

The Role of Hierarchical Dynamical Functions in Coding for Episodic Memory and Cognition

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Abstract

Behavioral research in human verbal memory function led to the initial definition of episodic memory and semantic memory. A complete model of the neural mechanisms of episodic memory must include the capacity to encode and mentally reconstruct everything that humans can recall from their experience. This article proposes new model features necessary to address the complexity of episodic memory encoding and recall in the context of broader cognition and the functional properties of neurons that could contribute to this broader scope of memory. Many episodic memory models represent individual snapshots of the world with a sequence of vectors, but a full model must represent complex functions encoding and retrieving the relations between multiple stimulus features across

space and time on multiple hierarchical scales. Episodic memory involves not only the space and time of an agent experiencing events within an episode but also features shown in neurophysiological data such as coding of speed, direction, boundaries, and objects. Episodic memory includes not only a spatio-temporal trajectory of a single agent but also segments of spatio-temporal trajectories for other agents and objects encountered in the environment consistent with data on encoding the position and angle of sensory features of objects and boundaries. We will discuss potential interactions of episodic memory circuits in the hippocampus and entorhinal cortex with distributed neocortical circuits that must represent all features of human cognition. ■

INTRODUCTION

Challenges for Episodic Memory Models

The challenge for episodic memory models is understanding how neural circuits could encode and retrieve the complex range of features that a human can recall from episodic memory of individual experiences. A complete model of episodic memory will require understanding of not only the neural mechanisms for encoding and retrieval in regions directly implicated in episodic memory such as the hippocampus and entorhinal cortex but also the interaction of regions coding episodic memory with higher cognitive function throughout distributed regions of the neocortex (Bhandari & Badre, 2018; Hasselmo & Stern, 2018; Lundqvist, Herman, Warden, Brincat, & Miller, 2018).

Episodic memory was first defined by Tulving (1972) to focus on the difference between the encoding and recollection of a specific sensory experience at a specific place and time versus the encoding and retrieval of facts in general knowledge, which was addressed by the term

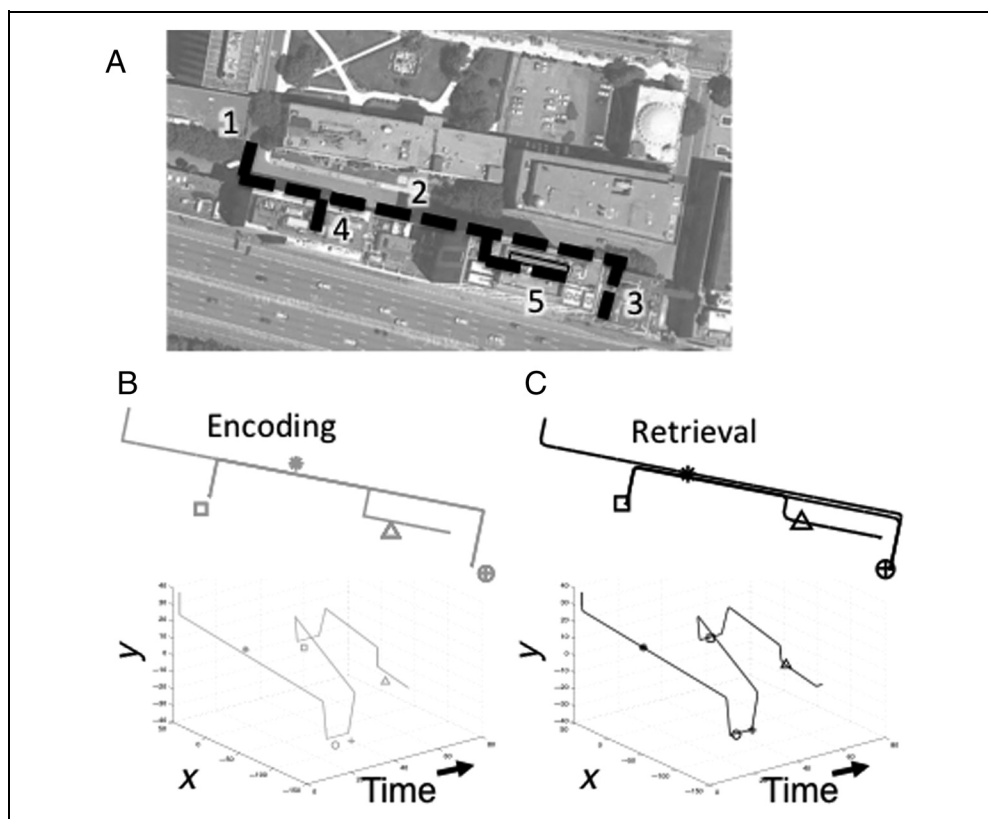
“semantic memory” (Baddeley, 2001; Tulving, 1984, 2001). The term “semantic memory” had been developed by Quillian (Collins & Quillian, 1969) as a description of memory for facts and general knowledge about the world. Episodic memory was later contrasted with other forms of memory such as knowing how to do things, referred to as procedural or implicit memory (Cohen & Eichenbaum, 1993; Cohen & Squire, 1980), and with the active, conscious maintenance of recent information, known as working memory (Baddeley, 2001). Despite being contrasted with semantic memory, a model of episodic memory must ultimately include its interaction with elements of semantic memory. When we remember throwing a ball to a dog, we code many features of the episodic memory in terms of general knowledge of the rules governing the interaction with both objects and agents (Buschman & Miller, 2014; Badre & Frank, 2012). In fact, human episodic memory does not accurately retrieve most details of episodes (Misra, Marconi, Peterson, & Kreiman, 2018), but instead, we reconstruct much of the world from general semantic knowledge.

