DOI: 10.1002/hipo.22956

WILEY

COMMENTARY

Three brain states in the hippocampus and cortex

Kenneth Kay | Loren M. Frank

Howard Hughes Medical Institute, Kavli Institute for Fundamental Neuroscience, Department of Physiology, University of California San Francisco, San Francisco, California

Correspondence
Kenneth Kay, Howard Hughes Medical Institute, Kavli Institute for Fundamental Neuroscience, Department of Physiology, University of California San Francisco, San Francisco, CA.
Email: kaykenneth@gmail.com

Abstract

Contemporary brain research seeks to understand how cognition is reducible to neural activity. Crucially, much of this effort is guided by a scientific paradigm that views neural activity as essentially driven by external stimuli. In contrast, recent perspectives argue that this paradigm is by itself inadequate and that understanding patterns of activity intrinsic to the brain is needed to explain cognition. Yet, despite this critique, the stimulus-driven paradigm still dominates—possibly because a convincing alternative has not been clear. Here, we review a series of findings suggesting such an alternative. These findings indicate that neural activity in the hippocampus occurs in one of three brain states that have radically different anatomical, physiological, representational, and behavioral correlates, together implying different functional roles in cognition. This three-state framework also indicates that neural representations in the hippocampus follow a surprising pattern of organization at the timescale of ~1 s or longer. Lastly, beyond the hippocampus, recent breakthroughs indicate three parallel states in the cortex, suggesting shared principles and brain-wide organization of intrinsic neural activity.

KEYWORDS

brain state, cortex, hippocampus, imagination, memory, naturalistic behavior, prospection, sharp wave–ripple

1 | INTRODUCTION

The study of cognition, spanning diverse disciplines, is faced with an apparent lack of common ground. In brain research, the neuron is the common ground—explanation of how the brain works rests on an account of what neurons do. More can be said here. The function of the brain is ultimately useful behavior, which requires that the brain actuate the right movements, often quickly. Therefore, explanation of the brain must also refer to the ability of neurons to signal with commensurate speed. We now know that this is accomplished through neural firing (action potentials or "spikes").

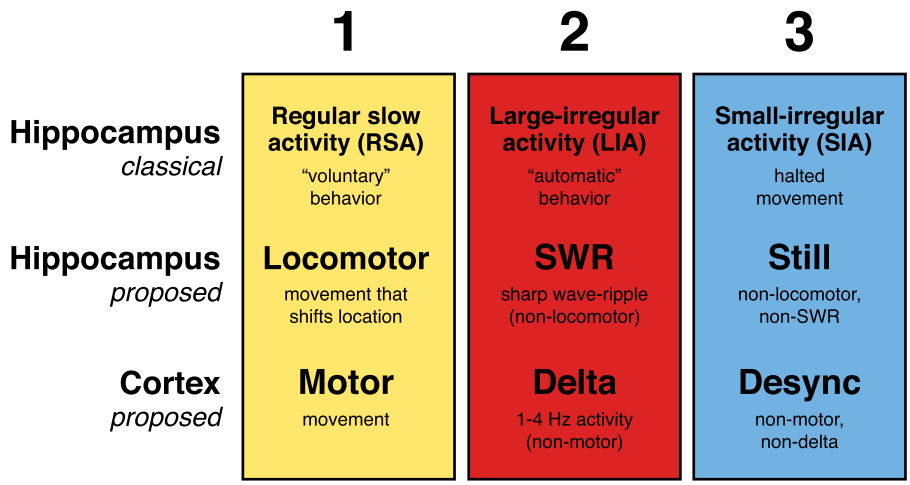
What remains unclear is how neural firing could be the basis of cognition: complex brain functions such as perception, memory, imagination, and decision-making. Indeed, the reduction of cognition to neural firing is a common goal for researchers focusing on different cognitive functions and associated structures (e.g., hippocampus, neocortex, basal ganglia, thalamus). This commonality is motivation to re-examine paradigms and consider alternatives.

In this review, we begin by pointing out that classic studies of neural firing at the sensory periphery established a lasting paradigm for studying the brain ("The stimulus-driven view"). We then refer to recent perspectives arguing that this paradigm is by itself inadequate and briefly outline what would make for a convincing alternative ("Brain state"). Toward such an alternative, we describe how a series of classic and recent experimental findings establish a framework for studying internally generated neural activity in the hippocampus ("Three brain states in the hippocampus"; see Overview 1), afterward discussing implications for hippocampal neural representation and cognitive function ("Temporal organization" and "Function"; these sections are geared to readers with particular interest in the hippocampus and can be skipped). Lastly, we consider how this framework from the hippocampus relates to other domains of the brain, focusing on recent breakthroughs in the sensory neocortex ("Three brain states in cortex").

2 | THE STIMULUS-DRIVEN VIEW

The earliest studies of neural firing were conducted at the sensory periphery (Adrian & Zotterman, 1926a; Adrian & Zotterman, 1926b; Barlow, 1953; Kuffler, 1953; Lettvin, Maturana, McCulloch, & Pitts, 1959), where it is simplest to infer that the relevant stimuli are external in origin. Subsequently, over the span of decades, the scientific paradigm established in this early work has been used to show that

 © 2018 Wiley Periodicals, Inc.



OVERVIEW 1 Three-state frameworks

Three brain state frameworks in awake subjects. Each approach (row) identifies three states (columns). The primary correlate of each state is indicated below the name of the state. Hippocampus classical refers to the framework established by Vanderwolf and colleagues in the late 1960s and 1970s (see "Naturalistic behavior"; reviewed in O'Keefe and Nadel (1978); O'Keefe (2007)), while the other two frameworks are proposed in the present discussion. Note that, across frameworks, the three states are approximately correspondent but not equivalent [Color figure can be viewed at wileyonlinelibrary.com]

neurons deeper in the brain tend to respond to more abstract external stimuli (Hubel & Wiesel, 1977). The scientific approach most closely associated with establishing and extending these early findings can be referred to as the "stimulus-driven view." This approach is related to the framework of "information processing" (Marr, 1982).

Our present aim is not a wholesale critique of this paradigm. Rather, we look to highlight a few methods and concepts that radically differ from the methods and concepts characterizing the research we review at length further below. In framing this later discussion, we seek to foster a broader perspective.

Methods associated with the stimulus-driven view include behavioral restraint, use of an artificial stimulus space, artificial task structure (i.e., cue-delay-response), and trial averaging. In physiology, emphasis is typically placed on single-neuron representational correlates. These approaches have established advantages yet may tend to address only a limited set of principles relating neural activity to cognition.

An important example is the efficient coding hypothesis (Atick, 1992; Attneave, 1954; Barlow, 1961; Barlow, 1972; Field, 1994; Simoncelli & Olshausen, 2001), which posits statistically efficient neural responses as an explanatory principle for understanding the brain. The idea of efficient coding holds particular appeal in that it appears to be a unifying principle, moreover one that offers tractability by way of formalization. However, one basic problem is that the efficiency of a neural representation is assessed with respect to the external world as interpreted by the human researcher, thus possibly obscuring what is in fact functionally (i.e., biologically) relevant. In other words, even though information in neural responses can be measured with respect to artificial stimuli, information of functional relevance is neither intrinsic to the physical world (in any modality) nor, for that matter, intelligible outside the ecological scope of the animal (Barlow, 1961; Laurent, 1999). Furthermore, characterization of neural representation without reference to natural behavior (ethology) is incomplete because partly if not primarily.

Of course, it is also the case that behavior itself, by virtue of sheer mechanics and also by internally routed motor signals, causally alters the external stimuli that impinge on the brain and thus what is represented in stimulus-driven neurons (Schroeder, Wilson, Radman, Scharfman, & Lakatos, 2010; Ahissar & Kleinfeld, 2003; Busse et al., 2017; Wolpert, Ghahramani, & Jordan, 1995). In fact, it is conceivable that the behavioral patterns of an organism influence stimulus-driven neural representation in a manner as important as what is commonly thought to be the case for statistical properties of natural sensory stimuli.

For these reasons, neural representation and its formal properties can only be bridged to cognitive function in light of ethological behavior. Indeed, this bridging requires us to know whether and how neural representation, or neural activity more broadly, systematically depends on ethological behavior (O'Keefe & Nadel, 1978; Paré & Quirk, 2017). As discussed further below, this systematic dependence has in fact proved essential in making sense of neural activity in the hippocampus.

3 | BRAIN STATE

Opposing the stimulus-driven view are critiques and alternatives via both experiment and theory (e.g., Buckner, Andrews-Hanna, & Schacter, 2008; Buzsáki, 2006; Cisek & Kalaska, 2010; Clark, 2013; Engel, Fries, & Singer, 2001; Friston, 2005; Gibson, 1979; Lamme & Roelfsema, 2000; Leopold & Logothetis, 1999; Mumford, 1992; Raichle, 2010; Rao & Ballard, 1999; Ringach, 2009; Salinas & Sejnowski, 2001; Von Der Malsburg, 1994; Wagemans et al., 2012; Wilson, 2002; Yuste, 2015). Still, depending on the researcher, it may be argued that there is not yet a convincing alternative to the stimulus-driven view.

Such an alternative must accomplish two things. First, as argued above, it must clarify how neural activity contributes to cognition given natural behavior. Second, it must also encompass a full range of empirical facts about neural activity. While these facts can be organized in many ways, here we propose four essential dimensions,

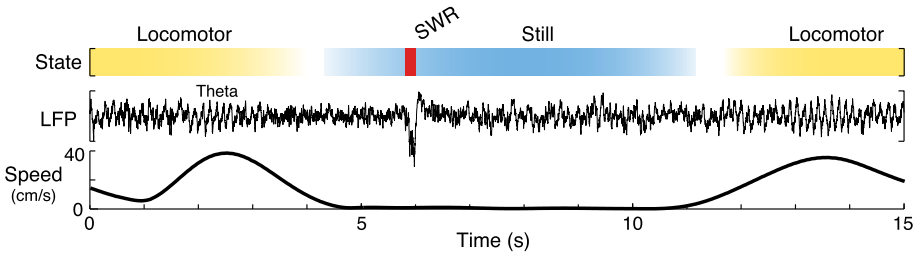


FIGURE 1 Illustration of three states in the hippocampus
Two correlates of brain state in the freely behaving rat: LFP and movement speed. LFP from hippocampal subregion CA1. Color bar: time periods corresponding to the three proposed hippocampal states (locomotor, SWR, still). The hippocampal theta rhythm (8 Hz), associated with locomotion, is visible in the LFP as a periodic pattern. Note the relationship of state to both LFP and behavior [Color figure can be viewed at wileyonlinelibrary.com]

loosely distinguished: anatomy, physiology, representation, and behavior. We choose these four because they together concisely define configurations of neural activity that (a) commonly occur throughout the life of an animal, (b) routinely switch from moment to moment (~1–10 s), and, critically, (c) are associated with comprehensive changes in neural firing patterns neither necessarily nor characteristically driven by sensory stimuli. In the following discussion, we refer to these configurations of neural activity as "brain states." (Note that these configurations are also called different "modes" of processing.) From these points, we suggest that knowledge of the principles underlying brain state will ultimately be necessary to relate neural firing to cognition.

A number of excellent reviews have been written on the topic of brain state (Buzsáki, 2006; Fontanini & Katz, 2008; Getting, 1989; Gilbert & Sigman, 2007; Harris & Thiele, 2011; Harris-Warrick & Marder, 1991; Lee & Dan, 2012; McGinley et al., 2015; Zagha & McCormick, 2014). Below, we focus on brain state in the hippocampus and neocortex, noting that the present definition of brain state is less granular than certain formulations in other work. Moreover, though we focus on the hippocampus and neocortex, there is considerable evidence that brain states are coordinated across the brain (see Overview 1 in Section 5). Lastly, it may also be useful to note that the state framework outlined here originates in the endeavor to understand hippocampal neural activity in awake subjects, mainly rats. As mentioned above and elaborated below, one theme essential to this endeavor has been ethological behavior. This is somewhat different than in study of the cortex, for which the matter of brain state in waking subjects has traditionally derived more from study of attention and awareness (Gilbert & Sigman, 2007; Harris & Thiele, 2011; Kanwisher, 2001; Lamme, 2003; Maunsell & Treue, 2006).

4 | THREE BRAIN STATES IN THE HIPPOCAMPUS

We offer the view that hippocampal neural firing occurs in one of three basic brain states (Figure 1). Each of these states is defined by a unique configuration of anatomy, physiology, representation, and behavior, together suggesting different respective functions (Table 1). To outline this framework, our strategy is to begin with what we see as its origin ("Naturalistic behavior"), after which we proceed state by state, roughly following the chronology of what was most clearly established first ("Locomotor," "Sharp wave-ripple (SWR)," "Still"). We then discuss implications of the three-state framework in relation to hippocampal neural representations ("Temporal organization") and function ("Functions").

4.1 | Naturalistic behavior

In our view, current understanding of brain state in the hippocampus originates in the landmark insights of studies published in the 1960s and early 1970s by Cornelius Vanderwolf and colleagues (Vanderwolf, 1969; Vanderwolf, 1971; Whishaw & Vanderwolf, 1973; reviewed in O'Keefe & Nadel, 1978; Vanderwolf, 1983; O'Keefe, 2007). Vanderwolf's ideas were formulated with reference to experiments from his own lab and others (Grastyan, Lissak, Madarasz, & Donhoffer, 1959; Pickenhain & Klingberg, 1967b; Stumpf, 1965; Vanderwolf & Heron, 1964) in which neural activity at the scale of the local field potential (LFP) was recorded in freely behaving animals during ethological behaviors, from sleep to feeding to exploration. In this experimental paradigm, the experimenter observes subjects' ongoing behavior with the aim to match behavioral patterns to LFP patterns. (Note that LFP in

TABLE 1 Three brain states in the hippocampus

	Locomotor	SWR	Still
Behavioral	movement that shifts location	rest, immobility	rest, immobility
Anatomical	CA1 fires more than CA3	CA3 generates	CA2 has specializers
Physiological	theta (in rodents)	sharp wave-ripple	non-SWR N wave
Representational	classic place code theta sequences	replay sequences	spatial code continuous code

Proposed framework for waking brain states in the hippocampus (see "Locomotor," "SWR," and "Still," and "Synopsis of hippocampal states").

this context is significant mainly as an adequately fast readout of neural activity in the recorded brain region.) While these studies are largely qualitative and may seem less rigorous by current conventions, the findings described are no less relevant to understanding neural activity today—indeed, we contend that their relevance has only grown. Here, we describe two implications of this early work: one broad (free behavior) and one specific (classical brain states).

Broadly, the move to permit free behavior serves to integrate neurophysiology with ethology. This amounts to a break not only with older hippocampal recording studies (in restrained animals; reviewed in O'Keefe & Nadel, 1978; O'Keefe, 2007), but also with the stimulus-driven paradigm. In essence, free behavior shifts the primary variable of interest from external stimuli to behavior since the unrestrained animal spontaneously expresses a set of behaviors that demand an account. Moreover, when combined with tasks, free behavior may in fact allow subjects to adopt strategies akin to those used under native conditions, whether behavioral or covert (Buzsaki, 2015; Redish, 2016). This matter of synthesizing ethology with controlled experimentation remains an open question (Cisek & Kalaska, 2010; Juavinett, Erlich, & Churchland, 2017; Krakauer, Ghazanfar, Gomez-Marin, MacIver, & Poeppel, 2017; Yartsev, 2017).

Specifically, Vanderwolf and colleagues defined three hippocampal brain states in the awake animal, establishing an influential framework that continues to be commonly referenced (Buzsaki, 2015; Buzsaki, Leung, & Vanderwolf, 1983; Hulse, Lubenov, & Siapas, 2017; Jarosiewicz & Skaggs, 2004b; Lever, Kaplan, & Burgess, 2014; O'Keefe, 2007; O'Keefe & Nadel, 1978; Redish, 1999; Skaggs, 1995; Wikenheiser & Redish, 2014). This lasting influence is testimony to the empirical accuracy of the original studies in conjunction with their firm rationale of matching neural activity strictly to behavioral observables (Buzsaki & Bland, 2015; Skaggs, 1995). In this framework, each (of three) brain state is defined by an LFP pattern ("Regular slow activity [RSA]," "Large irregular activity [LIA]," "Small irregular activity [SIA]") and behavioral correlate (O'Keefe, 2007; O'Keefe & Nadel, 1978; Vanderwolf, 1969; Vanderwolf, 1971; Vanderwolf, 1983):

1. *RSA* and "voluntary" behavior.
   Walking, running, climbing, rearing, jumping, head turning, postural shifts, and manipulating objects.
   (Note that RSA is now typically referred to as hippocampal theta.)
2. *LIA* and "automatic" behavior and immobility.
   These behaviors include sitting still, feeding, licking, chewing, and grooming.
3. *SIA* and sudden cessation of movement.

A few points of clarification are in order. The first is that the terms "voluntary" and "automatic" were meant purely as convenient shorthand for subsets of behaviors rather than as claims about cognitive constructs or mental states (Buzsaki & Bland, 2015; O'Keefe & Nadel, 1978; Vanderwolf, 1983). The second is that each of these waking LFP patterns were also observed in the sleeping animal, with RSA occurring during rapid eye movement (REM) sleep (Grastyan & Karmos, 1961; Montgomery, Sirota, & Buzsaki, 2008), LIA occurring during non-REM sleep (including slow-wave sleep [SWS]), and SIA occurring upon awakening from sleep either spontaneously or when aroused by a stimulus (Jarosiewicz & Skaggs, 2004b). While our focus in this review is waking brain states, these sleep analogs are a clue we will revisit later.

Past these clarifications, the larger point is that RSA, LIA, and SIA are closely related to the hippocampal brain states outlined below (Locomotor, Sharp wave–ripple, and Still). As we will elaborate, the grounds for an updated framework stem from a collection of subsequent findings at the level of neural firing. These findings suggest a way to reformulate brain states in terms that may help clarify the neural basis of cognitive functions within the hippocampus and possibly beyond.

4.2 | Locomotor

By the early 1970s, the ethological approach to hippocampal neural activity was extended in one respect that was to prove in its turn crucial—that is, neural activity began to be studied at the scale of neural firing. In 1971, John O'Keefe and Jonathan Dostrovsky reported the existence of single neuron (unit) firing in the hippocampus with a completely unprecedented correlate: namely, a subject's location in the world (O'Keefe & Dostrovsky, 1971; Figure 2). Neurons exhibiting this firing correlate, termed "place cells," were soon found to be ubiquitous in the hippocampus and readily observable under conditions in which an unrestrained subject visited different locations in an environment (Muller, 1996; O'Keefe, 1976; O'Keefe, 1979; O'Keefe, 2007). Subsequent work established that the locational correlate was indeed accurately described as reflecting an abstract representation of space in that place firing generally does not rely on single external cues or any particular sensory modality (Muller & Kubie, 1987; Muller, Kubie, & Ranck Jr., 1987; O'Keefe & Conway, 1978; Quirk, Muller, & Kubie, 1990; Save, Cressant, Thinus-Blanc, & Poucet, 1998). Importantly, place firing has been found to reflect an animal's estimate of location (behaviorally reported) rather than absolute location (Jeffery, 2008; O'Keefe & Speakman, 1987; Save & Poucet, 2008), indicating that place firing is not simply determined by external stimuli but in part generated internally.

What internally derived factors might contribute into a neural representation of location? One extremely influential answer comes from the insight that a navigating animal can update its locational representation using internal signals encoding direction and speed (O'Keefe, 1976), a cognitive function known as dead reckoning or path integration (Etienne & Jeffery, 2004; Gallistel, 1990; McNaughton et al., 1996; McNaughton, Battaglia, Jensen, Moser, & Moser, 2006; Mittelstaedt & Mittelstaedt, 1980; Redish, 1999). Neurons encoding heading direction and neurons encoding movement speeds are now known to exist in regions upstream of the hippocampus (Finkelstein et al., 2015; Hinman, Brandon, Climer, Chapman, & Hasselmo, 2016; Kropff, Carmichael, Moser, & Moser, 2015; Sargolini et al., 2006; Sharp, 1996; Sun et al., 2015; Taube, Muller, & Ranck, 1990; Taube, Muller, & Ranck Jr, 1990). Furthermore, neurons in the hippocampus and in upstream regions also show activity consistent with path integration (Chen, King, Burgess, & O'Keefe, 2013; Hardcastle, Ganguli, & Giocomo, 2015; McNaughton et al., 1996; McNaughton et al., 2006). Crucially, hippocampal place cells themselves, in particular in subregions CA1 and CA3, were found early on to encode speed as well

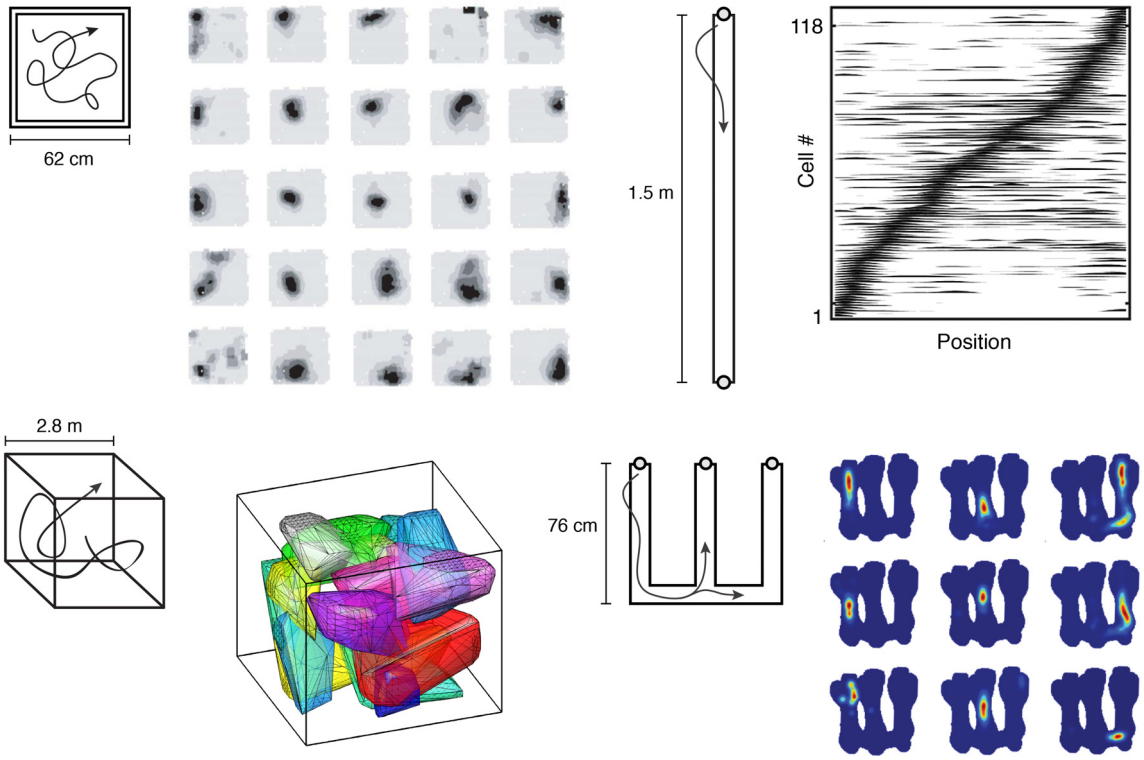


FIGURE 2 Locomotor place activity

Four examples of the locomotor place representation. At left in each example is a schematic of the recording environment, with an arrow path representing subjects' movement. At right in each example are maps indicating the locations at which single hippocampal principal neurons (place cells) predominantly fired. Data from hippocampal subregion CA1 and locomotor periods. Top left: 2D spatial maps (25 cells). Darker colors indicate higher firing rate locations. Top right: 1D spatial maps (118 cells). Darker colors indicate higher firing rate locations. Bottom left: 3D spatial maps (15 cells). Different colors indicate spatial firing fields from different cells. Bottom right: 2D spatial maps in a maze (9 cells). Warmer colors indicate higher firing rate locations. In each example, note that the firing fields collectively cover the environment. Top left, top right, and bottom left data reproduced with permission from O'Keefe (2007), Ambrose et al. (2016), Yartsev and Ulanovsky (2013), respectively. Bottom right data are described in Karlsson and Frank (2009) and Kay et al., 2016 [Color figure can be viewed at wileyonlinelibrary.com]

(McNaughton, Barnes, & O'Keefe, 1983). These neurons fire proportionally more at higher speeds, a result corroborated in numerous later studies (e.g., Czurko, Hirase, Csicsvari, & Buzsaki, 1999; Geisler, Robbe, Zugaro, Sirota, & Buzsaki, 2007; Hirase, Czurko, Csicsvari, & Buzsaki, 1999; Huxter, Burgess, & O'Keefe, 2003; Kay et al., 2016; Zhang, Ginzburg, McNaughton, & Sejnowski, 1998; Zheng, Bieri, Trettel, & Colgin, 2015). Complementing this result, it has also been observed that place cells in CA1 go silent when a completely restrained subject is manually transported to the spatial firing locations of these neurons (Foster, Castro, & McNaughton, 1989). If subjects are allowed to move in these same locations, the place cells resume firing. These findings, with path integration as the functional context, outline the conceptual and empirical link between classic hippocampal place cell firing and movement, in particular self-generated movement capable of changing a subject's position in an environment (O'Keefe, 2007; O'Keefe & Nadel, 1978). We here refer to this type of movement as "locomotor."

Importantly, these findings in single hippocampal neurons recall the previous observation made at LFP scale, namely, that hippocampal theta (i.e., RSA) becomes active when unrestrained animals move about (Vanderwolf, 1969; Whishaw & Vanderwolf, 1973). Thus, at least in rodents, place cell firing is closely associated with hippocampal theta in addition to locomotion. This suggests that the theta rhythm, a striking pattern of brain activity in its own right (Buzsaki, 2002; Buzsaki, 2005; Buzsáki, 2006; Green & Arduini, 1954; Hasselmo, 2005), might be a marker of the hippocampal state in which place firing occurs. Indeed, numerous results suggest that the theta rhythm has a functional role in the hippocampus (Ranck Jr, 1973; Winson, 1978; Buzsaki et al., 1983; O'Keefe & Recce, 1993; O'Keefe, 2007; Wang, Romani, Lustig, Leonardo, & Pastalkova, 2015; Redish, 2016; Wang, Roth, & Pastalkova, 2016; also see Brandon, Koenig, Leutgeb, & Leutgeb, 2014).

Despite this apparently compelling relationship between the single neuron (place cell) and neural population (LFP) levels, research in bats has established that hippocampal theta does not as a rule occur during locomotion (Ulanovsky & Moss, 2007) and place cell firing occurs during locomotion in the absence of theta (Yartsev & Ulanovsky, 2013). Thus, the role of theta is species-specific or not strictly associated with movement, indicating that the basis for distinguishing brain states in the hippocampus should be re-evaluated.

As we introduced earlier, we think this basis should encompass different dimensions of neural activity, including representation. In this respect, place firing currently provides the surest landmark: no other representational activity pattern in the hippocampus is known to be more ubiquitous, reliable, and consistently observed across conditions and species (Ekstrom et al., 2003; Las & Ulanovsky, 2014; McHugh, Blum, Tsien, Tonegawa, & Wilson, 1996; Muir et al., 2009; Ulanovsky & Moss, 2007; Yartsev, Witter, & Ulanovsky, 2011). It

should be added that adopting place firing as the basis for framing neural activity in the hippocampus, as opposed to the theta rhythm, implies that we regard neural representation of abstract variables as essential to understanding the hippocampus (Eichenbaum, 2013; Eichenbaum & Cohen, 2014; Eichenbaum, Dudchenko, Wood, Shapiro, & Tanila, 1999; Foster, 2017; O'Keefe, 2007; O'Keefe & Nadel, 1978; Quiroga, 2012).

Where does this take us? As outlined above, place firing is location-specific neural firing that has been found to depend on the capacity to move, and furthermore is most vigorous at higher locomotor speeds. This indicates that locomotion is the essential condition in which place firing—at least as classically observed—occurs. In practice, this is consistent with the methodological convention in place cell research of filtering for periods of movement. It is also in accord with the widespread use of behavioral paradigms that promote continuous locomotion (e.g., random foraging in an open arena; Muller et al., 1987). In sum, locomotion is the condition in which classical place firing is most clearly expressed.

Conceptually, our conclusion is that locomotion and place firing are the behavioral and representational correlates, respectively, of a single major brain state in the hippocampus, here referred to as the "locomotor" state. In the discussion below, we refer to the spatially specific firing that occurs in this state as "locomotor place" or simply "place" firing (in some contexts we add "locomotor" to avoid confusion). Anatomically, locomotor place firing has been established in CA1, CA3, and DG, with recent studies targeting CA2 also reporting spatially specific firing resembling that of classic place cells (Alexander et al., 2016; Kay et al., 2016; Lee, Wang, Deshmukh, & Knierim, 2015; Lu, Igarashi, Witter, Moser, & Moser, 2015; Mankin, Diehl, Sparks, Leutgeb, & Leutgeb, 2015; Oliva, Fernandez-Ruiz, Buzsaki, & Berenyi, 2016b). Physiologically, the locomotor state is associated with relatively low or intermediate excitability in the hippocampus (in principal neurons, as indexed by different measures of activity; Csicsvari, Hirase, Czurko, & Buzsaki, 1998; Csicsvari, Hirase, Czurko, Mamiya, & Buzsaki, 1999; Kay et al., 2016; Hulse et al., 2017).

4.3 | Sharp wave–ripple

The discovery of place firing has had an unparalleled influence on the effort to understand the hippocampus at the level of neural firing. As a consequence, most work has focused on the conditions, activity patterns, and experimental methods associated with place firing (i.e., locomotion, theta activity, and particular behavioral paradigms). Yet since their earliest characterizations (O'Keefe, 1976; O'Keefe & Nadel, 1978), place cells have also been found to fire intermittently in the absence of locomotion and theta. At the level of individual place cells, this firing at first appeared to lack spatial specificity, leading to speculation that such activity reflects the hippocampus in a representationally uninformative ("off-line") state (O'Keefe, 2007; O'Keefe & Nadel, 1978).

Subsequent work has led to an entirely different view (Buzsaki, 1989; Buzsaki, 2015). This view derives from the observation that, during periods of rest (non-locomotor periods or, alternatively, immobility and "consummatory" behaviors such as eating, drinking, and grooming), firing in place cells often occurs in association with a transient rhythmic activity pattern (~180 Hz) termed the hippocampal "ripple" (O'Keefe, 1976; O'Keefe & Nadel, 1978). The ripple pattern occurs in intermittent bursts lasting ~100 ms and occurs primarily during non-locomotor behavior. Physiologically, these bursts typically occur in conjunction with an aperiodic activity pattern termed the "sharp wave" (~100 ms/wave), with the term "sharp wave–ripple" (SWR) now commonly used to refer to the dual pattern (Figure 3; Buzsaki, Horvath, Urioste, Hetke, & Wise, 1992). SWRs are in practice detected in the LFP and correspond to the irregular large amplitude waves characteristic of the LIA state of Vanderwolf. Importantly, the hippocampus can generate SWRs autonomously: in vivo and in vitro work indicates that the hippocampus does not require external input to generate SWRs (reviewed in Buzsaki (2015)), and indeed SWRs appear to occur stochastically. These observations indicate that SWRs are internally generated patterns not dependent in any simple way on external stimuli—in short, internally generated.

What then of neural firing that occurs during SWRs? A comprehensive review can be found elsewhere (Buzsaki, 2015). Here, our goal is a concise outline of findings indicating that the pattern of neural firing in the hippocampus during SWRs is comprehensively different from that of the locomotor state. Toward this end, we outline three major findings.

The first is anatomical. By analyzing neural activity across anatomical sites, previous work has established that SWRs arise as a result of the synchronous activation of neurons in the CA3 subregion (Buzsáki, 1986; Buzsaki et al., 1983; Csicsvari, Hirase, Mamiya, & Buzsaki, 2000). CA3 is known to send unidirectional (feedforward) synaptic input onto CA1, the primary site of generation of the ripple component of the SWR, suggesting that CA3 provides input necessary to elicit the dual SWR pattern. Indeed measurements of synaptic activity indicate that the sharp wave component of SWRs is the manifestation of synchronous synaptic input from CA3 onto CA1 (Sullivan et al., 2011; Ylinen et al., 1995). In agreement, CA1 ripple power correlates with the amplitude of the sharp wave (Sullivan et al., 2011), and neural firing in CA3 increases earlier than neural firing in CA1 over the course of an SWR (Csicsvari et al., 2000; Oliva, Fernandez-Ruiz, Buzsaki, & Berenyi, 2016a). These results and numerous others (Buzsaki, 2015; Nakashiba, Buhl, McHugh, & Tonegawa, 2009) indicate that CA3 has an essential role in generating SWRs and, by inference, neural firing in the hippocampus during SWRs.

The second is physiological. SWRs are associated with an abrupt and dramatic increase in excitability across the hippocampus, manifesting as a burst of extremely synchronous neural firing. This increase in firing can be up to six-fold greater than when SWRs are absent (Buzsaki, 2015; Csicsvari et al., 1998; Csicsvari et al., 1999; Csicsvari et al., 2000).

The third is representational, and perhaps the most evocative. During SWRs, populations of place cells often fire in temporally compressed sequences reflecting spatial trajectories (example in Figure 4; reviewed in O'Neill, Pleydell-Bouverie, Dupret, & Csicsvari, 2010; Carr, Jadhav, & Frank, 2011; Buzsaki, 2015; Foster, 2017; Pfeiffer, 2017; Olafsdottir, Bush, & Barry, 2018). This sequential firing pattern, termed "replay sequences" or "replay," has been shown to represent (a) spatial trajectories in both forward and reverse order (Csicsvari, O'Neill, Allen, & Senior, 2007; Davidson, Kloosterman, & Wilson, 2009; Diba & Buzsaki, 2007; Foster & Wilson, 2006; Gupta, van der Meer, Touretzky, & Redish, 2010), (b) spatial trajectories in locations or environments remote from

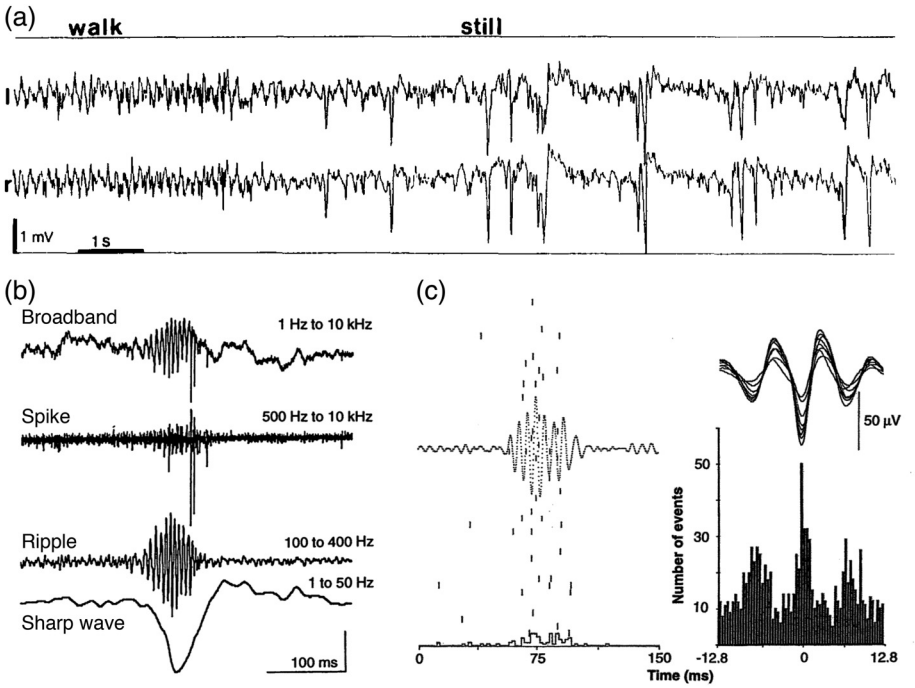


FIGURE 3 Sharp wave–ripple (SWR) activity

(a) SWRs and their occurrence during immobility. Plotted is LFP from left (l) and right (r) dorsal hippocampal CA1 (stratum radiatum) during periods of locomotion (walk) and immobility (still). SWRs correspond to the large intermittent sharp waves (SPW; Buzsaki et al., 1983; Buzsaki, 1986) seen specifically during immobility. Note also the bilateral synchrony of SWRs. (b) Example of a single SWR. The upper three traces are from a recording site in hippocampal subregion CA1 near the cell bodies of principal neurons (stratum pyramidale), while the sharp wave trace is from a recording site nearer apical dendites (stratum radiatum). (c) Neural firing during SWRs. Firing activity (rasters) from 50 CA1 neurons, with collected firing (histograms) at bottom. The LFP trace of the ripple rhythm, recorded in CA1, is also shown. Left: single SWR. Right: multiple SWRs.
Part a reproduced with permission from Buzsaki (1989)); parts b and c reproduced with permission from Buzsaki et al. (1992)

the subjects (Davidson, Kloosterman, & Wilson, 2009; Gupta et al., 2010; Karlsson & Frank, 2009), (c) spatial trajectories in novel combinations not seen in prior behavior (Gupta et al., 2010), (4) spatial trajectories extending over meters (Davidson, Kloosterman, & Wilson, 2009), and (5) spatial trajectories taken by subjects in subsequent goal-directed navigational behavior (Pfeiffer & Foster, 2013; see also Wu, Haggerty, Kemere, & Ji, 2017). These various findings indicate that hippocampal neural firing during SWRs represents spatial experience in an extremely flexible manner unlike classical place firing.

These three major groupings of findings (anatomical, physiological, representational) together establish a brain state in the hippocampus different from the locomotor state—we here refer to this as the "SWR state" as its most reliable and widely established correlate is the SWR. Note that the SWR is analogous to locomotion as a marker of brain state, though, in essential contrast to locomotion, the SWR is not an overt behavioral correlate.

Across hippocampal regions, SWR neural firing representing previously experienced spatial trajectories has been primarily studied in CA1

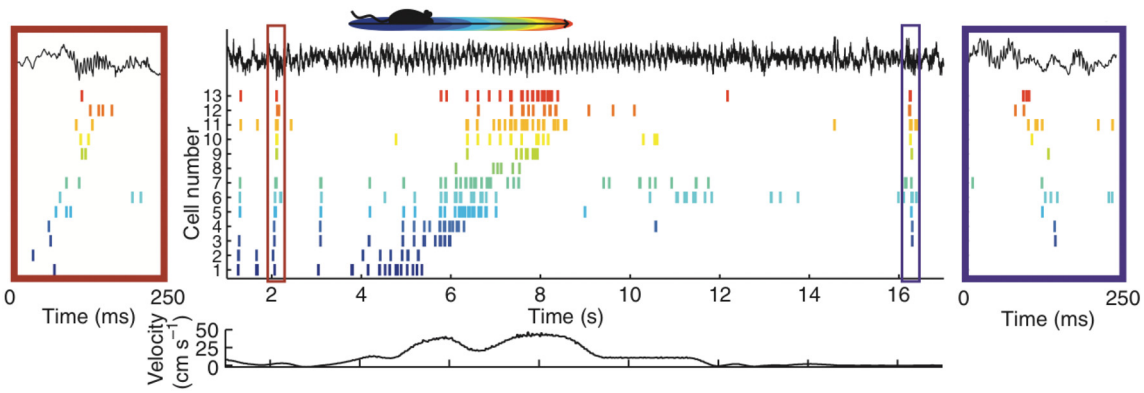


FIGURE 4 Place cell firing during SWRs

Place cell firing sequences during locomotion are replayed during SWRs. Firing activity (rasters) of 13 CA3 place cells are shown before, during, and after a single traversal through an environment. Sequences that occur during locomotion are reactivated during periods of immobility before and after the traversal. LFP from CA1 is shown above the rasters, and the animal's speed is shown below. In this example, the SWR replays occur in the forward (left example) and reverse (right) order relative to the locomotor sequence.
Adapted with permission from Diba and Buzsaki (2007) [Color figure can be viewed at wileyonlinelibrary.com]

but is known to occur also in CA3 (Diba & Buzsaki, 2007; Karlsson & Frank, 2009). Elevated firing during SWRs has also been reported in DG (Penttonen, Kamondi, Sik, Acsady, & Buzsaki, 1997; Szabo et al., 2017) and in certain neurons in CA2 (Kay et al., 2016; Oliva et al., 2016a). More broadly, it is important to keep in mind that the same hippocampal neurons participate in both the locomotor and SWR states—thus place cells (locomotor state) are just as well "replay cells" (SWR state). This illustrates structure in the hippocampus that is dynamic rather than static (Buzsaki, 2010; Buzsáki, 2006; Carr & Frank, 2012), unlike the "labeled line" property at the sensory periphery (Boring, 1942; Rieke, Warland, de Ruyter van Steveninck, & Bialek, 1997).

4.4 | Still

If we take a step back, the wider significance of the above findings comes down to *inclusivity*—comprehending a larger share of time (of the subject's ongoing experience or of the experiment) to be associated with functionally important neural activity. Furthermore, inclusivity with regard to the SWR state can be interpreted either specifically or generally. If specifically, then what we learned is that neural representation in the hippocampus occurs during SWRs, not only during periods of locomotion. By itself, this indicates that an adequate account of neural activity in the hippocampus must extend to SWR periods.

If, further, we interpret the above findings generally, then what we learned is that neural representation in the hippocampus does not require locomotion. Critically, this simple observation leads to a problematic ambiguity. Across various studies and conditions in waking subjects, the SWR state accounts for only a small proportion (<10%) of time when subjects are not in locomotion. What then does the hippocampus do during periods of rest in the absence of SWRs? More explicitly: is hippocampal neural activity during periods of rest a mixture of that of the locomotor and SWR states, or something else?

To our surprise, we recently found evidence indicating the latter. In examining neural firing in the hippocampus of subjects in a maze, we found neural firing that could not be classified as either of the locomotor or SWR states (Figures 5 and 6; Kay et al., 2016). This activity was most clearly distinguished from locomotor and SWR activity by virtue of a distinct population of neurons located in subregion CA2, an understudied subregion of the hippocampus (itself the focus of recent reviews, Jones & McHugh, 2011; Dudek, Alexander, & Farris, 2016; Robert, Cassim, Chevaleyre, & Piskorowski, 2018).

In contrast to locomotor place activity (associated with higher firing at higher movement speeds; discussed above), these neurons recorded in CA2 fired less at higher speeds and showed exceptionally high firing when subjects were stopped. Notably, akin to place cells, single neurons in this population fired when the subject was in particular locations.

In contrast to SWR activity (associated with enhanced firing in CA1, CA3, and DG; discussed above), these neurons did not fire more during SWRs, even over the course of thousands of recorded SWRs. This uniquely consistent lack of recruitment during SWRs could be used as the criterion for identifying neurons in this population: consequently "N" cells (nonpositively modulated by SWRs). Importantly, among CA1, CA2, and CA3 recording sites, only those located in CA2 reported N cells in considerable proportions, suggesting that the CA2 subregion has a privileged role in non-SWR neural activity. This link to CA2 establishes an anatomical correlate (at the level of subregion) reminiscent of the dominant contribution of CA3 to SWRs.

Taken together, these findings establish an overarching observation—namely, that there exists hippocampal neural firing that cannot be classified as either of the locomotor nor SWR states, with a neural population in CA2 (N cells) specializing in this neural firing. On the basis of the view that different configurations of neural firing define different brain states, this observation suggests a third hippocampal brain state corresponding to non-locomotor, non-SWR activity. If we operationally identify this putative brain state as occurring during non-locomotor, non-SWR periods, then we obtain a rough correspondence with Vander wolf's SIA state, which was identified behaviorally by halted movement. On the other hand, this updated view necessarily encompasses a larger proportion of time in the life of an animal or in naturalistic settings, as elaborated further below.

Are there other signatures of a third brain state? The striking differences in neural activity between the locomotor and SWR states suggest that an alternative state might have its own correlates. To evaluate this possibility, we focused on the activity of N cells in light of their consistent tendency to fire during non-locomotor, non-SWR periods (their "specialization" in an alternative state). Two additional correlates were clarified: one in awake subjects and the other during sleep.

The first correlate was a hippocampal LFP pattern. In awake subjects, N cells fired in association with an aperiodic LFP pattern lasting ~200 ms, which we termed the "N wave" (N cell-identified wave). The N wave is distinct from both theta and SWRs: unlike theta (~8 Hz), the N wave was characterized by lower frequencies (1–4 Hz)

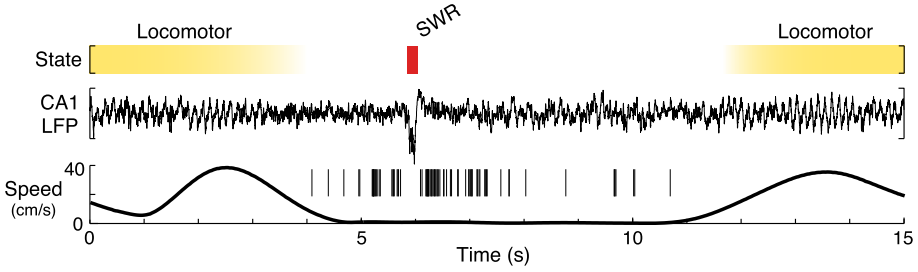


FIGURE 5 Non-classical firing in the hippocampus
Observation of non-locomotor, non-SWR neural firing in the hippocampus. Data are the same as presented in Figure 1, though here shown with firing (raster) from a simultaneously recorded hippocampal neuron located in subregion CA2 [Color figure can be viewed at wileyonlinelibrary.com]

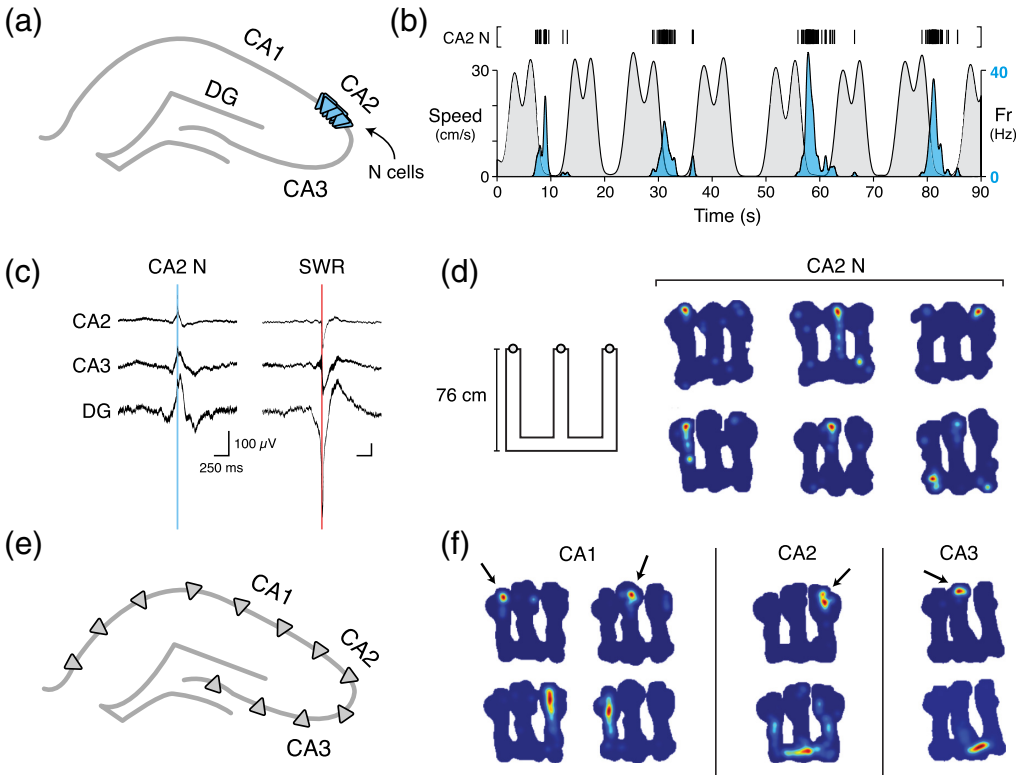


FIGURE 6 Still activity

(a) Diagram of hippocampal subregions and CA2 N cells. The cluster of blue triangular symbols in CA2 represents neurons specializing in non-locomotor, non-SWR activity (CA2 N cells). (b) Example of CA2 N cell firing during behavior. Left y-axis and grey fill trace: head speed (cm/s). Right y-axis and blue fill trace: instantaneous firing rate (Fr), estimated from the spike train (raster). (c) Physiological correlate of still firing. Left, CA2 N unit spike-triggered averages (STA) of hippocampal LFP recorded at CA2, CA3, and DG. Right, SWR-triggered averages from the same recording sites. (d) Spatially specific activity in CA2 N cells. Left, diagram of maze environment with three sites at which subjects routinely visited and ceased locomotion (wells holding food reward; circles). Right, spatial maps of six CA2 N units. Warmer colors indicate higher firing rates. (e) Visual summary of other hippocampal neurons (in CA1, CA2, CA3) that show spatially-specific still firing. (f) Example spatial firing maps from eight hippocampal neurons in CA1, CA2, and CA3 that are not CA2 N cells. Upper row: example neurons that fire at single still locations (indicated by arrows). Lower row, example neurons with conventional spatial firing fields. Units in each column were simultaneously recorded. Reproduced with permission from Kay et al. (2016) [Color figure can be viewed at wileyonlinelibrary.com]

and was not continuously oscillatory; unlike SWRs, the N wave was a positive pattern at the same recording sites at which the sharp wave component of the SWR was negative. Because theta and SWRs are markers of the locomotor and SWR states, this finding is a further indication that N-cell firing occurs in an alternative hippocampal brain state.

The second correlate relates to a sleep pattern known as microarousal (MA) (Figure 7). Some background here is necessary: MA is a relatively understudied pattern that occurs spontaneously throughout sleep (mainly non-REM) in short periods (~1 s to several seconds) (Bergmann, Winter, Rosenberg, & Rechtschaffen, 1987). In the brain, MA is grossly characterized by desynchronization of neural activity, manifesting as flattened EEG/LFP (Figure 7a). Although MA is not often studied (see (Hulse et al., 2017; Lapray et al., 2012; Miyawaki, Billeh, & Diba, 2017; Watson, Levenstein, Greene, Gelinas, & Buzsaki, 2016) for recent exceptions), there are two important precedents in the hippocampal literature. Indeed, we encountered one of these in the discussion above: studies correlating LFP to naturalistic behavior make note of a desynchronized hippocampal state (Grastyan et al., 1959; Pickenhain & Klingberg, 1967a; Vanderwolf, 1969)–Vander wolf's SIA state, as seen in sleeping subjects, corresponds closely to MA as described in other work (for simplicity, we will refer to sleep SIA here as MA). The other precedent comes from a series of studies conducted by Beata Jarosiewicz and William Skaggs, who found that ~5% of CA1 place cells fired at high rates specifically during MA (Figure 7a; Jarosiewicz, McNaughton, & Skaggs, 2002; Jarosiewicz & Skaggs, 2004a; Jarosiewicz & Skaggs, 2004b). Remarkably, these neurons were found to have spatial firing fields at the location at which the animal was sleeping. Conversely, neurons that did not fire during periods of SIA had spatial firing fields elsewhere. Thus, during MA, neurons in CA1 encode a subject's sleeping location (Figure 7b). Notably, the final study in the series found that this spatial code did not rely on visual input, suggesting that the spatial code activated during MA reflects an internally stored memory of a subject's location (Jarosiewicz & Skaggs, 2004a).

Building on this groundbreaking work, we found that MA is associated with N-cell firing in two ways. The first was that N cells generally fired more than neurons in CA1 and CA3 during MA. The second was that N-cell firing during MA, as with that of CA1 neurons, coded for subjects' sleeping location. For reasons that remain unclear, CA3 did not appear to show spatially specific firing during MA. Despite this, we note that individual CA3 neurons can be observed to fire at high rates during MA (unpublished observations). Broadly, these several findings (Figure 7c–e) further establish the existence of

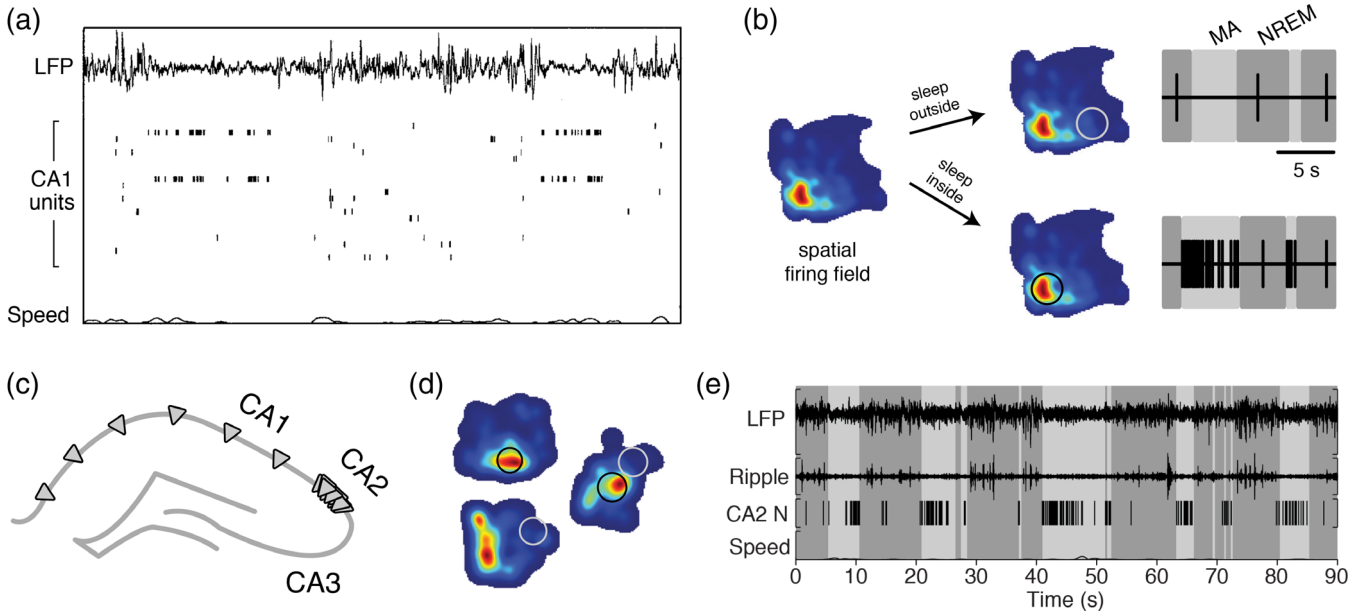


FIGURE 7 MA activity

(a) Observation of MA firing in CA1. Shown is 30 s of neural data (LFP and unit firing in CA1) recorded during sleep. Movement speed is plotted at bottom and reflects small head movements that occur during sleep. Note periods of desynchronization, reflected in the flattening of LFP, accompanied by continuous firing in two CA1 units. (b) Illustration of MA spatial coding. MA occurs between periods of conventional non-REM sleep; CA1 neurons that have spatial firing fields at the animal's sleeping location fire continuously during MA periods. (c) Visual summary of MA spatial coding in the hippocampus. Neurons in CA1 and CA2 have been found to encode sleeping location during MA periods. (d) Examples of MA spatial coding in CA2 N neurons. Shown are the spatial firing maps of three CA2 N neurons in a sleeping environment. Circles indicate sleep location of the subject, and are outlined in different colors depending on whether the neuron was active during MA (black circle: >2 Hz; white circle: <2 Hz). (e) Example firing of a CA2 N neuron during sleep. Wide-band LFP (0.5–400 Hz) and ripple-band LFP (150–250 Hz) was recorded in CA1. Light and dark grey zones correspond to detected MA and non-REM periods, respectively.

Part a is reproduced with permission from Jarosiewicz et al. (2002); parts d and e are reproduced with permission from (Kay et al. (2016) [Color figure can be viewed at wileyonlinelibrary.com]

hippocampal neural firing unambiguously unlike that of the locomotor and SWR states—even in sleep.

Lastly, we stress that spatial firing during periods of stillness was not limited to specialist neurons in CA2. In the maze, CA1, CA2, and CA3 neurons that not were not N cells could be seen to fire at high rates during immobility in the absence of SWRs. As with N cells, this firing in CA1 and CA3 neurons was location-specific and was associated with the N wave pattern. These shared properties indicate participation in non-locomotor non-SWR activity. At the same time, these neurons also commonly had typical spatial firing fields during locomotion ("place fields") and thus would simply be place cells from the perspective of traditional analyses. Moreover, these neurons showed enhanced firing during SWRs (as could be confirmed by inspection of SWR-averaged firing), and thus directly participate in the SWR state. Therefore there exist neurons in CA1, CA2, and CA3 that participate in every hippocampal state (locomotor, SWR, and a third state associated with neither locomotion nor SWRs). Further work is needed to clarify whether there exist hippocampal neurons that tend not to be active in multiple states. For example, it remains possible that there exist hippocampal neurons that generally do not engage in still firing, in converse fashion to the N-cell population.

We interpret the above findings as evidence of a non-locomotor, non-SWR brain state in the hippocampus. We refer to this state as the "still" state and propose that periods of time corresponding to this state be operationally identified by exclusion of the previously established hippocampal brain states: namely, when animals are not in locomotion and when SWRs are absent. Although it may be possible in future work to use non-exclusionary criteria (e.g., based on N-cell firing or N wave activity), we suggest this approach for three reasons: (a) we have found it to be robust in our efforts to account for hippocampal neural firing across subregions, (b) it promotes inclusive consideration of neural activity (discussed further below), and (c) it is relatively accessible to different experimental approaches. (We also note that the term "still" is, by itself, not fully semantically sufficient given its lack of reference to the SWR—the advantage of "still" is that it is readily comprehensible.) Physiologically, still state firing in the hippocampus is associated with lower or minimum excitability across the hippocampus (in principal neurons, as indexed by mean firing rate [Kay et al., 2016]; also indicated by results in Csicsvari et al., 1998; Csicsvari et al., 1999; Csicsvari et al., 2000; Hulse et al., 2017).

4.5 | Synopsis of hippocampal states

Three hippocampal brain states were established in early form by rigorously correlating neural activity, at the level of LFP, to naturalistic behavior. The subsequent discovery and elucidation of "place" firing then established locomotion as the essential correlate of one of these brain states (locomotor). Next, investigation of the hippocampal SWR established the SWR as the essential correlate of a second brain state (SWR). Lastly, recent findings indicate a third brain state (still) that can be identified operationally by excluding locomotor and SWR periods.

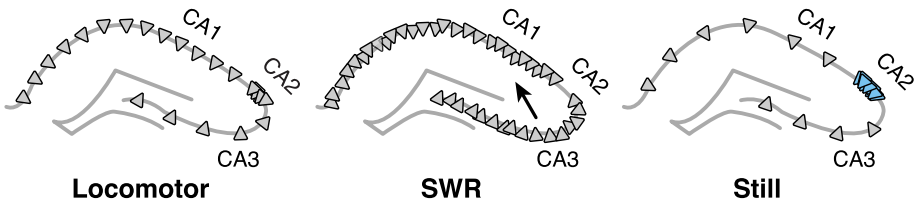


FIGURE 8 Differential recruitment of hippocampal subregions by state
Visual summary of differences in principal neuron recruitment across states. Locomotor: higher activation of CA1 compared to CA3. Neuron populations in CA2 have been found to be consistently active. SWR: CA1 and CA3 are both maximally active. A neuron population in CA2 (N cells) is minimally active. The arrow indicates strong synaptic drive from CA3 to CA1. Still: CA2 N cells (in blue) are maximally active. CA1 and CA3 are minimally active on average—however, subpopulations are active [Color figure can be viewed at wileyonlinelibrary.com]

A visual summary of the differential activity of hippocampal subregions by these three brain states is in Figure 8.

Illustration of this proposed three-state framework and a survey on example data is provided in Figure 9.

4.6 | Temporal organization

In this section, we discuss implications of the hippocampal three-state framework in relation to neural representation. This focus is important because phenomena and principles at the representational level recurrently inspire new thinking and paradigms in brain science (Barlow, 1953; Chang & Tsao, 2017; Desimone, Albright, Gross, & Bruce, 1984; di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992; Gross, Rocha-Miranda, & Bender, 1972; Hafting, Fyhn, Molden, Moser, & Moser, 2005; Hubel & Wiesel, 1962; Lettvin et al., 1959; O'Keefe & Dostrovsky, 1971; Quiroga, Reddy, Kreiman, Koch, & Fried, 2005; Taube, Muller, & Ranck Jr, 1990; Tsao, Freiwald, Tootell, & Livingstone, 2006), and frame theories relating neural activity to cognitive function (e.g., Barlow, 1972; Foster & Knierim, 2012; Gold & Shadlen, 2007; Johnson, 2000; Lisman & Redish, 2009; Marr, 1982; McNaughton et al., 2006; Mountcastle, 1998; O'Keefe & Nadel, 1978; Parker & Newsome, 1998; Rieke et al., 1997). This second point merits careful consideration because conceptual problems are incurred by certain views of single neuron (or for that matter population level) representation in relation to cognition (Krakauer et al., 2017; Smit & Hacker, 2014) and also to certain views of formal representation in relation to cognition (Dreyfus, 1992; Harnad, 1990; Searle, 1980). For instance, one extremely influential instance of the latter is a framework for explaining brain function (Marr, 1982) in which representation occupies an abstract level of analysis ("algorithmic") above physical instantiation ("implementational") yet below behavioral function ("computational"). This idea of fully abstracted levels may be misapplied easily, particularly because the nature of representation in the brain (much less exact algorithmic roles) generally remains unclear. At the same time, we think that insight can be gained by focusing on the representational level—this view motivates the following discussion.

Representational correlates in the hippocampus are often divided into those that are spatial versus nonspatial (Aronov, Nevers, & Tank, 2017; Eichenbaum & Cohen, 2014; Schiller et al., 2015a). In our outline of hippocampal states above, we dealt mainly with spatial representation in rats because of the breadth and depth of empirical facts accrued in this model system. Here, by contrast, we propose to approach the matter of hippocampal representation more generally—rather than ask what the hippocampus represents, we instead ask how it is that the hippocampus could represent any given thing.

Taking this approach leads us to one variable in particular: time. To begin with, the most apparent link between the hippocampus and time is episodic memory (Tulving, 1983; Tulving et al., 1972), a cognitive function that lies at the origin of modern hippocampal research and also continues to unify much of it (Aggleton & Brown, 1999; Andersen, 2007; Buzsaki, 2015; Buzsaki & Moser, 2013; Carr et al., 2011; Corkin, 2013; Eichenbaum, 2017c; Eichenbaum, 2017d; Eichenbaum & Cohen, 2001; Knierim, Lee, & Hargreaves, 2006; Kumaran & McClelland, 2012; Leutgeb, Leutgeb, Moser, & Moser, 2005; Nadel & Moscovitch, 1997; Nadel, Samsonovich, Ryan, & Moscovitch, 2000; Redish, 2016; Sanders, Renno-Costa, Idiart, & Lisman, 2015; Scoville & Milner, 1957; Tulving & Markowitsch, 1998; Vargha-Khadem et al., 1997). Episodic memory has long been recognized to entail the storage, in a neural substrate, of a large collection of arbitrarily associated features or items ("what") in a specific spatial ("where") and temporal ("when") context. Furthermore, it has been argued that these properties of episodic memory imply temporal organization of correspondent neural representations in the hippocampus (Eichenbaum, 2014; Eichenbaum, 2017e). Remarkably, recent work has shown that time is a representational correlate in the hippocampus, in analogous fashion as space (Eichenbaum, 2014; Eichenbaum, 2017e; MacDonald, Lepage, Eden, & Eichenbaum, 2011; Pastalkova, Itskov, Amarasingham, & Buzsaki, 2008).

Even so, the significance of time in the hippocampus is even more fundamental than as an explicitly encoded variable. Given experimental work (reviewed only briefly here), it is ever increasingly clear that time is intrinsic to what populations of hippocampal neurons must accomplish biophysically. In fact, it appears that temporal rather than spatial (anatomical) organization is essential. This point is most clearly illustrated by the representational challenge posed by the place representation: how would a group of place cells signal location to a downstream neuron? One conceivable answer is that the place representation is mapped onto the anatomy of the hippocampus (i.e., topographic organization), making it possible for downstream neurons to read out location on an anatomical basis. However, place cells are not in fact anatomically organized by the locations they represent—place cells representing nearby locations are no more likely to be anatomically near to each other than place cells representing distant locations (Redish et al., 2001) (see also Alme et al., 2014; Kubie & Muller, 1991; O'Keefe, 2007). Thus "reader" downstream neurons of place cells have no anatomic basis by which to respond to

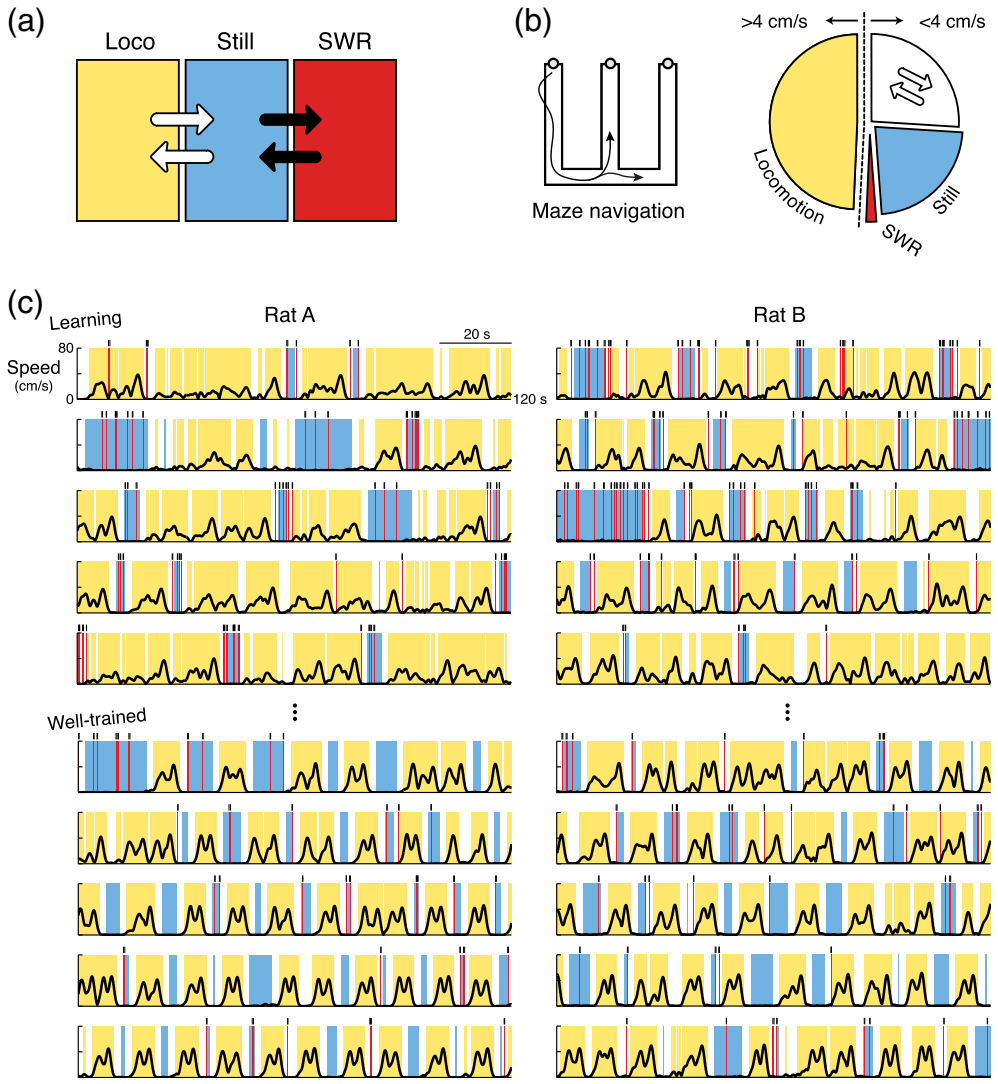


FIGURE 9 Illustration and survey of three hippocampal states

(a) Schematic of state changes in the hippocampus. Locomotor-still (white arrows) and still-SWR (black arrows) transitions are proposed to be important. (b) Proportion of time in each state. Hippocampal states were detected from eight rats navigating a simple maze (left), and proportion of time periods calculated (right). Locomotion was defined as times when speed was >4 cm/s (yellow; 49%); SWR periods were detected from hippocampal recordings (red: 2%); Still periods were defined as non-SWR, >4 cm/s periods at least 2 s separate from locomotor periods (blue; 23%). The remaining time was classified as locomotor-still transitions (white: 26%). (c) Four example 10-min periods of maze navigation. Each column corresponds to two 10-min blocks from an individual rat, with upper blocks from the earlier exposures of the rats' to the maze ("Learning") and bottom blocks from later exposures ("Well-trained"). Each individual row (2 min) displays the animal's speed (black trace) and is backgrounded by the color of the classified brain state. Still-SWR transitions are indicated above each trace as black ticks. Notice the irregularity of movement early in learning and the prevalence of all three states.

Part b reproduced with permission from Kay et al. (2016); part c is unpublished data from the same study [Color figure can be viewed at wileyonlinelibrary.com]

a given location. The only remaining possibility is that these downstream neurons detect whether incoming place cell inputs representing similar locations are coincident in time (Figure 10; Buzsáki, 2006; Curto & Itskov, 2008; Buzsaki, 2010; Dabaghian, Memoli, Frank, & Carlsson, 2012; Buzsaki & Moser, 2013; Dabaghian, Brandt, & Frank, 2014). Importantly, this line of reasoning applies to any given representation implemented in the hippocampus.

Are hippocampal neural representations in fact organized in time? If so, how? A number of decisive findings spanning decades of hippocampal research indicate extraordinary temporal organization of neural representations. This temporal organization is intrinsic to the brain because the timing in question is relative to activity patterns generated within the brain and because these patterns require and engage specific brain structures (e.g., medial septum [MS] and theta [Buzsaki, 2002; Fuhrmann et al., 2015], entorhinal cortex and theta [Kamondi, Acsady, Wang, & Buzsaki, 1998; Schlesiger et al., 2015], CA3 and low gamma [Csicsvari, Jamieson, Wise, & Buzsaki, 2003; Colgin et al., 2009], and microcircuits within the hippocampus [Freund & Buzsaki, 1996; Buzsaki, 2002; Klausberger et al., 2003; Klausberger & Somogyi, 2008; Somogyi, Katona, Klausberger, Lasztoczi, & Viney, 2014; Buzsaki, 2015]). Moreover, large numbers of hippocampal neurons are entrained to each of these patterns, explaining the presence of signature LFP patterns (Buzsáki, 2006; Buzsaki et al., 1983; Colgin, 2016; O'Keefe & Nadel, 1978). Note that earlier

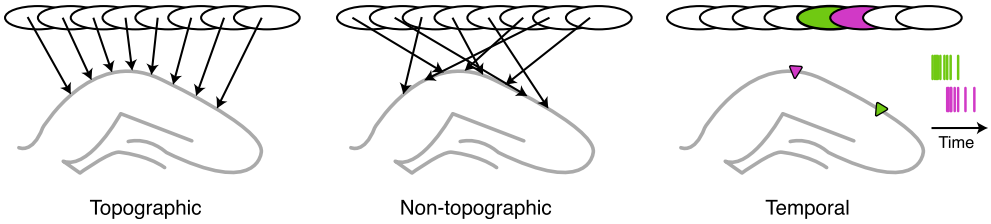


FIGURE 10 The role of time in the hippocampus
Left, topographic representation. In this hypothetical scheme, spatial locations in an environment (top) are mapped in the anatomy of the hipppocampus (bottom). Middle, non-topographic representation. Here, anatomical locus has no correspondence with spatial location. Experimental findings indicate this scenario (Redish et al., 2001). Right, temporal representation. Neurons representing similar locations fire together in time even though these neurons otherwise have no systematic anatomical relationship [Color figure can be viewed at wileyonlinelibrary.com]

in this discussion we encountered two of these patterns (theta and SWRs) as physiological markers of brain states. Here the point is rather that neural representations are organized by these patterns, and that this organization is strong enough to be observable in single trials and in single or few neurons (some striking examples are illustrated in Figure 11; studies include O'Keefe and Recce (1993); Skaggs, McNaughton, Wilson, and Barnes (1996); Pastalkova et al. (2008); Schmidt et al. (2009) Wu and Foster (2014); Pfeiffer and Foster (2015)); recent reviews include Buzsaki and Moser (2013); Buzsaki (2015); Colgin (2016); Redish (2016); Foster (2017)).

What is the significance of this temporal organization for function? Importantly, the above findings share a common property: organization at the short timescale (∼1–100 ms), which has been repeatedly suggested to be essential for various memory functions (Buzsaki, 2015; Buzsaki & Moser, 2013; Carr et al., 2011; Colgin, 2016; Dragoi & Buzsaki, 2006; Robbe et al., 2006; Roumis & Frank, 2015; Skaggs et al., 1996). Yet many questions remain. One concerns episodic memory—how could short timescale activity explain the role of the hippocampus, given that episodic memory entails representation of experience at longer timescales? To specify, episodic memory involves (a) single episodes encompassing longer periods of time (seconds to minutes and longer) (Ferbinteanu, Kennedy, & Shapiro, 2006; Shapiro, Kennedy, & Ferbinteanu, 2006; Smith & Mizumori, 2006a), (b) knowledge of temporal relationships across episodes, and (c) retrieval of episodes long after initial storage. Although recent work has provided promising clues (Attardo, Fitzgerald, & Schnitzer, 2015; Cai et al., 2016; Driscoll, Pettit, Minderer, Chettih, & Harvey, 2017; Eichenbaum, 2013; Eichenbaum, 2017b; Eichenbaum, 2017e; Ezzyat & Davachi, 2014; Ferbinteanu & Shapiro, 2003; Frank, Stanley, & Brown, 2004a; Hsieh, Gruber, Jenkins, & Ranganath, 2014; Karlsson & Frank, 2008; Kitamura et al., 2014; Ludvig, 1999; Mankin et al., 2012; Mankin et al., 2015; Manning, Polyn, Baltuch, Litt, & Kahana, 2011; Manns, Howard, & Eichenbaum, 2007; Murray et al., 2014; Ranganath & Hsieh, 2016; Rubin, Geva, Sheintuch, & Ziv, 2015; Runyan, Piasini, Panzeri, & Harvey, 2017; Suh, Rivest, Nakashiba, Tominaga, & Tonegawa, 2011; Ziv et al., 2013), the neural representation of events at longer timescales remains unclear. More knowledge and insight are needed.

In the following discussion, we consider the possibility that temporal organization associated with brain state may clarify how neural representations in the hippocampus relate to cognitive functions. In particular, we point out that the three-state framework implies temporal organization at both the short (∼1–100 ms) and long (∼1 s to minutes) timescales. We elaborate this observation in the four following points, noting in advance that what can be said here is far short of explanation and is rather meant to guide future investigation.

Point 1. At the long or short timescale, there are no "off-line" periods in the hippocampus.

Point 2. At the long timescale, hippocampal neural representations depend on behavior and subregional anatomy.

Point 3. At the short timescale, there may exist hippocampal neural representations specific to brain state transitions.

Point 4. Within the still state, the temporal organization of hippocampal neural representations is unknown.

Point 1. At the long or short timescale, there are no "off-line" periods in the hippocampus.

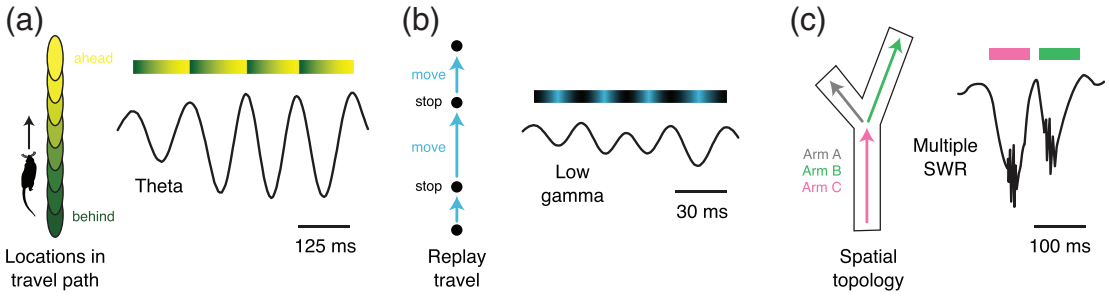


FIGURE 11 Temporal organization of hippocampal representations
(a) Hippocampal theta organizes representation of locations in ongoing travel path. See (Buzsaki & Moser, 2013; Colgin, 2016; Redish, 2016; Skaggs et al., 1996). (b) Hippocampal low gamma organizes replay travel. See (Carr et al., 2012; Pfeiffer & Foster, 2015). (c) SWRs organize representation of environment topology. See (Wu & Foster, 2014) [Color figure can be viewed at wileyonlinelibrary.com]

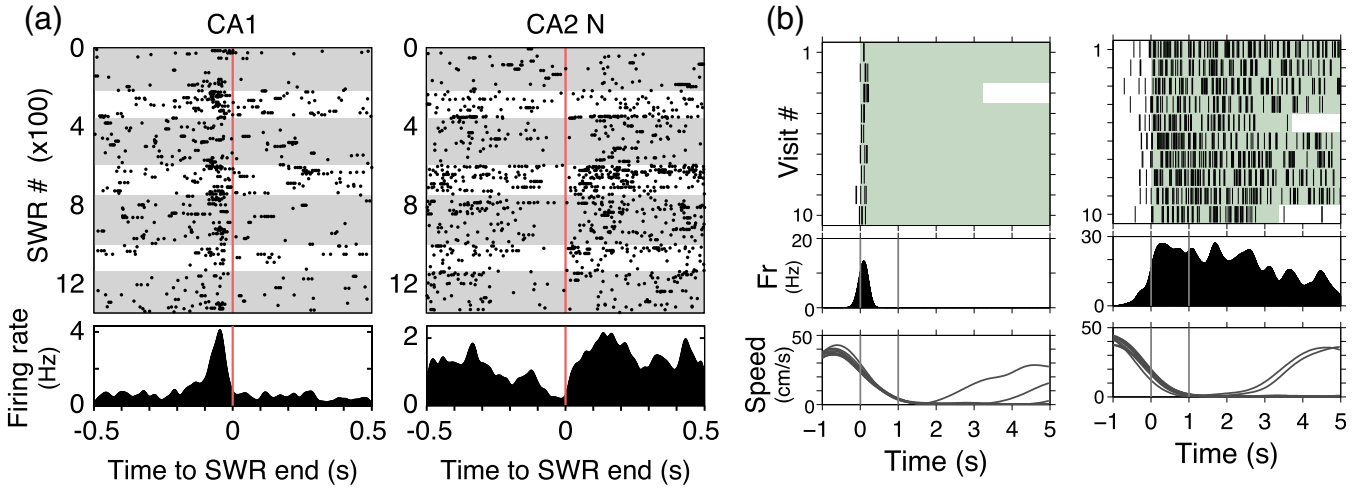


FIGURE 12 Fast firing dynamics at the time of transitions between hippocampal states
(a) Still-SWR transitions. Firing activity of two hippocampal neurons (left: CA1; right: CA2 N) aligned to the end of SWRs (t = 0; >1,200 single SWRs). Grey zones: data when subject was in a rest environment; white zones: data when subject was in maze. Note the fast offset of CA1 firing complemented by the fast onset of CA2 N firing. (b) Locomotor-still transitions. Firing activity of two hippocampal neurons (left: CA3; right: CA1) aligned to termination of running at a particular location (visit) (K.K., L.M.F., unpublished data) [Color figure can be viewed at wileyonlinelibrary.com]

In brain research, there is a tradition of interpreting brain activity that does not have an apparent neural representation as not having a function, hence terms such as "off-line" or "noise." On the one hand, these terms are used to denote a provisional lack of knowledge or simply activity not driven by sensory stimuli. At the same time, the implicit view is that such activity has no function unless shown otherwise. Early thinking on brain activity during sleep is perhaps a classic example of this outlook (Dement, 1990; Dement, 1998). A more recent example is the default mode network (Buckner, 2012; Raichle, 2015; Smith, 2012). In hippocampal research, neural firing associated with SWRs was at first thought to reflect an off-line state in part because this firing appeared not to be spatially specific (O'Keefe, 2007; O'Keefe & Nadel, 1978). The subsequent elucidation of SWR-associated replay sequences has since dissolved this view (Buzsaki, 2015; Carr et al., 2011; Foster, 2017; O'Neill et al., 2010). Possibly for similar reasons, neural activity occurring outside locomotor and SWR periods has largely has not been confronted in prior work in naturalistic behavioral paradigms (however, see Best & Ranck, 1982; Mizumori, Barnes, & McNaughton, 1990; Jarosiewicz et al., 2002; Tabuchi, Mulder, & Wiener, 2003; Takahashi, Lauwereyns, Sakurai, & Tsukada, 2009b).

From the outset, we advocate the opposite outlook—there are no periods of time that are absent functionally relevant firing or neural representation in the hippocampus. At least at the long timescale, we consider this now to be evident given that hippocampal neurons, understood as a population, fire continuously across periods of locomotion (outlined above in "Locomotor") and of rest ("Still" and "Sharp wave–ripple"), which together necessarily comprise the whole of waking experience.

There is also reason to think that at the short timescale, this outlook holds true. At the short timescale, the times in question are transitions between hippocampal states, whether between locomotor and still or between still and SWR. Though relatively little is known about neural activity during these times (though see Eichenbaum, Kuperstein, Fagan, & Nagode, 1987; Wiener & Korshunov, 1995; O'Neill, Senior, & Csicsvari, 2006; Jackson & Redish, 2007), prior observations of neural firing suggest fast transitions. For transitions from locomotor to still, associated changes in firing rate can occur in <1 s (Figure 12; Kay et al., 2016). For transitions between still and SWR, associated firing rate changes can be seen to occur in <100 ms (Kay et al., 2016; see also Oliva et al., 2016a). These observations suggest that hippocampal neural representations cover all of experience (Yu et al., 2017), including at the time of a change in state. This accords with the view that the hippocampus encodes experience into memory continuously by default (Eichenbaum, 2004; Morris & Frey, 1997).

Point 2. At the long timescale, hippocampal neural representations depend on behavior and subregional anatomy.

Most research on neural representation in the hippocampus focuses on the locomotor (or theta) state. Yet rest and immobility are intrinsic to natural behavior, naturalistic behavior, and behaviors that require the hippocampus (Bannerman et al., 2004; Christian & Thompson, 2003; Drai, Kafkafi, Benjamini, Elmer, & Golani, 2001; Eilam & Golani, 1989; Golani, Benjamini, & Eilam, 1993; Maren, Phan, & Liberzon, 2013; O'Keefe & Nadel, 1978; Pentkowski, Blanchard, Lever, Litvin, & Blanchard, 2006; Tchernichovski, Benjamini, & Golani, 1998; Wallace, Hamilton, & Whishaw, 2006; Wallace, Hines, & Whishaw, 2002; Wallace & Whishaw, 2003; Whishaw & Kolb, 2005), suggesting that understanding the hippocampus will ultimately require knowledge of neural activity during stillness. Moreover, as outlined above, neural activity in the hippocampus during these periods is qualitatively different from that of locomotion.

In relation to neural representation, these brain states imply a pattern of organization demanding future investigation. In the following discussion, we focus on the locomotor place representation and its relationship to the still state. We do so because the locomotor place representation remains the paradigmatic neural representation in the hippocampus and because the implications of the still state with

respect to the locomotor place representation are not only surprising (at least to us) but also relatively unexplored (e.g., as compared to the SWR state, associated with the burgeoning field of hippocampal replay; O'Neill et al., 2010; Carr et al., 2011; Buzsaki, 2015; Foster, 2017).

As outlined earlier, the place representation signals the current location of the subject and is active during locomotion. When the subject comes to a stop, an overlapping but different set of hippocampal neurons becomes active, with this alternative set of neurons also encoding the subject's location. During these transitions, hippocampal neurons active in the locomotor and still states often can have overlapping firing in time (Yu et al., 2017) as well as overlapping spatial firing fields, even for the same neuron in some instances (unpublished observations; examples in supplementary data from CA1 and CA3 in Kay et al. (2016)). However, these two sets of hippocampal neurons, while overlapping, are not equivalent because there is a different pattern of recruitment across hippocampal subregions (diagrammed in Figure 8)—CA1 has been found to be most active subregion during the locomotor place state (Karlsson & Frank, 2008; Leutgeb, Leutgeb, Treves, Moser, & Moser, 2004; Mizuseki, Royer, Diba, & Buzsaki, 2012; Oliva et al., 2016b), whereas neurons in CA2 have been found to specialize in the still state ("N" cells; see above). Also notable is that an additional set of neurons in CA2 is, like neurons in CA1, particularly active in the locomotor place state ("P" cells; see also Oliva et al. (2016b) and later discussion concerning generalization in CA2 ("Map switching").

These findings reduce to two observations referring to the long timescale (~1 s or longer; the resolution at which it is clearly the case that either the locomotor or still state is engaged). The first is that approximately the same location is represented by different neurons, with different neurons engaged depending on the behavior of the subject (considered in early work: Ranck (1973); O'Keefe (1976); Best and Ranck (1982); see discussion in Eichenbaum et al. (1999); Eichenbaum and Cohen (2001)). The second is that approximately the same location is represented by different anatomically defined sets of neurons. Thus, hippocampal neural representations that are expressed at this timescale (relevant to virtually all tasks and ethological behaviors) cannot be fully described unless both behavior and subregional anatomy are considered. We add that though this qualification may seem to complicate analysis and interpretation, it also suggests a path that may lead to better understanding of how neural representation relates to behavioral-level function and thereby behavior.

Because the above findings refer exclusively to the rodent model and spatial representation, caution is important. It is not yet fully clear which state-dependent principles apply across species and types of representations. We reference other sources on this issue (Las & Ulanovsky, 2014; O'Keefe, 2007), taking the overall view is that further empirical work is needed, particularly with behavioral paradigms comparable to those in rodent work. Notably, most available research indicates that different species have different correlates of the theta rhythm (Bohbot, Copara, Gotman, & Ekstrom, 2017; Bush et al., 2017; Jacobs, 2014; Jutras, Fries, & Buffalo, 2013; Lever et al., 2014; O'Keefe, 2007; Stewart & Fox, 1991; Ulanovsky & Moss, 2007; Watrous et al., 2013; Yartsev & Ulanovsky, 2013); though see (Aghajan et al., 2017).

Point 3. At the short timescale, there may exist hippocampal neural representations specific to brain state transitions.

As mentioned in the first point above, there are fast firing rate changes associated with state changes in the hippocampus. In particular, we observe fast firing rate changes at the time of locomotor to still transitions (Figure 12, (Kay, 2016; Kay et al., 2016); also see Hulse, Moreaux, Lubenov, & Siapas, 2016), suggesting that there may exist neural representations specifically associated with state transitions. Generally speaking, neural activity at the time of state transitions may be of interest for multiple reasons. One is that activity during these periods may simply be unexpectedly insightful. These are figuratively "off-line" periods in that they are conventionally not analyzed in hippocampal research. Speaking for ourselves, lower speed periods (e.g., when a running rat comes to a stop or an immobile rat begins to run) for which we claim no definite classification into locomotor versus still comprise a large proportion of data (26%) in a navigational setting (a simple maze; Karlsson & Frank, 2009; Carr, Karlsson, & Frank, 2012; Kay et al., 2016). A second reason is that neural activity during these transitional periods may clarify how states interrelate.

Point 4. Within the still state, the temporal organization of hippocampal neural representations is unknown.

Little is known about what the hippocampus represents in the still state. An initial clue is that neural firing in the still state encodes current location in the same way as locomotor place firing (Kay et al., 2016). In our view, this finding is only introductory because it does not refer to time: as discussed above, there is compelling reason to think that time is essential to the representational capacity of the hippocampus. Therefore, even though data are currently lacking, the question of whether temporal organization is the case in the still state is worth some thought. We believe that organization is likely and here consider in turn the short and long timescales.

At the short timescale, one clue is that activity patterns known to organize representations in other states are also engaged in the still state. In particular, the hippocampal low gamma rhythm (Bieri, Bobbitt, & Colgin, 2014; Cabral et al., 2014; Carr et al., 2012; Colgin et al., 2009; Lasztoczi & Klausberger, 2016; Pfeiffer & Foster, 2015; Takahashi, Nishida, Redish, & Lauwereyns, 2014; Tort, Komorowski, Manns, Kopell, & Eichenbaum, 2009; Zheng, Bieri, Hsiao, & Colgin, 2016) is at highest amplitude at lower speeds (Ahmed & Mehta, 2012; Kemere, Carr, Karlsson, & Frank, 2013; Zheng et al., 2015) and occurs at rest in the absence of theta (our unpublished observations; see also Buzsaki et al. (1983); Csicsvari et al. (2003); Takahashi et al. (2014)). Another clue is the N-wave pattern, a low-frequency pattern (1–4 Hz) expressed in hippocampal LFP at the time of location-specific neural firing in the still state (Kay et al., 2016). Notably, the N wave is detectable across hippocampal subregions (CA3 and DG in particular), suggesting coordinated activity across the hippocampus and thus plausible coordination of associated neural representations. Lastly, from a standpoint of cognitive function and ethological behavior, we point out that there is no obvious reason to think that the encoding (or expression) of episodic memory in the hippocampus cannot occur when subjects are in the still state. On the contrary, given the amount of time in an animal's life correspondent with the still state, it appears reasonable to expect otherwise. We thus might expect that the short timescale organization of hippocampal representations, traditionally

linked to episodic memory in other hippocampal states, is also present during stillness.

At the long timescale, we note that location-specific still firing at the single cell level appears to be relatively constant in some instances, while in others firing evolves over seconds (see example in Figure 6b; more below). We think this property is important and revisit this further below.

Lastly, several caveats merit mention. One is that the theta rhythm or a variant of it (atropine-sensitive theta) can be observed sometimes to occur when animals are not in locomotion (Kramis, Vanderwolf, & Bland, 1975; Sainsbury, Heynen, & Montoya, 1987; Sainsbury & Montoya, 1984; Vanderwolf, 1983). Indeed as Vanderwolf has pointed out, movements that are not necessarily or plainly locomotor (e.g., isolated limb movements) are associated with theta in the rodent (Vanderwolf, 2001). (Indeed the existence of two types of theta in waking subjects is reminiscent of distinction between phasic and tonic REM, two sleep states both associated with theta [Hobson & Pace-Schott, 2002; Montgomery et al., 2008; Mizuseki, Diba, Pastalkova, & Buzsaki, 2011].) This suggests that the theta rhythm or a variant of it can be active during non-locomotor periods, which we indeed observe in our data. At the same time, we find that periods of theta during non-locomotor periods do not appear to occur reliably. Moreover, taking measures to exclude periods of theta during non-locomotor periods does not eliminate location-specific firing (Kay et al., 2016). It is not yet clear what is the best way to view theta activity occurring during stillness. For now, we only point out that, in longer periods of immobility (more than a few seconds) in navigational paradigms, theta in LFP or theta-paced firing in the hippocampus is not reliably active (Yu et al., 2017). It is also worth noting that in paradigms imposing immobility, theta can be at times active (e.g., MacDonald, Carrow, Place, & Eichenbaum, 2013).

4.7 | Functions

The following discussion is divided into sections ("Outlook," "Memory vs. Prospection," "Prospection across states," "Abstractive state," "Three properties of prospection," "Prospection during stillness," "A prospective circuit during stillness," "Navigation," "Sleep," and "Synopsis of function by hippocampal state.")

4.7.1 | Outlook

Why do these three brain states exist in the hippocampus? The short answer is that we do not entirely know. As we review below, the most influential view is that these different states support different stages of memory processing, with the locomotor state corresponding to encoding, particularly in novel circumstances, while the SWR state corresponds to consolidation. This is a major insight yet, for reasons discussed below, cannot be the entire picture. We do think that activity in each hippocampal state supports a unique set of cognitive functions, even if these functions may not conform to conventional vocabularies used to describe how the mind works (Buzsáki, 2006). Past this caveat, state-specific function is plausible given that each dimension of state (anatomy, physiology, etc.) in isolation already suggests separate functions.

A few more introductory points are needed here. The first is that all aspects of a given state should be considered, not only representation. In particular, compared to prior research, it will be increasingly important to consider and probe anatomical structure, starting at least at the level of subregion. Because hippocampal subregions are differentially active in each state (Figure 8), given their different projection patterns (Andersen, 2007; van Strien, Cappaert, & Witter, 2009; Witter & Amaral, 2004), inferences about responses in neural populations downstream of the hippocampus (Buzsaki, 2010), and hence of eventual function, will be different. Moreover, at a finer anatomical scale within respective subregions (e.g., Cembrowski et al., 2016; Fanselow & Dong, 2010; Igarashi, Ito, Moser, & Moser, 2014; Katona et al., 2014; Klausberger & Somogyi, 2008; Lovett-Barron et al., 2014; Masurkar et al., 2017; Nakamura, Flasbeck, Maingret, Kitsukawa, & Sauvage, 2013; Okuyama, Kitamura, Roy, Itohara, & Tonegawa, 2016; Poppenk, Evensmoen, Moscovitch, & Nadel, 2013; Royer et al., 2012; Slomianka, Amrein, Knuesel, Sorensen, & Wolfer, 2011; Strange, Witter, Lein, & Moser, 2014; Sun et al., 2017; Xu et al., 2016), recent findings have identified physiologically distinct subpopulations of hippocampal principal neurons (Graves et al., 2012; Hongo et al., 2015; Jarsky, Mady, Kennedy, & Spruston, 2008; Kohara et al., 2014; Krook-Magnuson, Varga, Lee, & Soltesz, 2012; Lee et al., 2014; Maroso et al., 2016; Schmidt-Hieber, Jonas, & Bischofberger, 2004), some of which have state- or representation-specific activity (Ciocchi, Passecker, Malagon-Vina, Mikus, & Klausberger, 2015; Danielson, Kaifosh, et al., 2016; Danielson et al., 2016; Geiller, Fattahi, Choi, & Royer, 2017; GoodSmith et al., 2017; Henriksen et al., 2010; Kay et al., 2016; Lee et al., 2015; Lu et al., 2015; Mizuseki et al., 2011; Neunuebel & Knierim, 2012; Oliva et al., 2016a; Oliva et al., 2016b; Senior, Huxter, Allen, O'Neill, & Csicsvari, 2008; Stark et al., 2014; Valero et al., 2015). These findings highlight entanglement between hippocampal activity and anatomical structure, a theme that will only deepen in future work.

Second, we point out that because the majority of systems hippocampal research at the scale of neural firing has focused on the locomotor (or theta) state, neural activity in other states often cannot be inferred from prior studies. Addressing this ambiguity will require a return to explicit consideration of behavior in relation to neural activity (where we started), including at the finer scale of single trials and behavioral episodes. As mentioned earlier, this corresponds to a shift to considering temporal organization in neural activity at the timescale of differentiable ongoing behavior. Moreover, depending on research focus, the organization of activity by behavior-yoked brain states also recommends behavioral paradigms that require an intact hippocampus as such paradigms often elicit or even require behaviors that are not solely locomotor (Ainge, van der Meer, Langston, & Wood, 2007; Bannerman et al., 2004; Eichenbaum, 2017d; Kim & Fanselow, 1992; Kim & Frank, 2009; Maren et al., 2013; O'Keefe & Nadel, 1978; Olton & Samuelson, 1976; Pentkowski et al., 2006; Wallace et al., 2002; Wallace & Whishaw, 2003).

Third, we contend that understanding relationships between states will yield insight into the neural activity of any one state and for that matter the hippocampus as a whole. If anything, this is because brain states refer to the same physical substrate, here, the set of neurons comprising the hippocampus. Notably, the multiple-state approach is already a matter of scientific practice in the study of hippocampal replay sequences (Foster, 2017), though at present this is

an exceptional case. Looking forward, more specific insights will likely depend on our hypotheses about function, to which we now turn.

4.7.2 | Memory versus prospection

Theories of hippocampal function are numerous, varied, and fairly involved (e.g., Andersen, 2007; Bannerman et al., 2004; Buzsaki & Moser, 2013; Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001; Eichenbaum & Cohen, 2014; Fanselow & Dong, 2010; Nadel & Moscovitch, 1997; O'Keefe & Nadel, 1978; Squire, 1992; Sutherland & Rudy, 1989). For the sake of focus, our strategy here is contrastive—instead of a particular function as a starting point, we will start with previously established hypotheses.

The origin of current thinking about how hippocampal states relate to cognitive function is the "two-stage" memory formation hypothesis formulated by György Buzsáki in the late 1980s (Buzsaki, 1989). Subsequent work has clarified a number of points (Buzsaki, 2015), but the essential idea has endured: memory formation in the hippocampus occurs in an initial stage in which a short-lasting trace is weakly encoded, followed by subsequent stage in which a long-lasting trace is consolidated—and that these two stages correspond to neural activity during theta (locomotor) and SWR periods, respectively.

The two-stage hypothesis outlines a neural basis by which the hippocampus stores memories. In our view, this framework has proved most insightful with respect to the learning of novel experience. This is because subsequent studies have shown that SWRs are exceptionally upregulated by novelty, serving immediately to reactivate neural firing patterns that initially occurred during exploratory locomotor periods (Cheng & Frank, 2008; Foster & Wilson, 2006; Kudrimoti, Barnes, & McNaughton, 1999; O'Neill, Senior, Allen, Huxter, & Csicsvari, 2008; Wu & Foster, 2014). Here we only add that the labile encoding function attributed to theta-associated activity may need to be amended in light of the still state, which is not characteristically associated with theta. This is simply for behavioral reasons—the capacity to encode memories is evidently not specific to locomotor periods, thus the hippocampus should be able to encode experience in the still state, in the absence of locomotion and theta. Of course, the mechanisms and efficacy of an encoding process in the still state likely differ from that of locomotion and theta (Berry & Thompson, 1978; Seager, Johnson, Chabot, Asaka, & Berry, 2002). It is also worth pointing out that encoding of nonspatial variables may be most prominent in the absence of locomotion, only because at rest only one spatial location is directly experienced, in effect controlling for space (Gelbard-Sagiv, Mukamel, Harel, Malach, & Fried, 2008; MacDonald et al., 2013; Quiroga, 2012; Quiroga et al., 2005; Takahashi et al., 2009b).

Crucially, much subsequent work has extended the two-stage hypothesis, doing so in two major directions: namely, *theta sequences* and *replay sequences*. Each is a pattern of neural firing that occurs routinely in awake, task-engaged subjects (in practice, rats performing spatial memory tasks) and, critically, respectively, occurs in two different hippocampal brain states: theta sequences in the locomotor state and replay sequences in the SWR state. Here we briefly summarize these two patterns, noting that each can be understood as an avenue for investigating how memories formed by the two-stage mechanism are subsequently used to guide behavior (Foster, 2017).

Theta sequences, associated with the continuous 8 Hz theta rhythm and thus with locomotion, are ~100 ms sequences of hippocampal neural firing at the population level (Figure 13). These firing sequences represent the moving subject's current path through space, sweeping progressively from the subject's current location (or somewhat behind) to upcoming locations ("look-ahead"; Skaggs et al., 1996; Dragoi & Buzsaki, 2006; Foster & Wilson, 2007; Huxter, Senior, Allen, & Csicsvari, 2008; Gupta, van der Meer, Touretzky, & Redish, 2012a; Maurer, Burke, Lipa, Skaggs, & Barnes, 2012; Cei, Girardeau, Drieu, Kanbi, & Zugaro, 2014; Feng, Silva, & Foster, 2015; Sanders et al., 2015; Zheng et al., 2015). Furthermore, at path bifurcations, theta sequences have been shown to encode either one or the other upcoming path (Johnson & Redish, 2007; Redish, 2016). Importantly, the paths represented by theta sequences correlate with the paths taken in subsequent navigational behavior (Wikenheiser & Redish, 2015a), suggesting that theta sequences contribute to or reflect a spatial planning process.

Replay sequences, occurring during SWRs and thus during pauses in locomotion, are ~100 ms sequences of hippocampal neural firing at the population level (Figure 14), much like theta sequences. In comparison to theta sequences, replay sequences have been found to represent a wider variety of spatial paths with respect to subjects' navigational experience. (Also note that we earlier encountered replay sequences in discussing the representational correlates of the SWR state.) In brief, replay sequences have been shown to represent spatial experience in a manner that is temporally (Diba & Buzsaki, 2007; Foster & Wilson, 2006), geometrically (Wu & Foster, 2014), and unpredictably (Gupta et al., 2010; Karlsson & Frank, 2009) abstracted from the prior spatial experience of an animal. These findings suggest that replay sequences are, representationally, more flexible than theta sequences. Yet replay sequences are similar to theta sequences in two telling ways: replay sequences (a) most often represent paths that sweep out from the subject's current location (Ambrose, Pfeiffer, & Foster, 2016; Davidson, Kloosterman, & Wilson, 2009; Karlsson & Frank, 2009; Pfeiffer & Foster, 2013) and (b) represent alternative spatial paths that are relevant to upcoming navigational choice. Moreover, just as with theta sequences, the paths represented by replay sequences have been found to correlate with the paths taken in subsequent navigational behavior (Pfeiffer & Foster, 2013).

On the one hand, these two patterns can be seen as particularly different—replay sequences appear more flexible than theta sequences and furthermore these two patterns occur in different brain states (SWR and locomotor, respectively). More generally, the two-stage hypothesis and related experimental results articulate major functional differences between SWR and theta activity ([Girardeau, Benchenane, Wiener, Buzsaki, & Zugaro, 2009; Ego-Stengel & Wilson, 2010; Kovacs et al., 2016; van de Ven, Trouche, McNamara, Allen, & Dupret, 2016; Roux, Hu, Eichler, Stark, & Buzsaki, 2017]; discussed and reviewed in Buzsaki (2015)).

We suggest that, at least at first, it may be more insightful to focus on the opposite view—theta and replay sequences are remarkably similar. This similarity appears to be included two representational properties: first, that of encoding current circumstances

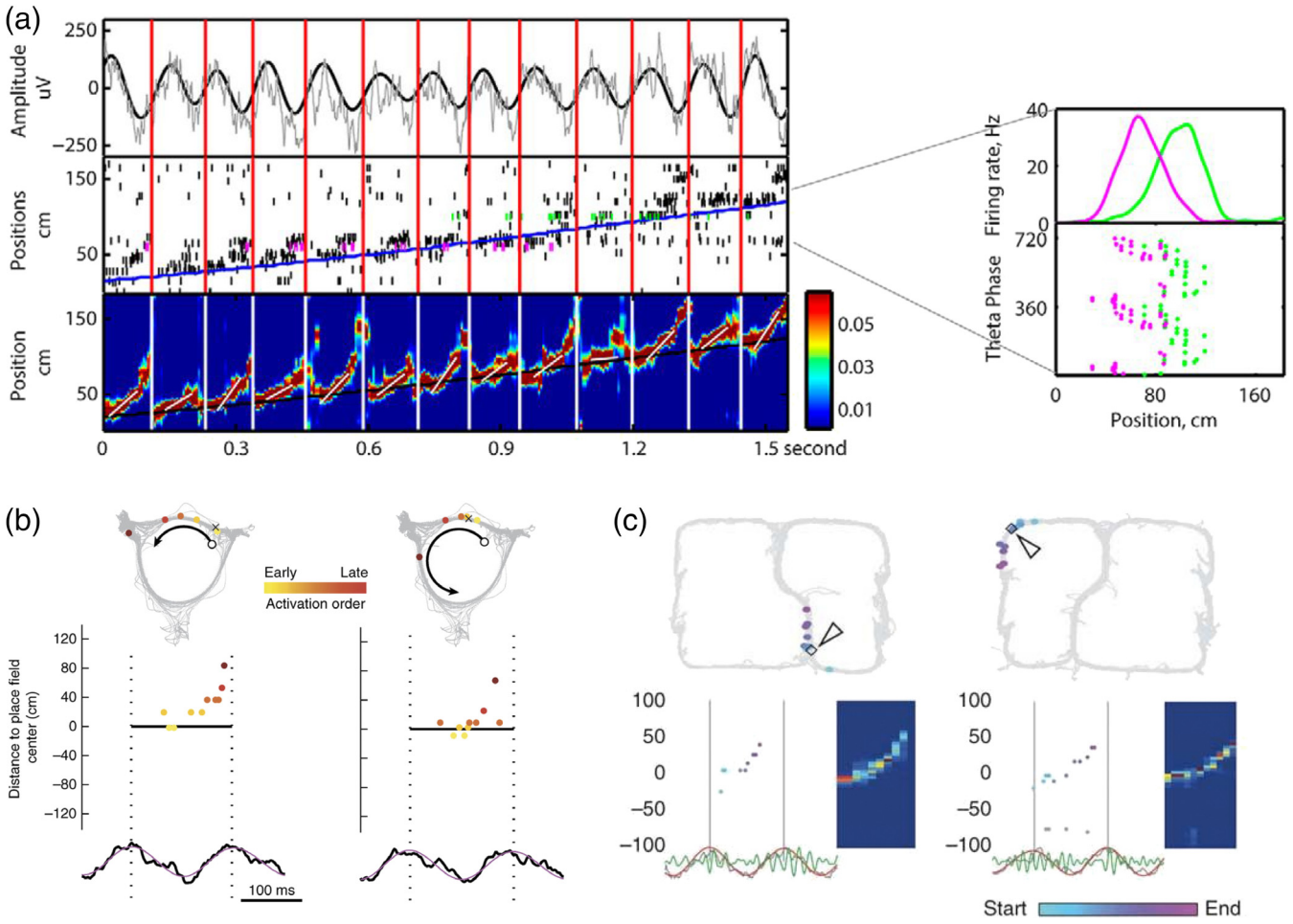


FIGURE 13 Theta sequences

Three examples of theta sequences. Data from locomotor periods. (a) Theta sequences in a linear maze. The linear track (1.65 m) is not shown. Top, LFP in CA1, with the trace filtered at theta frequency overlaid (black trace; 4–12 Hz). Middle, firing activity (rasters) of 107 CA1 principal neurons (place cells) ordered by their peak firing locations along the track. The position of the animal is shown as a blue line. Bottom, probability estimates of location corresponding to the place cell firing activity. The position of the animal is shown as a black line. Right, examples of theta phase precession; top panel shows overlapping spatial firing fields of two place cells; bottom panel shows phase-position relationship of spikes during the period plotted at left. (b) Theta sequences in a circular track. Two theta sequences shown. This environment has three goal locations (reward sites). Shown are two theta sequences. Top, plot of the locations visited by the rat, with the center locations of the spatial firing fields of the hippocampal neurons active during the theta sequence shown as colored dots. Colors corresponds to the time at which the neuron fired within the theta sequence (to show temporal order). The location of the subject is indicated by the white circle. The arrow indicates the subsequent path taken by subject. Bottom, firing activity (rasters) of the neurons active during the theta sequences. The neurons are ordered by the distance of their spatial firing fields relative to the subject's current location. LFP is plotted below the rasters (overlay trace; 6–10 Hz). (c) Theta sequences in a branching maze. Two theta sequences shown. Top, plot of the locations visited by the rat, with the center locations of the spatial firing fields of the hippocampal neurons active during each theta sequence shown as colored dots. Colors correspond to the time at which the neuron fired within the theta sequence (to show temporal order). The location of the subject is indicated by the white arrow. Bottom, firing activity (rasters) of neurons active during the theta sequences. The neurons are ordered by the distance of their spatial firing fields relative to the subject's current location. LFP is plotted below the rasters (overlaid traces are LFP filtered at 6–12 Hz and 40–100 Hz).
Part a reproduced with permission from Feng et al. (2015); part b reproduced with permission from Wikenheiser and Redish (2015b); part c reproduced with permission from Gupta et al. (2012a) [Color figure can be viewed at wileyonlinelibrary.com]

(externally driven in essence) and, second, that of encoding multiple possible options (internally generated in essence). Note that this duality is at the heart of any form of cognition (Buzsaki, 2013; Buzsaki, Peyrache, & Kubie, 2014).

To frame the following discussion, we identify these dual properties as hallmarks of the cognitive function of prospection—a radical form of prediction in which possible future scenarios are constructed in the brain (Foster, 2017; Gilbert & Wilson, 2007; Redish, 2016; Schacter & Addis, 2007; Suddendorf & Corballis, 2007). The capacity for prospection confers an immense adaptive advantage by enabling internal evaluation of alternative outcomes relevant to upcoming behavior.

How does prospection relate to the hippocampus? One way is through memory. In humans, prospection and episodic memory activate and require many of the same brain regions, including the hippocampus (Buckner & Carroll, 2007; Hassabis, Kumaran, & Maguire, 2007; Hassabis, Kumaran, Vann, & Maguire, 2007; Schacter et al., 2012). Indeed, the distinction between memory and prospection can

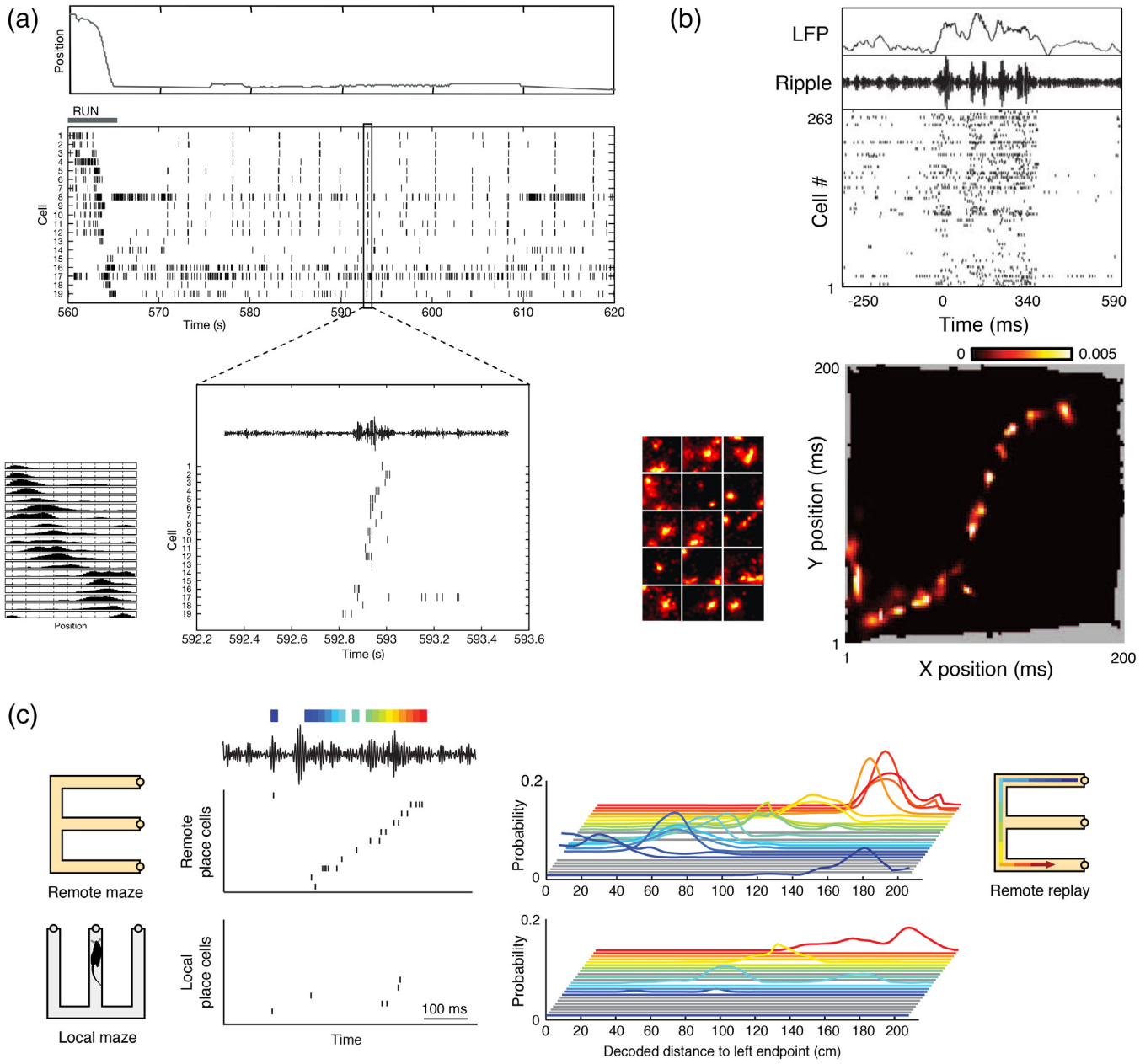


FIGURE 14 Replay sequences

Three examples of replay sequences. In each example, highlighted data from SWR periods. (a) Reverse replay. The subject was in a linear maze. Top, position of the subject over time. Bottom left, spatial firing fields in the linear maze for 19 CA1 neurons. Middle and bottom right, firing activity (raster) of the 19 neurons. LFP filtered in the ripple range (here 100–400 Hz) is shown above the expanded replay event to show the associated SWR activity. Note the reverse order firing of the replay sequence. (b) Replay in a 2D environment. The subject was in an open 2D arena (2 × 2 m). Top, neural data from CA1 at the time of an SWR. Ripple is LFP filtered in the ripple range (150–250 Hz). Bottom left, example spatial firing maps in the arena (15 of 263 CA1 neurons shown). Bottom right, decoded location (probability distribution) across all time frames of the SWR. Note that the trajectory depicted spans the arena. (c) Remote replay. First column, diagram of two different mazes encountered by the subject. In this example, the subject was located in the "local" maze. Second column, neural firing in 11 hippocampal neurons (CA1 and CA3) during an SWR event. At top is the filtered CA1 LFP (150–250 Hz). Color bar corresponds to time bins (15 ms) used for decoding location. Third column, decoded location (probability distribution) for each time bin; grey indicates time bins where no spikes occurred. Fourth column, diagram of the replay trajectory in the remote environment. Note that the neural firing depicts a coherent trajectory through the remote maze but not through the local maze.

Part a reproduced with permission from Foster and Wilson (2006); part b reproduced with permission from Pfeiffer and Foster (2015); part c adapted with permission from Karlsson and Frank (2009) [Color figure can be viewed at wileyonlinelibrary.com]

be thought of as purely heuristic, particularly for research in animal models. In other words, prospection is an interpretation of hippocampal function which suggests a shift from the concepts and terminology associated with memory to alternatives that may better describe the underlying neurobiology. One instance of such a shift is from learning and its physical substrates to decision-making and its accompanying behavioral output. Another concerns the common subdivision of memory processes into encoding, consolidation, and retrieval—concepts commonly invoked in memory research but possibly less useful in describing the use of memory to solve problems or realize

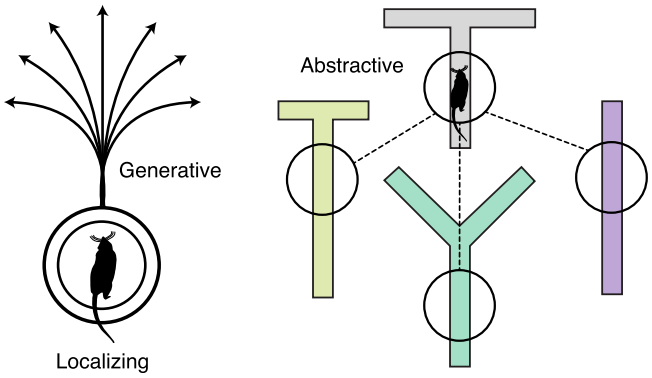


FIGURE 15 Conceptualizing prospective neural activity
Three representational properties of prospective neural activity: (a) localizing: representing current circumstances; (b) generative: representing multiple upcoming or possible scenarios; (c) localizing state: representing experience relevant to the current circumstance, that is, generalizing across different experiences. Left, visualization of (i) and (ii) as spatial representations. Right, visualization of (iii) as a representation shared across similar experiences in different navigational settings [Color figure can be viewed at wileyonlinelibrary.com]

goals. In short, conventional categories may constitute overly rigid paradigms for describing or explaining function.

By referring to the future and to upcoming behavior, the concept of prospection makes two needs explicit: (a) the need to represent current circumstances and (b) the need to represent multiple upcoming scenarios. We refer here to these properties as "localizing" and "generative," respectively (Figure 15), and suggest that neural activity in the hippocampus can be conceptualized along these lines. Note that "localizing" and "generative" are not unitary functions (such as encoding or consolidation) but are rather representation-level features that can be used to describe a given activity pattern—as we see it, better specification of representation-level description may in turn help us to understand function. We also note that we do not expect these properties to be obviously or even generally dissociable for an observed pattern of neural firing, a point we discuss further below ("Three properties of prospection").

Given this distinction between localizing versus generative, we reiterate two points (mentioned above in introducing theta sequences and replay sequences). One is that the distinction between localizing versus generative is expected to be most relevant in the awake and task-engaged subject, for whom the appropriate synthesis of localizing and generative neural activity has short-term consequences for the subject by way of upcoming behavior. The other is that theta sequences and replay sequences each have both localizing and generative properties (Buzsaki, 2015; Carr et al., 2011; Foster, 2017; Olafsdottir et al., 2018; Pfeiffer, 2017; Redish, 2016).

4.7.3 | Prospection across states

Prospection may offer insight into the function of hippocampal brain states, and vice versa. Recent reviews of theta sequences (Redish, 2016) and replay sequences (Buzsaki, 2015; Foster, 2017; Olafsdottir et al., 2018; Pfeiffer, 2017) respectively cover what is currently known of neural-level prospection in the hippocampus in the locomotor and SWR states. Given these available perspectives, we choose a particular approach in the present section. First, we start by considering what periods of time prospective neural activity might be expected to occur in awake behaving subjects. Second, we consider whether prospective neural activity occurs in the still state, a possibility that leads directly to the question of how replay sequences—a remarkable pattern of activity thought to underlie prospection—can possibly represent counterfactual experience. This question is taken by us to be pivotal: from it, we motivate the need to enlarge our present definition of prospection, which we then clarify ("Abstractive state," "Three properties of prospection") and extend ("Prospection during stillness," "A prospective circuit during stillness") in the two subsequent sections.

When does the hippocampus produce prospective neural activity? More specifically, does prospection predominate in particular brain states in the hippocampus? To help frame an answer, some basic facts about behavior and hippocampal states are in order. In a range of behavioral paradigms requiring the hippocampus, substantial time is spent outside locomotion. For example, in navigational paradigms, animals routinely pause or reduce locomotion, whether over the course of spontaneous exploratory excursions, upon attainment of the goal location, or as a consequence of imposed delays that render tasks hippocampus-dependent (Ainge et al., 2007; Eilam & Golani, 1989; Papale, Zielinski, Frank, Jadhav, & Redish, 2016; Redish, 2016; Tolman, 1948; Wallace & Whishaw, 2003). In our own experiments using a simple navigational maze, we find that unambiguous still state periods comprise ~25% of all time in the task (Kay et al., 2016). This moreover corresponds to ~90% of non-locomotor periods, with the other ~10% corresponding to SWR periods (Figure 9b); note that the proportion of SWR periods will increase somewhat due to the up-regulation of SWRs by novelty (Cheng & Frank, 2008) and reward (Ambrose et al., 2016; Singer & Frank, 2009). We also note that most task paradigms impose a motivational component (food or water deprivation or aversive stimuli) to elicit prompt behavior—the subjects (rats) perform the task with urgency. These aspects outline the prototypical experimental settings in which to consider when prospective neural activity might occur.

We suggest that prospective neural firing in the hippocampus occurs throughout waking task behavior. Above, we generically defined a pattern of neural activity to be prospective if it is both localizing and generative. This is true of both theta and replay sequences, activity patterns that occur (abundantly) during locomotor and SWR periods, respectively. Thus neural activity in the hippocampus during either locomotor and SWR periods is consistent with prospection. What remains unclear is whether prospection is the case for other periods of time, in particular, when the hippocampus is in the still state. To answer this, we can directly ask whether neural firing in the still state qualifies as prospective.

To begin with, still firing has been found to be localizing. In the same way that locomotor place firing encodes a subject's current location (manifestly a localizing representation), neural firing in the still state encodes an animal's current location (Kay et al., 2016). (Note that this result is from taking a spatial average over extended recording periods, that is, ~10 minutes or longer, thus ignoring any temporal pattern in firing; a complementary assessment that refers to time is needed, and indeed this is the crux of the following observation.)

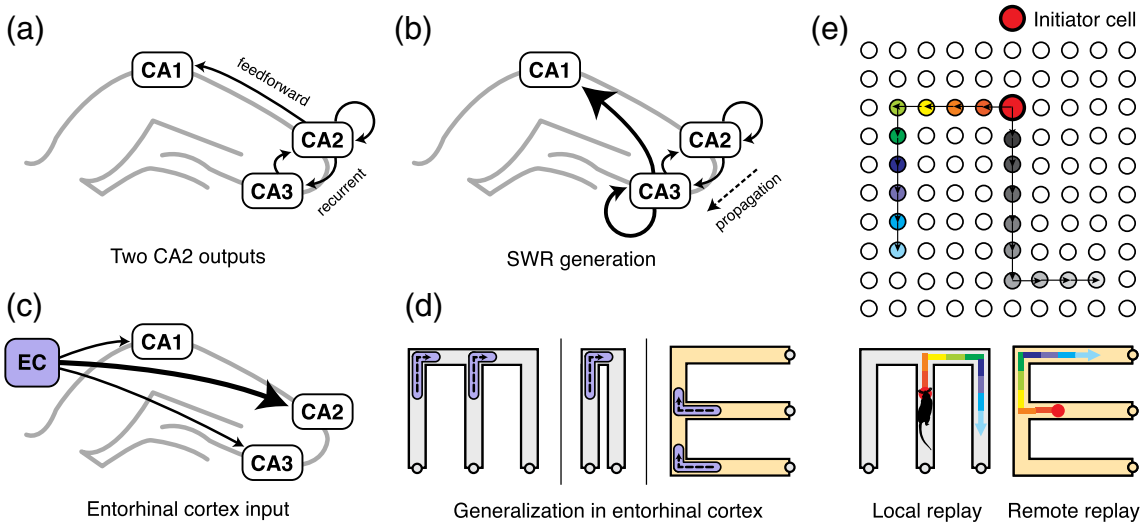


FIGURE 16 CA2 inputs, outputs, and putative role in replay
(a) Diagram of two CA2 outputs. The recurrently connected CA2 network sends feedforward input to CA1 and is also part of a recurrent network with CA3. (b) Diagram of subregional inputs involved in SWR generation. SWRs are initiated by activity in the CA2-CA3 recurrent network, with activity propagating along the hippocampal transverse axis from CA2 to CA3. CA3 provides major feedforward input to CA1. (c) Diagram of entorhinal cortex (EC) input to CA1, CA2, and CA3. EC sends exceptionally strong input to CA2. See (Bartesaghi & Gessi, 2004; Chevaleyre & Siegelbaum, 2010; Srinivas et al., 2017; Sun et al., 2014). (d) Illustration of generalizing spatial representation in EC. Diagram of spatial firing fields (purple zones) of an EC neuron across three environments (left, middle, right) with similar spatial features. Here the spatial firing field is specific to rightward corner turns. See (Derdikman et al., 2009; Frank, Brown, & Wilson, 2000b; Mizuseki et al., 2012; Singer et al., 2010). (e) Illustration of the possible role of generalizing spatial input in replay. Sensory information relating to the animal's actual location (local) activates cells with spatial fields at that location (top diagram; one such cell diagrammed as a red circle). These cells may act to initiate the reactivation of previously stored spatial sequences (diagrammed above as two series of arrows; diagram below shows corresponding spatial locations). Because these "initiator" cells can also generalize to a similar location in a remote environment (red location), these cells can initiate sequential replay of either the local (bottom left) or remote (bottom right) environment. The geometry of the neural ensemble at top is for illustration and does not represent anatomical topographic organization in the hippocampus.
Part e adapted with permission from Carr et al. (2011) [Color figure can be viewed at wileyonlinelibrary.com]

Is still firing also generative? It is not currently known whether still firing can represent multiple upcoming scenarios. Despite this, a collection of observations suggests that something related to generativity may be the case. These observations, discussed in turn here, concern specifically the relationship between the still and SWR states.

The leading observation is that SWR periods are characteristically temporally embedded in still state periods in a way that is not the case for locomotor periods (see Figure 9c). This is because the locomotor state in natural behavior is often continuously active, and thus locomotor neural firing patterns (i.e., place firing and theta sequences) are in general separated in time from still state activity by seconds or longer. In contrast, still state firing evidently occurs immediately up to the time of SWR periods and even immediately after (<100 ms; right example in Figure 12a; [Kay et al., 2016; Oliva et al., 2016a]). In this way, still firing is typically separated from SWR firing by about an order of magnitude less time than between locomotor and SWR firing. It is thus plausible that still firing has a direct physiological role in eliciting SWR firing, whether by direct or decaying synaptic activity (Buzsaki, 1989; Buzsaki, 2015) or both. Thus behavioral patterning and physiology together imply a direct and reciprocal relationship between neural activity in the still and SWR states.

A second observation is anatomical and comes from the fact that neurons specializing in the still state (N cells) are found in CA2 rather than CA1 or CA3 (Kay et al., 2016; Oliva et al., 2016a). Importantly, past work indicates that CA2 principal neurons are interconnected with CA3 (Figure 16a; Lorente de Nó, 1934; Traub & Wong, 1982; Wong & Traub, 1983; Tamamaki, Abe, & Nojyo, 1988; Ishizuka, Weber, & Amaral, 1990; Mercer, Trigg, & Thomson, 2007), the primary locus of generation of SWRs. Thus N cells, insofar as they correspond to CA2 principal neurons, likely input onto CA3 and may thus contribute to the onset of SWRs, and thus of neural activity in the SWR state (Oliva et al., 2016a); see also (Boehringer et al., 2017). Notably, this observation suggests a refinement in our understanding of SWR generation, because contribution of glutamatergic input from CA2 principal neurons would rule out an SWR gating mechanism solely dependent on disinhibition or subcortical input (Atherton, Dupret, & Mellor, 2015; Buzsaki, 2015; Hulse et al., 2016; Wang et al., 2015).

There is also a telling correspondence at the representational level. As we mentioned earlier, SWR-associated replay sequences in the awake subject predominantly represent trajectories that begin near the current location of the subject (Ambrose et al., 2016; Davidson, Kloosterman, & Wilson, 2009; Foster, 2017; Karlsson & Frank, 2009; Pfeiffer & Foster, 2013). Along similar lines, other studies in awake subjects have found that the degree of a neuron's recruitment in SWR firing correlates with the proximity of the subject to the neuron's place field (Csicsvari et al., 2007; O'Neill et al., 2006). These results indicate that neural representation during SWRs is predominantly local, paralleling the fact that still state firing predominantly encodes an animal's current location.

These three observations suggest that still state activity initiates and biases SWR firing. These observations also suggest possible mechanisms. Even so, this assessment thus far is not adequate at the representational level because it does not account for the remarkable generativity of SWR firing (as manifest in representational flexibility of replay sequences, for example, forward and reverse replay, remote replay, replay of novel paths). If still firing imposes localizing activity on SWR firing, how can it be that the neural representations associated with SWR firing are often overtly not simply localizing?

One clue lies at the timescale of behavior, in particular single periods of rest during navigation. Prior work suggests that replay sequences occurring near the start of a rest period tend to represent spatial sequences in the reverse order, whereas replay sequences near the end of a rest period represent spatial sequences in the forward order (Diba & Buzsaki, 2007; though see Ambrose et al. (2016). In addition, it has been observed that replay sequences occurring near the onset of a period of waking rest are more likely to represent task-relevant spatial sequences (Karlsson & Frank, 2009; Olafsdottir, Carpenter, & Barry, 2017). The first finding suggests a progression from representing the recent past to representing the future (upcoming navigational behavior), while the second observation indicates a progression from representing immediate circumstances to experience either further in the past or at lower fidelity. In all, these findings suggest that the machinery underlying the generation of replay sequences may evolve over the course of a given period of rest.

A number of mechanisms for biasing replay sequences have been proposed (Buzsaki, 2015; Foster, 2017; Pfeiffer, 2017), but so far none are adequate. To begin with, it is clear that inputs encoding an animal's current location in a manner continuous with the classic place representation (e.g., place field "tails") are not sufficient to account for various capacities of awake replay (discussed in Atherton et al. (2015); Buzsaki (2015)), for instance, remote representation (Davidson, Kloosterman, & Wilson, 2009; Gupta et al., 2010; Karlsson & Frank, 2009). Consequently various physiological mechanisms have been proposed, including neuromodulatory input and the excitatory contribution of place cells that represent locations across multiple environments (Buzsaki, 2015; Carr et al., 2011; Karlsson & Frank, 2009). While these physiology-oriented explanatory approaches are important, they do not as yet fully account for how the hippocampus could implement replay sequences.

4.7.4 | Abstractive state

We suggest that we can begin to tackle this explanatory gap by adopting the functional perspective of prospection. If we interpret replay sequences as prospective, then the problem at stake is *selectivity*. Recall that replay sequences reflect prior spatial experience and derive from SWRs, a pattern of neural activity associated extensively with memory. On the one hand, these properties of replay sequences simply accord with the truism that any conception of the future derives from the past (i.e., memory). On the other hand, these properties clarify the problem. In facing the future or solving a task, what knowledge from the past is relevant? In neural terms, which stored representations or patterns are best activated?

This need to abstract from prior experience means that our account of prospection thus far has been incomplete. Prospection requires not only representation with regard to ongoing circumstances (localizing) and multiple possible scenarios (generative) but also the capacity to represent specific features, shared between past and ongoing experience, which are useful for the subject with respect to the future or to upcoming behavior. In other words, prospection requires representation of similar experiences as abstracted from different single episodes in the life of the subject. Accordingly—following our earlier rubric of identifying properties needed for useful prospection—we adopt the term "abstractive" as a descriptor for neural activity that represents this kind of knowledge (Figure 15). The abstractive property makes explicit the idea that generative mechanisms in the brain need not operate only on the representation of ongoing circumstances (e.g., of sensory stimuli or veridical estimates of current location) but can flexibly support a subject's cognitive need, which may or may not be directly inferable from localizing information.

When would neural activity be abstractive? To start, we would expect that abstractive neural activity is generally less prevalent during periods of movement because moving behaviors (e.g., active sensing, locomotion, exploration) consistently demand processing of incoming sensory input (localizing information), presumably at the expense of other types of activity. In contrast, sensory influx is not necessarily the case when movement is absent.

Further, it is also the case that the cognitive need to abstract across past and current experience can evolve not only in the absence of movement but also in the absence of any changing sensory input—that is, purely as a consequence of internal processes requiring time (deliberative processes such as retrieval from memory; Shadlen & Shohamy, 2016). In other words, the knowledge that a prospecting subject needs to abstract from prior experience does not necessarily derive from incoming sensory input. This independence from sensory input indicates that abstractive neural activity can evolve over time covertly.

To return to replay sequences: the possibility of an "abstractive state" that can continuously evolve in the absence of movement can help us tackle the apparent flexibility of replay sequences. If neural activity that implements a covert abstractive state is not known to, or monitored by, the experimenter, then it would be necessarily difficult to explain how replay sequences ($\sim$100 ms events occurring intermittently at $\sim$1 Hz; Figure 14) could be both extremely flexible and relevant to upcoming behavior. Note that the concept of an internally evolving abstractive state is consistent with the findings that replay sequences change systematically over the course of rest periods (Diba & Buzsaki, 2007; Karlsson & Frank, 2009; Olafsdottir et al., 2017). In addition, an evolving abstractive state is consistent with the possibility that replay events occurring successively in a given period of rest during navigation may represent an evolving sequence of plans as opposed to a series of independent guesses. Notably, preliminary observations suggest that replay sequences in a single rest period can represent trajectories suggestive of multistep planning (Foster, 2017).

4.7.5 | Three properties of prospection

Here we look to clarify the concepts from above and in subsequent discussion. First, we summarize these concepts; second, we relate these concepts to prior thinking in memory and spatial cognition

TABLE 2 Three properties of prospection

	Localizing	Generative	Abstractive
Definition	encodes ongoing circumstance, veridical	encodes possible future scenario, counterfactual	encodes repeated commonalities, inferential
Locus in time	present	past, future	none
Spatial framework	current location, current environment	non-current location in one environment	similar locations in any environment
Memory framework	current episode (what, where, when)	constructed episode (what, where, when)	semantic (what)
Putative organization	associative	sequential	schematic

Proposed framework for representation-level properties of prospective neural activity (see "Three properties of prospection"). Related concepts can be found in in earlier work (e.g., Buzsaki & Moser, 2013; Eichenbaum et al., 1999). The types of possible organization (associative, sequential, schematic) refer to Eichenbaum, 2017a.

research; lastly, we highlight one area that remains unclear and which we address in the following sections ("Prospection during stillness," "A prospective circuit during stillness"), subsequently returning to the question of brain state.

First, a brief summary. Prospection is the capacity to represent possible future scenarios. Given this definition, it stands to reason that useful prospection has particular properties. We propose three: (a) representing ongoing (current) circumstances ("localizing"), (b) representing multiple future scenarios ("generative"), (c) representing abstracted (generalized) features of experience ("abstractive"). Furthermore, the need to abstract across experience with respect to specific features can evolve independently of movement or sensory input and is thus a covert variable ("abstractive state").

These several ideas have many precursors. We have chosen a set of terms and definitions that we think is appropriate to describe the experimental findings of present concern and that we think could be useful in other areas of inquiry. Our immediate goal is to establish useful representation-level categories for patterns of activity (particularly neural firing) in the hippocampus—past this, we look to determine whether these categories can help us understand the function of these patterns, and, by inference, the function of their associated brain states.

Before categorizing specific activity patterns, some clarification and context is required. The categories of localizing, generative, and abstractive are generic and as such do not specify the timescale at which the activity pattern in question is representational nor how the activity pattern in question is interpreted by downstream neurons. Ultimately, neither of these "implementation" specifications can be ignored. Moreover, in the hippocampus, it has been unambiguously established that timescale makes all the difference for the same set of spikes: for instance, neural firing in the locomotor state is localizing at the seconds timescale (representing current location; Wilson & McNaughton, 1993; Brown, Frank, Tang, Quirk, & Wilson, 1998; Zhang et al., 1998) but often nonlocalizing at shorter timescales (representing locations besides where the subject is; Muller & Kubie, 1989; Johnson & Redish, 2007; Gupta et al., 2012a; Wikenheiser & Redish, 2015b).

Next, it is essential to note that the categorization of localizing, generative, and abstractive is deeply related to concepts found in prior work (summarized in Table 2; e.g., Eichenbaum et al., 1999; Eichenbaum & Cohen, 2001; Buzsaki & Moser, 2013; Eichenbaum & Cohen, 2014; Eichenbaum, 2017a). An important example is the categorization of "event," "sequence," and "nodal" coding as proposed by Howard Eichenbaum and colleagues to distinguish between different kinds of memory representations. This framework was meant to capture the system of representations empirically found to underlie hippocampal neural activity (particularly in the locomotor state)—neural activity which Eichenbaum understood as implementing a more general set of relationships than strictly those of spatial map (O'Keefe, 1999).

One vital point emphasized by Eichenbaum and colleagues is the implication of nodal representation. To appreciate this implication, we need first to consider nodal coding in the hippocampus as observed empirically. In single hippocampal neurons, nodal coding manifests in a wide variety of firing patterns that occur in a general manner across different single experiences: for example, firing in place cells that encodes regular features of a subject's spatial experience (e.g., spatial firing fields in similar or analogous locations across different environments) rather than single locations (e.g., Skaggs & McNaughton, 1998). The existence and ubiquity of this type of coding is reported in a collection of place cell studies reporting two contrasting firing patterns (typically observed in different cells—often CA1 neurons—in the same recording): firing that is specific to a spatial location or spatial behavior (referred to as "context"-specific place firing; e.g., directional place firing, trajectory or "splitter" place firing, journey place firing) as opposed to firing that occurs across these locations and behaviors (e.g., "pure" place cells, "bidirectional" place cells, "path equivalent" firing; findings reviewed in Eichenbaum et al. (1999); Eichenbaum and Cohen (2014); example studies include McNaughton et al. (1983); Gothard, Skaggs, Moore, and McNaughton (1996); Skaggs and McNaughton (1998); Wood, Dudchenko, and Eichenbaum (1999); Frank, Brown, and Wilson (2000a); Wood, Dudchenko, Robitsek, and Eichenbaum (2000); Ferbinteanu and Shapiro (2003); Battaglia, Sutherland, and McNaughton (2004); Smith and Mizumori (2006b); Royer, Sirota, Patel, and Buzsaki (2010); Singer, Karlsson, Nathe, Carr, and Frank (2010); Grieves, Wood, and Dudchenko (2016); Geiller et al. (2017)). In addition to this work in the rodent model, it is also important to note that nodal coding

encompasses the invariant firing correlates of hippocampal neurons reported in humans (Quiroga, 2012; Quiroga et al., 2005).

The functional implication of nodal coding is that the hippocampus supports neural representations that are not purely associative or recapitulative but are capable of supporting inferential operations. Note that this view of function has numerous precursors, from that of schemas and cognitive maps (Bartlett, 1932; O'Keefe & Nadel, 1978; Schiller et al., 2015b; Tolman, 1948) to the essential role of the hippocampus in forming declarative memories in the brain (Frankland & Bontempi, 2005; Scoville & Milner, 1957; Squire, 1992). We stress this last precedent—in particular, the division of declarative memory into episodic versus semantic memory (Nadel & Moscovitch, 1997; Tulving, 2002; Tulving & Markowitsch, 1998; Vargha-Khadem et al., 1997).

Semantic memory is understood to result from a process that abstracts out specific spatial and temporal contexts from experience (e.g., Buzsaki (2013)). The resulting semantic representation is in turn capable of supporting cognition and behavior across a wide variety of circumstances, that is, is extremely flexible (Cohen & Eichenbaum, 1993; Eichenbaum & Cohen, 2001). It is also important to keep in mind that episodic memory, taken by itself, can only have an adaptive function by way of some process of abstraction between current circumstances and the recollected episode, a requirement that we sought to illustrate in the above discussion focusing on prospection and replay sequences.

Many influential views of hippocampal function and representation emphasize episodic over semantic aspects (e.g., context-specific vs. context-free, pattern separation, context discrimination). While there is clearly good reason to do so, other views emphasize the requirement and involvement of abstractive processes, whether expressed in terms of computational operations (Kumaran, Hassabis, & McClelland, 2016; Kumaran & McClelland, 2012), schemas (Tse et al., 2011) or inferential behaviors (Eichenbaum & Cohen, 2014; Zeithamova, Schlichting, & Preston, 2012).

To summarize, abstractive neural activity is prevalent in the hippocampus and abstractive processes are essential to a range of accounts of hippocampal function.

What are the neural substrates for abstractive processes in the hippocampus? An extremely large number of findings and ideas bear on this question—here we mention just three. The first is that most of the observations of nodal coding mentioned above were from recordings in CA1. Second, a form of generalization termed pattern completion is commonly ascribed to be function of the highly recurrent neural network in CA3 (reviewed in Le Duigou, Simonnet, Telenczuk, Fricker, and Miles (2014); Knierim and Neunuebel (2016)); recent studies include Neunuebel and Knierim (2014); Lee et al. (2015); Lu et al. (2015)). Third, past work has shown that brain regions beyond the hippocampus encode similarities across spatial-navigational experience (e.g., prefrontal [Jung, Qin, McNaughton, & Barnes, 1998], parietal [Nitz, 2006], retrosplenial [Alexander & Nitz, 2015; Alexander & Nitz, 2017], and entorhinal cortex [Frank et al., 2000a; Derdikman et al., 2009]; discussion in [Grieves, Duvelle, Wood, & Dudchenko, 2017]). These brain regions can thus contribute spatially abstractive neural activity to target structures, among them the hippocampus.

These and other observations are clues to an answer that ultimately remains unclear. In the following section, we consider the possibility of a specific association between abstractive processes in the hippocampus and the CA2 subregion. As we elaborate, this putative association provides several clues relevant to our original inquiry into the functions of hippocampal brain state.

4.7.6 | Prospection during stillness

In this section, we extend the line of reasoning, introduced in the previous several sections, to the CA2 subregion and the still state. We previously concluded that an abstractive dimension of hippocampal neural activity was required not only to account for prospective replay sequences but also for prospection more generally. Furthermore, we speculated that an "abstractive state," an underlying pattern of activity that could evolve in the absence of behavior or even changing sensory input, would help explain how replay sequences appropriately abstract across previous experience with extreme flexibility (e.g., Carr et al., 2011; Davidson, Kloosterman, & Wilson, 2009; Foster, 2017; Gupta et al., 2010; Pfeiffer & Foster, 2013). In this section, we look to elaborate one possibility regarding the neural substrates of abstractive state.

A pattern of neural activity implementing abstractive state must access prior experience relevant to ongoing experience. A clue regarding such activity was reported in a study that focused on replay sequences and moreover used two different environments (two mazes in different overall locations; Karlsson & Frank, 2009). In particular, it was observed that hippocampal neurons that fire first in a replay sequence representing a remote environment were more likely to be active at the location in the environment where the subject actually was in other words, these neurons were active in *both* environments outside replay activity. This finding suggests that putative "initiator cells" (Buzsaki, 1989; posited originally for SWRs) that bias or help generate awake replay sequences might also act as abstractive nodes across different spatial environments (Carr et al., 2011). These observations raise the possibility of a neural network that initiates replay sequences and also specializes in abstractive (generalizing) representation.

Our basic hypothesis is that, during stillness, neural activity within the hippocampus encodes abstractive state rather than only local position. In this way, neural firing in the still state may have not only a localizing but also an abstractive role in the prospective capacity of the hippocampus.

As we see it, still firing can be updated over the course of a period of rest by a combination of three inputs: (a) externally driven input, such as from reward or changing sensory stimuli, (b) internally generated input from within the hippocampus, and (c) internally generated input from regions beyond the hippocampus. Input (c) could in turn be thought of as dependent on recurrent connectivity in the hippocampus or dependent on prior hippocampal activity. This prior activity would relate to either the still state or the SWR state.

Note that the influence of prior SWR firing on still activity would indicate an ongoing reciprocal relationship between the still and SWR states. This possibility is plausible given a similar behavioral–physiological argument as presented above for the causal influence of still activity on SWR activity (Figure 9c). Indeed, we routinely observe in our data that still firing can commence rapidly after SWRs (within

~100 ms; Kay et al., 2016; Figure 12a). On this point, it is notable that a recent study reports that precise disruption of neural activity normally following SWRs causes impaired performance on a classic hippocampus-dependent memory task (trace conditioning; Nokia, Mikkonen, Penttonen, & Wikgren, 2012)—it is possible that this effect was due to disruption of still state activity.

More generally, we think it is important to point out that all forms of state-dependent activity, including still state firing, likely engage processing loops both within the hippocampus and between the hippocampus and the rest of the brain (Buzsáki, 2006; Buzsaki et al., 2014; Lisman, Talamini, & Raffone, 2005). Apart from this, we emphasize that though spatial location is an easily inferable correlate of still state firing, given the line of reasoning presented here we think there is reason to suspect that nonspatial factors (which we describe generically as "abstractive") are indispensible in the actual representational properties and functional role of still state firing. Lastly, we stress that abstractive representation is not exclusive to neural activity in one hippocampal brain state. As reviewed above, abstractive firing in the hippocampus has been traditionally established in studies focusing on the locomotor state. Our present focus on still state activity has aimed specifically to address a major difficulty regarding replay sequences (i.e., SWR state activity) and otherwise, more generally, to address an area of hippocampal research that has been largely overlooked (still state activity), possibly with important consequences for ongoing attempts to explain hippocampal function.

4.7.7 | A prospective circuit during stillness

How might the hippocampus in the still state "compute" abstractive state? One approach to this question is through anatomy, namely to determine where in the hippocampus this process would occur. As discussed above ("Still"), cells specializing in the still state (N cells) are found in CA2 and anatomical and physiological findings are consistent with CA2 as a site of initiation or biasing of SWRs (Figure 16b). Thus, CA2 neurons likely have some role in SWR-associated firing—in particular, replay sequences (Kay, 2016; Oliva et al., 2016a), which is argued above to involve abstractive input.

We suggest that neural activity in CA2 encodes abstractive state. Several additional findings suggest that this is plausible. The first is that among the CA subregions, CA2 receives uniquely strong input from entorhinal cortex (Figure 16c; Bartesaghi & Gessi, 2004; Chevaleyre & Siegelbaum, 2010; Sun, Srinivas, Sotayo, & Siegelbaum, 2014; Srinivas et al., 2017), a region of the brain that exhibits spatial representations that are remarkably general across locations and environments (Figure 16d; Frank et al., 2000a; Hafting et al., 2005; Fyhn, Hafting, Treves, Moser, & Moser, 2007; Solstad, Boccara, Kropff, Moser, & Moser, 2008; Derdikman et al., 2009; Hartley, Lever, Burgess, & O'Keefe, 2014; Knierim, Neunuebel, & Deshmukh, 2014; Moser et al., 2014; Rowland, Roudi, Moser, & Moser, 2016). These general representations may enable abstraction across different episodes of experience or across different structured representations thereof (i.e., schemas or map-like representations). There are also distinct intracellular properties and rules for synaptic plasticity in CA2 (Zhao, Choi, Obrietan, & Dudek, 2007; Lee et al., 2010; Caruana, Alexander, & Dudek, 2012; Simons, Caruana, Zhao, & Dudek, 2012; Srinivas et al., 2017; Sun et al., 2017; reviewed in [Chevaleyre & Piskorowski, 2016; Dudek et al., 2016), lending further plausibility to unique representational properties in CA2 neurons. In addition, anatomical work suggests the CA2 network is as recurrently connected as neighboring neurons in CA3, corresponding to one extreme of a continuum of recurrent connectivity along the proximal to distal axis of CA3 (Ishizuka et al., 1990; Li, Somogyi, Ylinen, & Buzsaki, 1994; Tamamaki et al., 1988). Notably, neurons located in CA2 show spatial firing fields most likely to generalize across different or altered spatial contexts (Lee et al., 2015; Lu et al., 2015; Mankin et al., 2015; consider also Wintzer, Boehringer, Polygalov, and McHugh (2014); Alexander et al. (2016)). This observation is particularly striking and is discussed in greater detail further below ("Map switching").

Apart from CA2, we can approach the question by focusing on still state firing (to reiterate, neural firing in non-locomotor non-SWR periods). To date, few recording studies permitting free behavior have explicitly addressed still state firing (Takahashi, Lauwereyns, Sakurai, & Tsukada, 2009a; Takahashi et al., 2009b; Takahashi et al., 2014; Kay et al., 2016; Yu et al., 2017; see also results in Hulse et al. (2017)); it should also be noted that data shown in other work and from other experimental paradigms may also be relevant. Despite this relative lack of knowledge, the available work indicates three features of still firing. We outline these as *continuousness*, *memory coding*, and *non-stationarity*.

Continuousness

The first is that still firing appears continuous (Figure 17a; see also Figures 5 and 6b). This property is unusual in the hippocampus because neural firing in the locomotor and SWR states is characterized by recurrent ~100 ms sequences (theta sequences and replay sequences, respectively; for replay sequences, some plotted examples of firing can be found in Figures 4 and 14; Foster & Wilson, 2007; Davidson, Kloosterman, & Wilson, 2009; Wu & Foster, 2014); for theta sequences, Figure 13; Gupta, van der Meer, Touretzky, & Redish, 2012b; Feng et al., 2015; Wikenheiser & Redish, 2015b).

Continuous firing is also reminiscent of neural activity in other systems. One case expressly relevant to prospection is neural firing that continues even after an initial stimulus is no longer present or "persistent" firing (Guo et al., 2017; Major & Tank, 2004; Wang, 2001; Zylberberg & Strowbridge, 2017). Persistent firing in effect stores a previously set variable (e.g., bodily position or an external cue to be remembered) using a rate-based neural code and as such is a putative neural basis for memory and, by inference, cognitive functions dependent on memory. Importantly, persistent firing is thought to underlie working memory (Funahashi, Bruce, & Goldman-Rakic, 1989; Fuster & Alexander, 1971; Liu et al., 2014; Romo, Brody, Hernandez, & Lemus, 1999; Wang, 2005), a function dependent on the hippocampus in various settings (e.g., Olton, Becker, & Handelmann, 1979; Spellman et al., 2015; Wang & Cai, 2006). These links suggest that continuous firing in the still state can generically support maintenance of information over time and furthermore suggest a possible role in hippocampus-dependent working memory. Indeed, this observation may help resolve apparently paradoxical relationships, noted in prior work, between working memory requirement in hippocampus-dependent tasks and the expression of hippocampal neural activity

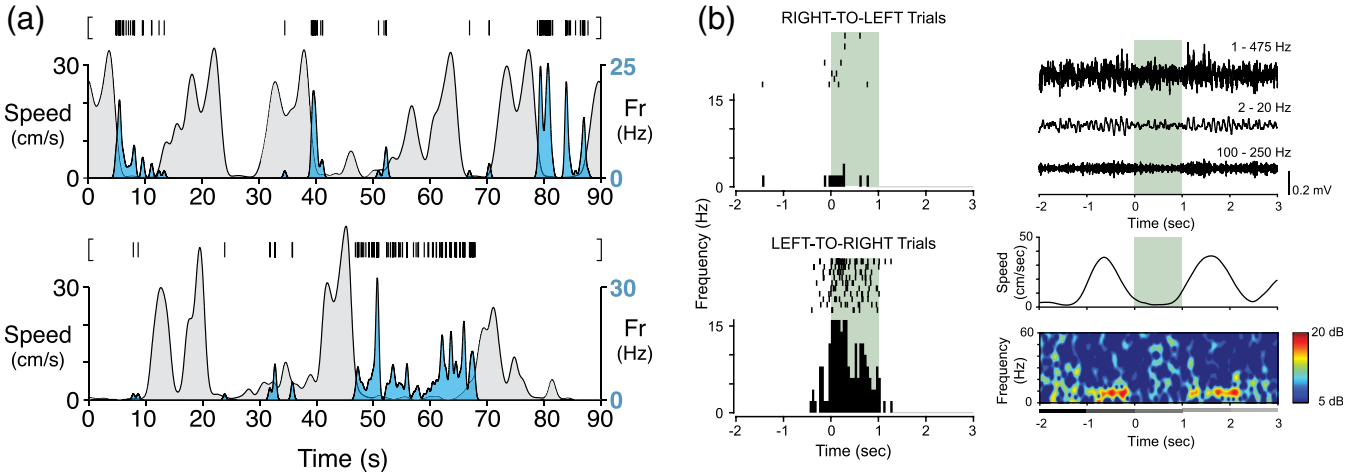


FIGURE 17 Three properties of still firing

Continuousness, memory coding, and non-stationarity. (a) Firing activity of two example CA2 N cells during behavior. Spike rasters are plotted above each example. Left y axis and grey fill trace: movement speed. Right *y*-axis and blue fill trace: instantaneous firing rate (Hz). Note that over a course of single periods of immobility, firing appears continuous and moreover evolves over time. (b) Memory coding of still firing. Left, spike rasters of an example CA1 cell at the time a rat held its head fixed at a single location (1 s; green zone) in a continuous alternation behavioral task. Data were separated depending on the trial type (10 trials each; upper: Right-to-Left trials; lower: Left-to-Right trials). Right, LFP and behavior at the time of head fixation. Note that the neural activity at the time of fixation indicates inactivation of both theta (~8 Hz) and ripple (150–250 Hz) activity. Part a reproduced with permission from Kay et al. (2016); part b reproduced with permission from Takahashi et al. (2009b) [Color figure can be viewed at wileyonlinelibrary.com]

that could putatively support working memory (Ainge et al., 2007; Ainge, Dudchenko, & Wood, 2008).

It is also worth mentioning that continuous firing in the hippocampus may have a more general role in bridging time. Indeed, it has been proposed that a fundamental function of the hippocampus is to associate temporally discontiguous stimuli or events (Rawlins, 1985; Wallenstein, Eichenbaum, & Hasselmo, 1998). Empirical support for this view comes from the fact that tasks otherwise not dependent on the hippocampus become dependent when a time delay is introduced (Ainge et al., 2007; Christian & Thompson, 2003; Clark & Squire, 1998; Eichenbaum, 2013; Rawlins, 1985). Though additional knowledge is needed, continuous firing in the still state manifestly suggests a solution.

Persistent firing is also suggestive of network-level mechanisms. One prominent example is attractor dynamics as implemented in recurrently connected neural network (Brody, Romo, & Kepecs, 2003; Wang, 2001; Wang, 2008). Another set of possible mechanisms concerns neural integrators, neural circuits that update a stably stored continuous variable in response to transient external input, a function useful elsewhere in the brain (Green et al., 2017; Koulakov, Raghavachari, Kepecs, & Lisman, 2002; Robinson, 1989; Seung, Lee, Reis, & Tank, 2000; Shadmehr, 2017; Wang, 2001). In the cases that are best characterized, an explicit physical variable—velocity—is integrated to obtain an explicit representation of position. Notably, it has been proposed that an abstract velocity representation is integrated in hippocampal–entorhinal circuitry (Sanders et al., 2015). Our suggestion here in relation to still state firing is broader: we suggest that the hippocampus may integrate extra-hippocampal inputs that are expressly nonspatial (abstractive representation) in a manner similar to that of classical neural integrators, though not necessarily or overtly for parametric information (Brody et al., 2003; Romo et al., 1999; Wang, 2005). The mechanisms underlying neural integrators (much less whether a common mechanism applies across systems) remain an area of active investigation (e.g., Green et al., 2017; Miri et al., 2011).

Memory coding

In an elegant series of studies (Takahashi et al., 2009a; Takahashi et al., 2009b; Takahashi et al., 2014), Takahashi and colleagues report a large subset of CA1 neurons that not only mainly fire during behavioral immobility (42/135 or ~30% of CA1 neurons, if not more; see classification of behavioral period types in Takahashi et al. (2009a)) but also show memory-dependent firing during immobility (>50% of neurons firing during immobility). The authors specifically used a spatial alternation task that required rats to come to a rest at a choice port for 1 s before traveling to separate left and right target ports (L-R-L-R and so on). Remarkably, unequivocal differences in firing rates during the rest period were observed between R-to-L versus L-to-R trials (Figure 17b)—this firing thus constitutes a memory-based neural code that would be useful for planning future action. Importantly, the rest periods in this paradigm, though brief, meet our proposed criteria for the still state (non-locomotor, non-SWR periods). It should be noted that because neural firing in these experiments showed theta rhythmicity, which may be due to residual locomotor theta or the presence of a theta variant, longer delay periods will help further clarify the hippocampal state during which this activity occurs.

Non-stationarity

In our experiments, we observe that neural firing in N cells can change dramatically over the course of a single period of rest (Figure 17a; see also Figures 5 and 6B; Takahashi et al., 2009b)—individual N cells can routinely go from active to silent and back, indicating an underlying process that evolves over time. Notably, this dynamic occurs with

little or at times no overt behavior. Apart from the likely involvement of intracellular mechanisms (Magee, 2003; Spruston, 2008; Wang, 2001), this pattern of activity suggests that network- and systems-level operations are changing this form of hippocampal activity through some internally evolving process. The above suggestion of a continuously integrating process is relevant here. At the same time, it is important to keep in mind that non-stationary activity does not necessarily mean that the overall neural representation is in fact changing (Brody et al., 2003; Druckmann & Chklovskii, 2012).

Given these three properties and the functional context of prospection in the hippocampus, we suggest that neurons located in CA2 specializing in the still state (N cells; discussed in "Still") may function to integrate the three sources of input outlined above (a, b, c) during periods of rest. As a result of this integration, N cells would continuously encode abstractive state. As described above, abstractive neural activity is required for effective prospection and would need to operate in conjunction with a generative neural mechanism that accesses a qualitatively different kind of stored memory (episodic counterfactuals), possibly via sequential neural activity—we suppose that this corresponds to the mechanisms and mnemonic representations of the SWR state and its associated pattern of replay sequences. This concerted operation between states would be implemented in part by synaptic input from N cells in CA2 to neurons in CA3, the critical site of SWR generation.

It is not clear whether neurons in CA2 can in fact encode abstractive state: in other words, whether relevant nonspatial (and nontemporal) factors can be encoded by these neurons. As part of this assessment, it would be critical to evaluate whether external stimuli can be continuously integrated by neurons in CA2, and whether the resulting neural code could indeed be useful for abstracting between past and current episodes of experience—for instance, via an influence on the spatial trajectories represented in replay sequences. Indeed, recent work focusing on the spatial firing properties of neurons located in CA2 shows that this is plausible, if not likely. Given this established connection to spatial representation, we discuss this matter in depth further below in the functional context of navigation (see "Map switching").

Parenthetically, we also note that representation in which spatial and temporal information is partially or fully abstracted out would help explain why CA2 is apparently needed for social memory (Hitti & Siegelbaum, 2014; reviewed in Dudek et al. (2016)).

4.7.8 | Navigation

A state-based view of neural activity in the hippocampus may also contribute to more strictly spatial interpretations of hippocampal function. The function of the place code has long been conceptualized as a spatial "cognitive map," the means by which spatial relationships between items in the world (i.e., independent of the observer) are represented such as to enable superlatively flexible navigation (O'Keefe, 2007; O'Keefe & Nadel, 1978). Under this view, neural firing in the hippocampus during locomotion constitutes a localizing signal indicating where the subject is in such a map. Indeed, a wealth of experimental data is consistent with this basic interpretation (e.g., Muller, 1996; Wilson & McNaughton, 1993; Zhang et al., 1998). However, fundamental problems remain unresolved. Here we consider four, which we refer to as *self-localization*, *initializing position*, *map switching*, and *navigational plan*. Our basic proposal is that differences and putative relationships between the locomotor and still states may clarify each of these four interrelated problems.

Self-localization

For a cognitive map to be useful, one requirement is that the correct map be selected for a given environment. This process has been referred to as self-localization (Redish, 1999; Redish & Touretzky, 1998). Prior work has shown that populations of neurons in CA1 and in CA3 are each capable of encoding different environments (Alme et al., 2014; Jezek, Henriksen, Treves, Moser, & Moser, 2011; Karlsson & Frank, 2008; Leutgeb et al., 2004; Leutgeb, Leutgeb, Barnes, et al., 2005; Mizuseki et al., 2012; Muller & Kubie, 1987; Tanila, 1999), thereby constituting neural codes for self-localization. But if there are many accessible cognitive maps in the hippocampus, how is the right one selected? Insofar as external stimuli, a putative brain mechanism is largely thought to rely on a constellation of visual cues in the background of a given environment ("distal" cues, to a first approximation; see discussion in Knierim and Hamilton (2011)). At the neural level, theoretical work suggests that neural networks underlying self-localization use winner-take-all dynamics implemented by local excitation and global inhibition (McNaughton et al., 1996; Redish, 1999; Samsonovich & McNaughton, 1997). This work also suggests a role for recurrently connected attractor networks capable of transitioning between population-level locational codes, with transitions occurring at times gradually and at times abruptly ("jumps") (Gothard, Skaggs, & McNaughton, 1996; Jezek et al., 2011; Redish, Rosenzweig, Bohanick, McNaughton, & Barnes, 2000; Samsonovich & McNaughton, 1997; Wills, Lever, Cacucci, Burgess, & O'Keefe, 2005; Zugaro, Arleo, Berthoz, & Wiener, 2003). It remains unclear where in the brain these mechanisms are implemented.

One possible reason for this gap in understanding is that isolation of the moment in which self-localization occurs may be insufficiently precise in prior work. Studies of hippocampal activity relevant to self-localization ordinarily consider data from over an entire recording session or over extended periods. Greater precision in time may be necessary to isolate what may be a rapid process (Redish et al., 2000; see discussion in Redish (1999)). Furthermore, we suggest that tackling this problem by considering neural firing at a shorter timescale (e.g., Frank, Stanley, & Brown, 2004b; Geiller et al., 2017; Hill, 1978; Zugaro et al., 2003) may give greater insight into both the relevant neural activity patterns and behaviors. Of note is a recent study (Monaco, Rao, Roth, & Knierim, 2014) that relates a specific behavior (head scanning; Lever, Burton, & O'Keefe, 2006) to the formation of hippocampal place firing, illustrating the point that there may be important relationships between neural representation and behavior-yoked mechanisms in the hippocampus.

When could self-localization occur? One possibility is that the hippocampus may generate or access self-localization information in any hippocampal state (whether locomotor, SWR, or still). Notably, an earlier proposal has suggested that self-localization might occur upon entry into an environment by means of a single SWR (Redish, 1999;

Redish & Touretzky, 1998). This was proposed given the known link between SWRs and reactivation of prior experience (Skaggs & McNaughton, 1996; Wilson & McNaughton, 1994) and also the link between SWRs and CA3, a neural network known to have suitable properties for memory recall (O'Reilly & McClelland, 1994; Redish & Touretzky, 1997; discussed further below). More broadly, this proposal suggests that self-localization may occur during rest, that is, when SWRs occur (also see Poucet et al., 2015). If it is the case that self-localization is optimal during rest, then it would be optimal behaviorally to come to a rest when self-location is ambiguous (e.g., upon entry into an environment or after disorientation). Notably, in our own informal observations, rats abruptly manually transferred between navigational environments do not necessarily move immediately in the environment they are moved to but often remain still for a period prior to movement.

Along similar lines, we point out that the transition from sleep to waking, an ethological universal, is a scenario in which self-localization would be not only routinely useful to an animal but also necessarily dependent on brain state. During sleep, it is evident that an animal is relatively unreceptive to external stimuli and furthermore that conscious awareness, much less spatial awareness, is relatively diminished. The capacity to self-localize under these conditions would have adaptive value upon awakening in an environment with few external cues (discussed in more detail below; "Sleep"). At the neural level, we simply point out that self-localization in sleep cannot rely on mechanisms dependent on locomotion. Thus, upon awakening in an environment, self-localization—if in fact accomplished—could rely only on a mechanism that persists through sleep. Indeed it has been established that subsets of hippocampal neurons express a self-localization signal during sleep (Jarosiewicz et al., 2002; Jarosiewicz & Skaggs, 2004a; Kay et al., 2016).

With regard to specific neural substrates, we offer a few additional observations. Prior work has suggested CA3 as a candidate substrate for self-localization given that the extensive recurrent connectivity of CA3 can plausibly implement the memory recall operation needed for self-localization (Jeffery, 2007; Redish, 1999; Redish & Touretzky, 1997). Notably, neural populations in CA3 better distinguish between different environments as compared to CA1 (Guzowski, Knierim, & Moser, 2004; Lee, Rao, & Knierim, 2004; Lee, Yoganarasimha, Rao, & Knierim, 2004; Leutgeb et al., 2004; Vazdarjanova & Guzowski, 2004). Interestingly, the possible role of CA3 in turn implicates specific physiological patterns and behaviors. Apart from the rest-associated SWRs, CA3 is also associated with low-frequency gamma rhythm (low gamma, 30–50 Hz; Csicsvari et al., 2003; Colgin et al., 2009), which is expressed at higher amplitudes downstream in CA1 at lower movement speeds and rest (Ahmed & Mehta, 2012; Kemere et al., 2013; Zheng et al., 2015). Thus, with SWRs and low gamma as an indicator of CA3-driven activity, the influence of CA3 on the hippocampal circuit is highest at low speeds and periods of rest. It is also notable that low movement speed and rest is associated with lower cholinergic tone in the hippocampus, a change known to gate recurrent input in the CA3 network (Hasselmo, 1999; Hasselmo, 2006; Tsanov, 2017; Vandecasteele et al., 2014). This gating is thought to bias the operation of the hippocampus toward recall (versus encoding) and as such can be understood to favor a process for self-localization.

These findings implicating CA3 just as well implicate CA2. As in CA3, CA2 is also characterized by recurrent circuitry (Ishizuka et al., 1990; Lorente de Nó, 1934; Mercer et al., 2007; Tamamaki et al., 1988), consistent with neural architecture supporting memory recall. Moreover, gating of recurrent input upon periods of rest parallels the observation that CA2 contains a subpopulation of neurons that fires preferentially at low speeds and rest (Kay et al., 2016). It is also worth noting that neural firing in this neural population is associated with an activity pattern detectable in hippocampal LFP ("N wave"; discussed above in "Still") that may be consistent with widespread inhibitory activity, reminiscent of the winner-take-all network mechanism thought to support self-localization (Redish, 1999).

Initializing position

Another requirement of a putative cognitive map is the ability to keep track of one's spatial position given knowledge of starting location in conjunction with self-motion cues, a process (mentioned earlier) known as path integration (McNaughton et al., 1996; McNaughton et al., 2006). Path integration implies dependence between the locomotor place representation and self-generated movement, which is consistent with experimental results (McNaughton et al., 1996). However, path integration also requires an initial position, presumably determined during periods of rest prior to self-generated movement. (This is similar to the need to "reset" path integration; discussion in Etienne and Jeffery (2004); Hafting et al. (2005); Hardcastle et al. (2015); Poucet et al. (2015)). Notably, the ability to path integrate does not require a particular pattern of movement and rest over the course of navigational behavior. Naturalistic exploratory behavior is characteristically punctuated by periods of rest that often occur at irregular intervals and locations (Drai, Benjamini, & Golani, 2000; Eilam & Golani, 1989; Golani et al., 1993; Tchernichovski et al., 1998; Wallace et al., 2002; Whishaw, Hines, & Wallace, 2001). Given that path integration occurs under such conditions (Wallace et al., 2002; Wallace et al., 2006), we might expect that the mechanism underlying path integration, and neural activity supporting or relying on path integration, encompasses all types of behaviors over the course of navigation, including rest. Thus, the hippocampal place representation should have access to or itself generate a neural representation of current location during rest.

As described earlier, neural firing encoding current location during rest has been identified in the hippocampus, in particular, in the still state (Best & Ranck, 1982; Kay et al., 2016). However, the qualitative difference between the still and locomotor brain states raises a question—why would there be different anatomical and physiological correlates (by brain state) for the purpose of representing current location? In our view, it is not evident whether or how the spatial representation in the hippocampus, characterized on the basis of the locomotor place representation, is related to location-specific firing in the still state. The respective self-location signals in locomotor and still states could be thus interpreted as coincidental.

We think that this relationship may be more than coincidental. While more work is needed, it may be that the continuity of the self-localization signal across behaviors (locomotion and rest) is only possible due to mutual dependence between neural activity in the

locomotor and still states. In this view, the self-location representation is distributed in different hippocampal (or upstream) networks during behavioral shifts between locomotion and rest. (Note that these networks would not be segregated strictly along brain regions or subregions. Rather, the proportion of active neurons in each region would systematically differ for each state-associated locational network.) This extends the view that the hippocampal spatial representation is "gated" by the path integrator by simply adding that the reverse is also worth consideration: that when subjects come to a stop, activity encoding the computed output of the path integrator gates a self-localization signal that is otherwise not dependent on the path integrator. The update of location within the brain would be different depending on whether an animal was continuously in locomotion or not. If not, then different networks of neurons would be updated in a manner dependent on regional anatomy, rather than as a homogeneous network (McNaughton et al., 1996; McNaughton et al., 2006; Muller, Stead, & Pach, 1996; Samsonovich & McNaughton, 1997).

Map switching

A wealth of experimental findings indicates that, in a given environment, there are in fact multiple forms of representation coactive in the hippocampus. This was initially indicated in environments with linear paths, where it was found that place cells often fire only in one direction of travel (McNaughton et al., 1983), thus ruling out purely spatial representation. Subsequent work has found that a variety of additional variables have roles in determining the place representation (in short, variables based on task, memory, behavior, motivational state, sensory modality, and nonspatial cues; reviewed in Eichenbaum et al. (1999); Shapiro et al. (2006); O'Keefe (2007); Eichenbaum and Cohen (2014); Eichenbaum (2017d)); also see recent relevant work [Geva-Sagiv, Romani, Las, & Ulanovsky, 2016; Sarel, Finkelstein, Las, & Ulanovsky, 2017; Danjo, Toyoizumi, & Fujisawa, 2018; Omer, Maimon, Las, & Ulanovsky, 2018]).

From the spatial viewpoint, the consequence of these additional correlates is that place firing can be understood to occur in different "maps" within a given environment (e.g., Gothard, Skaggs, & McNaughton, 1996; Gothard, Skaggs, Moore, & McNaughton, 1996; Shapiro, Tanila, & Eichenbaum, 1997; Skaggs & McNaughton, 1998). Indeed it has since become clear that simultaneously recorded populations of hippocampal neurons can collectively switch between different map representations in the same environment (Harris, Csicsvari, Hirase, Dragoi, & Buzsaki, 2003; Jezek et al., 2011; Kelemen & Fenton, 2010; Kelemen & Fenton, 2016; Markus et al., 1995; Redish et al., 2000). Note that map switching can be understood as an extension of self-localization (Poucet et al., 2015) and may use similar mechanisms. In particular, focusing on the remarkable capacity of the hippocampus to switch between representations is possibly a way to understand why, in the first place, there are multiple map representations. What then are the conditions and mechanisms of map switching?

One clue is that map switching can occur as fast as at the subsecond timescale (Harris et al., 2003; Jackson & Redish, 2007; Jezek et al., 2011; Kelemen & Fenton, 2010; Kelemen & Fenton, 2016) and is thus temporally flexible enough to support a rapidly evolving

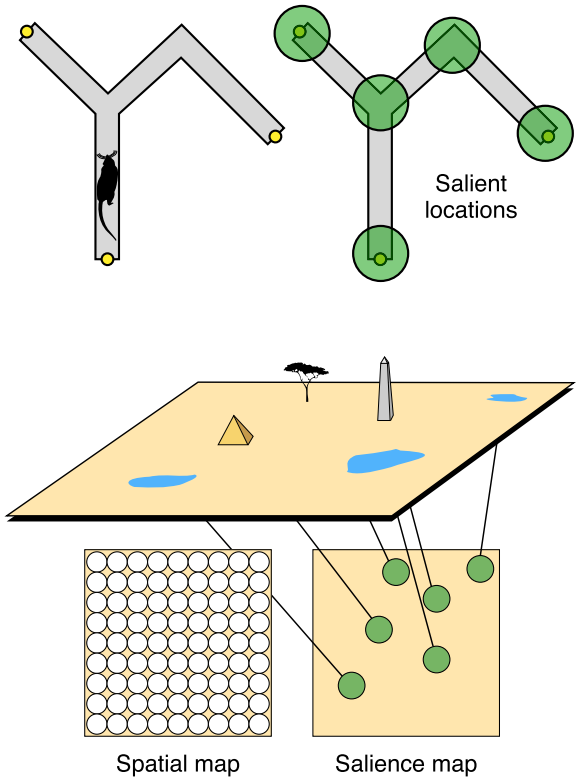


FIGURE 18 A salience map
(A) Salient locations (encircled in green) in mazes include reward sites (yellow circle), path junctions, and path crossings. Generalization across different experiences may occur predominantly at these locations. (B) Illustration of a homogeneous representation of space ("Spatial map") versus a representation of space based on salient locations ("Salience map"). These map-like representations may coexist in the hippocampus; moreover, a map based on salient locations may be useful for generalization across different individual experiences [Color figure can be viewed at wileyonlinelibrary.com]

ongoing behavioral need. It has been argued before that the interlinking of multiple maps through switching allows for flexible recall of similar experiences for the sake of effective problem solving, particularly in circumstances requiring inference (e.g., goal-directed navigation; Cohen & Eichenbaum, 1993; Eichenbaum et al., 1999; Eichenbaum & Cohen, 2001). The relevance of generalization in hippocampal function has also been emphasized in other experimental contexts (Bunsey & Eichenbaum, 1996; Eichenbaum, 2017a; Eichenbaum & Cohen, 2014; McKenzie, Robinson, Herrera, Churchill, & Eichenbaum, 2013; Schlichting & Preston, 2015; Shohamy & Wagner, 2008; Tse et al., 2007; Tse et al., 2011; Zeithamova, Dominick, & Preston, 2012).

Given this clue, we suggest that map switching can be clarified by considering brain states in the hippocampus, in particular the locomotor and still states. The idea that map switching is associated with generalization may relate to a basic observation: that locations where animals tend to reduce locomotion or come to a rest also tend to be locations at which generalization, and therefore map switching, appears most relevant. Three examples common to navigational paradigms include reward sites, sites with local cues (landmarks), and path crossings, each a type of location where cognitive access to additional representations would be desirable for learning and decision-making. A unifying interpretation of these locations is that they are salient

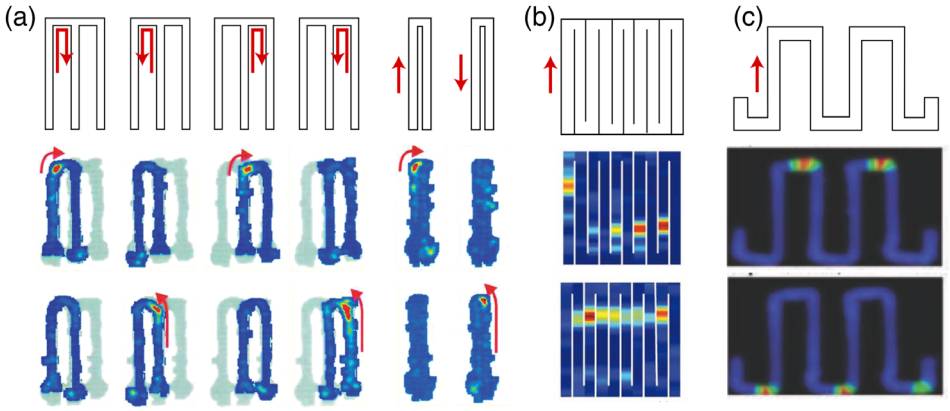


FIGURE 19 Spatial generalization in the brain
Three examples (a, b, c) of generalized spatial representations from neural data. Top row in each example, a diagram of the environment in which neural activity was recorded. Red arrows indicate that the data plotted are from periods when the subject moved along a specific path. The middle and bottom row of each example show spatial firing maps from two example neurons. (a) Spatial generalization in deep entorhinal cortex. Here, data were recorded in two different environments (W- and U- mazes). The first example neuron (middle row) fired at rightward corner turns in both environments, while the second example neuron (bottom row) fired at leftward corner turns in both environments. (b) Spatial generalization in entorhinal cortex. (c) Spatial generalization in the hippocampus. Neurons recorded in CA1.
Part a reproduced with permission from Frank et al. (2000b); part b reproduced with permission from Derdikman et al. (2009)); part c reproduced with permission from Mizuseki et al. (2012) [Color figure can be viewed at wileyonlinelibrary.com]

(Figure 18). Furthermore, if we adopt an interpretation that adheres strictly to salience, these locations do not necessarily entail low movement speeds. Indeed we think it important to point out that it is possible, given what we currently know, that hippocampal neural firing as has been observed the still state primarily encodes some form of salience, and that higher still state firing at low speeds is the consequence of a subject's (here a rat) behavioral tendency to come a rest at salient locations. Additional experiments are needed to evaluate this possibility.

This scenario suggests that there may be an important relationship between still state firing and map switching. Rather than a neural code necessarily dependent on rest (though typically so), still state firing in the hippocampus may be a clue that, in conjunction with various spatial maps in a given environment, there exists a more specialized map (Figure 18) that represents locations where switching between various spatial maps is appropriate. Prior work has proposed similar ideas: locations relevant to multiple cognitive maps have been called "wormholes" where switching between maps would occur (McNaughton et al., 1996), and locations common across different episodes of experience have been referred to as "nodes" (Buzsaki & Moser, 2013; Eichenbaum et al., 1999); see also above discussion "Three properties of prospection"). It may be conceptually useful to view such a salience map in an inverse way, where rather than reflecting a subject's cognitive need at a given place, salient locations can be thought of as triggering map switches in the hippocampus if a subject spends time at them, whether moving or not. Like the dynamics of hippocampal neural populations (e.g., Jezek et al., 2011; Kelemen & Fenton, 2010), switching would not be deterministically triggered but would vary probabilistically such that the greater time spent at a salient location the more likely to trigger a map switch. This scheme speaks to what we would expect ethologically when an animal comes to a lengthy rest from locomotion—a subject's goals and thus relevant representations are most likely to switch following an extended period of rest (when "consummatory" behaviors, such as drinking and feeding, take place; Buzsaki, 2015).

Several experimental findings are also relevant to the plausibility of a saliency map for generalization. The first stems from the fact that if such a map exists and is associated with still state firing, then the saliency map would be selectively represented in the activity of the distinct N-cell population in CA2, thereby implicating subregional anatomy. This possibility is reminiscent of subregional differences in the place representation between CA1 and CA3 (e.g., Alvernhe, Van, Save, & Poucet, 2008; Dupret, O'Neill, Pleydell-Bouverie, & Csicsvari, 2010; Lee, Rao, & Knierim, 2004; Lee, Yoganarasimha, et al., 2004; Leutgeb et al., 2004; Mizuseki et al., 2012), and more recent work in CA2 (Alexander et al., 2016; Kay et al., 2016; Lee et al., 2015; Lu et al., 2015; Mankin et al., 2015; Oliva et al., 2016b). It is also relevant that neurons in the hippocampus and in directly connected regions show firing patterns consistent with anchoring of generalized spatial maps to salient features or locations (Figure 19; O'Keefe & Burgess, 1996; Skaggs & McNaughton, 1998; Frank et al., 2000a; Derdikman et al., 2009; Singer et al., 2010; Mizuseki et al., 2012); reviewed in (Grieves et al., 2017).

More specifically, a set of experimental results suggests that neurons in CA2 have a privileged role in generalizing across different experiences. It is important to note that these results refer to neural activity averaged over longer periods of time (minutes and longer): our point here is that these time-averaged responses may reflect what is in fact covert, flexible, and frequent switching between cognitive maps at a faster timescale (<1 s; Harris et al., 2003; Jezek et al., 2011; Kelemen & Fenton, 2016). For clarity, we organize these results into two main findings.

The first is that neurons in CA2 are exceptionally active across different environments and conditions. This is indicated by exceptionally high mean firing rates regardless of specific conditions, and by measures of the similarity of spatial firing across environments and

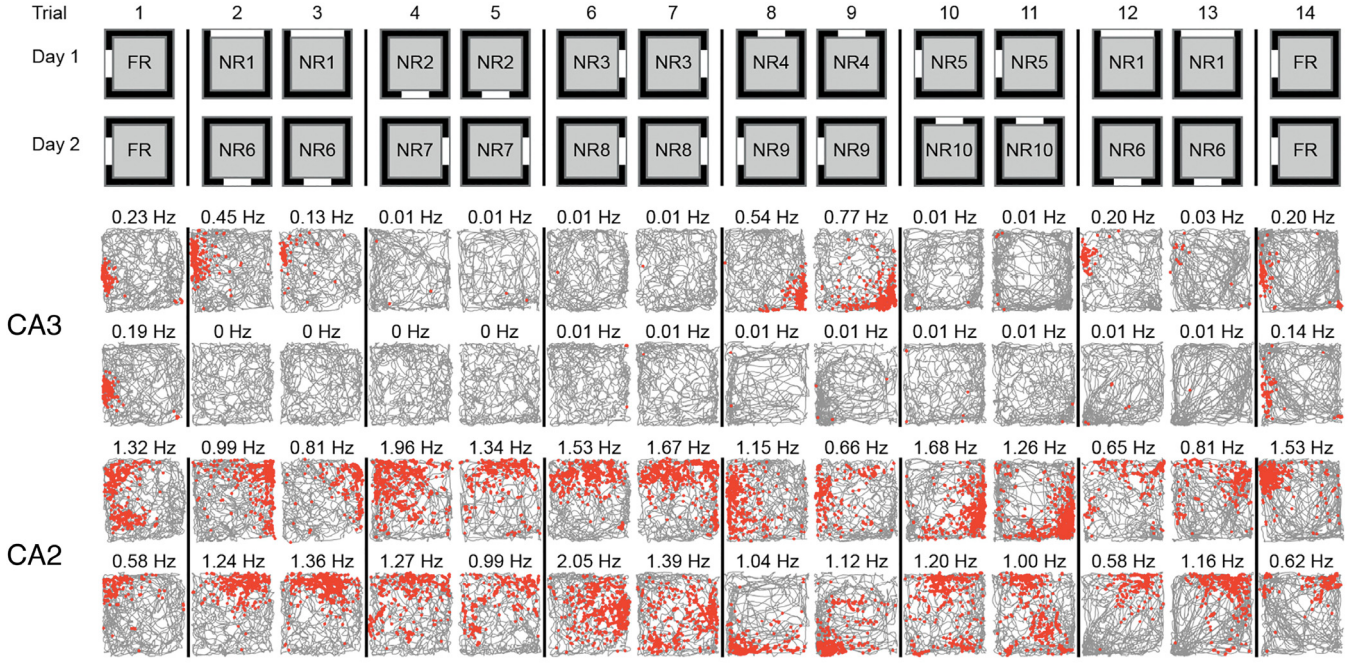


FIGURE 20 Spatial generalization in CA2

Spatial firing maps from two example neurons: one recorded in CA3 (upper) and the other in CA2 (lower). Top, schematic of the experimental paradigm. Across 2 days, subjects were placed in a series of different 2D arenas (11 total; vertical lines separate trials in different rooms). Bottom, raw spatial firing maps of the two neurons. Grey indicates locations visited by subjects; locations of individual spikes shown in red. Mean firing rate is reported at top. Note that the neuron recorded in CA2 fired across environments.

Reproduced with permission from Lu et al. (2015) [Color figure can be viewed at wileyonlinelibrary.com]

altered local cues (Alexander et al., 2016;Lee et al., 2015 ; Lu et al., 2015 ; Mankin et al., 2015). In one impressive study (Lu et al., 2015), firing activity was evaluated for neurons in CA1, CA2, and CA3 in 11 different environments, with neurons in CA2 exhibiting an unmatched tendency to fire in every environment (Figure 20). Remarkably, considerable similarity of spatial firing between environments was found for neurons in CA2, demonstrating a type of generalization that does not occur in either the CA1 or CA3 neuron populations (Alme et al., 2014; Leutgeb et al., 2004). This finding is indication that generalizing activity ("nodal" or "abstractive" above) in the hippocampus is concentrated anatomically at CA2, a possibility also indicated by results comparing CA1, CA2, and CA3 in altered environment paradigms (Lee et al., 2015; Mankin et al., 2015). Interestingly, two studies find that neural activity in CA2 is sensitive to changes in the environment (Alexander et al., 2016; Wintzer et al., 2014), suggesting additional complexity or the importance of additional factors (such as social stimuli and novelty; Alexander et al., 2016; also see Hitti and Siegelbaum (2014)). More work is needed, and we again suggest that finer-grained analyses, particularly with respect to behavior, may provide insight.

The second finding is that CA2 is associated with a subpopulation of CA1 neurons that have been shown to have extremely robust generalizing activity. This association stems from an important study in which CA2 was genetically targeted (Kohara et al., 2014). This study found that CA2 neurons provide more synaptic input to CA1 neurons located deeper along the radial axis of the hippocampus, in accordance with the tendency of axonal fibers of CA2 neurons to project to radially deeper layers in CA1 (unlike CA3 projections to CA1; Ishizuka et al., 1990; Shinohara et al., 2012; Cui, Gerfen, & Young, 2013; Hitti & Siegelbaum, 2014). Recent complementary work in vivo has found that deep CA1 neurons in fact fire more overall (Mizuseki et al., 2011), fire at more locations in a given environment (Mizuseki et al., 2011), and fire when the subject is near specific landmarks (Danielson, Zaremba et al., 2016; Geiller et al., 2017). Remarkably, a recent study reports that systematically removing and introducing specific landmarks completely controls this landmark-based firing (Geiller et al., 2017). The robustness of this firing pattern is indicated by the elicitation and elimination of landmark-tied firing within a single trial. Importantly, because this firing could be instantly elicited by a cue in an entirely novel location, this firing constitutes generalization across different locations. Notably, landmark firing was found disproportionately more in CA1 versus CA3, and strength of this firing was observed also to depend on the salience of the specific landmark. In conjunction with this study, similar findings have been reported for deep CA1 neurons in relation to the location of goals (Danielson, Zaremba et al., 2016; also see McKenzie et al. (2013)).

We point out that this generalizing neural activity may be due to inputs from CA2, and that the properties of such activity may account for the correlation of spatial firing patterns across different environments observed in CA2 studies (Lee et al., 2015; Lu et al., 2015; Mankin et al., 2015). The overall finding of generalizing activity in CA2 may in turn help explain prior differences in spatial firing patterns (observed during locomotion) between CA1 and CA3, including differences in goal representation (Dupret et al., 2010), differences in spatially abstractive firing (Mizuseki et al., 2012), differences in bidirectionality (a generalizing representation, [Mizuseki et al., 2012]; see

also Battaglia et al. (2004)), and differences in orthogonalization between different environments (Guzowski et al., 2004; Leutgeb et al., 2004). At a finer temporal scale, it is also worth mentioning that there may also be some relationship between salient locations encoded by CA2 neurons and the tendency of locomotor theta sequences to conform to salient features of environments (observed in CA1; Gupta et al., 2012b).

Here it is worth noting that CA2 input to CA1 is unlike putative input from CA2 onto CA3. With CA1, CA2 input is diffuse and strictly feedforward, while with CA3, CA2 input is restricted to the portion of CA3 nearest CA2, and moreover reciprocal and apparently part of a recurrent network (reviewed in Dudek et al. (2016); Oliva et al. (2016a)). It is possible that these distinct anatomical outputs from CA2 are differentially efficacious depending on brain state: for instance, CA2 inputs to CA1 may be primarily engaged during locomotion, whereas CA2 inputs to CA3 would be engaged primarily during immobility. State-based neuromodulatory mechanisms previously postulated for gating CA3 outputs onto CA1 may be similarly relevant here (Hasselmo, 1999; Hasselmo, 2006).

In summary, findings at the anatomical, physiological, and representational levels are consistent with the scenario in which CA2 contributes abstractive (generalizing) activity to both CA3 and CA1. This activity from CA2 may have a role in the map switching observed in the hippocampal place representation.

Navigational plan

Lastly, we point out how hippocampal state suggests a way to relate prior findings on spatial prospection to active navigation. Recent findings indicate that the hippocampal replay sequences characteristic of the SWR state are capable of representing upcoming navigational trajectories (Buzsaki, 2015; Foster, 2017; Pfeiffer & Foster, 2013; Wu et al., 2017), consistent with a prospective role of SWR activity in navigation. In agreement, disruption of SWRs in a navigational task results in a performance deficit (Jadhav, Kemere, German, & Frank, 2012), consistent with a role of SWRs in planning upcoming behavior.

However, SWRs and associated replay sequences are typically brief (~100 ms) and occur only sporadically. Indeed SWRs do not necessarily occur just prior to movement. While different scenarios are possible for how SWR activity may contribute to behavior (Foster, 2017), it is worth taking into account that still state firing is commonly active just prior to locomotion (Figure 17a; additional examples in Kay et al., 2016; also see Tabuchi et al., 2003; Takahashi et al., 2009b; Takahashi et al., 2009a; Takahashi et al., 2014). Therefore, it is possible that still state firing in the hippocampus has a role in specifying a particular navigational plan, whether motoric or more abstract. Moreover, if replay sequences function in part to alter still firing (discussed earlier), then still firing could at least partially mediate the prospective contribution of replay sequences to upcoming behavior. We also note that, even in the absence of SWRs, still state activity may be sufficient to maintain and specify navigational plans for upcoming behavior.

4.7.9 | Sleep

Each of the three hippocampal states proposed here has an analogous state during sleep: REM sleep is similar to the locomotor state, non-REM sleep approximately to the SWR state, and MA sleep to the still state. Furthermore, it appears to be the case that during these sleep states, neural firing in the hippocampus and other brain regions follows the same temporal dynamics as during their waking analogs (e.g., Louie & Wilson, 2001; Harris et al., 2002; Peyrache, Lacroix, Petersen, & Buzsaki, 2015; reviewed in Buzsaki (2015)). Still, there are a number of important differences between waking and sleep states (Karlsson & Frank, 2009; Mizuseki et al., 2011; Montgomery et al., 2008; Poe, Nitz, McNaughton, & Barnes, 2000; Roumis & Frank, 2015; Wikenheiser & Redish, 2013). Furthermore, additional sleep patterns of thalamic or cortical origin are known to have systematic relationships with various forms of hippocampal activity, indicating that a full account of what distinguishes sleep will require knowledge of activity in both anatomical domains. Some broad reviews of sleep include Jouvet (1967); Siegel (2005); Stickgold (2005); Buzsáki (2006); Diekelmann and Born (2010)). Below, we highlight a few points of interest.

Less is known about hippocampal neural firing during REM than during non-REM sleep. In REM, recapitulation of waking spatial sequences in hippocampal neurons has been reported (Louie & Wilson, 2001). Furthermore, a separate study focusing on head-direction neurons in extra-hippocampal regions shows similar activity (Peyrache et al., 2015). Recent work has related REM activity to homeostatic regulation (Grosmark, Mizuseki, Pastalkova, Diba, & Buzsaki, 2012; Watson et al., 2016) and memory consolidation (Boyce, Glasgow, Williams, & Adamantidis, 2016).

Non-REM sleep encompasses transitional periods of sleep (e.g., involving sleep spindles) and also SWS, both of which are associated with a high incidence of SWRs (Buzsaki, 1989; Buzsaki, 2015; O'Neill et al., 2010; Roumis & Frank, 2015). In agreement with the original two-stage hypothesis, numerous studies have shown that neural firing during sleep SWRs replays prior spatial experience (Buzsaki, 2015). Furthermore, experiments disrupting hippocampal activity at the time of SWRs suggests a role of SWR-associated hippocampal neural activity in consolidation of spatial memory (Girardeau et al., 2009; Ego-Stengel & Wilson, 2010; Nokia et al., 2012; van de Ven et al., 2016; see also (Maingret, Girardeau, Todorova, Goutierre, & Zugaro, 2016; Roux et al., 2017).

As discussed earlier ("Still"), during periods of sleep that correspond approximately to MA, hippocampal neurons in CA1 and CA2 become continuously active and encode the sleeping subject's current location. This code is qualitatively different from recapitulative firing patterns seen in REM and non-REM sleep and may have different functions. A spatial code for current location during sleep may make it possible to recover one's bearings quickly upon awakening, moreover even without external cues. Immediately accessible spatial knowledge in sleep may also be critical in imminently dangerous circumstances (e.g., predators, flooding) interrupting sleep. An active representation of current location during MA may also have a role in biasing the reactivation of waking activity related to an animal's sleeping context. This may be adaptive because a subject's sleeping location and related experiences are guaranteed to be of ethological significance.

4.7.10 | Synopsis of function by hippocampal state

The classic view of the function of hippocampal brain states concerns memory, with the locomotor state supporting memory encoding and the SWR state supporting memory consolidation (two-stage hypothesis). Recent work in waking subjects has extended this view via the characterization of two neural firing patterns in the hippocampus: theta sequences and replay sequences. These two patterns encode current circumstances (localizing) and also multiple possible options (generative), and thus have been suggested to support prospection, the hippocampus-dependent capacity to represent future scenarios.

Critically, replay sequences have been found to represent experience in an abstracted and extremely flexible manner—an observation that remains unexplained. This suggests the existence and contribution of neural activity representing features of experience that are similar across behavioral episodes (abstractive). Abstractive neural activity has been described in earlier work as "nodal" coding, and its possible role underscores the relevance of semantic memory and generalization to hippocampal function.

In principle, abstractive neural activity could evolve in the absence of changing sensory input, thus constituting a covertly changing variable (abstractive state). Neural activity in the still state may encode abstractive state, a possibility suggested on the basis of physiological and anatomical findings. Physiologically, still state firing appears continuous, dependent on memory, and non-stationary. Anatomically, still state firing implicates CA2, a hippocampal subregion that may contribute direct (synaptic) input to replay sequences and that exhibits extreme representational generalization in spatial paradigms.

Besides memory and prospection, the hippocampus has also been linked to navigation. The specific contribution of the hippocampus to navigation is in need of clarification and can be approached through different component processes. It is proposed that still state activity, and also subregion CA2, may help explain how these processes are implemented by the hippocampus.

Lastly, the three waking hippocampal brain states have roughly analogous states during sleep (locomotor, SWR, and still corresponding to REM, non-REM, and MA).

5 | THREE BRAIN STATES IN CORTEX

The following discussion is divided into sections ("Overview," "Parallel states," "Notes on function," and "Synopsis of cortical states.")

5.1 | Overview

Hippocampal brain states are a paradigm case of neural activity that is not characteristically stimulus-driven. Beyond this, we think it important to consider more specific implications given the relationship between the hippocampus and the rest of the brain. To motivate this discussion, we briefly sketch this relationship in three threads (function, anatomy, and physiology).

The first is function. To begin with, episodic memory and prospection are multimodal, coherent, and also associated with cognitive control, implicating coordination of hippocampal activity with that of various sensory and associative brain regions, and prefrontal cortex (Addis & Schacter, 2011; Eichenbaum, 2017c; Schacter et al., 2012; Teyler & DiScenna, 1986; Teyler & Rudy, 2007; Tulving & Markowitsch, 1998; Wheeler, Stuss, & Tulving, 1997). In addition, the role of the hippocampus in consolidating memories implies coordination of activity with extra-hippocampal regions (Buzsaki, 2015; Diekelmann & Born, 2010; Frankland & Bontempi, 2005; Schwindel & McNaughton, 2011; Squire & Alvarez, 1995; Wang & Morris, 2010), and complementary computational roles between hippocampus and neocortex have been postulated (Marr, 1971; McClelland, McNaughton, & O'Reilly, 1995). With respect to navigation, brain regions required for navigation and representing navigational variables coherent with hippocampal spatial representations are known to exist in certain cortical and subcortical regions (Grieves & Jeffery, 2017; Knierim, 2006; O'Keefe, 2007). Lastly, studies of motor substrates in the brain have long recognized the segregation of systems involved in movement versus holding still (Noorani & Carpenter, 2017; Shadmehr, 2017). In the present review, we do not explore this conspicuous parallel to brain states in hippocampus (and sensory neocortex below).

Another thread is anatomy (Amaral & Witter, 1989; David & Pierre, 2007; van Strien et al., 2009). Hippocampal neurons project directly to prefrontal cortex, other structures in the medial temporal lobe, and numerous subcortical structures, among them the striatum and amygdala. The hippocampus receives a dense projection from medial temporal lobe regions (in particular entorhinal cortex) and inputs from many subcortical regions, among them the MS and lateral septum, ventral tegmental area, locus coeruleus, and the median raphe. It also deserves mention that the hippocampus has been conceptualized as at the top of a cortical anatomical hierarchy (Felleman & Van Essen, 1991).

Lastly, physiological findings indicate mutual organization between neural activity in the hippocampus and that of the rest of the brain. For instance, hippocampal theta has been shown to entrain much of cortex (Grion, Akrami, Zuo, Stella, & Diamond, 2016; Sirota et al., 2008), and task-specific coordination of theta activity between hippocampus and cortex has been observed (Jones & Wilson, 2005; Benchenane et al., 2010; see also Kleinfeld, Deschenes, & Ulanovsky, 2016). In addition, hippocampal SWRs are now known to be coordinated with essentially the entire brain (Logothetis et al., 2012) (Kaplan et al., 2016; Ramirez-Villegas, Logothetis, & Besserve, 2015). Intriguingly, both low-frequency rhythms and SWRs have also recently been shown to relate to non-neural physiology with global influence (respiration; Liu, McAfee, & Heck, 2017; Lockmann & Tort, 2018; Tort, Brankack, & Draguhn, 2018). Studies at the level of neural firing have moreover identified interregional coordination of representations relevant to task behaviors (e.g., (Jadhav, Rothschild, Roumis, & Frank, 2016; Ji & Wilson, 2007; Pennartz, Ito, Verschure, Battaglia, & Robbins, 2011; Peyrache, Khamassi, Benchenane, Wiener, & Battaglia, 2009; Pezzulo, van der Meer, Lansink, & Pennartz, 2014; Rothschild, Eban, & Frank, 2017). Importantly, the influence between hippocampus and cortex is bidirectional: cortical activity patterns (e.g., slow oscillations and spindles) also entrain hippocampal activity (Buzsaki, 2015; Fujisawa & Buzsaki, 2011; Hahn, McFarland, Berberich, Sakmann, & Mehta, 2012; Hahn, Sakmann, & Mehta, 2006; Hahn,

TABLE 3 Summary of three cortical states

	Motor	Delta	Desync
Behavioral	movement	rest, immobility	rest, immobility
Anatomical	layer specific	?	?
Physiological	decorrelation	1-4 Hz activity high correlation	decorrelation desynchronization
Representational	change in gain, spatial integration	low sensory selectivity	max sensory selectivity

Proposed framework for waking brain states in cortex (see "Motor," "Delta," and "Desynchronous," and "Synopsis of cortical states").

Sakmann, & Mehta, 2007; Isomura et al., 2006; Sirota, Csicsvari, Buhl, & Buzsaki, 2003).

In all, this accumulated knowledge establishes that the influence between brain structures is immensely rich. What appears to be missing, as we (the authors) see it, is a broader view—namely an account of interregional neural activity encompassing all or most of waking experience instead of only particular activity patterns (e.g., theta, gamma, SWRs). This broader account could be necessary or useful to bridge finer-grained analysis of neural activity (i.e., single firing patterns or rhythms) to cognitive- and behavior-level functions, especially functions associated with multiple brain regions.

Here a series of recent breakthroughs in sensory neocortex in awake subjects suggests a way forward (Crochet & Petersen, 2006; Ferezou et al., 2007; Poulet & Petersen, 2008; Gentet, Avermann, Matyas, Staiger, & Petersen, 2010; Niell & Stryker, 2010; Gentet et al., 2012; Keller, Bonhoeffer, & Hubener, 2012; Poulet, Fernandez, Crochet, & Petersen, 2012; Ayaz, Saleem, Scholvinck, & Carandini, 2013; Bennett, Arroyo, & Hestrin, 2013; Luczak, Bartho, & Harris, 2013; Polack, Friedman, & Golshani, 2013; Saleem, Ayaz, Jeffery, Harris, & Carandini, 2013; Zagha, Casale, Sachdev, McGinley, & McCormick, 2013; Eggermann, Kremer, Crochet, & Petersen, 2014; Erisken et al., 2014; Froudarakis et al., 2014; Fu et al., 2014; Lee et al., 2014; Reimer et al., 2014; Schneider, Nelson, & Mooney, 2014; Tan, Chen, Scholl, Seidemann, & Priebe, 2014; Zhou et al., 2014; Zhuang et al., 2014; McGinley, David, & McCormick, 2015; Scholvinck, Saleem, Benucci, Harris, & Carandini, 2015; Vinck, Batista-Brito, Knoblich, & Cardin, 2015; Engel et al., 2016; Mineault, Tring, Trachtenberg, & Ringach, 2016; Pakan et al., 2016; Roth et al., 2016; Rummell, Klee, & Sigurdsson, 2016; Zhao, Kremkow, & Poulet, 2016; Dadarlat & Stryker, 2017; Munoz, Tremblay, Levenstein, & Rudy, 2017; see McGinley, Vinck, et al. (2015) for an overview). In the following discussion, our primary aim is to establish one overarching observation ("Parallel states"). Afterwards, we offer a few remarks on function ("Notes on function").

We think it important to stress in advance (as have others; e.g., Harris & Thiele, 2011; Zagha & McCormick, 2014; McGinley, Vinck, et al., 2015) that the classification of brain states is not meant as a rigid prescription but as a guide. For instance, the existence of major brain states does not rule out important transitional states (e.g., Erisken et al., 2014; Vinck et al., 2015) or substates defined by single activity patterns (e.g., Engel et al., 2001; Buzsáki, 2006; Cohen & Maunsell, 2009; Mitchell, Sundberg, & Reynolds, 2009; Buschman & Kastner, 2015; Fries, 2015; Lockmann & Tort, 2018; also consider Saalmann & Kastner, 2015; Roth et al., 2016; Sherman, 2016; Nakajima & Halassa, 2017). Also, it is clearly the case that specific activity patterns (e.g., gamma rhythms, low-frequency patterns) occur in multiple hippocampal and cortical brain states with varying amplitudes and incidences (Colgin, 2016; Csicsvari et al., 2003; Einstein, Polack, Tran, & Golshani, 2017; Engel et al., 2016; Fries, 2015; Hall, de Carvalho, & Jackson, 2014;

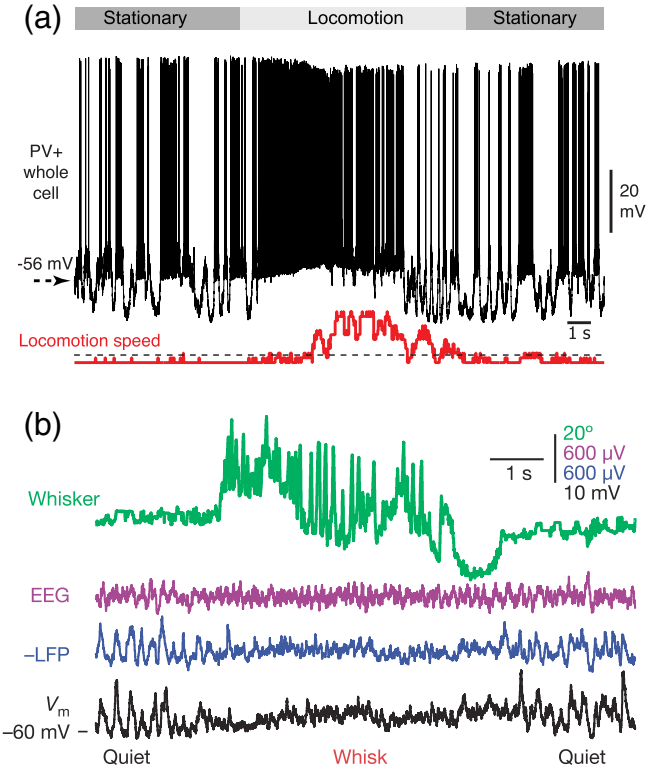


FIGURE 21 Movement changes cortical state
Two examples of neural activity across periods of movement (here, locomotion and whisking) and rest. (a) Locomotion example. Intracellular recording from an interneuron in mouse V1. Note the depolarization of the neuron and the elimination of low-frequency fluctuations during locomotion. (b) Whisking example. Recording from mouse S1. Whisker deflections (in degrees) were measured using a high-speed camera. EEG was recorded from the surface of cortex, while LFP (sign inverted) and intracellular (Vm) recordings were taken from layer 2/3. Note the synchronization of low frequency fluctuations during nonmovement periods (quiet) and reduction of low-frequency fluctuations across recordings during whisking. Part a reproduced with permission from Polack et al. (2013); part b reproduced with permission from Poulet and Petersen (2008) [Color figure can be viewed at wileyonlinelibrary.com]

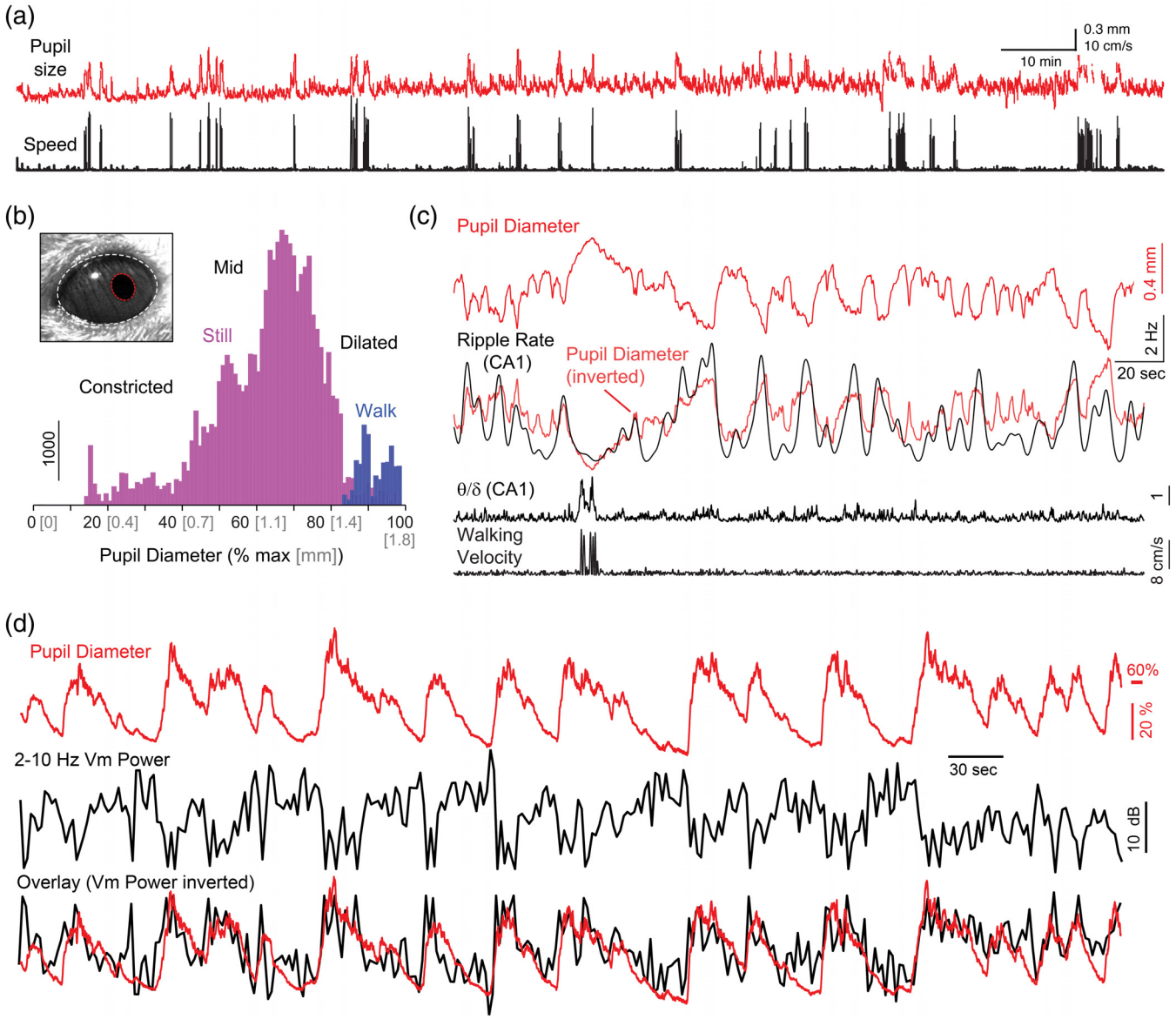


FIGURE 22 Pupil size indexes brain state

Data from head-fixed mice allowed to run spontaneously on a treadmill. (a) Pupil size and locomotor speed measured. Total recording time is ~2.4 hr. (b) Histogram of pupil sizes across behavioral states. (c) Pupil size (diameter) and SWR (ripple) rate (sign inverted for comparison). Note the inverse relationship between SWR rate and pupil size. (d) Pupil size (diameter) and low frequency neural activity. Neural activity is from an intracellular recording of a neuron in primary auditory cortex, filtered at low frequencies and inverted at bottom for comparison. Note the inverse relationship between low frequency activity and pupil size.

Part a adapted with permission from Reimer et al. (2014); parts b–d adapted with permission from McGinley, David, and McCormick (2015) [Color figure can be viewed at wileyonlinelibrary.com]

Niell & Stryker, 2010; Saleem et al., 2017; Schroeder & Lakatos, 2009; Tort et al., 2018; Vyazovskiy et al., 2011), and that this overlap also applies to neuromodulatory signals (e.g., Aston-Jones & Cohen, 2005; Cohen, Haesler, Vong, Lowell, & Uchida, 2012; Hasselmo & Sarter, 2011; Lee & Dan, 2012; Lee, Hoy, et al., 2014; Lisman & Grace, 2005; Pi et al., 2013; Takeuchi et al., 2016). These activity patterns, considered singly, may be more consistent with a view of intrinsic brain activity as being expressed along continua. All the same, we reiterate that identifying major brain states—on the basis of multiple-correlate configurations—may provide an appropriate framework for bridging brain structures (e.g., *hippocampus* and neocortex) and levels of analysis (e.g., single neurons and neural populations).

5.2 | Parallel states

A series of recent findings in the sensory neocortex of awake subjects indicates three basic cortical states (Table 3). Here we refer to these waking cortical states as "motor," "delta," and "desynchronous," and describe in the following sections how these states are defined and how they correspond approximately to the locomotor, SWR, and still states, respectively, in the hippocampus. For the sake of clarity, we discuss anatomical correlates separately afterwards.

5.2.1 | Motor

We first suggest a cortical state characterized by self-generated movement (Figure 21). Recent advances relevant to this state began

with groundbreaking work investigating sensory cortex during locomotion (Niell & Stryker, 2010) and active sensing behavior (Crochet & Petersen, 2006; Poulet & Petersen, 2008). From a wider point of view, it may help to note that these studies isolate the effect of self-generated movement on sensory-evoked neural activity by combining well-controlled experimental paradigms with awake subjects allowed to move spontaneously. In this way, these studies represent a synthesis of stimulus-driven (Hubel & Wiesel, 1962; Mountcastle, 1957) and ethological (Gervasoni et al., 2004; Vanderwolf, 1969) methodologies.

The essential correlate of the motor state is overt behavior: thus, identification of this brain state relies on detection of movement. As we review below, detection of movement distinguishes between unambiguously different patterns of cortical activity. It should be kept in mind that different types of movements likely influence brain state differently—for example, locomotion versus isolated movements such as saccades, sniffing, and whisking. (It is important to note that in early hippocampal studies, distinctions between more specific behaviors were proposed to be important [Vanderwolf, 1971; O'Keefe & Nadel, 1978; Vanderwolf, 1983; Vanderwolf, 2001; O'Keefe, 2007].) On the other hand, at least some forms of movement may indeed have correlates that are global—an important case of this is locomotion, which has recently been found to correlate with maximal pupillary dilation (Figure 22a,b; Erisken et al., 2014;McGinley, David, & McCormick, 2015 ; Reimer et al., 2014 ; Vinck et al., 2015).

At the neural level, the motor state is characterized by global decorrelation of activity relative to non-motor periods (examples in Poulet and Petersen (2008); Polack et al. (2013); Schneider et al. (2014)). While additional correlates have appeared to depend systematically on cortical region and layer (discussed further below), one principle that has emerged (e.g., Erisken et al., 2014; Mineault et al., 2016; Niell & Stryker, 2010; Sofroniew, Vlasov, Hires, Freeman, & Svoboda, 2015; Zhou et al., 2014) is that the magnitude of stimulus-evoked responses systematically changes during motor periods, while in some neurons selectivity does not (consider also Ayaz et al., 2013; Erisken et al., 2014, concerning spatial integration). Enhanced signal-to-noise ratios and other integrated measures of stimulus encoding have also been reported (Bennett et al., 2013; Dadarlat & Stryker, 2017; Erisken et al., 2014; McGinley, David, & McCormick, 2015; Polack et al., 2013; Poulet & Petersen, 2008; Reimer et al., 2014; Vinck et al., 2015; Zagha et al., 2013; Zhou et al., 2014). Importantly, the motor state and associated circuit mechanisms (e.g., Fu et al., 2014) have begun to be linked to functional consequences: for example, enhancement of performance on psychophysical tasks (Bennett et al., 2013) and enhancement of experience-dependent plasticity (Fu, Kaneko, Tang, Alvarez-Buylla, & Stryker, 2015; Kaneko, Fu, & Stryker, 2017; Kaneko & Stryker, 2014).

5.2.2 | Delta

In addition to the motor state, we suggest a cortical state characterized by neural activity in a frequency range often designated as the "delta" band (1–4 Hz or up to 10 Hz in some experimental settings). Delta-range activity in cortex has long been observed in sleeping and anesthetized subjects (McGinley, Vinck, et al., 2015; Steriade, Timofeev, & Grenier, 2001)—the more recent insight is that delta activity in awake subjects occurs commonly and globally (examples in Poulet and Petersen (2008); Gentet et al. (2010); Zagha et al. (2013); McGinley, David, and McCormick (2015); also see Vyazovskiy et al. (2011)) and has several crucial correlates.

One of these correlates is the hippocampal SWR, the marker of a specific brain state in the hippocampus (the SWR state, outlined above). This link is important as earlier work already indicated a broad correspondence between delta cortical activity and hippocampal SWRs. First, both have been known to be most prevalent in non-REM sleep, particularly SWS (Buzsaki et al., 1983; Buzsáki, 1986; Steriade, McCormick, & Sejnowski, 1993; Steriade, 2000; Buzsaki, 2015; example data in Gervasoni et al., 2004; Wierzynski, Lubenov, Gu, & Siapas, 2009; Kay et al., 2016; Watson et al., 2016). Second, in the awake subject, both have long been known to occur particularly in behavioral states associated with low arousal (Buzsaki, 2015; example data in Buzsaki, 1989; Poulet & Petersen, 2008; McGinley, David, & McCormick, 2015; Vinck et al., 2015; Jadhav et al., 2016).

Building on these basic observations, a recent study in awake subjects (McGinley, David, & McCormick, 2015) has explicitly established that cortical delta activity is strongest when SWR incidence is highest. Crucially, these high delta-high SWR periods correspond to times of minimum arousal and diminished sensory perceptual performance (minimum arousal was indicated by minimum pupil size). Remarkably, pupil size reliably tracks both delta activity and SWRs at the timescale of a few seconds, indicating rapid global regulation (Figure 22c,d; see also Reimer et al., 2014; Vinck et al., 2015, linking delta to pupil size). An additional study has confirmed the link between SWR activity and pupillary changes at a rapid timescale (Hulse et al., 2017). Thus, correlates of minimum arousal (delta activity, SWRs, and pupil size) fluctuate together from moment to moment, indicating relatively fast coordination of brain state between the hippocampus and cortex.

Despite this correspondence, the cortical delta state (as defined here) and the hippocampal SWR state are not formally equivalent: delta refers to ~1–4 Hz activity (whether in single cells or in LFP/EEG), while the SWR state is identified by SWRs detected in a high-frequency LFP band (bursts of power at 150–250 Hz in CA1; some recent studies detecting SWRs include Csicsvari et al., 1999; Davidson et al., 2009; McGinley, David, & McCormick, 2015; Pfeiffer & Foster, 2015; Kay et al., 2016; Yu et al., 2017; alternatively, the sharp wave component can be detected instead of high-frequency power (Buzsáki, 1986; Buzsaki et al., 1983; Oliva et al., 2016a; Suzuki & Smith, 1987). Further investigation in awake subjects is needed to clarify the relationship between these characteristic patterns.

Representational correlates of the cortical delta state have begun to be clarified. In sensory cortex, the delta state has been analyzed in paradigms assessing stimulus coding and perception (Engel et al., 2016; McGinley, David, & McCormick, 2015; Poulet & Petersen, 2008;Reimer et al., 2014 ; Vinck et al., 2015). In these paradigms, the amplitude of stimulus-evoked responses and also their selectivity are at a minimum (McGinley, David, & McCormick, 2015; Reimer et al., 2014). Furthermore, population measures of sensory coding are also at their lowest values (Reimer et al., 2014; Vinck et al., 2015). These results broadly accord with diminished perceptual performance (McGinley, David, & McCormick, 2015; also see Engel et al., 2016).

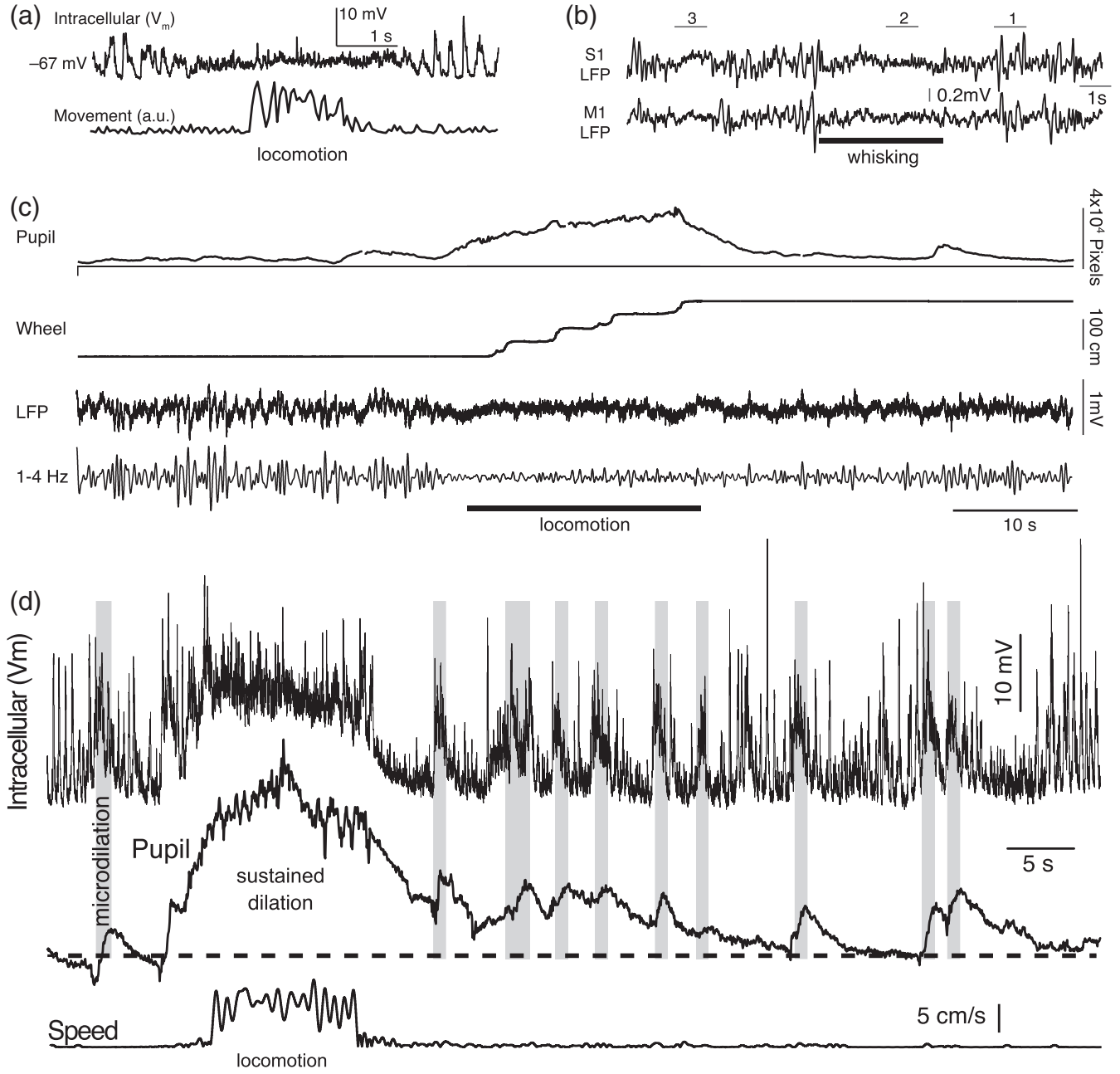


FIGURE 23 Examples of cortical state

(a) Auditory cortex. Example intracellular recording of an excitatory neuron in an unrestrained awake mouse. Note periods of low-frequency activity and also periods of desynchronization (flattened trace). (b) Somatosensory and motor cortex. Example extracellular recording in S1 and M1 in a head-fixed awake mouse. A detected period of movement (whisking) is indicated. A period of high-amplitude low frequency fluctuation is highlighted as (1). Also highlighted are periods of desynchronization, which occur both during movement (2) and absent movement (3). (c) Visual cortex. Example extracellular recording in V1 in a head-fixed awake mouse. LFP is filtered at the delta range (1–4 Hz) at bottom. A period of locomotion is indicated (yellow zone). Note the reduction of 1–4 Hz activity during movement. (d) Auditory cortex. Example intracellular recording of an L5 pyramidal neuron in a head-fixed awake mouse. The second trace (Pupil) is the reflectance of infrared light from the pupil, used as a proxy for pupil size. Brief periods of pupil dilation are indicated (microdilations; grey zones). Note that pupil size varies considerably in the absence of movement, and that the resulting variability correlates with intracellular neural activity.

Part a reproduced with permission from Schneider et al. (2014); part b reproduced with permission from Zagha et al. (2013); part c reproduced with permission from Vinck et al., 2015); part d reproduced with permission from McGinley, Vinck, et al. (2015)

Lastly, it is important to note that correlated neural activity is at maximal levels (in the presence or absence of stimuli and as indexed by different measures, including EEG/LFP and population firing correlations; e.g., Poulet & Petersen, 2008; Reimer et al., 2014; Vinck et al., 2015) during the cortical delta state.

5.2.3 | Desynchronous

A pivotal series of studies has established a distinction between arousal and movement in relation to brain state (McGinley, David, & McCormick, 2015; Reimer et al., 2014; Vinck et al., 2015). The basic observation is that periods of intermediate arousal (indexed by

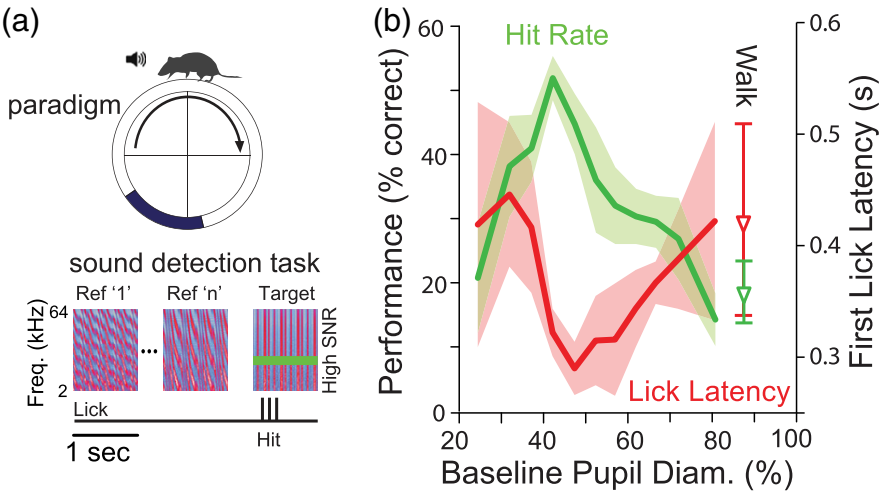


FIGURE 24 Optimal perceptual performance in the desynchronous state
(a) Behavioral paradigm of an auditory detection task. Mice spontaneously walked or remained at rest during the task. Subjects were presented with 1 s periods of complex sounds within which a pure tone was occasionally played. If the subject licked during the presentation of the tone, a hit was recorded and the animal received a liquid reward. (b) Performance on a sound detection task (requiring a lick response) varies with pupil size. Hit rate (green) was maximal at intermediate pupil size (desynchronous state), while lick latency (red) was shortest. Reponses obtained during locomotion are plotted separately from those obtained during rest. Performance during locomotion (walk) was similar to that of high arousal (large pupil diameter) non-locomotor periods, with lower performance and higher lick latency.
Reproduced with permission from McGinley, Vinck, et al. (2015) [Color figure can be viewed at wileyonlinelibrary.com]

pupillary dilation) occur routinely in the absence of motor activity, furthermore when delta activity is minimal (Figure 23). As with delta activity, the incidence of SWRs is also minimal during these times (Hulse et al., 2017; McGinley, David, & McCormick, 2015). These non-motor periods of elevated arousal occur spontaneously or, notably, can be induced simply by delivering a stimulus to the subject (e.g., an air puff [Vinck et al., 2015] or a visual stimulus [Tan et al., 2014]).

These findings indicate a cortical state associated neither with movement nor with delta activity. One readily observable correlate of this state is maximal desynchronization of neural activity, indicated by flattening of LFP/EEG and minimum variability of intracellular V_m (examples in McGinley, David, & McCormick, 2015; Vinck et al., 2015). Correlated neural firing is also at a minimum (Reimer et al., 2014; McGinley, David, & McCormick, 2015; Vinck et al., 2015). Accordingly, we here refer to this state as the "desynchronous" state. The term "asynchronous" has also been used, particularly in modeling contexts (e.g., Brunel, 2000; Harris & Thiele, 2011; Ostojic, 2014; Renart et al., 2010; Tan et al., 2014).

In sensory paradigms, analysis of stimulus-evoked neural responses suggests that the brain is maximally receptive to sensory input in this state. Across modalities, stimulus selectivity in single neurons is enhanced or maximal, as are additional measures of the fidelity, reliability, and efficacy of sensory coding (McGinley, David, & McCormick, 2015; Reimer et al., 2014; Vinck et al., 2015; Zhuang et al., 2014). Notably, this state has been found to correspond to optimal behavioral performance on sensory perceptual tasks (Figure 24; McGinley, David, & McCormick, 2015). Here it is important to note that performance does not correlate monotonically with arousal, because extreme arousal (indexed by pupil size) actually corresponds to lower task performance. This manifests as an inverted-U relationship between arousal and performance, in agreement with prior psychophysical research (Diamond, Campbell, Park, Halonen, & Zoladz, 2007; McGinley, David, & McCormick, 2015; McGinley, Vinck, et al., 2015). This finding highlights that this brain state is associated with a level of arousal intermediate between that of the delta (low) and motor (generally high) states. The observation of optimal perceptual performance in this state, in conjunction with the observation of maximally informative sensory coding, indicates that one functional characteristic of this brain state is optimal receptivity to external stimuli.

When does this brain state occur? It is possible to use criteria based on either neural activity (e.g., desynchronization) or pupillometry (intermediate pupil size). Our suggestion here is based on a particular view, namely that the desynchronous state is approximately correspondent with the hippocampal still state, for which we adopted exclusionary criteria (i.e., non-locomotor, non-SWR periods) based on findings in the hippocampus (Kay et al., 2016). For cortex, we suggest analogous exclusionary criteria because this minimizes unclassified time periods, thus promoting an inclusive approach to neural data. As discussed earlier, opting for inclusivity is in line with the outlook that functional neural activity occurs throughout experience. We therefore suggest that desynchronous state periods be defined as non-motor, non-delta periods.

5.2.4 | Anatomical correlates of cortical states

Various studies have focused on neuromodulatory and microcircuit mechanisms of cortical state (reviewed in Harris and Thiele (2011) and Lee and Dan (2012); recent studies include Gentet et al. (2010); Gentet et al. (2012); Poulet et al. (2012); Polack et al. (2013); Zagha et al. (2013); Fu et al. (2014); Reimer et al. (2014); Schneider et al. (2014); Pakan et al. (2016); Munoz et al. (2017)).

It is less clear whether and which anatomically defined subsets of principal neurons in cortex are differentially recruited by different cortical states. This matter may be fundamental because such recruitment implies dynamic routing of cortical inputs and outputs (Douglas & Martin, 2004; Mountcastle, 1998) as fast as changes in

brain state, that is, within ~1 s. Notably, systematic differences between sensory modalities somewhat complicate this issue (see discussion in Vinck et al. (2015); Krupa, Wiest, Shuler, Laubach, and Nicolelis (2004); de Kock and Sakmann (2009); Sakata and Harris (2009); Sakata and Harris (2012); Andermann et al. (2013); Zagha et al. (2013); Erisken et al. (2014); Zhou et al. (2014); Makino and Komiyama (2015); McGinley, David, and McCormick (2015); Williamson, Hancock, Shinn-Cunningham, and Polley (2015); Zhao et al. (2016); Dadarlat and Stryker (2017); Munoz et al. (2017); van Kerkoerle, Self, and Roelfsema (2017)).

Nonetheless, early findings indicate that subpopulations of principal neurons in cortex are differentially engaged by cortical state (Andermann et al., 2013; Saleem et al., 2013; Vinck et al., 2015). In one study that imaged neural activity across cortical layers in V1 (Andermann et al., 2013), subpopulations of layer six neurons were found to have suppressed activity at the onset of locomotion. Another study of V1 (Vinck et al., 2015) also hints at the possibility of principal neuron subpopulations that fire differently between the delta and desynchronous states. State-dependent neurons have also been found in thalamic nuclei projecting to these cortical regions (Erisken et al., 2014; Roth et al., 2016; also see Williamson et al., 2015). These various findings are reminiscent of the anatomic localization of state-yoked neurons in the hippocampus (Figure 8) and the anatomic segregation of moving versus still circuits in motor systems (Shadmehr, 2017). These commonalities suggest a widespread principle that encompasses cortex and possibly other domains in the brain.

5.3 | Notes on function

Why are there different cortical brain states? To formulate a satisfactory answer, it would be best to assess specific functions linked to cortex. This is beyond our present purview—rather, our goal is to facilitate this kind of assessment by suggesting a basic framework (Overview 1; Table 2) and making a few introductory observations.

To start, we contend that distinguishing between states is probably relevant to any cognitive function associated with cortex. To reiterate, this view is based on the premise that (a) neural firing is the basis of cognitive function and (b) major brain states correspond to comprehensive reconfigurations of neural firing that are not characteristically stimulus-driven. From this, we sought in the above discussion to classify major brain states, doing so by considering four essential dimensions of neural firing (anatomy, physiology, behavior, representation).

Below we offer a few more specific remarks (divided into delta, motor, desynchronous) with the caveat that our (the authors') viewpoint is from the hippocampus. Our aim is to spur broader thinking in future studies of cortex, and, beyond this, to suggest that cortical brain states have functional implications that run deeper than variability ("noise") in stimulus-evoked responses. Our basic view is that cortex and hippocampus must operate jointly throughout waking experience—therefore, the state-specific properties discussed above for hippocampal neural activity (e.g., localizing, generative, and abstractive properties at the representational level) must somehow be appropriately matched or complemented by properties of state-specific neural activity in cortex, whatever these properties may in fact be. We grant that the phenomena and properties we outlined for hippocampal neural activity may seem foreign, particularly in sensory experimental paradigms. Insight into the relationship between neural activity in cortex and hippocampus will likely become clearer as distinctions between stimulus-driven and internally generated activity patterns come into focus.

5.3.1 | Delta

Essentially, all findings concerning the delta state are consistent with the view that subjects are less attentive or aware of ongoing external stimuli during this state (Fries, Reynolds, Rorie, & Desimone, 2001; Gregoriou, Gotts, Zhou, & Desimone, 2009; McGinley, David, & McCormick, 2015; Mitchell et al., 2009). However, this should not be taken to mean that the subject is necessarily any less engaged in solving a task (e.g., "intentional mind-wandering"; Smallwood & Schooler, 2015; Seli, Risko, Smilek, & Schacter, 2016).

This possibility is illustrated by what is known of the corresponding hippocampal brain state, that is, the SWR state. As described earlier, neural firing in the hippocampus during SWRs routinely represents remote past experience (Davidson, Kloosterman, & Wilson, 2009; Gupta et al., 2010; Karlsson & Frank, 2009) and can furthermore represent entire episodes of upcoming experience not immediately acted upon (e.g., Diba & Buzsaki, 2007; Pfeiffer & Foster, 2013; Wu et al., 2017). These neural representations do not encode ongoing sensory stimuli yet may be useful or even necessary for solving a task. Indeed, even for sensory perceptual tasks, it may be useful to access types of memory that are not strictly required (Shadlen & Shohamy, 2016).

In addition, the direct influence of hippocampal SWRs (and their associated non-sensory representations) on cortical activity suggests that non-sensory representations are expressed in cortex during the delta state (Xu, Jiang, Poo, & Dan, 2012). Thus, even though cortical encoding of ongoing sensory stimuli is diminished during the delta state, the actual fidelity and the functional contribution of cortical neural representations may not be.

5.3.2 | Motor

Research in sensory cortex has traditionally eliminated or isolated self-generated movement. Other work has addressed the direct contribution of internally routed motor signals (Allen et al., 2017; Busse et al., 2017; Eliades & Wang, 2008; Fanselow & Nicolelis, 1999; Fee, Mitra, & Kleinfeld, 1997; Lee, Hoy, et al., 2014; Lee, Kruglikov, Huang, Fishell, & Rudy, 2013; Nelson et al., 2013; Petreanu et al., 2012; Schneider et al., 2014), particularly with respect to perceptual stability (Hall & Colby, 2011; Kleinfeld, Ahissar, & Diamond, 2006; Kleinfeld, Berg, & O'Connor, 1999; Sommer & Wurtz, 2002; Wurtz, Joiner, & Berman, 2011). This focus has led to valuable insights but may also be limited in the premise that, during movement, cortex functions to construct a single factual representation. Indeed some authors have argued that prospective representations occur during movement out of ecological necessity and moreover engage much of the brain (Cisek, 2012; Cisek & Kalaska, 2010; Cisek & Pastor-Bernier, 2014).

Hippocampal activity across states may provide some insight here. During the locomotor state, populations of hippocampal neurons continuously generate a form of prospective activity termed theta sequences (discussed in detail above). Theta sequences are population

firing patterns (each ~100 ms) that represent sequences of locations that begin near the subject's current location and sweep to a location ahead of the animal (Johnson & Redish, 2007; Redish, 2016). Notably, analysis of neural firing underlying theta sequences suggests that there is a limited representational range (here, the spatial extent of represented locations) of this prospective activity (Buzsaki & Moser, 2013), in contrast to the extreme representational range of spatial sequences that occur in the SWR state (replay sequences), which can be chained together to represent long sequences of locations remote from the subject (at least several meters; Davidson, Kloosterman, & Wilson, 2009). If cortex follows a similar principle between its analogous states (motor and delta), then we might expect that the representational range of nonlocalizing activity in cortex tends also to be limited in the motor state relative to the delta state.

5.3.3 | Desynchronous

As outlined above, one remarkable aspect of the desynchronous state is that measures of sensory coding and sensory perceptual performance are maximal in this state. This suggests that neural activity in this state is characteristically localizing (encoding current circumstances) at the representational level. In a stimulus-driven paradigm of the brain, this in turn would suggest that feedforward sensory processing is quintessential to this state. However, the parallel (or direct relationship) between the desynchronous state in cortex and the still state in the hippocampus offers a possible twist: that it may also be the case that the desynchronous state in cortex supports abstractive neural activity (see "Abstractive state" and "Three properties of prospection") essential for prospection. Furthermore, by analogy to the hippocampus, cortical neural activity in the desynchronous state may have a specialized role in selecting stored experience for reactivation (namely in the delta state). Following the same deduction from the hippocampus, this process of selection would ideally generalize (abstract) across relevant prior experience and thus would neither simply or necessarily represent ongoing sensory stimuli. Thus in the desynchronous state there may be considerable neural activity in cortex that is better characterized as internally derived rather than stimulus-driven. Notably, desynchronous states in artificial cortical networks have been shown to be suitable for internally driven operations on external input (Goudar & Buonomano, 2014; Ostojic, 2014).

5.4 | Synopsis of cortical states

The synthesis of stimulus-driven and ethological methodologies has established three waking brain states in cortex. The first of these is defined by spontaneous movement (motor). For periods of time absent movement, recent studies distinguish between a state characterized by low-frequency activity and minimal arousal (delta) versus a state characterized by relative desynchronization of activity (desynchronous). In sensory neocortex, each of these states has representational correlates.

These three states in cortex approximately correspond to the three states in the hippocampus outlined earlier.

6 | SUMMARY

1. To understand cognition in the brain, we may need to understand routinely occurring yet comprehensively different configurations of neural activity (brain states).
2. Brain states can be defined concisely by anatomical, physiological, representational, and behavioral correlates.
3. Classic and recent findings indicate three brain states in the hippocampus: "locomotor," "SWR," "still."
4. The CA1, CA2, and CA3 subregions are differentially active within and across these three states.
5. Neural representations in the hippocampus (e.g., of location) are organized by brain state.
6. This organization by state implicates temporal organization of hippocampal neural representations at the scale of ~1 s or longer and also dependence on anatomy and behavior.
7. Functionally, the hippocampus is known to contribute to memory, navigation, and prospection (the capacity to represent possible future scenarios).
8. Different hippocampal brain states have been linked to different memory functions, such as encoding and consolidation.
9. Recent work focusing on awake subjects suggests that hippocampal neural activity supports prospection.
10. Prospective neural activity has three representation-level properties—termed "localizing," "generative," "abstractive"—corresponding to veridical, counterfactual, and inferential representation, respectively.
11. CA2 and neural activity in the still state may have a role in abstracting across episodes of experience and thus may specialize in semantic (vs. episodic) elements of memory.
12. CA2 and neural activity in the still state may have roles in navigation—specifically in self-localization, initializing path integration, switching between spatial maps, and navigational planning—via influence on locomotor and SWR state activity.
13. Still state activity in the hippocampus has three features: continuousness, memory coding, and non-stationarity.
14. Still state activity in the hippocampus may enable remembering across delays.
15. Still state activity in the hippocampus may continuously integrate abstract inputs.
16. In sensory neocortex, recent work focusing on awake subjects indicates three parallel states in cortex: "motor," "delta," "desynchronous."
17. Neural activity in each of these cortical states is expected to be representationally and functionally coherent with neural activity in the parallel hippocampal state.
18. The three-state framework may extend beyond the hippocampus and cortex.

7 | QUESTIONS

1. Does state-specific neural activity support specific cognitive functions?

2. Do different aspects of a given cognitive function correspond to different states?
3. Why do properties of neural representation in the hippocampus and cortex depend on state?
4. Is there activity specific to transitions between states?
5. Does the temporal organization of hippocampal representations by state relate to the structure and implementation of episodic memory?
6. How do different dimensions of prospective representation (localizing, generative, abstractive) change with state?
7. Does CA2 have a specialized role in abstractive representation or in inferential behavioral tasks?
8. Does still state firing encode abstractive state?
9. Does a continuously evolving abstractive state help explain replay sequences?
10. What correlates of brain states are species-specific?
11. In awake subjects, what are the exact relationships between hippocampal and cortical brain states?
12. Are neural representations in the hippocampus and in cortex coherent across states?
13. Are there correspondent brain states in other domains of the brain?

ACKNOWLEDGMENTS

We thank György Buzsáki, Beata Jarosiewicz, Lucas Tian, Marielena Sosa, Morgane Roth, Paul Jaffe, Jermyn See, Ryan Morrill, Maria Dadarlat, and the anonymous reviewers for their constructive feedback on the manuscript.

REFERENCES

Addis, D. R., & Schacter, D. L. (2011). The hippocampus and imagining the future: Where do we stand? *Frontiers in Human Neuroscience*, *5*, 173.

Adrian, E. D., & Zotterman, Y. (1926a). The impulses produced by sensory nerve endings: Part 3. Impulses set up by touch and pressure. *The Journal of Physiology*, *61*(4), 465–483.

Adrian, E. D., & Zotterman, Y. (1926b). The impulses produced by sensory nerve-endings: Part II. The response of a single end-organ. *The Journal of Physiology*, *61*(2), 151–171.

Aggleton, J. P., & Brown, M. W. (1999). Episodic memory, amnesia, and the hippocampal-anterior thalamic axis. *The Behavioral and Brain Sciences*, *22*(3), 425–444 discussion 444–89.

Aghajan, Z., Schuette, P., Fields, T. A., Tran, M. E., Siddiqui, S. M., Hasulak, N. R., … others. (2017). Theta oscillations in the human medial temporal lobe during real-world ambulatory movement. *Current Biology*, *27*(24), 3743–3751.e3.

Ahissar, E., & Kleinfeld, D. (2003). Closed-loop neuronal computations: Focus on vibrissa somatosensation in rat. *Cerebral Cortex*, *13*(1), 53–62.

Ahmed, O. J., & Mehta, M. R. (2012). Running speed alters the frequency of hippocampal gamma oscillations. *The Journal of Neuroscience*, *32*(21), 7373–7383.

Ainge, J. A., Dudchenko, P. A., & Wood, E. R. (2008). Context-dependent firing of hippocampal place cells: Does it underlie memory. In *Hippocampal place fields: Relevance to learning and memory* (pp. 44–58). Oxford: Oxford University Press.

Ainge, J. A., van der Meer, M. A., Langston, R. F., & Wood, E. R. (2007). Exploring the role of context-dependent hippocampal activity in spatial alternation behavior. *Hippocampus*, *17*(10), 988–1002.

Alexander, A. S., & Nitz, D. A. (2015). Retrosplenial cortex maps the conjunction of internal and external spaces. *Nature Neuroscience*, *18*(8), 1143–1151.

Alexander, A. S., & Nitz, D. A. (2017). Spatially periodic activation patterns of retrosplenial cortex encode route sub-spaces and distance traveled. *Current Biology*, *27*(11), 1551–1560.e4.

Alexander, G. M., Farris, S., Pirone, J. R., Zheng, C., Colgin, L. L., & Dudek, S. M. (2016). Social and novel contexts modify hippocampal CA2 representations of space. *Nature Communications*, *7*, 10300.

Allen, W. E., Kauvar, I. V., Chen, M. Z., Richman, E. B., Yang, S. J., Chan, K., … Deisseroth, K. (2017). Global representations of goal-directed behavior in distinct cell types of mouse neocortex. *Neuron*, *94*(4), 891–907.e6.

Alme, C. B., Miao, C., Jezek, K., Treves, A., Moser, E. I., & Moser, M. B. (2014). Place cells in the hippocampus: Eleven maps for eleven rooms. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(52), 18428–18435.

Alvernhe, A., Van, C. T., Save, E., & Poucet, B. (2008). Different CA1 and CA3 representations of novel routes in a shortcut situation. *Journal of Neuroscience*, *28*(29), 7324–7333.

Amaral, D. G., & Witter, M. P. (1989). The three-dimensional organization of the hippocampal formation: A review of anatomical data. *Neuroscience*, *31*(3), 571–591.

Ambrose, R. E., Pfeiffer, B. E., & Foster, D. J. (2016). Reverse replay of hippocampal place cells is uniquely modulated by changing reward. *Neuron*, *91*(5), 1124–1136.

Andermann, M. L., Gilfoy, N. B., Goldey, G. J., Sachdev, R. N., Wolfel, M., McCormick, D. A., … Levene, M. J. (2013). Chronic cellular imaging of entire cortical columns in awake mice using microprisms. *Neuron*, *80*(4), 900–913.

Andersen, P. (2007). *The hippocampus book*. Oxford: Oxford University Press.

Aronov, D., Nevers, R., & Tank, D. W. (2017). Mapping of a non-spatial dimension by the hippocampal-entorhinal circuit. *Nature*, *543*(7647), 719–722.

Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function: Adaptive gain and optimal performance. *Annual Review of Neuroscience*, *28*, 403–450.

Atherton, L. A., Dupret, D., & Mellor, J. R. (2015). Memory trace replay: The shaping of memory consolidation by neuromodulation. *Trends in Neurosciences*, *38*(9), 560–570.

Atick, J. J. (1992). Could information theory provide an ecological theory of sensory processing? *Network: Computation in Neural Systems*, *3*(2), 213–251.

Attardo, A., Fitzgerald, J. E., & Schnitzer, M. J. (2015). Impermanence of dendritic spines in live adult CA1 hippocampus. *Nature*, *523*(7562), 592–596.

Attneave, F. (1954). Some informational aspects of visual perception. *Psychological Review*, *61*(3), 183–193.

Ayaz, A., Saleem, A. B., Scholvinck, M. L., & Carandini, M. (2013). Locomotion controls spatial integration in mouse visual cortex. *Current Biology*, *23*(10), 890–894.

Bannerman, D. M., Rawlins, J. N., McHugh, S. B., Deacon, R. M., Yee, B. K., Bast, T., … Feldon, J. (2004). Regional dissociations within the hippocampus—Memory and anxiety. *Neuroscience and Biobehavioral Reviews*, *28*(3), 273–283.

Barlow, H. B. (1953). Summation and inhibition in the frog's retina. *The Journal of Physiology*, *119*(1), 69–88.

Barlow, H. B. (1961). Possible principles underlying the transformations of sensory messages. In W. Rosenblith (Ed.), *Sensory communication* (pp. 217–234). Cambridge, MA: MIT Press.

Barlow, H. B. (1972). Single units and sensation: A neuron doctrine for perceptual psychology? *Perception*, *1*(4), 371–394.

Bartesaghi, R., & Gessi, T. (2004). Parallel activation of field CA2 and dentate gyrus by synaptically elicited perforant path volleys. *Hippocampus*, *14*(8), 948–963.

Bartlett, F. C. (1932). *Remembering*. London: Cambridge University Press.

Battaglia, F. P., Sutherland, G. R., & McNaughton, B. L. (2004). Local sensory cues and place cell directionality: Additional evidence of prospective coding in the hippocampus. *The Journal of Neuroscience*, *24*(19), 4541–4550.

Benchenane, K., Peyrache, A., Khamassi, M., Tierney, P. L., Gioanni, Y., Battaglia, F. P., & Wiener, S. I. (2010). Coherent Theta oscillations and reorganization of spike timing in the hippocampal-prefrontal network upon learning. *Neuron*, *66*(6), 921–936.

Bennett, C., Arroyo, S., & Hestrin, S. (2013). Subthreshold mechanisms underlying state-dependent modulation of visual responses. *Neuron*, *80*(2), 350–357.

Bergmann, B. M., Winter, J. B., Rosenberg, R. S., & Rechtschaffen, A. (1987). NREM sleep with low-voltage EEG in the rat. *Sleep*, *10* (1), 1–11.

Berry, S. D., & Thompson, R. F. (1978). Prediction of learning rate from the hippocampal electroencephalogram. *Science*, *200*(4347), 1298–1300.

Best, P. J., & Ranck, J. B., Jr. (1982). Reliability of the relationship between hippocampal unit activity and sensory-behavioral events in the rat. *Experimental Neurology*, *75*(3), 652–664.

Bieri, K. W., Bobbitt, K. N., & Colgin, L. L. (2014). Slow and fast gamma rhythms coordinate different spatial coding modes in hippocampal place cells. *Neuron*, *82*(3), 670–681.

Boehringer, R., Polygalov, D., Huang, A. J. Y., Middleton, S. J., Robert, V., Wintzer, M. E., … McHugh, T. J. (2017). Chronic loss of CA2 transmission leads to hippocampal Hyperexcitability. *Neuron*, *94*(3), 642–655.e9.

Bohbot, V. D., Copara, M. S., Gotman, J., & Ekstrom, A. D. (2017). Low-frequency theta oscillations in the human hippocampus during real-world and virtual navigation. *Nature Communications*, *8*, 14415.

Boring, E. G. (1942). Sensation and perception. Scientific books: Sensation and perception in the history of experimental psychology. *Science*, *96*, 64–65.

Boyce, R., Glasgow, S. D., Williams, S., & Adamantidis, A. (2016). Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation. *Science*, *352*(6287), 812–816.

Brandon, M. P., Koenig, J., Leutgeb, J. K., & Leutgeb, S. (2014). New and distinct hippocampal place codes are generated in a new environment during septal inactivation. *Neuron*, *82*(4), 789–796.

Brody, C. D., Romo, R., & Kepecs, A. (2003). Basic mechanisms for graded persistent activity: Discrete attractors, continuous attractors, and dynamic representations. *Current Opinion in Neurobiology*, *13*(2), 204–211.

Brown, E. N., Frank, L. M., Tang, D., Quirk, M. C., & Wilson, M. A. (1998). A statistical paradigm for neural spike train decoding applied to position prediction from ensemble firing patterns of rat hippocampal place cells. *The Journal of Neuroscience*, *18*(18), 7411–7425.

Brunel, N. (2000). Dynamics of sparsely connected networks of excitatory and inhibitory spiking neurons. *Journal of Computational Neuroscience*, *8*(3), 183–208.

Buckner, R. L. (2012). The serendipitous discovery of the brain's default network. *NeuroImage*, *62*(2), 1137–1145.

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: Anatomy, function, and relevance to disease. *Annals of the New York Academy of Sciences*, *1124*, 1–38.

Buckner, R. L., & Carroll, D. C. (2007). Self-projection and the brain. *Trends in Cognitive Sciences*, *11*(2), 49–57.

Bunsey, M., & Eichenbaum, H. (1996). Conservation of hippocampal memory function in rats and humans. *Nature*, *379*(6562), 255–257.

Buschman, T. J., & Kastner, S. (2015). From behavior to neural dynamics: An integrated theory of attention. *Neuron*, *88*(1), 127–144.

Bush, D., Bisby, J. A., Bird, C. M., Gollwitzer, S., Rodionov, R., Diehl, B., … Burgess, N. (2017). Human hippocampal theta power indicates movement onset and distance travelled. *Proceedings of the National Academy of Sciences of the United States of America*, *114*(46), 12297–12302.

Busse, L., Cardin, J. A., Chiappe, M. E., Halassa, M. M., McGinley, M. J., Yamashita, T., & Saleem, A. B. (2017). Sensation during active behaviors. *The Journal of Neuroscience*, *37*(45), 10826–10834.

Buzsaki, G. (1986). Hippocampal sharp waves—Their origin and significance. *Brain Research*, *398*(2), 242–252.

Buzsáki, G. (1986). Hippocampal sharp waves: Their origin and significance. *Brain Research*, *398*(2), 242–252.

Buzsaki, G. (1989). Two-stage model of memory trace formation: A role for "noisy" brain states. *Neuroscience*, *31*(3), 551–570.

Buzsaki, G. (2002). Theta oscillations in the hippocampus. *Neuron*, *33*(3), 325–340.

Buzsaki, G. (2005). Theta rhythm of navigation: Link between path integration and landmark navigation, episodic and semantic memory. *Hippocampus*, *15*(7), 827–840.

Buzsáki, G. (2006). *Rhythms of the brain* (Vol. xiv, p. 448). Oxford; New York: Oxford University Press.

Buzsaki, G. (2010). Neural syntax: Cell assemblies, synapsembles, and readers. *Neuron*, *68*(3), 362–385.

Buzsaki, G. (2013). Cognitive neuroscience: Time, space and memory. *Nature*, *497*(7451), 568–569.

Buzsaki, G. (2015). Hippocampal sharp wave-ripple: A cognitive biomarker for episodic memory and planning. *Hippocampus*, *25*(10), 1073–1188.

Buzsaki, G., & Bland, B. H. (2015). Obituary: Cornelius H. Vanderwolf. *Hippocampus*, *25*(11), 1191–1192.

Buzsaki, G., Horvath, Z., Urioste, R., Hetke, J., & Wise, K. (1992). High-frequency network oscillation in the hippocampus. *Science*, *256*(5059), 1025–1027.

Buzsaki, G., Leung, L. W., & Vanderwolf, C. H. (1983). Cellular bases of hippocampal EEG in the behaving rat. *Brain Research*, *287*(2), 139–171.

Buzsaki, G., & Moser, E. I. (2013). Memory, navigation and theta rhythm in the hippocampal-entorhinal system. *Nature Neuroscience*, *16*(2), 130–138.

Buzsaki, G., Peyrache, A., & Kubie, J. (2014). Emergence of cognition from action. *Cold Spring Harbor Symposia on Quantitative Biology*, *79*, 41–50.

Cabral, H. O., Vinck, M., Fouquet, C., Pennartz, C. M., Rondi-Reig, L., & Battaglia, F. P. (2014). Oscillatory dynamics and place field maps reflect hippocampal ensemble processing of sequence and place memory under NMDA receptor control. *Neuron*, *81*(2), 402–415.

Cai, D. J., Aharoni, D., Shuman, T., Shobe, J., Biane, J., Song, W., … others. (2016). A shared neural ensemble links distinct contextual memories encoded close in time. *Nature*, *534*(7605), 115–118.

Carr, M. F., & Frank, L. M. (2012). A single microcircuit with multiple functions: State dependent information processing in the hippocampus. *Current Opinion in Neurobiology*, *22*(4), 704–708.

Carr, M. F., Jadhav, S. P., & Frank, L. M. (2011). Hippocampal replay in the awake state: A potential substrate for memory consolidation and retrieval. *Nature Neuroscience*, *14*(2), 147–153.

Carr, M. F., Karlsson, M. P., & Frank, L. M. (2012). Transient slow gamma synchrony underlies hippocampal memory replay. *Neuron*, *75*(4), 700–713.

Caruana, D. A., Alexander, G. M., & Dudek, S. M. (2012). New insights into the regulation of synaptic plasticity from an unexpected place: Hippocampal area CA2. *Learning & Memory*, *19*(9), 391–400.

Cei, A., Girardeau, G., Drieu, C., Kanbi, K. E., & Zugaro, M. (2014). Reversed theta sequences of hippocampal cell assemblies during backward travel. *Nature Neuroscience*, *17*(5), 719–724.

Cembrowski, M. S., Bachman, J. L., Wang, L., Sugino, K., Shields, B. C., & Spruston, N. (2016). Spatial gene-expression gradients underlie prominent heterogeneity of CA1 pyramidal neurons. *Neuron*, *89*(2), 351–368.

Chang, L., & Tsao, D. Y. (2017). The code for facial identity in the primate brain. *Cell*, *169*(6), 1013–1028.e14.

Chen, G., King, J. A., Burgess, N., & O'Keefe, J. (2013). How vision and movement combine in the hippocampal place code. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(1), 378–383.

Cheng, S., & Frank, L. M. (2008). New experiences enhance coordinated neural activity in the hippocampus. *Neuron*, *57*(2), 303–313.

Chevaleyre, V., & Piskorowski, R. A. (2016). Hippocampal area CA2: An overlooked but promising therapeutic target. *Trends in Molecular Medicine*, *22*(8), 645–655.

Chevaleyre, V., & Siegelbaum, S. A. (2010). Strong CA2 pyramidal neuron synapses define a powerful disynaptic cortico-hippocampal loop. *Neuron*, *66*(4), 560–572.

Christian, K. M., & Thompson, R. F. (2003). Neural substrates of eyeblink conditioning: Acquisition and retention. *Learning & Memory*, *10*(6), 427–455.

Ciocchi, S., Passecker, J., Malagon-Vina, H., Mikus, N., & Klausberger, T. (2015). Brain computation. Selective information routing by ventral hippocampal CA1 projection neurons. *Science*, *348*(6234), 560–563.

Cisek, P. (2012). Making decisions through a distributed consensus. *Current Opinion in Neurobiology*, *22*(6), 927–936.

Cisek, P., & Kalaska, J. F. (2010). Neural mechanisms for interacting with a world full of action choices. *Annual Review of Neuroscience*, *33*, 269–298.

Cisek, P., & Pastor-Bernier, A. (2014). On the challenges and mechanisms of embodied decisions. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *369*(1655).

Clark, A. (2013). Whatever next? Predictive brains, situated agents, and the future of cognitive science. *The Behavioral and Brain Sciences*, *36*(3), 181–204.

Clark, R. E., & Squire, L. R. (1998). Classical conditioning and brain systems: The role of awareness. *Science*, *280*(5360), 77–81.

Cohen, J. Y., Haesler, S., Vong, L., Lowell, B. B., & Uchida, N. (2012). Neuron-type-specific signals for reward and punishment in the ventral tegmental area. *Nature*, *482*(7383), 85–88.

Cohen, M. R., & Maunsell, J. H. (2009). Attention improves performance primarily by reducing interneuronal correlations. *Nature Neuroscience*, *12*(12), 1594–1600.

Cohen, N. J., & Eichenbaum, H. (1993). *Memory, amnesia, and the hippocampal system*. Cambridge, MA: MIT Press.

Colgin, L. L. (2016). Rhythms of the hippocampal network. *Nature Reviews. Neuroscience*, *17*(4), 239–249.

Colgin, L. L., Denninger, T., Fyhn, M., Hafting, T., Bonnevie, T., Jensen, O., … Moser, E. I. (2009). Frequency of gamma oscillations routes flow of information in the hippocampus. *Nature*, *462*(7271), 353–357.

Corkin, S. (2013). *Permanent present tense: The unforgettable life of the amnesic patient* (Vol. xix). H.M. New York: Basic Books 364 pages, 16 pages of plates.

Crochet, S., & Petersen, C. C. (2006). Correlating whisker behavior with membrane potential in barrel cortex of awake mice. *Nature Neuroscience*, *9*(5), 608–610.

Csicsvari, J., Hirase, H., Czurko, A., & Buzsaki, G. (1998). Reliability and state dependence of pyramidal cell-interneuron synapses in the hippocampus: An ensemble approach in the behaving rat. *Neuron*, *21*(1), 179–189.

Csicsvari, J., Hirase, H., Czurko, A., Mamiya, A., & Buzsaki, G. (1999). Oscillatory coupling of hippocampal pyramidal cells and interneurons in the behaving rat. *The Journal of Neuroscience*, *19*(1), 274–287.

Csicsvari, J., Hirase, H., Mamiya, A., & Buzsaki, G. (2000). Ensemble patterns of hippocampal CA3-CA1 neurons during sharp wave-associated population events. *Neuron*, *28*(2), 585–594.

Csicsvari, J., Jamieson, B., Wise, K. D., & Buzsaki, G. (2003). Mechanisms of gamma oscillations in the hippocampus of the behaving rat. *Neuron*, *37*(2), 311–322.

Csicsvari, J., O'Neill, J., Allen, K., & Senior, T. (2007). Place-selective firing contributes to the reverse-order reactivation of CA1 pyramidal cells during sharp waves in open-field exploration. *The European Journal of Neuroscience*, *26*(3), 704–716.

Cui, Z., Gerfen, C. R., & Young, W. S., 3rd. (2013). Hypothalamic and other connections with dorsal CA2 area of the mouse hippocampus. *The Journal of Comparative Neurology*, *521*(8), 1844–1866.

Curto, C., & Itskov, V. (2008). Cell groups reveal structure of stimulus space. *PLoS Computational Biology*, *4*(10), e1000205.

Czurko, A., Hirase, H., Csicsvari, J., & Buzsaki, G. (1999). Sustained activation of hippocampal pyramidal cells by 'space clamping' in a running wheel. *The European Journal of Neuroscience*, *11*(1), 344–352.

Dabaghian, Y., Brandt, V. L., & Frank, L. M. (2014). Reconceiving the hippocampal map as a topological template. *eLife*, *3*, e03476.

Dabaghian, Y., Memoli, F., Frank, L., & Carlsson, G. (2012). A topological paradigm for hippocampal spatial map formation using persistent homology. *PLoS Computational Biology*, *8*(8), e1002581.

Dadarlat, M. C., & Stryker, M. P. (2017). Locomotion enhances neural encoding of visual stimuli in mouse V1. *The Journal of Neuroscience*, *37*(14), 3764–3775.

Danielson, N. B., Kaifosh, P., Zaremba, J. D., Lovett-Barron, M., Tsai, J., Denny, C. A., … Kheirbek, M. A. (2016). Distinct contribution of adult-born hippocampal granule cells to context encoding. *Neuron*, *90*, 101–112.

Danielson, N. B., Zaremba, J. D., Kaifosh, P., Bowler, J., Ladow, M., & Losonczy, A. (2016). Sublayer-specific coding dynamics during spatial navigation and learning in hippocampal area CA1. *Neuron*, *91*(3), 652–665.

Danjo, T., Toyoizumi, T., & Fujisawa, S. (2018). Spatial representations of self and other in the hippocampus. *Science*, *359*(6372), 213–218.

David, A., & Pierre, L. (2007). *Hippocampal neuroanatomy. The hippocampus book*. Oxford: Oxford University Press.

Davidson, T. J., Kloosterman, F., & Wilson, M. A. (2009). Hippocampal replay of extended experience. *Neuron*, *63*(4), 497–507.

Davidson, T. L., Chan, K., Jarrard, L. E., Kanoski, S. E., Clegg, D. J., & Benoit, S. C. (2009). Contributions of the hippocampus and medial prefrontal cortex to energy and body weight regulation. *Hippocampus*, *19*(3), 235–252.

de Kock, C. P., & Sakmann, B. (2009). Spiking in primary somatosensory cortex during natural whisking in awake head-restrained rats is cell-type specific. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(38), 16446–16450.

Dement, W. C. (1990). A personal history of sleep disorders medicine. *Journal of Clinical Neurophysiology*, *7*(1), 17–47.

Dement, W. C. (1998). The study of human sleep: A historical perspective. *Thorax*, *53*(Suppl 3), S2–S7.

Derdikman, D., Whitlock, J. R., Tsao, A., Fyhn, M., Hafting, T., Moser, M. B., & Moser, E. I. (2009). Fragmentation of grid cell maps in a multicompartment environment. *Nature Neuroscience*, *12*, 1325–1332.

Desimone, R., Albright, T. D., Gross, C. G., & Bruce, C. (1984). Stimulus-selective properties of inferior temporal neurons in the macaque. *The Journal of Neuroscience*, *4*(8), 2051–2062.

di Pellegrino, G., Fadiga, L., Fogassi, L., Gallese, V., & Rizzolatti, G. (1992). Understanding motor events: A neurophysiological study. *Experimental Brain Research*, *91*(1), 176–180.

Diamond, D. M., Campbell, A. M., Park, C. R., Halonen, J., & Zoladz, P. R. (2007). The temporal dynamics model of emotional memory processing: A synthesis on the neurobiological basis of stress-induced amnesia, flashbulb and traumatic memories, and the Yerkes-Dodson law. *Neural Plasticity*, *2007*, 60803.

Diba, K., & Buzsaki, G. (2007). Forward and reverse hippocampal place-cell sequences during ripples. *Nature Neuroscience*, *10*(10), 1241–1242.

Diekelmann, S., & Born, J. (2010). The memory function of sleep. *Nature Reviews. Neuroscience*, *11*(2), 114–126.

Douglas, R. J., & Martin, K. A. (2004). Neuronal circuits of the neocortex. *Annual Review of Neuroscience*, *27*, 419–451.

Dragoi, G., & Buzsaki, G. (2006). Temporal encoding of place sequences by hippocampal cell assemblies. *Neuron*, *50*(1), 145–157.

Drai, D., Benjamini, Y., & Golani, I. (2000). Statistical discrimination of natural modes of motion in rat exploratory behavior. *Journal of Neuroscience Methods*, *96*(2), 119–131.

Drai, D., Kafkafi, N., Benjamini, Y., Elmer, G., & Golani, I. (2001). Rats and mice share common ethologically relevant parameters of exploratory behavior. *Behavioural Brain Research*, *125*(1–2), 133–140.

Dreyfus, H. L. (1992). *What computers still can't do: A critique of artificial reason*. Cambridge: MIT Press.

Driscoll, L. N., Pettit, N. L., Minderer, M., Chettih, S. N., & Harvey, C. D. (2017). Dynamic reorganization of neuronal activity patterns in parietal cortex. *Cell*, *170*(5), 986–999.e16.

Druckmann, S., & Chklovskii, D. B. (2012). Neuronal circuits underlying persistent representations despite time varying activity. *Current Biology*, *22*(22), 2095–2103.

Dudek, S. M., Alexander, G. M., & Farris, S. (2016). Rediscovering area CA2: Unique properties and functions. *Nature Reviews. Neuroscience*, *17*(2), 89–102.

Dupret, D., O'Neill, J., Pleydell-Bouverie, B., & Csicsvari, J. (2010). The reorganization and reactivation of hippocampal maps predict spatial memory performance. *Nature Neuroscience*, *13*(8), 995–1002.

Eggermann, E., Kremer, Y., Crochet, S., & Petersen, C. C. (2014). Cholinergic signals in mouse barrel cortex during active whisker sensing. *Cell Reports*, *9*(5), 1654–1660.

Ego-Stengel, V., & Wilson, M. A. (2010). Disruption of ripple-associated hippocampal activity during rest impairs spatial learning in the rat. *Hippocampus*, *20*(1), 1–10.

Eichenbaum, H. (2004). Hippocampus: Cognitive processes and neural representations that underlie declarative memory. *Neuron*, *44*(1), 109–120.

Eichenbaum, H. (2013). Memory on time. *Trends in Cognitive Sciences*, *17*(2), 81–88.

Eichenbaum, H. (2014). Time cells in the hippocampus: A new dimension for mapping memories. *Nature Reviews. Neuroscience*, *15*(11), 732–744.

Eichenbaum, H. (2017a). Memory: Organization and control. *Annual Review of Psychology*, *68*, 19–45.

Eichenbaum, H. (2017b). On the integration of space, time, and memory. *Neuron*, *95*(5), 1007–1018.

Eichenbaum, H. (2017c). Prefrontal-hippocampal interactions in episodic memory. *Nature Reviews. Neuroscience*, *18*, 547–558.

Eichenbaum, H. (2017d). The role of the hippocampus in navigation is memory. *Journal of Neurophysiology*, *117*(4), 1785–1796.

Eichenbaum, H. (2017e). Time (and space) in the hippocampus. *Current Opinion in Behavioral Sciences*, *17*, 65–70.

Eichenbaum, H., & Cohen, N. J. (2001). *From conditioning to conscious recollection*. New York: Oxford University Press.

Eichenbaum, H., & Cohen, N. J. (2014). Can we reconcile the declarative memory and spatial navigation views on hippocampal function? *Neuron*, *83*(4), 764–770.

Eichenbaum, H., Dudchenko, P., Wood, E., Shapiro, M., & Tanila, H. (1999). The hippocampus, memory, and place cells: Is it spatial memory or a memory space? *Neuron*, *23*(2), 209–226.

Eichenbaum, H., Kuperstein, M., Fagan, A., & Nagode, J. (1987). Cue-sampling and goal-approach correlates of hippocampal unit activity in rats performing an odor-discrimination task. *The Journal of Neuroscience*, *7*(3), 716–732.

Eilam, D., & Golani, I. (1989). Home base behavior of rats (*Rattus norvegicus*) exploring a novel environment. *Behavioural Brain Research*, *34*(3), 199–211.

Einstein, M. C., Polack, P. O., Tran, D. T., & Golshani, P. (2017). Visually evoked 3-5 Hz membrane potential oscillations reduce the responsiveness of visual cortex neurons in awake behaving mice. *The Journal of Neuroscience*, *37*(20), 5084–5098.

Ekstrom, A. D., Kahana, M. J., Caplan, J. B., Fields, T. A., Isham, E. A., Newman, E. L., & Fried, I. (2003). Cellular networks underlying human spatial navigation. *Nature*, *425*(6954), 184–188.

Eliades, S. J., & Wang, X. (2008). Neural substrates of vocalization feedback monitoring in primate auditory cortex. *Nature*, *453*(7198), 1102–1106.

Engel, A. K., Fries, P., & Singer, W. (2001). Dynamic predictions: Oscillations and synchrony in top-down processing. *Nature Reviews. Neuroscience*, *2*(10), 704–716.

Engel, T. A., Steinmetz, N. A., Gieselmann, M. A., Thiele, A., Moore, T., & Boahen, K. (2016). Selective modulation of cortical state during spatial attention. *Science*, *354*(6316), 1140–1144.

Erisken, S., Vaiceliunaite, A., Jurjut, O., Fiorini, M., Katzner, S., & Busse, L. (2014). Effects of locomotion extend throughout the mouse early visual system. *Current Biology*, *24*(24), 2899–2907.

Etienne, A. S., & Jeffery, K. J. (2004). Path integration in mammals. *Hippocampus*, *14*(2), 180–192.

Ezzyat, Y., & Davachi, L. (2014). Similarity breeds proximity: Pattern similarity within and across contexts is related to later mnemonic judgments of temporal proximity. *Neuron*, *81*(5), 1179–1189.

Fanselow, E. E., & Nicolelis, M. A. (1999). Behavioral modulation of tactile responses in the rat somatosensory system. *The Journal of Neuroscience*, *19*(17), 7603–7616.

Fanselow, M. S., & Dong, H. W. (2010). Are the dorsal and ventral hippocampus functionally distinct structures? *Neuron*, *65*(1), 7–19.

Fee, M. S., Mitra, P. P., & Kleinfeld, D. (1997). Central versus peripheral determinants of patterned spike activity in rat vibrissa cortex during whisking. *Journal of Neurophysiology*, *78*(2), 1144–1149.

Felleman, D. J., & Van Essen, D. C. (1991). Distributed hierarchical processing in the primate cerebral cortex. *Cerebral Cortex*, *1*(1), 1–47.

Feng, T., Silva, D., & Foster, D. J. (2015). Dissociation between the experience-dependent development of hippocampal theta sequences and single-trial phase precession. *The Journal of Neuroscience*, *35*(12), 4890–4902.

Ferbinteanu, J., Kennedy, P. J., & Shapiro, M. L. (2006). Episodic memory--from brain to mind. *Hippocampus*, *16*(9), 691–703.

Ferbinteanu, J., & Shapiro, M. L. (2003). Prospective and retrospective memory coding in the hippocampus. *Neuron*, *40*(6), 1227–1239.

Ferezou, I., Haiss, F., Gentet, L. J., Aronoff, R., Weber, B., & Petersen, C. C. (2007). Spatiotemporal dynamics of cortical sensorimotor integration in behaving mice. *Neuron*, *56*(5), 907–923.

Field, D. J. (1994). What is the goal of sensory coding? *Neural Computation*, *6*(4), 559–601.

Finkelstein, A., Derdikman, D., Rubin, A., Foerster, J. N., Las, L., & Ulanovsky, N. (2015). Three-dimensional head-direction coding in the bat brain. *Nature*, *517*(7533), 159–164.

Fontanini, A., & Katz, D. B. (2008). Behavioral states, network states, and sensory response variability. *Journal of Neurophysiology*, *100*(3), 1160–1168.

Foster, D. J. (2017). Replay comes of age. *Annual Review of Neuroscience*, *40*, 581–602.

Foster, D. J., & Knierim, J. J. (2012). Sequence learning and the role of the hippocampus in rodent navigation. *Current Opinion in Neurobiology*, *22*(2), 294–300.

Foster, D. J., & Wilson, M. A. (2006). Reverse replay of behavioural sequences in hippocampal place cells during the awake state. *Nature*, *440*(7084), 680–683.

Foster, D. J., & Wilson, M. A. (2007). Hippocampal theta sequences. *Hippocampus*, *17*(11), 1093–1099.

Foster, T. C., Castro, C. A., & McNaughton, B. L. (1989). Spatial selectivity of rat hippocampal neurons: Dependence on preparedness for movement. *Science*, *244*(4912), 1580–1582.

Frank, L. M., Brown, E. N., & Wilson, M. (2000a). Trajectory encoding in the hippocampus and entorhinal cortex. *Neuron*, *27*(1), 169–178.

Frank, L. M., Brown, E. N., & Wilson, M. A. (2000b). Trajectory encoding in the hippocampus and entorhinal cortex. *Neuron*, *27*, 169–178.

Frank, L. M., Stanley, G. B., & Brown, E. N. (2004a). Hippocampal plasticity across multiple days of exposure to novel environments. *The Journal of Neuroscience*, *24*(35), 7681–7689.

Frank, L. M., Stanley, G. B., & Brown, E. N. (2004b). Hippocampal plasticity across multiple days of exposure to novel environments. *Journal of Neuroscience*, *24*(35), 7681–7689.

Frankland, P. W., & Bontempi, B. (2005). The organization of recent and remote memories. *Nature Reviews Neuroscience*, *6*, 119–130.

Freund, T. F., & Buzsaki, G. (1996). Interneurons of the hippocampus. *Hippocampus*, *6*(4), 347–470.

Fries, P. (2015). Rhythms for cognition: Communication through coherence. *Neuron*, *88*(1), 220–235.

Fries, P., Reynolds, J. H., Rorie, A. E., & Desimone, R. (2001). Modulation of oscillatory neuronal synchronization by selective visual attention. *Science*, *291*(5508), 1560–1563.

Friston, K. (2005). A theory of cortical responses. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *360*(1456), 815–836.

Froudarakis, E., Berens, P., Ecker, A. S., Cotton, R. J., Sinz, F. H., Yatsenko, D., … Tolias, A. S. (2014). Population code in mouse V1 facilitates readout of natural scenes through increased sparseness. *Nature Neuroscience*, *17*(6), 851–857.

Fu, Y., Kaneko, M., Tang, Y., Alvarez-Buylla, A., & Stryker, M. P. (2015). A cortical disinhibitory circuit for enhancing adult plasticity. *eLife*, *4*, e05558.

Fu, Y., Tucciarone, J. M., Espinosa, J. S., Sheng, N., Darcy, D. P., Nicoll, R. A., … Stryker, M. P. (2014). A cortical circuit for gain control by behavioral state. *Cell*, *156*(6), 1139–1152.

Fuhrmann, F., Justus, D., Sosulina, L., Kaneko, H., Beutel, T., Friedrichs, D., … Remy, S. (2015). Locomotion, Theta oscillations, and the speed-correlated firing of hippocampal neurons are controlled by a medial Septal Glutamatergic circuit. *Neuron*, *86*(5), 1253–1264.

Fujisawa, S., & Buzsaki, G. (2011). A 4 Hz oscillation adaptively synchronizes prefrontal, VTA, and hippocampal activities. *Neuron*, *72*(1), 153–165.

Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. S. (1989). Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. *Journal of Neurophysiology*, *61*(2), 331–349.

Fuster, J. M., & Alexander, G. E. (1971). Neuron activity related to short-term memory. *Science*, *173*(3997), 652–654.

Fyhn, M., Hafting, T., Treves, A., Moser, M. B., & Moser, E. I. (2007). Hippocampal remapping and grid realignment in entorhinal cortex. *Nature*, *446*(7132), 190–194.

Gallistel, C. R. (1990). *The organization of learning* (Vol. viii, p. 648). Cambridge, MA: MIT Press.

Geiller, T., Fattahi, M., Choi, J. S., & Royer, S. (2017). Place cells are more strongly tied to landmarks in deep than in superficial CA1. *Nature Communications*, *8*, 14531.

Geisler, C., Robbe, D., Zugaro, M., Sirota, A., & Buzsaki, G. (2007). Hippocampal place cell assemblies are speed-controlled oscillators. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(19), 8149–8154.

Gelbard-Sagiv, H., Mukamel, R., Harel, M., Malach, R., & Fried, I. (2008). Internally generated reactivation of single neurons in human Hippocampus during free recall. *Science*, *322*, 96–101.

Gentet, L. J., Avermann, M., Matyas, F., Staiger, J. F., & Petersen, C. C. (2010). Membrane potential dynamics of GABAergic neurons in the barrel cortex of behaving mice. *Neuron*, *65*(3), 422–435.

Gentet, L. J., Kremer, Y., Taniguchi, H., Huang, Z. J., Staiger, J. F., & Petersen, C. C. (2012). Unique functional properties of somatostatin-expressing GABAergic neurons in mouse barrel cortex. *Nature Neuroscience*, *15*(4), 607–612.

Gervasoni, D., Lin, S. C., Ribeiro, S., Soares, E. S., Pantoja, J., & Nicolelis, M. A. (2004). Global forebrain dynamics predict rat behavioral states and their transitions. *The Journal of Neuroscience*, *24*(49), 11137–11147.

Getting, P. A. (1989). Emerging principles governing the operation of neural networks. *Annual Review of Neuroscience*, *12*, 185–204.

Geva-Sagiv, M., Romani, S., Las, L., & Ulanovsky, N. (2016). Hippocampal global remapping for different sensory modalities in flying bats. *Nature Neuroscience*, *19*, 952–958.

Gibson, J. J. (1979). *The ecological approach to visual perception* (Vol. xiv, p. 332). Boston: Houghton Mifflin Harcourt.

Gilbert, C. D., & Sigman, M. (2007). Brain states: Top-down influences in sensory processing. *Neuron*, *54*(5), 677–696.

Gilbert, D. T., & Wilson, T. D. (2007). Prospection: Experiencing the future. *Science*, *317*(5843), 1351–1354.

Girardeau, G., Benchenane, K., Wiener, S. I., Buzsaki, G., & Zugaro, M. B. (2009). Selective suppression of hippocampal ripples impairs spatial memory. *Nature Neuroscience*, *12*(10), 1222–1223.

Golani, I., Benjamini, Y., & Eilam, D. (1993). Stopping behavior: Constraints on exploration in rats (*Rattus norvegicus*). *Behavioural Brain Research*, *53*(1–2), 21–33.

Gold, J. I., & Shadlen, M. N. (2007). The neural basis of decision making. *Annual Review of Neuroscience*, *30*, 535–574.

GoodSmith, D., Chen, X., Wang, C., Kim, S. H., Song, H., Burgalossi, A., … Knierim, J. J. (2017). Spatial representations of granule cells and mossy cells of the dentate Gyrus. *Neuron*, *93*(3), 677–690 e5.

Gothard, K. M., Skaggs, W. E., & McNaughton, B. L. (1996). Dynamics of mismatch correction in the hippocampal ensemble code for space: Interaction between path integration and environmental cues. *Journal of Neuroscience*, *16*(24), 8027–8040.

Gothard, K. M., Skaggs, W. E., Moore, K. M., & McNaughton, B. L. (1996). Binding of hippocampal CA1 neural activity to multiple reference frames in a landmark-based navigation task. *Journal of Neuroscience*, *16*(2), 823–835.

Goudar, V., & Buonomano, D. V. (2014). Useful dynamic regimes emerge in recurrent networks. *Nature Neuroscience*, *17*(4), 487–489.

Grastyan, E., & Karmos, G. (1961). A study of a possible "dreaming" mechanism in the cat. *Acta Physiologica Academiae Scientiarum Hungaricae*, *20*, 41–50.

Grastyan, E., Lissak, K., Madarasz, I., & Donhoffer, H. (1959). Hippocampal electrical activity during the development of conditioned reflexes. *Electroencephalography and Clinical Neurophysiology*, *11*(3), 409–430.

Graves, A. R., Moore, S. J., Bloss, E. B., Mensh, B. D., Kath, W. L., & Spruston, N. (2012). Hippocampal pyramidal neurons comprise two distinct cell types that are countermodulated by metabotropic receptors. *Neuron*, *76*(4), 776–789.

Green, J., Adachi, A., Shah, K. K., Hirokawa, J. D., Magani, P. S., & Maimon, G. (2017). A neural circuit architecture for angular integration in drosophila. *Nature*, *546*(7656), 101–106.

Green, J. D., & Arduini, A. A. (1954). Hippocampal electrical activity in arousal. *Journal of Neurophysiology*, *17*(6), 533–557.

Gregoriou, G. G., Gotts, S. J., Zhou, H., & Desimone, R. (2009). High-frequency, long-range coupling between prefrontal and visual cortex during attention. *Science*, *324*(5931), 1207–1210.

Grieves, R. M., Duvelle, É., Wood, E. R., & Dudchenko, P. A. (2017). Field repetition and local mapping in the hippocampus and the medial entorhinal cortex. *Journal of Neurophysiology*, *118*(4), 2378–2388.

Grieves, R. M., & Jeffery, K. J. (2017). The representation of space in the brain. *Behavioural Processes*, *135*, 113–131.

Grieves, R. M., Wood, E. R., & Dudchenko, P. A. (2016). Place cells on a maze encode routes rather than destinations. *eLife*, *5*, e15986.

Grion, N., Akrami, A., Zuo, Y., Stella, F., & Diamond, M. E. (2016). Coherence between rat sensorimotor system and Hippocampus is enhanced during tactile discrimination. *PLoS Biology*, *14*(2), e1002384.

Grosmark, A. D., Mizuseki, K., Pastalkova, E., Diba, K., & Buzsaki, G. (2012). REM sleep reorganizes hippocampal excitability. *Neuron*, *75*(6), 1001–1007.

Gross, C. G., Rocha-Miranda, C. E., & Bender, D. B. (1972). Visual properties of neurons in inferotemporal cortex of the macaque. *Journal of Neurophysiology*, *35*(1), 96–111.

Guo, Z. V., Inagaki, H. K., Daie, K., Druckmann, S., Gerfen, C. R., & Svoboda, K. (2017). Maintenance of persistent activity in a frontal thalamocortical loop. *Nature*, *545*(7653), 181–186.

Gupta, A. S., van der Meer, M. A., Touretzky, D. S., & Redish, A. D. (2010). Hippocampal replay is not a simple function of experience. *Neuron*, *65*(5), 695–705.

Gupta, A. S., van der Meer, M. A., Touretzky, D. S., & Redish, A. D. (2012a). Segmentation of spatial experience by hippocampal theta sequences. *Nature Neuroscience*, *15*(7), 1032–1039.

Gupta, A. S., van der Meer, M. A. A., Touretzky, D. S., & Redish, A. D. (2012b). Segmentation of spatial experience by hippocampal θ sequences. *Nature Neuroscience*, *15*(7), 1032–1039.

Guzowski, J. F., Knierim, J. J., & Moser, E. I. (2004). Ensemble dynamics of hippocampal regions CA3 and CA1. *Neuron*, *44*(4), 581–584.

Hafting, T., Fyhn, M., Molden, S., Moser, M. B., & Moser, E. I. (2005). Microstructure of a spatial map in the entorhinal cortex. *Nature*, *436*(7052), 801–806.

Hahn, T. T., McFarland, J. M., Berberich, S., Sakmann, B., & Mehta, M. R. (2012). Spontaneous persistent activity in entorhinal cortex modulates cortico-hippocampal interaction in vivo. *Nature Neuroscience*, *15*, 1531–1538.

Hahn, T. T., Sakmann, B., & Mehta, M. R. (2006). Phase-locking of hippocampal interneurons' membrane potential to neocortical up-down states. *Nature Neuroscience*, *9*(11), 1359–1361.

Hahn, T. T., Sakmann, B., & Mehta, M. R. (2007). Differential responses of hippocampal subfields to cortical up-down states. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(12), 5169–5174.

Hall, N. J., & Colby, C. L. (2011). Remapping for visual stability. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *366*(1564), 528–539.

Hall, T. M., de Carvalho, F., & Jackson, A. (2014). A common structure underlies low-frequency cortical dynamics in movement, sleep, and sedation. *Neuron*, *83*(5), 1185–1199.

Hardcastle, K., Ganguli, S., & Giocomo, L. M. (2015). Environmental boundaries as an error correction mechanism for grid cells. *Neuron*, *86*(3), 827–839.

Harnad, S. (1990). The symbol grounding problem. *Physica D: Nonlinear Phenomena*, *42*(1–3), 335–346.

Harris, K. D., Csicsvari, J., Hirase, H., Dragoi, G., & Buzsaki, G. (2003). Organization of cell assemblies in the hippocampus. *Nature*, *424*(6948), 552–556.

Harris, K. D., Henze, D. A., Hirase, H., Leinekugel, X., Dragoi, G., Czurko, A., & Buzsaki, G. (2002). Spike train dynamics predicts theta-related phase precession in hippocampal pyramidal cells. *Nature*, *417*(6890), 738–741.

Harris, K. D., & Thiele, A. (2011). Cortical state and attention. *Nature Reviews. Neuroscience*, *12*(9), 509–523.

Harris-Warrick, R. M., & Marder, E. (1991). Modulation of neural networks for behavior. *Annual Review of Neuroscience*, *14*, 39–57.

Hartley, T., Lever, C., Burgess, N., & O'Keefe, J. (2014). Space in the brain: How the hippocampal formation supports spatial cognition. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *369*(1635), 20120510.

Hassabis, D., Kumaran, D., & Maguire, E. A. (2007). Using imagination to understand the neural basis of episodic memory. *The Journal of Neuroscience*, *27*(52), 14365–14374.

Hassabis, D., Kumaran, D., Vann, S. D., & Maguire, E. A. (2007). Patients with hippocampal amnesia cannot imagine new experiences. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(5), 1726–1731.

Hasselmo, M. E. (1999). Neuromodulation: Acetylcholine and memory consolidation. *Trends in Cognitive Sciences*, *3*(9), 351–359.

Hasselmo, M. E. (2005). What is the function of hippocampal theta rhythm?-linking behavioral data to phasic properties of field potential and unit recording data. *Hippocampus*, *15*(7), 936–949.

Hasselmo, M. E. (2006). The role of acetylcholine in learning and memory. *Current Opinion in Neurobiology*, *16*(6), 710–715.

Hasselmo, M. E., & Sarter, M. (2011). Modes and models of forebrain cholinergic neuromodulation of cognition. *Neuropsychopharmacology*, *36* (1), 52–73.

Henriksen, E. J., Colgin, L. L., Barnes, C. A., Witter, M. P., Moser, M. B., & Moser, E. I. (2010). Spatial representation along the proximodistal axis of CA1. *Neuron*, *68*(1), 127–137.

Hill, A. J. (1978). First occurrence of hippocampal spatial firing in a new environment. *Experimental Neurology*, *62*(2), 282–297.

Hinman, J. R., Brandon, M. P., Climer, J. R., Chapman, G. W., & Hasselmo, M. E. (2016). Multiple running speed signals in medial Entorhinal cortex. *Neuron*, *91*(3), 666–679.

Hirase, H., Czurko, A., Csicsvari, J., & Buzsaki, G. (1999). Firing rate and theta-phase coding by hippocampal pyramidal neurons during 'space clamping'. *The European Journal of Neuroscience*, *11*(12), 4373–4380.

Hitti, F. L., & Siegelbaum, S. A. (2014). The hippocampal CA2 region is essential for social memory. *Nature*, *508*(7494), 88–92.

Hobson, J. A., & Pace-Schott, E. F. (2002). The cognitive neuroscience of sleep: Neuronal systems, consciousness and learning. *Nature Reviews Neuroscience*, *3*(9), 679–693.

Hongo, Y., Ogawa, K., Takahara, Y., Takasu, K., Royer, S., Hasegawa, M., … Ikegaya, Y. (2015). Topological organization of CA3-to-CA1 excitation. *The European Journal of Neuroscience*, *42*(5), 2135–2143.

Hsieh, L. T., Gruber, M. J., Jenkins, L. J., & Ranganath, C. (2014). Hippocampal activity patterns carry information about objects in temporal context. *Neuron*, *81*(5), 1165–1178.

Hubel, D. H., & Wiesel, T. N. (1962). Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *The Journal of Physiology*, *160*, 106–154.

Hubel, D. H., & Wiesel, T. N. (1977). Ferrier lecture. Functional architecture of macaque monkey visual cortex. *Proceedings of the Royal Society of London—Series B: Biological Sciences*, *198*(1130), 1–59.

Hulse, B. K., Lubenov, E. V., & Siapas, A. G. (2017). Brain state dependence of hippocampal subthreshold activity in awake mice. *Cell Reports*, *18*(1), 136–147.

Hulse, B. K., Moreaux, L. C., Lubenov, E. V., & Siapas, A. G. (2016). Membrane potential dynamics of CA1 pyramidal neurons during hippocampal ripples in awake mice. *Neuron*, *89*(4), 800–813.

Huxter, J., Burgess, N., & O'Keefe, J. (2003). Independent rate and temporal coding in hippocampal pyramidal cells. *Nature*, *425*(6960), 828–832.

Huxter, J. R., Senior, T. J., Allen, K., & Csicsvari, J. (2008). Theta phase-specific codes for two-dimensional position, trajectory and heading in the hippocampus. *Nature Neuroscience*, *11*(5), 587–594.

Igarashi, K. M., Ito, H. T., Moser, E. I., & Moser, M. B. (2014). Functional diversity along the transverse axis of hippocampal area CA1. *FEBS Letters*, *588*(15), 2470–2476.

Ishizuka, N., Weber, J., & Amaral, D. G. (1990). Organization of intrahippocampal projections originating from CA3 pyramidal cells in the rat. *The Journal of Comparative Neurology*, *295*(4), 580–623.

Isomura, Y., Sirota, A., Ozen, S., Montgomery, S., Mizuseki, K., Henze, D. A., & Buzsaki, G. (2006). Integration and segregation of activity in entorhinal-hippocampal subregions by neocortical slow oscillations. *Neuron*, *52*(5), 871–882.

Jackson, J., & Redish, A. D. (2007). Network dynamics of hippocampal cell-assemblies resemble multiple spatial maps within single tasks. *Hippocampus*, *17*(12), 1209–1229.

Jacobs, J. (2014). Hippocampal theta oscillations are slower in humans than in rodents: Implications for models of spatial navigation and memory. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *369*(1635), 20130304.

Jadhav, S. P., Kemere, C., German, P. W., & Frank, L. M. (2012). Awake hippocampal sharp-wave ripples support spatial memory. *Science*, *336* (6087), 1454–1458.

Jadhav, S. P., Rothschild, G., Roumis, D. K., & Frank, L. M. (2016). Coordinated excitation and inhibition of prefrontal ensembles during awake hippocampal Sharp-wave ripple events. *Neuron*, *90*(1), 113–127.

Jarosiewicz, B., McNaughton, B. L., & Skaggs, W. E. (2002). Hippocampal population activity during the small-amplitude irregular activity state in the rat. *The Journal of Neuroscience*, *22*(4), 1373–1384.

Jarosiewicz, B., & Skaggs, W. E. (2004a). Hippocampal place cells are not controlled by visual input during the small irregular activity state in the rat. *The Journal of Neuroscience*, *24*(21), 5070–5077.

Jarosiewicz, B., & Skaggs, W. E. (2004b). Level of arousal during the small irregular activity state in the rat hippocampal EEG. *Journal of Neurophysiology*, *91*(6), 2649–2657.

Jarsky, T., Mady, R., Kennedy, B., & Spruston, N. (2008). Distribution of bursting neurons in the CA1 region and the subiculum of the rat hippocampus. *The Journal of Comparative Neurology*, *506*(4), 535–547.

Jeffery, K. (2008). *The Place cells—Cognitive map or memory system?* Oxford: Oxford University Press.

Jeffery, K. J. (2007). Self-localization and the entorhinal-hippocampal system. *Current Opinion in Neurobiology*, *17*(6), 684–691.

Jezek, K., Henriksen, E. J., Treves, A., Moser, E. I., & Moser, M. B. (2011). Theta-paced flickering between place-cell maps in the hippocampus. *Nature*, *478*(7368), 246–249.

Ji, D., & Wilson, M. A. (2007). Coordinated memory replay in the visual cortex and hippocampus during sleep. *Nature Neuroscience*, *10*(1), 100–107.

Johnson, A., & Redish, A. D. (2007). Neural ensembles in CA3 transiently encode paths forward of the animal at a decision point. *The Journal of Neuroscience*, *27*(45), 12176–12189.

Johnson, K. O. (2000). Neural coding. *Neuron*, *26*(3), 563–566.

Jones, M. W., & McHugh, T. J. (2011). Updating hippocampal representations: CA2 joins the circuit. *Trends in Neurosciences*, *34*(10), 526–535.

Jones, M. W., & Wilson, M. A. (2005). Phase precession of medial prefrontal cortical activity relative to the hippocampal theta rhythm. *Hippocampus*, *15*(7), 867–873.

Jouvet, M. (1967). The states of sleep. *Scientific American*, *216*(2), 62–68.

Juavinett, A. L., Erlich, J. C., & Churchland, A. K. (2017). Decision-making behaviors: Weighing ethology, complexity, and sensorimotor compatibility. *Current Opinion in Neurobiology*, *49*, 42–50.

Jung, M. W., Qin, Y., McNaughton, B. L., & Barnes, C. A. (1998). Firing characteristics of deep layer neurons in prefrontal cortex in rats performing spatial working memory tasks. *Cerebral Cortex*, *8*(5), 437–450.

Jutras, M. J., Fries, P., & Buffalo, E. A. (2013). Oscillatory activity in the monkey hippocampus during visual exploration and memory formation. *Proceedings of the National Academy of Sciences of the United States of America*, *110*(32), 13144–13149.

Kamondi, A., Acsady, L., Wang, X. J., & Buzsaki, G. (1998). Theta oscillations in somata and dendrites of hippocampal pyramidal cells in vivo: Activity-dependent phase-precession of action potentials. *Hippocampus*, *8*(3), 244–261.

Kaneko, M., Fu, Y., & Stryker, M. P. (2017). Locomotion induces stimulus-specific response enhancement in adult visual cortex. *The Journal of Neuroscience*, *37*(13), 3532–3543.

Kaneko, M., & Stryker, M. P. (2014). Sensory experience during locomotion promotes recovery of function in adult visual cortex. *eLife*, *3*, e02798.

Kanwisher, N. (2001). Neural events and perceptual awareness. *Cognition*, *79*(1–2), 89–113.

Kaplan, R., Adhikari, M. H., Hindriks, R., Mantini, D., Murayama, Y., Logothetis, N. K., & Deco, G. (2016). Hippocampal sharp-wave ripples influence selective activation of the default mode network. *Current Biology*, *26*(5), 686–691.

Karlsson, M. P., & Frank, L. M. (2008). Network dynamics underlying the formation of sparse, informative representations in the hippocampus. *The Journal of Neuroscience*, *28*(52), 14271–14281.

Karlsson, M. P., & Frank, L. M. (2009). Awake replay of remote experiences in the hippocampus. *Nature Neuroscience*, *12*(7), 913–918.

Katona, L., Lapray, D., Viney, T. J., Oulhaj, A., Borhegyi, Z., Micklem, B. R., … Somogyi, P. (2014). Sleep and movement differentiates actions of two types of somatostatin-expressing GABAergic interneuron in rat hippocampus. *Neuron*, *82*(4), 872–886.

Kay, K. (2016). *Novel patterns of activity in the hippocampus*. San Francisco: University of California.

Kay, K., Sosa, M., Chung, J. E., Karlsson, M. P., Larkin, M. C., & Frank, L. M. (2016). A hippocampal network for spatial coding during immobility and sleep. *Nature*, *531*(7593), 185–190.

Kelemen, E., & Fenton, A. A. (2010). Dynamic grouping of hippocampal neural activity during cognitive control of two spatial frames. *PLoS Biology*, *8*(6), e1000403.

Kelemen, E., & Fenton, A. A. (2016). Coordinating different representations in the hippocampus. *Neurobiology of Learning and Memory*, *129*, 50–59.

Keller, G. B., Bonhoeffer, T., & Hubener, M. (2012). Sensorimotor mismatch signals in primary visual cortex of the behaving mouse. *Neuron*, *74*(5), 809–815.

Kemere, C., Carr, M. F., Karlsson, M. P., & Frank, L. M. (2013). Rapid and continuous modulation of hippocampal network state during exploration of new places. *PLoS One*, *8*(9), e73114.

Kim, J. J., & Fanselow, M. S. (1992). Modality-specific retrograde amnesia of fear. *Science*, *256*(5057), 675–677.

Kim, S. M., & Frank, L. M. (2009). Hippocampal lesions impair rapid learning of a continuous spatial alternation task. *PLoS One*, *4*(5), e5494.

Kitamura, T., Pignatelli, M., Suh, J., Kohara, K., Yoshiki, A., Abe, K., & Tonegawa, S. (2014). Island cells control temporal association memory. *Science*, *343*(6173), 896–901.

Klausberger, T., Magill, P. J., Marton, L. F., Roberts, J. D., Cobden, P. M., Buzsaki, G., & Somogyi, P. (2003). Brain-state- and cell-type-specific firing of hippocampal interneurons in vivo. *Nature*, *421*(6925), 844–848.

Klausberger, T., & Somogyi, P. (2008). Neuronal diversity and temporal dynamics: The unity of hippocampal circuit operations. *Science*, *321* (5885), 53–57.

Kleinfeld, D., Ahissar, E., & Diamond, M. E. (2006). Active sensation: Insights from the rodent vibrissa sensorimotor system. *Current Opinion in Neurobiology*, *16*(4), 435–444.

Kleinfeld, D., Berg, R. W., & O'Connor, S. M. (1999). Anatomical loops and their electrical dynamics in relation to whisking by rat. *Somatosensory & Motor Research*, *16*(2), 69–88.

Kleinfeld, D., Deschenes, M., & Ulanovsky, N. (2016). Whisking, sniffing, and the hippocampal theta-rhythm: A tale of two oscillators. *PLoS Biology*, *14*(2), e1002385.

Knierim, J. J. (2006). Neural representations of location outside the hippocampus. *Learning & Memory*, *13*(4), 405–415.

Knierim, J. J., & Hamilton, D. A. (2011). Framing spatial cognition: Neural representations of proximal and distal frames of reference and their roles in navigation. *Physiological Reviews*, *91*(4), 1245–1279.

Knierim, J. J., Lee, I., & Hargreaves, E. L. (2006). Hippocampal place cells: Parallel input streams, subregional processing, and implications for episodic memory. *Hippocampus*, *16*(9), 755–764.

Knierim, J. J., & Neunuebel, J. P. (2016). Tracking the flow of hippocampal computation: Pattern separation, pattern completion, and attractor dynamics. *Neurobiology of Learning and Memory*, *129*, 38–49.

Knierim, J. J., Neunuebel, J. P., & Deshmukh, S. S. (2014). Functional correlates of the lateral and medial entorhinal cortex: Objects, path integration and local-global reference frames. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *369*(1635), 20130369.

Kohara, K., Pignatelli, M., Rivest, A. J., Jung, H. Y., Kitamura, T., Suh, J., … Obata, Y. (2014). Cell type-specific genetic and optogenetic tools reveal hippocampal CA2 circuits. *Nature Neuroscience*, *17*(2), 269–279. Wickersham IR, Tonegawa S

Koulakov, A. A., Raghavachari, S., Kepecs, A., & Lisman, J. E. (2002). Model for a robust neural integrator. *Nature Neuroscience*, *5*(8), 775–782.

Kovacs, K. A., O'Neill, J., Schoenenberger, P., Penttonen, M., Ranguel Guerrero, D. K., & Csicsvari, J. (2016). Optogenetically blocking Sharp wave ripple events in sleep does not interfere with the formation of stable spatial representation in the CA1 area of the Hippocampus. *PLoS One*, *11*(10), e0164675.

Krakauer, J. W., Ghazanfar, A. A., Gomez-Marin, A., MacIver, M. A., & Poeppel, D. (2017). Neuroscience needs behavior: Correcting a reductionist Bias. *Neuron*, *93*(3), 480–490.

Kramis, R., Vanderwolf, C. H., & Bland, B. H. (1975). Two types of hippocampal rhythmical slow activity in both the rabbit and the rat: Relations to behavior and effects of atropine, diethyl ether, urethane, and pentobarbital. *Experimental Neurology*, *49*(1 Pt 1), 58–85.

Krook-Magnuson, E., Varga, C., Lee, S. H., & Soltesz, I. (2012). New dimensions of interneuronal specialization unmasked by principal cell heterogeneity. *Trends in Neurosciences*, *35*(3), 175–184.

Kropff, E., Carmichael, J. E., Moser, M. B., & Moser, E. I. (2015). Speed cells in the medial entorhinal cortex. *Nature*, *523*(7561), 419–424.

Krupa, D. J., Wiest, M. C., Shuler, M. G., Laubach, M., & Nicolelis, M. A. (2004). Layer-specific somatosensory cortical activation during active tactile discrimination. *Science*, *304*(5679), 1989–1992.

Kubie, J. L., & Muller, R. U. (1991). Multiple representations in the hippocampus. *Hippocampus*, *1*(3), 240–242.

Kudrimoti, H. S., Barnes, C. A., & McNaughton, B. L. (1999). Reactivation of hippocampal cell assemblies: Effects of behavioral state, experience, and EEG dynamics. *The Journal of Neuroscience*, *19*(10), 4090–4101.

Kuffler, S. W. (1953). Discharge patterns and functional organization of mammalian retina. *Journal of Neurophysiology*, *16*(1), 37–68.

Kumaran, D., Hassabis, D., & McClelland, J. L. (2016). What learning systems do intelligent agents need? Complementary learning systems theory updated. *Trends in Cognitive Sciences*, *20*(7), 512–534.

Kumaran, D., & McClelland, J. L. (2012). Generalization through the recurrent interaction of episodic memories: A model of the hippocampal system. *Psychological Review*, *119*(3), 573–616.

Lamme, V. A. (2003). Why visual attention and awareness are different. *Trends in Cognitive Sciences*, *7*(1), 12–18.

Lamme, V. A., & Roelfsema, P. R. (2000). The distinct modes of vision offered by feedforward and recurrent processing. *Trends in Neurosciences*, *23*(11), 571–579.

Lapray, D., Lasztoczi, B., Lagler, M., Viney, T. J., Katona, L., Valenti, O., … Klausberger, T. (2012). Behavior-dependent specialization of identified hippocampal interneurons. *Nature Neuroscience*, *15*(9), 1265–1271.

Las, L., & Ulanovsky, N. (2014). Hippocampal neurophysiology across species. In D. Derdikman & J. J. Knierim (Eds.), *Space, time and memory in the hippocampal formation* (pp. 431–461). Vienna: Springer Vienna.

Lasztoczi, B., & Klausberger, T. (2016). Hippocampal place cells couple to three different gamma oscillations during place field traversal. *Neuron*, *91*(1), 34–40.

Laurent, G. (1999). A systems perspective on early olfactory coding. *Science*, *286*(5440), 723–728.

Le Duigou, C., Simonnet, J., Telenczuk, M. T., Fricker, D., & Miles, R. (2014). Recurrent synapses and circuits in the CA3 region of the hippocampus: An associative network. *Frontiers in Cellular Neuroscience*, *7*, 262.

Lee, A. M., Hoy, J. L., Bonci, A., Wilbrecht, L., Stryker, M. P., & Niell, C. M. (2014). Identification of a brainstem circuit regulating visual cortical state in parallel with locomotion. *Neuron*, *83*(2), 455–466.

Lee, H., Wang, C., Deshmukh, S. S., & Knierim, J. J. (2015). Neural population evidence of functional heterogeneity along the CA3 transverse axis: Pattern completion versus pattern separation. *Neuron*, *87*(5), 1093–1105.

Lee, I., Rao, G., & Knierim, J. J. (2004). A double dissociation between hippocampal subfields: Differential time course of CA3 and CA1 place cells for processing changed environments. *Neuron*, *42*(5), 803–815.

Lee, I., Yoganarasimha, D., Rao, G., & Knierim, J. J. (2004). Comparison of population coherence of place cells in hippocampal subfields CA1 and CA3. *Nature*, *430*(6998), 456–459.

Lee, S., Kruglikov, I., Huang, Z. J., Fishell, G., & Rudy, B. (2013). A disinhibitory circuit mediates motor integration in the somatosensory cortex. *Nature Neuroscience*, *16*(11), 1662–1670.

Lee, S. E., Simons, S. B., Heldt, S. A., Zhao, M., Schroeder, J. P., Vellano, C. P., … Hepler, J. R. (2010). RGS14 is a natural suppressor of both synaptic plasticity in CA2 neurons and hippocampal-based learning and memory. *Proceedings of the National Academy of Sciences of the United States of America*, *107*(39), 16994–16998.

Lee, S. H., & Dan, Y. (2012). Neuromodulation of brain states. *Neuron*, *76* (1), 209–222.

Lee, S. H., Marchionni, I., Bezaire, M., Varga, C., Danielson, N., Lovett-Barron, M., … Soltesz, I. (2014). Parvalbumin-positive basket cells differentiate among hippocampal pyramidal cells. *Neuron*, *82*(5), 1129–1144.

Leopold, D. A., & Logothetis, N. K. (1999). Multistable phenomena: Changing views in perception. *Trends in Cognitive Sciences*, *3*(7), 254–264.

Lettvin, J. Y., Maturana, H. R., McCulloch, W. S., & Pitts, W. H. (1959). What the frog's eye tells the frog's brain. *Proceedings of the IRE*, *47*(11), 1940–1951.

Leutgeb, S., Leutgeb, J. K., Barnes, C. A., Moser, E. I., McNaughton, B. L., & Moser, M. B. (2005). Independent codes for spatial and episodic memory in hippocampal neuronal ensembles. *Science*, *309*(5734), 619–623.

Leutgeb, S., Leutgeb, J. K., Moser, M. B., & Moser, E. I. (2005). Place cells, spatial maps and the population code for memory. *Current Opinion in Neurobiology*, *15*(6), 738–746.

Leutgeb, S., Leutgeb, J. K., Treves, A., Moser, M. B., & Moser, E. I. (2004). Distinct ensemble codes in hippocampal areas CA3 and CA1. *Science*, *305*(5688), 1295–1298.

Lever, C., Burton, S., & O'Keefe, J. (2006). Rearing on hind legs, environmental novelty, and the hippocampal formation. *Reviews in the Neurosciences*, *17*(1–2), 111–133.

Lever, C., Kaplan, R., & Burgess, N. (2014). The function of oscillations in the hippocampal formation. In *Space, time and memory in the hippocampal formation* (pp. 303–350). Vienna, Austria: Springer.

Li, X. G., Somogyi, P., Ylinen, A., & Buzsaki, G. (1994). The hippocampal CA3 network: An in vivo intracellular labeling study. *The Journal of Comparative Neurology*, *339*(2), 181–208.

Lisman, J., & Redish, A. D. (2009). Prediction, sequences and the hippocampus. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *364*(1521), 1193–1201.

Lisman, J. E., & Grace, A. A. (2005). The hippocampal-VTA loop: Controlling the entry of information into long-term memory. *Neuron*, *46*(5), 703–713.

Lisman, J. E., Talamini, L. M., & Raffone, A. (2005). Recall of memory sequences by interaction of the dentate and CA3: A revised model of the phase precession. *Neural Networks*, *18*(9), 1191–1201.

Liu, D., Gu, X., Zhu, J., Zhang, X., Han, Z., Yan, W., … Hou, R. (2014). Medial prefrontal activity during delay period contributes to learning of a working memory task. *Science*, *346*(6208), 458–463.

Liu, Y., McAfee, S. S., & Heck, D. H. (2017). Hippocampal sharp-wave ripples in awake mice are entrained by respiration. *Scientific Reports*, *7*(1), 8950.

Lockmann, A. L. V., & Tort, A. B. L. (2018). Nasal respiration entrains delta-frequency oscillations in the prefrontal cortex and hippocampus of rodents. *Brain Structure & Function*, *223*(1), 1–3.

Logothetis, N. K., Eschenko, O., Murayama, Y., Augath, M., Steudel, T., Evrard, H. C., … Oeltermann, A. (2012). Hippocampal-cortical interaction during periods of subcortical silence. *Nature*, *491*(7425), 547–553.

Lorente de Nó, R. (1934). Studies on the structure of the cerebral cortex. II. Continuation of the study of the ammonic system. *Journal für Psychologie Und Neurologie*, *46*, 113–177.

Louie, K., & Wilson, M. A. (2001). Temporally structured replay of awake hippocampal ensemble activity during rapid eye movement sleep. *Neuron*, *29*(1), 145–156.

Lovett-Barron, M., Kaifosh, P., Kheirbek, M. A., Danielson, N., Zaremba, J. D., Reardon, T. R., … Losonczy, A. (2014). Dendritic inhibition in the hippocampus supports fear learning. *Science*, *343*(6173), 857–863.

Lu, L., Igarashi, K. M., Witter, M. P., Moser, E. I., & Moser, M. B. (2015). Topography of place maps along the CA3-to-CA2 axis of the hippocampus. *Neuron*, *87*(5), 1078–1092.

Luczak, A., Bartho, P., & Harris, K. D. (2013). Gating of sensory input by spontaneous cortical activity. *The Journal of Neuroscience*, *33*(4), 1684–1695.

Ludvig, N. (1999). Place cells can flexibly terminate and develop their spatial firing. A new theory for their function. *Physiology & Behavior*, *67*(1), 57–67.

MacDonald, C. J., Carrow, S., Place, R., & Eichenbaum, H. (2013). Distinct hippocampal time cell sequences represent odor memories in immobilized rats. *The Journal of Neuroscience*, *33*(36), 14607–14616.

MacDonald, C. J., Lepage, K. Q., Eden, U. T., & Eichenbaum, H. (2011). Hippocampal "time cells" bridge the gap in memory for discontiguous events. *Neuron*, *71*(4), 737–749.

Magee, J. C. (2003). A prominent role for intrinsic neuronal properties in temporal coding. *Trends in Neurosciences*, *26*(1), 14–16.

Maingret, N., Girardeau, G., Todorova, R., Goutierre, M., & Zugaro, M. (2016). Hippocampo-cortical coupling mediates memory consolidation during sleep. *Nature Neuroscience*, *19*(7), 959–964.

Major, G., & Tank, D. (2004). Persistent neural activity: Prevalence and mechanisms. *Current Opinion in Neurobiology*, *14*(6), 675–684.

Makino, H., & Komiyama, T. (2015). Learning enhances the relative impact of top-down processing in the visual cortex. *Nature Neuroscience*, *18*(8), 1116–1122.

Mankin, E. A., Diehl, G. W., Sparks, F. T., Leutgeb, S., & Leutgeb, J. K. (2015). Hippocampal CA2 activity patterns change over time to a larger extent than between spatial contexts. *Neuron*, *85*(1), 190–201.

Mankin, E. A., Sparks, F. T., Slayyeh, B., Sutherland, R. J., Leutgeb, S., & Leutgeb, J. K. (2012). Neuronal code for extended time in the hippocampus. *Proceedings of the National Academy of Sciences of the United States of America*, *109*(47), 19462–19467.

Manning, J. R., Polyn, S. M., Baltuch, G. H., Litt, B., & Kahana, M. J. (2011). Oscillatory patterns in temporal lobe reveal context reinstatement during memory search. *Proceedings of the National Academy of Sciences of the United States of America*, *108*(31), 12893–12897.

Manns, J. R., Howard, M. W., & Eichenbaum, H. (2007). Gradual changes in hippocampal activity support remembering the order of events. *Neuron*, *56*(3), 530–540.

Maren, S., Phan, K. L., & Liberzon, I. (2013). The contextual brain: Implications for fear conditioning, extinction and psychopathology. *Nature Reviews. Neuroscience*, *14*(6), 417–428.

Markus, E. J., Qin, Y. L., Leonard, B., Skaggs, W. E., Mcnaughton, B. L., & Barnes, C. A. (1995). Interactions between location and task affect the spatial and directional firing of hippocampal neurons. *The Journal of Neuroscience*, *15*(11), 7079–7094.

Maroso, M., Szabo, G. G., Kim, H. K., Alexander, A., Bui, A. D., Lee, S. H., … Soltesz, I. (2016). Cannabinoid control of learning and memory through HCN channels. *Neuron*, *89*(5), 1059–1073.

Marr, D. (1971). Simple memory: A theory for archicortex. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *262*(841), 23–81.

Marr, D. (1982). *Vision: A computational investigation into the human representation and processing of visual information* (Vol. xvii, p. 397). San Francisco: W.H. Freeman.

Masurkar, A. V., Srinivas, K. V., Brann, D. H., Warren, R., Lowes, D. C., & Siegelbaum, S. A. (2017). Medial and lateral entorhinal cortex differentially excite deep versus superficial CA1 pyramidal neurons. *Cell Reports*, *18*(1), 148–160.

Maunsell, J. H., & Treue, S. (2006). Feature-based attention in visual cortex. *Trends in Neurosciences*, *29*(6), 317–322.

Maurer, A. P., Burke, S. N., Lipa, P., Skaggs, W. E., & Barnes, C. A. (2012). Greater running speeds result in altered hippocampal phase sequence dynamics. *Hippocampus*, *22*(4), 737–747.

McClelland, J. L., McNaughton, B. L., & O'Reilly, R. C. (1995). Why there are complementary learning systems in the hippocampus and neocortex: Insights from the successes and failures of connectionist models of learning and memory. *Psychological Review*, *102*(3), 419–457.

McGinley, M. J., David, S. V., & McCormick, D. A. (2015). Cortical membrane potential signature of optimal states for sensory signal detection. *Neuron*, *87*(1), 179–192.

McGinley, M. J., Vinck, M., Reimer, J., Batista-Brito, R., Zagha, E., Cadwell, C. R., … McCormick, D. A. (2015). Waking state: Rapid variations modulate neural and behavioral responses. *Neuron*, *87*(6), 1143–1161.

McHugh, T. J., Blum, K. I., Tsien, J. Z., Tonegawa, S., & Wilson, M. A. (1996). Impaired hippocampal representation of space in CA1-specific NMDAR1 knockout mice. *Cell*, *87*(7), 1339–1349.

McKenzie, S., Robinson, N. T., Herrera, L., Churchill, J. C., & Eichenbaum, H. (2013). Learning causes reorganization of neuronal firing patterns to represent related experiences within a hippocampal schema. *The Journal of Neuroscience*, *33*(25), 10243–10256.

McNaughton, B. L., Barnes, C. A., Gerrard, J. L., Gothard, K., Jung, M. W., Knierim, J. J., … others. (1996). Deciphering the hippocampal polyglot: The hippocampus as a path integration system. *The Journal of Experimental Biology*, *199*(Pt 1), 173–185.

McNaughton, B. L., Barnes, C. A., & O'Keefe, J. (1983). The contributions of position, direction, and velocity to single unit activity in the hippocampus of freely-moving rats. *Experimental Brain Research*, *52*(1), 41–49.

McNaughton, B. L., Battaglia, F. P., Jensen, O., Moser, E. I., & Moser, M. B. (2006). Path integration and the neural basis of the 'cognitive map'. *Nature Reviews Neuroscience*, *7*(8), 663–678.

Mercer, A., Trigg, H. L., & Thomson, A. M. (2007). Characterization of neurons in the CA2 subfield of the adult rat hippocampus. *The Journal of Neuroscience*, *27*(27), 7329–7338.

Mineault, P. J., Tring, E., Trachtenberg, J. T., & Ringach, D. L. (2016). Enhanced spatial resolution during locomotion and heightened attention in mouse primary visual cortex. *The Journal of Neuroscience*, *36*(24), 6382–6392.

Miri, A., Daie, K., Arrenberg, A. B., Baier, H., Aksay, E., & Tank, D. W. (2011). Spatial gradients and multidimensional dynamics in a neural integrator circuit. *Nature Neuroscience*, *14*(9), 1150–1159.

Mitchell, J. F., Sundberg, K. A., & Reynolds, J. H. (2009). Spatial attention decorrelates intrinsic activity fluctuations in macaque area V4. *Neuron*, *63*(6), 879–888.

Mittelstaedt, L. M., & Mittelstaedt, H. (1980). Homing by path integration in a mammal. *Naturwissenschaften*, *67*, 566–567.

Miyawaki, H., Billeh, Y. N., & Diba, K. (2017). Low activity microstates during sleep. *Sleep*, *40*(6).

Mizumori, S. J., Barnes, C. A., & McNaughton, B. L. (1990). Behavioral correlates of theta-on and theta-off cells recorded from hippocampal formation of mature young and aged rats. *Experimental Brain Research*, *80*(2), 365–373.

Mizuseki, K., Diba, K., Pastalkova, E., & Buzsaki, G. (2011). Hippocampal CA1 pyramidal cells form functionally distinct sublayers. *Nature Neuroscience*, *14*(9), 1174–1181.

Mizuseki, K., Royer, S., Diba, K., & Buzsaki, G. (2012). Activity dynamics and behavioral correlates of CA3 and CA1 hippocampal pyramidal neurons. *Hippocampus*, *22*(8), 1659–1680.

Monaco, J. D., Rao, G., Roth, E. D., & Knierim, J. J. (2014). Attentive scanning behavior drives one-trial potentiation of hippocampal place fields. *Nature Neuroscience*, *17*(5), 725–731.

Montgomery, S. M., Sirota, A., & Buzsaki, G. (2008). Theta and gamma coordination of hippocampal networks during waking and rapid eye movement sleep. *The Journal of Neuroscience*, *28*(26), 6731–6741.

Morris, R. G., & Frey, U. (1997). Hippocampal synaptic plasticity: Role in spatial learning or the automatic recording of attended experience? *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *352*(1360), 1489–1503.

Moser, E. I., Roudi, Y., Witter, M. P., Kentros, C., Bonhoeffer, T., & Moser, M. B. (2014). Grid cells and cortical representation. *Nature Reviews. Neuroscience*, *15*(7), 466–481.

Mountcastle, V. B. (1957). Modality and topographic properties of single neurons of cat's somatic sensory cortex. *Journal of Neurophysiology*, *20*(4), 408–434.

Mountcastle, V. B. (1998). *Perceptual neuroscience: The cerebral cortex* (Vol. 20, p. 486). Cambridge, Mass: Harvard University Press.

Muir, G. M., Brown, J. E., Carey, J. P., Hirvonen, T. P., Della Santina, C. C., Minor, L. B., & Taube, J. S. (2009). Disruption of the head direction cell signal after occlusion of the semicircular canals in the freely moving chinchilla. *The Journal of Neuroscience*, *29*(46), 14521–14533.

Muller, R. (1996). A quarter of a century of place cells. *Neuron*, *17*(5), 813–822.

Muller, R. U., & Kubie, J. L. (1987). The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *The Journal of Neuroscience*, *7*(7), 1951–1968.

Muller, R. U., & Kubie, J. L. (1989). The firing of hippocampal place cells predicts the future position of freely moving rats. *Journal of Neuroscience*, *9*(12), 4101–4110.

Muller, R. U., Kubie, J. L., & Ranck, J. B., Jr. (1987). Spatial firing patterns of hippocampal complex-spike cells in a fixed environment. *The Journal of Neuroscience*, *7*(7), 1935–1950.

Muller, R. U., Stead, M., & Pach, J. (1996). The hippocampus as a cognitive graph. *The Journal of General Physiology*, *107*(6), 663–694.

Mumford, D. (1992). On the computational architecture of the neocortex. II. The role of cortico-cortical loops. *Biological Cybernetics*, *66*(3), 241–251.

Munoz, W., Tremblay, R., Levenstein, D., & Rudy, B. (2017). Layer-specific modulation of neocortical dendritic inhibition during active wakefulness. *Science*, *355*(6328), 954–959.

Murray, J. D., Bernacchia, A., Freedman, D. J., Romo, R., Wallis, J. D., Cai, X., … others. (2014). A hierarchy of intrinsic timescales across primate cortex. *Nature Neuroscience*, *17*(12), 1661–1663.

Nadel, L., & Moscovitch, M. (1997). Memory consolidation, retrograde amnesia and the hippocampal complex. *Current Opinion in Neurobiology*, *7*(2), 217–227.

Nadel, L., Samsonovich, A., Ryan, L., & Moscovitch, M. (2000). Multiple trace theory of human memory: Computational, neuroimaging, and neuropsychological results. *Hippocampus*, *10*(4), 352–368.

Nakajima, M., & Halassa, M. M. (2017). Thalamic control of functional cortical connectivity. *Current Opinion in Neurobiology*, *44*, 127–131.

Nakamura, N. H., Flasbeck, V., Maingret, N., Kitsukawa, T., & Sauvage, M. M. (2013). Proximodistal segregation of nonspatial information in CA3: Preferential recruitment of a proximal CA3-distal CA1 network in nonspatial recognition memory. *The Journal of Neuroscience*, *33*(28), 11506–11514.

Nakashiba, T., Buhl, D. L., McHugh, T. J., & Tonegawa, S. (2009). Hippocampal CA3 output is crucial for ripple-associated reactivation and consolidation of memory. *Neuron*, *62*(6), 781–787.

Nelson, A., Schneider, D. M., Takatoh, J., Sakurai, K., Wang, F., & Mooney, R. (2013). A circuit for motor cortical modulation of auditory cortical activity. *The Journal of Neuroscience*, *33*(36), 14342–14353.

Neunuebel, J. P., & Knierim, J. J. (2012). Spatial firing correlates of physiologically distinct cell types of the rat dentate gyrus. *The Journal of Neuroscience*, *32*(11), 3848–3858.

Neunuebel, J. P., & Knierim, J. J. (2014). CA3 retrieves coherent representations from degraded input: Direct evidence for CA3 pattern completion and dentate gyrus pattern separation. *Neuron*, *81*(2), 416–427.

Niell, C. M., & Stryker, M. P. (2010). Modulation of visual responses by behavioral state in mouse visual cortex. *Neuron*, *65*(4), 472–479.

Nitz, D. A. (2006). Tracking route progression in the posterior parietal cortex. *Neuron*, *49*(5), 747–756.

Nokia, M. S., Mikkonen, J. E., Penttonen, M., & Wikgren, J. (2012). Disrupting neural activity related to awake-state sharp wave-ripple complexes prevents hippocampal learning. *Frontiers in Behavioral Neuroscience*, *6*, 84.

Noorani, I., & Carpenter, R. (2017). Not moving: The fundamental but neglected motor function. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *372*(1718), 20160190.

O'Keefe, J. (1976). Place units in the hippocampus of the freely moving rat. *Experimental Neurology*, *51*(1), 78–109.

O'Keefe, J. (1979). A review of the hippocampal place cells. *Progress in Neurobiology*, *13*(4), 419–439.

O'Keefe, J. (1999). Do hippocampal pyramidal cells signal non-spatial as well as spatial information? *Hippocampus*, *9*(4), 352–364.

O'Keefe, J. (2007). Hippocampal neurophysiology in the behaving animal. In P. Anderson (Ed.), *The hippocampus book* (pp. 475–548). Oxford: Oxford University Press.

O'Keefe, J., & Burgess, N. (1996). Geometric determinants of the place fields of hippocampal neurons. *Nature*, *381*(6581), 425–428.

O'Keefe, J., & Conway, D. H. (1978). Hippocampal place units in the freely moving rat: Why they fire where they fire. *Experimental Brain Research*, *31*(4), 573–590.

O'Keefe, J., & Dostrovsky, J. (1971). The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Research*, *34*(1), 171–175.

O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. London: Oxford University Press.

O'Keefe, J., & Recce, M. L. (1993). Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus*, *3*(3), 317–330.

O'Keefe, J., & Speakman, A. (1987). Single unit activity in the rat hippocampus during a spatial memory task. *Experimental Brain Research*, *68*(1), 1–27.

Okuyama, T., Kitamura, T., Roy, D. S., Itohara, S., & Tonegawa, S. (2016). Ventral CA1 neurons store social memory. *Science*, *353*(6307), 1536–1541.

Olafsdottir, H. F., Bush, D., & Barry, C. (2018). The role of hippocampal replay in memory and planning. *Current Biology*, *28*(1), R37–r50.

Olafsdottir, H. F., Carpenter, F., & Barry, C. (2017). Task demands predict a dynamic switch in the content of awake hippocampal replay. *Neuron*, *96*(4), 925–935.e6.

Oliva, A., Fernandez-Ruiz, A., Buzsaki, G., & Berenyi, A. (2016a). Role of hippocampal CA2 region in triggering sharp-wave ripples. *Neuron*, *91*(6), 1342–1355.

Oliva, A., Fernandez-Ruiz, A., Buzsaki, G., & Berenyi, A. (2016b). Spatial coding and physiological properties of hippocampal neurons in the Cornu Ammonis subregions. *Hippocampus*, *26*(12), 1593–1607.

Olton, D. S., Becker, J. T., & Handelmann, G. E. (1979). Hippocampus, space, and memory. *The Behavioral and Brain Sciences*, *2*, 313–365.

Olton, D. S., & Samuelson, R. J. (1976). Remembrance of places passed: Spatial memory in rats. *Journal of Experimental Psychology: Animal Behavior Processes*, *2*, 97–116.

Omer, D. B., Maimon, S. R., Las, L., & Ulanovsky, N. (2018). Social place-cells in the bat hippocampus. *Science*, *359*(6372), 218–224.

O'Neill, J., Pleydell-Bouverie, B., Dupret, D., & Csicsvari, J. (2010). Play it again: Reactivation of waking experience and memory. *Trends in Neurosciences*, *33*(5), 220–229.

O'Neill, J., Senior, T., & Csicsvari, J. (2006). Place-selective firing of CA1 pyramidal cells during sharp wave/ripple network patterns in exploratory behavior. *Neuron*, *49*(1), 143–155.

O'Neill, J., Senior, T. J., Allen, K., Huxter, J. R., & Csicsvari, J. (2008). Reactivation of experience-dependent cell assembly patterns in the hippocampus. *Nature Neuroscience*, *11*(2), 209–215.

O'Reilly, R. C., & McClelland, J. L. (1994). Hippocampal conjunctive encoding, storage, and recall: Avoiding a trade-off. *Hippocampus*, *4*(6), 661–682.

Ostojic, S. (2014). Two types of asynchronous activity in networks of excitatory and inhibitory spiking neurons. *Nature Neuroscience*, *17*(4), 594–600.

Pakan, J. M., Lowe, S. C., Dylda, E., Keemink, S. W., Currie, S. P., Coutts, C. A., & Rochefort, N. L. (2016). Behavioral-state modulation of inhibition is context-dependent and cell type specific in mouse visual cortex. *eLife*, *5*, e14985.

Papale, A. E., Zielinski, M. C., Frank, L. M., Jadhav, S. P., & Redish, A. D. (2016). Interplay between hippocampal Sharp-wave-ripple events and vicarious trial and error behaviors in decision making. *Neuron*, *92*(5), 975–982.

Paré, D., & Quirk, G. J. (2017). When scientific paradigms lead to tunnel vision: Lessons from the study of fear. *Npj Science of Learning*, *2*(1), 6.

Parker, A. J., & Newsome, W. T. (1998). Sense and the single neuron: Probing the physiology of perception. *Annual Review of Neuroscience*, *21*, 227–277.

Pastalkova, E., Itskov, V., Amarasingham, A., & Buzsaki, G. (2008). Internally generated cell assembly sequences in the rat hippocampus. *Science*, *321*(5894), 1322–1327.

Pennartz, C. M., Ito, R., Verschure, P. F., Battaglia, F. P., & Robbins, T. W. (2011). The hippocampal-striatal axis in learning, prediction and goal-directed behavior. *Trends in Neurosciences*, *34*(10), 548–559.

Pentkowski, N. S., Blanchard, D. C., Lever, C., Litvin, Y., & Blanchard, R. J. (2006). Effects of lesions to the dorsal and ventral hippocampus on defensive behaviors in rats. *The European Journal of Neuroscience*, *23*(8), 2185–2196.

Penttonen, M., Kamondi, A., Sik, A., Acsady, L., & Buzsaki, G. (1997). Feed-forward and feed-back activation of the dentate gyrus in vivo during dentate spikes and sharp wave bursts. *Hippocampus*, *7*(4), 437–450.

Petreanu, L., Gutnisky, D. A., Huber, D., Xu, N. L., O'Connor, D. H., Tian, L., … Svoboda, K. (2012). Activity in motor-sensory projections reveals distributed coding in somatosensation. *Nature*, *489*(7415), 299–303.

Peyrache, A., Khamassi, M., Benchenane, K., Wiener, S. I., & Battaglia, F. P. (2009). Replay of rule-learning related neural patterns in the prefrontal cortex during sleep. *Nature Neuroscience*, *12*(7), 919–926.

Peyrache, A., Lacroix, M. M., Petersen, P. C., & Buzsaki, G. (2015). Internally organized mechanisms of the head direction sense. *Nature Neuroscience*, *18*(4), 569–575.

Pezzulo, G., van der Meer, M. A., Lansink, C. S., & Pennartz, C. M. (2014). Internally generated sequences in learning and executing goal-directed behavior. *Trends in Cognitive Sciences*, *18*(12), 647–657.

Pfeiffer, B. E. (2017). The content of hippocampal "replay". *Hippocampus*, *91*, 1–13.

Pfeiffer, B. E., & Foster, D. J. (2013). Hippocampal place-cell sequences depict future paths to remembered goals. *Nature*, *497*(7447), 74–79.

Pfeiffer, B. E., & Foster, D. J. (2015). Autoassociative dynamics in the generation of sequences of hippocampal place cells. *Science*, *349*(6244), 180–183.

Pi, H. J., Hangya, B., Kvitsiani, D., Sanders, J. I., Huang, Z. J., & Kepecs, A. (2013). Cortical interneurons that specialize in disinhibitory control. *Nature*, *503*(7477), 521–524.

Pickenhain, L., & Klingberg, F. (1967a). Changes of electrophysiological and behavioural indicators during the delay period of conditioned reflexes in rats. *Activitas Nervosa Superior (Praha)*, *9*(3), 330.

Pickenhain, L., & Klingberg, F. (1967b). Hippocampal slow wave activity as a correlate of basic behavioral mechanisms in the rat. *Progress in Brain Research*, *27*, 218–227.

Poe, G. R., Nitz, D. A., McNaughton, B. L., & Barnes, C. A. (2000). Experience-dependent phase-reversal of hippocampal neuron firing during REM sleep. *Brain Research*, *855*(1), 176–180.

Polack, P. O., Friedman, J., & Golshani, P. (2013). Cellular mechanisms of brain state-dependent gain modulation in visual cortex. *Nature Neuroscience*, *16*(9), 1331–1339.

Poppenk, J., Evensmoen, H. R., Moscovitch, M., & Nadel, L. (2013). Long-axis specialization of the human hippocampus. *Trends in Cognitive Sciences*, *17*(5), 230–240.

Poucet, B., Chaillan, F., Truchet, B., Save, E., Sargolini, F., & Hok, V. (2015). Is there a pilot in the brain? Contribution of the self-positioning system to spatial navigation. *Frontiers in Behavioral Neuroscience*, *9*, 292.

Poulet, J. F., Fernandez, L. M., Crochet, S., & Petersen, C. C. (2012). Thalamic control of cortical states. *Nature Neuroscience*, *15*(3), 370–372.

Poulet, J. F., & Petersen, C. C. (2008). Internal brain state regulates membrane potential synchrony in barrel cortex of behaving mice. *Nature*, *454*(7206), 881–885.

Quirk, G. J., Muller, R. U., & Kubie, J. L. (1990). The firing of hippocampal place cells in the dark depends on the rat's recent experience. *Journal of Neuroscience*, *10*(6), 2008–2017.

Quiroga, R. Q. (2012). Concept cells: The building blocks of declarative memory functions. *Nature Reviews. Neuroscience*, *13*(8), 587–597.

Quiroga, R. Q., Reddy, L., Kreiman, G., Koch, C., & Fried, I. (2005). Invariant visual representation by single neurons in the human brain. *Nature*, *435*(7045), 1102–1107.

Raichle, M. E. (2010). Two views of brain function. *Trends in Cognitive Sciences*, *14*(4), 180–190.

Raichle, M. E. (2015). The brain's default mode network. *Annual Review of Neuroscience*, *38*, 433–447.

Ramirez-Villegas, J. F., Logothetis, N. K., & Besserve, M. (2015). Diversity of sharp-wave-ripple LFP signatures reveals differentiated brain-wide dynamical events. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(46), E6379–E6387.

Ranck, J. B., Jr. (1973). Studies on single neurons in dorsal hippocampal formation and septum in unrestrained rats. I. Behavioral correlates and firing repertoires. *Experimental Neurology*, *41*(2), 461–531.

Ranganath, C., & Hsieh, L. T. (2016). The hippocampus: A special place for time. *Annals of the New York Academy of Sciences*, *1369*(1), 93–110.

Rao, R. P., & Ballard, D. H. (1999). Predictive coding in the visual cortex: A functional interpretation of some extra-classical receptive-field effects. *Nature Neuroscience*, *2*(1), 79–87.

Rawlins, J. (1985). Associations across time: The hippocampus as a temporary memory store. *Behavioral and Brain Sciences*, *8*(3), 479–497.

Redish, A. D. (1999). *Beyond the cognitive map: From place cells to episodic memory*. Cambridge, MA: MIT Press.

Redish, A. D. (2016). Vicarious trial and error. *Nature Reviews. Neuroscience*, *17*(3), 147–159.

Redish, A. D., Battaglia, F. P., Chawla, M. K., Ekstrom, A. D., Gerrard, J. L., Lipa, P., … Barnes, C. A. (2001). Independence of firing correlates of anatomically proximate hippocampal pyramidal cells. *Journal of Neuroscience*, *21*(5), RC134.

Redish, A. D., Rosenzweig, E. S., Bohanick, J. D., McNaughton, B. L., & Barnes, C. A. (2000). Dynamics of hippocampal ensemble activity

realignment: Time versus space. *Journal of Neuroscience*, *20*(24), 9298–9309.
Redish, A. D., & Touretzky, D. S. (1997). Cognitive maps beyond the hippocampus. *Hippocampus*, *7*(1), 15–35.
Redish, A. D., & Touretzky, D. S. (1998). The role of the hippocampus in solving the Morris water maze. *Neural Computation*, *10*(1), 73–111.
Reimer, J., Froudarakis, E., Cadwell, C. R., Yatsenko, D., Denfield, G. H., & Tolias, A. S. (2014). Pupil fluctuations track fast switching of cortical states during quiet wakefulness. *Neuron*, *84*(2), 355–362.
Renart, A., de la Rocha, J., Bartho, P., Hollender, L., Parga, N., Reyes, A., & Harris, K. D. (2010). The asynchronous state in cortical circuits. *Science*, *327*(5965), 587–590.
Rieke, F., Warland, D., de Ruyter van Steveninck, R. R., & Bialek, W. (1997). In T. J. Sejnowski & T. A. Poggio (Eds.), *Spikes: Exploring the neural code*. Cambridge, MA: The MIT Press.
Ringach, D. L. (2009). Spontaneous and driven cortical activity: Implications for computation. *Current Opinion in Neurobiology*, *19*(4), 439–444.
Robbe, D., Montgomery, S. M., Thome, A., Rueda-Orozco, P. E., McNaughton, B. L., & Buzsaki, G. (2006). Cannabinoids reveal importance of spike timing coordination in hippocampal function. *Nature Neuroscience*, *9*(12), 1526–1533.
Robert, V., Cassim, S., Chevaleyre, V., & Piskorowski, R. A. (2018). Hippocampal area CA2: Properties and contribution to hippocampal function. *Cell and Tissue Research*, *373*, 525–540.
Robinson, D. A. (1989). Integrating with neurons. *Annual Review of Neuroscience*, *12*, 33–45.
Romo, R., Brody, C. D., Hernandez, A., & Lemus, L. (1999). Neuronal correlates of parametric working memory in the prefrontal cortex. *Nature*, *399*(6735), 470–473.
Roth, M. M., Dahmen, J. C., Muir, D. R., Imhof, F., Martini, F. J., & Hofer, S. B. (2016). Thalamic nuclei convey diverse contextual information to layer 1 of visual cortex. *Nature Neuroscience*, *19*(2), 299–307.
Rothschild, G., Eban, E., & Frank, L. M. (2017). A cortical-hippocampal-cortical loop of information processing during memory consolidation. *Nature Neuroscience*, *20*(2), 251–259.
Roumis, D. K., & Frank, L. M. (2015). Hippocampal sharp-wave ripples in waking and sleeping states. *Current Opinion in Neurobiology*, *35*, 6–12.
Roux, L., Hu, B., Eichler, R., Stark, E., & Buzsaki, G. (2017). Sharp wave ripples during learning stabilize the hippocampal spatial map. *Nature Neuroscience*, *20*(6), 845–853.
Rowland, D. C., Roudi, Y., Moser, M. B., & Moser, E. I. (2016). Ten years of grid cells. *Annual Review of Neuroscience*, *39*, 19–40.
Royer, S., Sirota, A., Patel, J., & Buzsaki, G. (2010). Distinct representations and theta dynamics in dorsal and ventral hippocampus. *Journal of Neuroscience*, *30*(5), 1777–1787.
Royer, S., Zemelman, B. V., Losonczy, A., Kim, J., Chance, F., Magee, J. C., & Buzsaki, G. (2012). Control of timing, rate and bursts of hippocampal place cells by dendritic and somatic inhibition. *Nature Neuroscience*, *15*(5), 769–775.
Rubin, A., Geva, N., Sheintuch, L., & Ziv, Y. (2015). Hippocampal ensemble dynamics timestamp events in long-term memory. *eLife*, *4*, e12247.
Rummell, B. P., Klee, J. L., & Sigurdsson, T. (2016). Attenuation of responses to Self-generated sounds in auditory cortical neurons. *The Journal of Neuroscience*, *36*(47), 12010–12026.
Runyan, C. A., Piasini, E., Panzeri, S., & Harvey, C. D. (2017). Distinct timescales of population coding across cortex. *Nature*, *548*(7665), 92–96.
Saalmann, Y. B., & Kastner, S. (2015). The cognitive thalamus. *Frontiers in Systems Neuroscience*, *9*, 39.
Sainsbury, R. S., Heynen, A., & Montoya, C. P. (1987). Behavioral correlates of hippocampal type 2 theta in the rat. *Physiology & Behavior*, *39*(4), 513–519.
Sainsbury, R. S., & Montoya, C. P. (1984). The relationship between type 2 theta and behavior. *Physiology & Behavior*, *33*(4), 621–626.
Sakata, S., & Harris, K. D. (2009). Laminar structure of spontaneous and sensory-evoked population activity in auditory cortex. *Neuron*, *64*(3), 404–418.
Sakata, S., & Harris, K. D. (2012). Laminar-dependent effects of cortical state on auditory cortical spontaneous activity. *Frontiers in Neural Circuits*, *6*, 109.
Saleem, A. B., Ayaz, A., Jeffery, K. J., Harris, K. D., & Carandini, M. (2013). Integration of visual motion and locomotion in mouse visual cortex. *Nature Neuroscience*, *16*(12), 1864–1869.
Saleem, A. B., Lien, A. D., Krumin, M., Haider, B., Roson, M. R., Ayaz, A., … Harris, K. D. (2017). Subcortical source and modulation of the narrowband gamma oscillation in mouse visual cortex. *Neuron*, *93*(2), 315–322.
Salinas, E., & Sejnowski, T. J. (2001). Correlated neuronal activity and the flow of neural information. *Nature Reviews. Neuroscience*, *2*(8), 539–550.
Samsonovich, A., & McNaughton, B. L. (1997). Path integration and cognitive mapping in a continuous attractor neural network model. *Journal of Neuroscience*, *17*(15), 5900–5920.
Sanders, H., Renno-Costa, C., Idiart, M., & Lisman, J. (2015). Grid cells and place cells: An integrated view of their navigational and memory function. *Trends in Neurosciences*, *38*(12), 763–775.
Sarel, A., Finkelstein, A., Las, L., & Ulanovsky, N. (2017). Vectorial representation of spatial goals in the hippocampus of bats. *Science*, *355*(6321), 176–180.
Sargolini, F., Fyhn, M., Hafting, T., McNaughton, B. L., Witter, M. P., Moser, M. B., & Moser, E. I. (2006). Conjunctive representation of position, direction, and velocity in entorhinal cortex. *Science*, *312*(5774), 758–762.
Save, E., Cressant, A., Thinus-Blanc, C., & Poucet, B. (1998). Spatial firing of hippocampal place cells in blind rats. *Journal of Neuroscience*, *18*(5), 1818–1826.
Save, E., & Poucet, B. (2008). Do place cells guide spatial behaviors? In *Hippocampal place fields: Relevance to learning and memory*. Oxford: Oxford University Press.
Schacter, D. L., & Addis, D. R. (2007). The cognitive neuroscience of constructive memory: Remembering the past and imagining the future. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *362*(1481), 773–786.
Schacter, D. L., Addis, D. R., Hassabis, D., Martin, V. C., Spreng, R. N., & Szpunar, K. K. (2012). The future of memory: Remembering, imagining, and the brain. *Neuron*, *76*(4), 677–694.
Schiller, D., Eichenbaum, H., Buffalo, E. A., Davachi, L., Foster, D. J., Leutgeb, S., & Ranganath, C. (2015a). Memory and space: Towards an understanding of the cognitive map. *The Journal of Neuroscience*, *35*(41), 13904–13911.
Schiller, D., Eichenbaum, H., Buffalo, E. A., Davachi, L., Foster, D. J., Leutgeb, S., & Ranganath, C. (2015b). Memory and space: Towards an understanding of the cognitive map. *Journal of Neuroscience*, *35*(41), 13904–13911.
Schlesiger, M. I., Cannova, C. C., Boublil, B. L., Hales, J. B., Mankin, E. A., Brandon, M. P., … Leutgeb, S. (2015). The medial entorhinal cortex is necessary for temporal organization of hippocampal neuronal activity. *Nature Neuroscience*, *18*(8), 1123–1132.
Schlichting, M. L., & Preston, A. R. (2015). Memory integration: Neural mechanisms and implications for behavior. *Current Opinion in Behavioral Sciences*, *1*, 1–8.
Schmidt, R., Diba, K., Leibold, C., Schmitz, D., Buzsaki, G., & Kempter, R. (2009). Single-trial phase precession in the hippocampus. *Journal of Neuroscience*, *29*(42), 13232–13241.
Schmidt-Hieber, C., Jonas, P., & Bischofberger, J. (2004). Enhanced synaptic plasticity in newly generated granule cells of the adult hippocampus. *Nature*, *429*(6988), 184–187.
Schneider, D. M., Nelson, A., & Mooney, R. (2014). A synaptic and circuit basis for corollary discharge in the auditory cortex. *Nature*, *513*(7517), 189–194.
Scholvinck, M. L., Saleem, A. B., Benucci, A., Harris, K. D., & Carandini, M. (2015). Cortical state determines global variability and correlations in visual cortex. *The Journal of Neuroscience*, *35*(1), 170–178.
Schroeder, C. E., & Lakatos, P. (2009). Low-frequency neuronal oscillations as instruments of sensory selection. *Trends in Neurosciences*, *32*(1), 9–18.
Schroeder, C. E., Wilson, D. A., Radman, T., Scharfman, H., & Lakatos, P. (2010). Dynamics of active sensing and perceptual selection. *Current Opinion in Neurobiology*, *20*(2), 172–176.
Schwindel, C. D., & McNaughton, B. L. (2011). Hippocampal-cortical interactions and the dynamics of memory trace reactivation. *Progress in Brain Research*, *193*, 163–177.

Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery, and Psychiatry*, *20*(1), 11–21.

Seager, M. A., Johnson, L. D., Chabot, E. S., Asaka, Y., & Berry, S. D. (2002). Oscillatory brain states and learning: Impact of hippocampal theta-contingent training. *Proceedings of the National Academy of Sciences of the United States of America*, *99*(3), 1616–1620.

Searle, J. R. (1980). Minds, brains, and programs. *Behavioral and Brain Sciences*, *3*(3), 417–424.

Seli, P., Risko, E. F., Smilek, D., & Schacter, D. L. (2016). Mind-wandering with and without intention. *Trends in Cognitive Sciences*, *20*(8), 605–617.

Senior, T. J., Huxter, J. R., Allen, K., O'Neill, J., & Csicsvari, J. (2008). Gamma oscillatory firing reveals distinct populations of pyramidal cells in the CA1 region of the hippocampus. *Journal of Neuroscience*, *28*(9), 2274–2286.

Seung, H. S., Lee, D. D., Reis, B. Y., & Tank, D. W. (2000). Stability of the memory of eye position in a recurrent network of conductance-based model neurons. *Neuron*, *26*(1), 259–271.

Shadlen, M. N., & Shohamy, D. (2016). Decision making and sequential sampling from memory. *Neuron*, *90*(5), 927–939.

Shadmehr, R. (2017). Distinct neural circuits for control of movement vs. holding still. *Journal of Neurophysiology*, *117*(4), 1431–1460.

Shapiro, M. L., Kennedy, P. J., & Ferbinteanu, J. (2006). Representing episodes in the mammalian brain. *Current Opinion in Neurobiology*, *16*(6), 701–709.

Shapiro, M. L., Tanila, H., & Eichenbaum, H. (1997). Cues that hippocampal place cells encode: Dynamic and hierarchical representation of local and distal stimuli. *Hippocampus*, *7*(6), 624–642.

Sharp, P. E. (1996). Multiple spatial/behavioral correlates for cells in the rat postsubiculum: Multiple regression analysis and comparison to other hippocampal areas. *Cerebral Cortex*, *6*(2), 238–259.

Sherman, S. M. (2016). Thalamus plays a central role in ongoing cortical functioning. *Nature Neuroscience*, *19*(4), 533–541.

Shinohara, Y., Hosoya, A., Yahagi, K., Ferecsko, A. S., Yaguchi, K., Sik, A., … Hirase, H. (2012). Hippocampal CA3 and CA2 have distinct bilateral innervation patterns to CA1 in rodents. *The European Journal of Neuroscience*, *35*(5), 702–710.

Shohamy, D., & Wagner, A. D. (2008). Integrating memories in the human brain: Hippocampal-midbrain encoding of overlapping events. *Neuron*, *60*(2), 378–389.

Siegel, J. M. (2005). Clues to the functions of mammalian sleep. *Nature*, *437*(7063), 1264–1271.

Simoncelli, E. P., & Olshausen, B. A. (2001). Natural image statistics and neural representation. *Annual Review of Neuroscience*, *24*, 1193–1216.

Simons, S. B., Caruana, D. A., Zhao, M., & Dudek, S. M. (2012). Caffeine-induced synaptic potentiation in hippocampal CA2 neurons. *Nature Neuroscience*, *15*(1), 23–25.

Singer, A. C., & Frank, L. M. (2009). Rewarded outcomes enhance reactivation of experience in the hippocampus. *Neuron*, *64*(6), 910–921.

Singer, A. C., Karlsson, M. P., Nathe, A. R., Carr, M. F., & Frank, L. M. (2010). Experience-dependent development of coordinated hippocampal spatial activity representing the similarity of related locations. *The Journal of Neuroscience*, *30*(35), 11586–11604.

Sirota, A., Csicsvari, J., Buhl, D., & Buzsaki, G. (2003). Communication between neocortex and hippocampus during sleep in rodents. *Proceedings of the National Academy of Sciences of the United States of America*, *100*(4), 2065–2069.

Sirota, A., Montgomery, S., Fujisawa, S., Isomura, Y., Zugaro, M., & Buzsaki, G. (2008). Entrainment of neocortical neurons and gamma oscillations by the hippocampal theta rhythm. *Neuron*, *60*(4), 683–697.

Skaggs, W. E. (1995). *Relations between the theta rhythm and activity patterns of hippocampal neurons*. Tucson, AZ: The University of Arizona.

Skaggs, W. E., & McNaughton, B. L. (1996). Replay of neuronal firing sequences in rat hippocampus during sleep following spatial experience. *Science*, *271*(5257), 1870–1873.

Skaggs, W. E., & McNaughton, B. L. (1998). Spatial firing properties of hippocampal CA1 populations in an environment containing two visually identical regions. *Journal of Neuroscience*, *18*(20), 8455–8466.

Skaggs, W. E., McNaughton, B. L., Wilson, M. A., & Barnes, C. A. (1996). Theta phase precession in hippocampal neuronal populations and the compression of temporal sequences. *Hippocampus*, *6*(2), 149–172.

Slomianka, L., Amrein, I., Knuesel, I., Sorensen, J. C., & Wolfer, D. P. (2011). Hippocampal pyramidal cells: The reemergence of cortical lamination. *Brain Structure & Function*, *216*(4), 301–317.

Smallwood, J., & Schooler, J. W. (2015). The science of mind wandering: Empirically navigating the stream of consciousness. *Annual Review of Psychology*, *66*, 487–518.

Smit, H., & Hacker, P. M. (2014). Seven misconceptions about the mereological fallacy: A compilation for the perplexed. *Erkenntnis*, *79*(5), 1077–1097.

Smith, D. M., & Mizumori, S. J. (2006a). Hippocampal place cells, context, and episodic memory. *Hippocampus*, *16*(9), 716–729.

Smith, D. M., & Mizumori, S. J. (2006b). Learning-related development of context-specific neuronal responses to places and events: The hippocampal role in context processing. *The Journal of Neuroscience*, *26*(12), 3154–3163.

Smith, K. (2012). Idle minds. *Nature*, *489*(7416), 356–358.

Sofroniew, N. J., Vlasov, Y. A., Hires, S. A., Freeman, J., & Svoboda, K. (2015). Neural coding in barrel cortex during whisker-guided locomotion. *eLife*, *4*, e12559.

Solstad, T., Boccara, C. N., Kropff, E., Moser, M. B., & Moser, E. I. (2008). Representation of geometric borders in the entorhinal cortex. *Science*, *322*(5909), 1865–1868.

Sommer, M. A., & Wurtz, R. H. (2002). A pathway in primate brain for internal monitoring of movements. *Science*, *296*(5572), 1480–1482.

Somogyi, P., Katona, L., Klausberger, T., Lasztoczi, B., & Viney, T. J. (2014). Temporal redistribution of inhibition over neuronal subcellular domains underlies state-dependent rhythmic change of excitability in the hippocampus. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *369*(1635), 20120518.

Spellman, T., Rigotti, M., Ahmari, S. E., Fusi, S., Gogos, J. A., & Gordon, J. A. (2015). Hippocampal-prefrontal input supports spatial encoding in working memory. *Nature*, *522*(7556), 309–314.

Spruston, N. (2008). Pyramidal neurons: Dendritic structure and synaptic integration. *Nature Reviews. Neuroscience*, *9*(3), 206–221.

Squire, L. R. (1992). Memory and the hippocampus: A synthesis from findings with rats, monkeys, and humans [published erratum appears in Psychol Rev 1992 Jul;99(3):582]. *Psychological Review*, *99*(2), 195–231.

Squire, L. R., & Alvarez, P. (1995). Retrograde amnesia and memory consolidation: A neurobiological perspective. *Current Opinion in Neurobiology*, *5*(2), 169–177.

Srinivas, K. V., Buss, E. W., Sun, Q., Santoro, B., Takahashi, H., Nicholson, D. A., & Siegelbaum, S. A. (2017). The dendrites of CA2 and CA1 pyramidal neurons differentially regulate information flow in the Cortico-hippocampal circuit. *The Journal of Neuroscience*, *37*(12), 3276–3293.

Stark, E., Roux, L., Eichler, R., Senzai, Y., Royer, S., & Buzsaki, G. (2014). Pyramidal cell-interneuron interactions underlie hippocampal ripple oscillations. *Neuron*, *83*(2), 467–480.

Steriade, M. (2000). Corticothalamic resonance, states of vigilance and mentation. *Neuroscience*, *101*(2), 243–276.

Steriade, M., McCormick, D. A., & Sejnowski, T. J. (1993). Thalamocortical oscillations in the sleeping and aroused brain. *Science*, *262*(5134), 679–685.

Steriade, M., Timofeev, I., & Grenier, F. (2001). Natural waking and sleep states: A view from inside neocortical neurons. *Journal of Neurophysiology*, *85*(5), 1969–1985.

Stewart, M., & Fox, S. (1991). Hippocampal theta activity in monkeys. *Brain Research*, *538*(1), 59–63.

Stickgold, R. (2005). Sleep-dependent memory consolidation. *Nature*, *437*(7063), 1272–1278.

Strange, B. A., Witter, M. P., Lein, E. S., & Moser, E. I. (2014). Functional organization of the hippocampal longitudinal axis. *Nature Reviews. Neuroscience*, *15*(10), 655–669.

Stumpf, C. (1965). The fast component in the electrical activity of rabbit's hippocampus. *Electroencephalography and Clinical Neurophysiology*, *18*(5), 477–486.

Suddendorf, T., & Corballis, M. C. (2007). The evolution of foresight: What is mental time travel, and is it unique to humans? *The Behavioral and Brain Sciences*, *30*(3), 299–313 discussion 313–51.

Suh, J., Rivest, A. J., Nakashiba, T., Tominaga, T., & Tonegawa, S. (2011). Entorhinal cortex layer III input to the hippocampus is crucial for temporal association memory. *Science*, *334*(6061), 1415–1420.

Sullivan, D., Csicsvari, J., Mizuseki, K., Montgomery, S., Diba, K., & Buzsaki, G. (2011). Relationships between hippocampal Sharp waves, ripples, and fast gamma oscillation: Influence of dentate and entorhinal cortical activity. *The Journal of Neuroscience*, *31*(23), 8605–8616.

Sun, C., Kitamura, T., Yamamoto, J., Martin, J., Pignatelli, M., Kitch, L. J., … Tonegawa, S. (2015). Distinct speed dependence of entorhinal Island and ocean cells, including respective grid cells. *Proceedings of the National Academy of Sciences of the United States of America*, *112*(30), 9466–9471.

Sun, Q., Sotayo, A., Cazzulino, A. S., Snyder, A. M., Denny, C. A., & Siegelbaum, S. A. (2017). Proximodistal heterogeneity of hippocampal CA3 pyramidal neuron intrinsic properties, connectivity, and reactivation during memory recall. *Neuron*, *95*(3), 656–672.e3.

Sun, Q., Srinivas, K. V., Sotayo, A., & Siegelbaum, S. A. (2014). Dendritic Na + spikes enable cortical input to drive action potential output from hippocampal CA2 pyramidal neurons. *eLife*, *3*, e04551.

Sutherland, R. J., & Rudy, J. W. (1989). Configural association theory: The role of the hippocampal formation in learning, memory and amnesia. *Psychobiology*, *17*(2), 129–144.

Suzuki, S. S., & Smith, G. K. (1987). Spontaneous EEG spikes in the normal hippocampus. I. Behavioral correlates, laminar profiles and bilateral synchrony. *Electroencephalography and Clinical Neurophysiology*, *67*(4), 348–359.

Szabo, G. G., Du, X., Oijala, M., Varga, C., Parent, J. M., & Soltesz, I. (2017). Extended Interneuronal network of the dentate gyrus. *Cell Reports*, *20*(6), 1262–1268.

Tabuchi, E., Mulder, A. B., & Wiener, S. I. (2003). Reward value invariant place responses and reward site associated activity in hippocampal neurons of behaving rats. *Hippocampus*, *13*(1), 117–132.

Takahashi, M., Lauwereyns, J., Sakurai, Y., & Tsukada, M. (2009a). Behavioral state-dependent episodic representations in rat CA1 neuronal activity during spatial alternation. *Cognitive Neurodynamics*, *3*(2), 165–175.

Takahashi, M., Lauwereyns, J., Sakurai, Y., & Tsukada, M. (2009b). A code for spatial alternation during fixation in rat hippocampal CA1 neurons. *Journal of Neurophysiology*, *102*(1), 556–567.

Takahashi, M., Nishida, H., Redish, A. D., & Lauwereyns, J. (2014). Theta phase shift in spike timing and modulation of gamma oscillation: A dynamic code for spatial alternation during fixation in rat hippocampal area CA1. *Journal of Neurophysiology*, *111*(8), 1601–1614.

Takeuchi, T., Duszkiewicz, A. J., Sonneborn, A., Spooner, P. A., Yamasaki, M., Watanabe, M., … others. (2016). Locus coeruleus and dopaminergic consolidation of everyday memory. *Nature*, *537*(7620), 357–362.

Tamamaki, N., Abe, K., & Nojyo, Y. (1988). Three-dimensional analysis of the whole axonal arbors originating from single CA2 pyramidal neurons in the rat hippocampus with the aid of a computer graphic technique. *Brain Research*, *452*(1–2), 255–272.

Tan, A. Y., Chen, Y., Scholl, B., Seidemann, E., & Priebe, N. J. (2014). Sensory stimulation shifts visual cortex from synchronous to asynchronous states. *Nature*, *509*(7499), 226–229.

Tanila, H. (1999). Hippocampal place cells can develop distinct representations of two visually identical environments. *Hippocampus*, *9*(3), 235–246.

Taube, J. S., Muller, R. U., & Ranck, J. B., Jr. (1990). Head-direction cells recorded from the postsubiculum in freely moving rats. II. Effects of environmental manipulations. *Journal of Neuroscience*, *10*(2), 436–447.

Taube, J. S., Muller, R. U., & Ranck, J. B., Jr. (1990). Head-direction cells recorded from the postsubiculum in freely moving rats. I. Description and quantitative analysis. *Journal of Neuroscience*, *10*(2), 420–435.

Tchernichovski, O., Benjamini, Y., & Golani, I. (1998). The dynamics of long-term exploration in the rat. Part I. A phase-plane analysis of the relationship between location and velocity. *Biological Cybernetics*, *78*(6), 423–432.

Teyler, T. J., & DiScenna, P. (1986). The hippocampal memory indexing theory. *Behavioral Neuroscience*, *100*(2), 147–154.

Teyler, T. J., & Rudy, J. W. (2007). The hippocampal indexing theory and episodic memory: Updating the index. *Hippocampus*, *17*(12), 1158–1169.

Tolman, E. C. (1948). Cognitive maps in rats and men. *Psychological Review*, *55*(4), 189–208.

Tort, A. B., Komorowski, R. W., Manns, J. R., Kopell, N. J., & Eichenbaum, H. (2009). Theta-gamma coupling increases during the learning of item-context associations. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(49), 20942–20947.

Tort, A. B. L., Brankack, J., & Draguhn, A. (2018). Respiration-entrained brain rhythms are global but often overlooked. *Trends in Neurosciences*, *41*, 186–197.

Traub, R. D., & Wong, R. K. (1982). Cellular mechanism of neuronal synchronization in epilepsy. *Science*, *216*(4547), 745–747.

Tsanov, M. (2017). Speed and oscillations: Medial septum integration of attention and navigation. *Frontiers in Systems Neuroscience*, *11*, 67.

Tsao, D. Y., Freiwald, W. A., Tootell, R. B., & Livingstone, M. S. (2006). A cortical region consisting entirely of face-selective cells. *Science*, *311*(5761), 670–674.

Tse, D., Langston, R. F., Kakeyama, M., Bethus, I., Spooner, P. A., Wood, E. R., … Morris, R. G. (2007). Schemas and memory consolidation. *Science*, *316*(5821), 76–82.

Tse, D., Takeuchi, T., Kakeyama, M., Kajii, Y., Okuno, H., Tohyama, C., … Morris, R. G. (2011). Schema-dependent gene activation and memory encoding in neocortex. *Science*, *333*(6044), 891–895.

Tulving, E. (1983). *Elements of episodic memory* (Vol. xi, p. 351). Oxford Oxfordshire New York: Clarendon Press; Oxford University Press.

Tulving, E. (2002). Episodic memory: From mind to brain. *Annual Review of Psychology*, *53*, 1–25.

Tulving, E., Donaldson, W., Bower, G. H., & United States. Office of Naval Research. (1972). *Organization of memory* (Vol. xiii, p. 423). New York: Academic Press.

Tulving, E., & Markowitsch, H. J. (1998). Episodic and declarative memory: Role of the hippocampus. *Hippocampus*, *8*(3), 198–204.

Ulanovsky, N., & Moss, C. F. (2007). Hippocampal cellular and network activity in freely moving echolocating bats. *Nature Neuroscience*, *10*(2), 224–233.

Valero, M., Cid, E., Averkin, R. G., Aguilar, J., Sanchez-Aguilera, A., Viney, T. J., … de la Prida, L. M. (2015). Determinants of different deep and superficial CA1 pyramidal cell dynamics during sharp-wave ripples. *Nature Neuroscience*, *18*(9), 1281–1290.

van de Ven, G. M., Trouche, S., McNamara, C. G., Allen, K., & Dupret, D. (2016). Hippocampal offline reactivation consolidates recently formed cell assembly patterns during Sharp wave-ripples. *Neuron*, *92*(5), 968–974.

van Kerkoerle, T., Self, M. W., & Roelfsema, P. R. (2017). Layer-specificity in the effects of attention and working memory on activity in primary visual cortex. *Nature Communications*, *8*, 13804.

van Strien, N. M., Cappaert, N. L., & Witter, M. P. (2009). The anatomy of memory: An interactive overview of the parahippocampal-hippocampal network. *Nature Reviews. Neuroscience*, *10*(4), 272–282.

Vandecasteele, M., Varga, V., Berenyi, A., Papp, E., Bartho, P., Venance, L., … Buzsaki, G. (2014). Optogenetic activation of septal cholinergic neurons suppresses sharp wave ripples and enhances theta oscillations in the hippocampus. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(37), 13535–13540.

Vanderwolf, C. (1983). The role of the cerebral cortex and ascending activating systems in the control of behavior. In *Motivation* (pp. 67–104). Boston, MA: Springer.

Vanderwolf, C., & Heron, W. (1964). Electroencephalographic waves with voluntary movement: Study in the rat. *Archives of Neurology*, *11*(4), 379–384.

Vanderwolf, C. H. (1969). Hippocampal electrical activity and voluntary movement in the rat. *Electroencephalography and Clinical Neurophysiology*, *26*(4), 407–418.

Vanderwolf, C. H. (1971). Limbic-diencephalic mechanisms of voluntary movement. *Psychological Review*, *78*(2), 83–113.

Vanderwolf, C. H. (2001). The hippocampus as an olfacto-motor mechanism: Were the classical anatomists right after all? *Behavioural Brain Research*, *127*(1–2), 25–47.

Vargha-Khadem, F., Gadian, D. G., Watkins, K. E., Connelly, A., Van Paesschen, W., & Mishkin, M. (1997). Differential effects of early hippocampal pathology on episodic and semantic memory [published erratum appears in science 1997 Aug 22; 277(5329):1117]. *Science*, *277* (5324), 376–380.

Vazdarjanova, A., & Guzowski, J. F. (2004). Differences in hippocampal neuronal population responses to modifications of an environmental context: Evidence for distinct, yet complementary, functions of CA3 and CA1 ensembles. *The Journal of Neuroscience*, *24*(29), 6489–6496.

Vinck, M., Batista-Brito, R., Knoblich, U., & Cardin, J. A. (2015). Arousal and locomotion make distinct contributions to cortical activity patterns and visual encoding. *Neuron*, *86*(3), 740–754.

Von Der Malsburg, C. (1994). The correlation theory of brain function. In *Models of Neural Networks* (pp. 95–119). New York: Springer.

Vyazovskiy, V. V., Olcese, U., Hanlon, E. C., Nir, Y., Cirelli, C., & Tononi, G. (2011). Local sleep in awake rats. *Nature*, *472*(7344), 443–447.

Wagemans, J., Elder, J. H., Kubovy, M., Palmer, S. E., Peterson, M. A., Singh, M., & von der Heydt, R. (2012). A century of gestalt psychology in visual perception: I. Perceptual grouping and figure-ground organization. *Psychological Bulletin*, *138*(6), 1172–1217.

Wallace, D. G., Hamilton, D. A., & Whishaw, I. Q. (2006). Movement characteristics support a role for dead reckoning in organizing exploratory behavior. *Animal Cognition*, *9*(3), 219–228.

Wallace, D. G., Hines, D. J., & Whishaw, I. Q. (2002). Quantification of a single exploratory trip reveals hippocampal formation mediated dead reckoning. *Journal of Neuroscience Methods*, *113*(2), 131–145.

Wallace, D. G., & Whishaw, I. Q. (2003). NMDA lesions of Ammon's horn and the dentate gyrus disrupt the direct and temporally paced homing displayed by rats exploring a novel environment: Evidence for a role of the hippocampus in dead reckoning. *The European Journal of Neuroscience*, *18*(3), 513–523.

Wallenstein, G. V., Eichenbaum, H., & Hasselmo, M. E. (1998). The hippocampus as an associator of discontiguous events. *Trends in Neuroscience*, *21*(8), 317–323.

Wang, D. V., Yau, H. J., Broker, C. J., Tsou, J. H., Bonci, A., & Ikemoto, S. (2015). Mesopontine median raphe regulates hippocampal ripple oscillation and memory consolidation. *Nature Neuroscience*, *18*(5), 728–735.

Wang, G. W., & Cai, J. X. (2006). Disconnection of the hippocampal-prefrontal cortical circuits impairs spatial working memory performance in rats. *Behavioural Brain Research*, *175*(2), 329–336.

Wang, S. H., & Morris, R. G. (2010). Hippocampal-neocortical interactions in memory formation, consolidation, and reconsolidation. *Annual Review of Psychology*, *61*(49–79), C1–C4.

Wang, X. J. (2001). Synaptic reverberation underlying mnemonic persistent activity. *Trends in Neurosciences*, *24*(8), 455–463.

Wang, X. J. (2005). Discovering spatial working memory fields in prefrontal cortex. *Journal of Neurophysiology*, *93*(6), 3027–3028.

Wang, X. J. (2008). Decision making in recurrent neuronal circuits. *Neuron*, *60*(2), 215–234.

Wang, Y., Romani, S., Lustig, B., Leonardo, A., & Pastalkova, E. (2015). Theta sequences are essential for internally generated hippocampal firing fields. *Nature Neuroscience*, *18*(2), 282–288.

Wang, Y., Roth, Z., & Pastalkova, E. (2016). Synchronized excitability in a network enables generation of internal neuronal sequences. *eLife*, *5*, e20697.

Watrous, A. J., Lee, D. J., Izadi, A., Gurkoff, G. G., Shahlaie, K., & Ekstrom, A. D. (2013). A comparative study of human and rat hippocampal low-frequency oscillations during spatial navigation. *Hippocampus*, *23*(8), 656–661.

Watson, B. O., Levenstein, D., Greene, J. P., Gelinas, J. N., & Buzsaki, G. (2016). Network homeostasis and state dynamics of neocortical sleep. *Neuron*, *90*(4), 839–852.

Wheeler, M. A., Stuss, D. T., & Tulving, E. (1997). Toward a theory of episodic memory: The frontal lobes and autonoetic consciousness. *Psychological Bulletin*, *121*(3), 331–354.

Whishaw, I. Q., Hines, D. J., & Wallace, D. G. (2001). Dead reckoning (path integration) requires the hippocampal formation: Evidence from spontaneous exploration and spatial learning tasks in light (allothetic) and dark (idiothetic) tests. *Behavioural Brain Research*, *127*(1–2), 49–69.

Whishaw, I. Q., & Kolb, B. (2005). *The behavior of the laboratory rat: A handbook with tests*. Oxford: Oxford University Press.

Whishaw, I. Q., & Vanderwolf, C. H. (1973). Hippocampal EEG and behavior: Changes in amplitude and frequency of RSA (theta rhythm) associated with spontaneous and learned movement patterns in rats and cats. *Behavioral Biology*, *8*(4), 461–484.

Wiener, S. I., & Korshunov, V. A. (1995). Place-independent behavioural correlates of hippocampal neurones in rats. *Neuroreport*, *7*(1), 183–188.

Wierzynski, C. M., Lubenov, E. V., Gu, M., & Siapas, A. G. (2009). State-dependent spike-timing relationships between hippocampal and prefrontal circuits during sleep. *Neuron*, *61*(4), 587–596.

Wikenheiser, A. M., & Redish, A. D. (2013). The balance of forward and backward hippocampal sequences shifts across behavioral states. *Hippocampus*, *23*(1), 22–29.

Wikenheiser, A. M., & Redish, A. D. (2014). Decoding the cognitive map: Ensemble hippocampal sequences and decision making. *Current Opinion in Neurobiology*, *32C*, 8–15.

Wikenheiser, A. M., & Redish, A. D. (2015a). Hippocampal theta sequences reflect current goals. *Nature Neuroscience*, *18*, 289–294.

Wikenheiser, A. M., & Redish, A. D. (2015b). Hippocampal theta sequences reflect current goals. *Nature Neuroscience*, *18*(2), 289–294.

Williamson, R. S., Hancock, K. E., Shinn-Cunningham, B. G., & Polley, D. B. (2015). Locomotion and task demands differentially modulate thalamic audiovisual processing during active search. *Current Biology*, *25*(14), 1885–1891.

Wills, T. J., Lever, C., Cacucci, F., Burgess, N., & O'Keefe, J. (2005). Attractor dynamics in the hippocampal representation of the local environment. *Science*, *308*(5723), 873–876.

Wilson, M. (2002). Six views of embodied cognition. *Psychonomic Bulletin & Review*, *9*(4), 625–636.

Wilson, M. A., & McNaughton, B. L. (1993). Dynamics of the hippocampal ensemble code for space. *Science*, *261*(5124), 1055–1058.

Wilson, M. A., & McNaughton, B. L. (1994). Reactivation of hippocampal ensemble memories during sleep. *Science*, *265*(5172), 676–679.

Winson, J. (1978). Loss of hippocampal theta rhythm results in spatial memory deficit in the rat. *Science*, *201*(4351), 160–163.

Wintzer, M. E., Boehringer, R., Polygalov, D., & McHugh, T. J. (2014). The hippocampal CA2 ensemble is sensitive to contextual change. *The Journal of Neuroscience*, *34*(8), 3056–3066.

Witter, M. P., & Amaral, D. G. (2004). Hippocampal formation. In G. Paxinos (Ed.), *The rat nervous system* (pp. 635–704). San Diego, CA: Elsevier Academic Press.

Wolpert, D. M., Ghahramani, Z., & Jordan, M. I. (1995). An internal model for sensorimotor integration. *Science*, *269*(5232), 1880–1882.

Wong, R. K., & Traub, R. D. (1983). Synchronized burst discharge in disinhibited hippocampal slice. I. Initiation in CA2-CA3 region. *Journal of Neurophysiology*, *49*(2), 442–458.

Wood, E. R., Dudchenko, P. A., & Eichenbaum, H. (1999). The global record of memory in hippocampal neuronal activity. *Nature*, *397*(6720), 613–616.

Wood, E. R., Dudchenko, P. A., Robitsek, R. J., & Eichenbaum, H. (2000). Hippocampal neurons encode information about different types of memory episodes occurring in the same location. *Neuron*, *27*(3), 623–633.

Wu, C. T., Haggerty, D., Kemere, C., & Ji, D. (2017). Hippocampal awake replay in fear memory retrieval. *Nature Neuroscience*, *20*(4), 571–580.

Wu, X., & Foster, D. J. (2014). Hippocampal replay captures the unique topological structure of a novel environment. *The Journal of Neuroscience*, *34*(19), 6459–6469.

Wurtz, R. H., Joiner, W. M., & Berman, R. A. (2011). Neuronal mechanisms for visual stability: Progress and problems. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *366*(1564), 492–503.

Xu, C., Krabbe, S., Grundemann, J., Botta, P., Fadok, J. P., Osakada, F., … Lüthi, A. (2016). Distinct hippocampal pathways mediate dissociable roles of context in memory retrieval. *Cell*, *167*(4), 961–972.e16.

Xu, S., Jiang, W., Poo, M. M., & Dan, Y. (2012). Activity recall in a visual cortical ensemble. *Nature Neuroscience*, *15*(3), 449–455 S1-2.

Yartsev, M. M. (2017). The emperor's new wardrobe: Rebalancing diversity of animal models in neuroscience research. *Science*, *358*(6362), 466–469.

Yartsev, M. M., & Ulanovsky, N. (2013). Representation of three-dimensional space in the hippocampus of flying bats. *Science*, *340* (6130), 367–372.

Yartsev, M. M., Witter, M. P., & Ulanovsky, N. (2011). Grid cells without theta oscillations in the entorhinal cortex of bats. *Nature*, *479*(7371), 103–107.

Ylinen, A., Bragin, A., Nadasdy, Z., Jando, G., Szabo, I., Sik, A., & Buzsaki, G. (1995). Sharp wave-associated high-frequency oscillation (200 Hz) in the intact hippocampus: Network and intracellular mechanisms. *The Journal of Neuroscience*, *15*(1 Pt 1), 30–46.

Yu, J. Y., Kay, K., Liu, D. F., Grossrubatscher, I., Loback, A., Sosa, M., … Frank, L. M. (2017). Distinct hippocampal-cortical memory representations for experiences associated with movement versus immobility. *eLife*, *6*.

Yuste, R. (2015). From the neuron doctrine to neural networks. *Nature Reviews. Neuroscience*, *16*(8), 487–497.

Zagha, E., Casale, A. E., Sachdev, R. N., McGinley, M. J., & McCormick, D. A. (2013). Motor cortex feedback influences sensory processing by modulating network state. *Neuron*, *79*(3), 567–578.

Zagha, E., & McCormick, D. A. (2014). Neural control of brain state. *Current Opinion in Neurobiology*, *29*, 178–186.

Zeithamova, D., Dominick, A. L., & Preston, A. R. (2012). Hippocampal and ventral medial prefrontal activation during retrieval-mediated learning supports novel inference. *Neuron*, *75*(1), 168–179.

Zeithamova, D., Schlichting, M., & Preston, A. (2012). The hippocampus and inferential reasoning: Building memories to navigate future decisions. *Frontiers in Human Neuroscience*, *6*(70).

Zhang, K., Ginzburg, I., McNaughton, B. L., & Sejnowski, T. J. (1998). Interpreting neuronal population activity by reconstruction: Unified framework with application to hippocampal place cells. *Journal of Neurophysiology*, *79*(2), 1017–1044.

Zhao, M., Choi, Y. S., Obrietan, K., & Dudek, S. M. (2007). Synaptic plasticity (and the lack thereof) in hippocampal CA2 neurons. *The Journal of Neuroscience*, *27*(44), 12025–12032.

Zhao, W. J., Kremkow, J., & Poulet, J. F. (2016). Translaminar cortical membrane potential synchrony in behaving mice. *Cell Reports*, *15*(11), 2387–2399.

Zheng, C., Bieri, K. W., Hsiao, Y. T., & Colgin, L. L. (2016). Spatial sequence coding differs during slow and fast gamma rhythms in the Hippocampus. *Neuron*, *89*(2), 398–408.

Zheng, C., Bieri, K. W., Trettel, S. G., & Colgin, L. L. (2015). The relationship between gamma frequency and running speed differs for slow and fast gamma rhythms in freely behaving rats. *Hippocampus*, *25*, 924–938.

Zhou, M., Liang, F., Xiong, X. R., Li, L., Li, H., Xiao, Z., … Zhang, L. I. (2014). Scaling down of balanced excitation and inhibition by active behavioral states in auditory cortex. *Nature Neuroscience*, *17*(6), 841–850.

Zhuang, J., Bereshpolova, Y., Stoelzel, C. R., Huff, J. M., Hei, X., Alonso, J. M., & Swadlow, H. A. (2014). Brain state effects on layer 4 of the awake visual cortex. *The Journal of Neuroscience*, *34*(11), 3888–3900.

Ziv, Y., Burns, L. D., Cocker, E. D., Hamel, E. O., Ghosh, K. K., Kitch, L. J., … Schnitzer, M. J. (2013). Long-term dynamics of CA1 hippocampal place codes. *Nature Neuroscience*, *16*(3), 264–266.

Zugaro, M. B., Arleo, A., Berthoz, A., & Wiener, S. I. (2003). Rapid spatial reorientation and head direction cells. *The Journal of Neuroscience*, *23* (8), 3478–3482.

Zylberberg, J., & Strowbridge, B. W. (2017). Mechanisms of persistent activity in cortical circuits: Possible neural substrates for working memory. *Annual Review of Neuroscience*, *40*, 603–627.

How to cite this article: Kay K, Frank LM. Three brain states in the hippocampus and cortex. *Hippocampus*. 2019;29: 184–238. https://doi.org/10.1002/hipo.22956