Here, we address some of the challenges for a complete model of episodic memory within the framework of an earlier model (Hasselmo, 2009, 2012; Hasselmo, Giacomo, Brandon, & Yoshida, 2010). This earlier model addressed how neural mechanisms for coding of grid cells in entorhinal cortex could provide the coding of the spatial location and time of events within an episode, linking

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Boston University

Figure 1. (A) Example of a model of an individual episodic memory encoded and retrieved as a spatio-temporal trajectory (dotted black line) of a person moving through the Boston University campus, including encounters with people at different positions. (B) The encoded trajectory is shown in gray, with people encountered at different positions (asterisk, circle, square). (C) The retrieval of the spatio-temporal trajectory by the model is shown in black, with shapes indicating the accurate retrieval of individual people encountered at their proper positions.



individual events and items with neural representations of spatio-temporal trajectories (see Figure 1). This framework describes the neural encoding of all features of episodic memory in terms of multiple spatio-temporal functions corresponding not only to the movement of an agent within a scene but also to the regular features of objects and barriers in the environment as well as the movement of other agents and objects (Hasselmo et al., 2010). A recent extension of this framework proposes that dynamical gating matrices represented and regulated by neural activity (Hasselmo, 2018) can mediate encoding and retrieval of the spatio-temporal functions with the capacity for interpolation or extrapolation of complex functions. This could involve creation of dynamical matrices within structures such as the hippocampus, entorhinal cortex, and retrosplenial cortex.

As an example, Figure 2 shows how sampling of specific points on a trajectory (asterisks) allows computational creation of a dynamical matrix and starting state vector representing properties such as location, velocity, and acceleration. The dynamical matrix and initial state vector can be represented by patterns of neural activity, and Figure 2 shows how a dynamical matrix and state vector can encode and retrieve the spatio-temporal trajectory of an object (Hasselmo, 2018). Retrieval of the full trajectory can be generated by sequential multiplication of the initial state vector by the dynamical matrix (Hasselmo, 2018). More complex trajectories can be encoded by higher level dynamical matrices resetting the component

elements of lower level dynamical matrices, to allow transitions between different trajectory segments. This direct influence of higher matrices on the elements of lower level matrices is an important part of the framework. The encoding of spatio-temporal trajectories by dynamical matrices can facilitate the subsequent retrieval of the memories through reactivation of these functions. The coding of

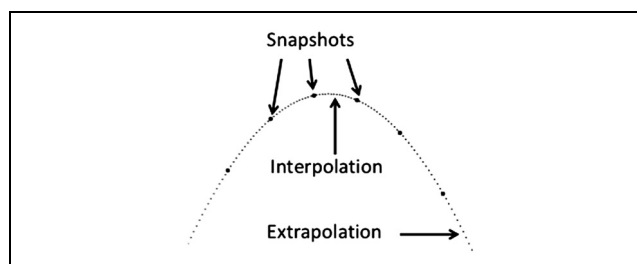


Figure 2. Interpolation and extrapolation of a trajectory. The parabolic trajectory of a thrown ball could be encoded as a series of six snapshots of the trajectory, with coding of the location and velocity of the ball at each position (shown with large black circles). However, this snapshots coding does not contain information about the dynamics of the ball. In contrast, the same number of elements of encoded information can be used to encode and retrieve the starting position and velocity and the dynamical matrix that describes the full trajectory, allowing accurate recall of the trajectory (gray dots) that interpolates between positions along the trajectory (including between snapshots) and also extrapolation of the trajectory beyond the last snapshots. This is a much more efficient representation than the snapshots.

multiple spatio-temporal functions moves beyond the coding used in many models in which episodic memories are represented as arrays of feature vectors (Norman & O'Reilly, 2003; Hasselmo & Wyble, 1997; Treves & Rolls, 1994; McNaughton & Morris, 1987).

This framework addresses the problem that a complete theory of episodic memory function must account for the encoding and retrieval of all aspects of mental experience, including not only the overall spatial location and time of an event but also the detailed sensory features of individual objects and agents within that event, including their location and time of appearance, as described previously (Hasselmo et al., 2010), as well as their direction of movement, their speed of movement, the configuration of component features (Hasselmo et al., 2010), and semantic knowledge about these objects and agents. Episodic memory also includes encoding and retrieval of memory for internal thoughts, motivations, and intentions of an individual agent and their conjectures about the thoughts and intentions of other agents. Thus, a complete neural model of episodic memory requires a general neural code for representing all aspects of human cognition that ultimately includes all dimensions of cognition and rule learning that contribute to the experiences that can be retrieved from episodic memory.

Tulving defined a query for episodic memory as “What did you do at time T in place P?” (Tulving, 1984) and also described retrieval as the mental voyage from the current time to the past episode being remembered, but he did not focus on time within the past episode or independent coding of the evolution of different features. Tulving (1984) states that his model “describes a ‘snapshot view’ of episodic memory [that] produces many snapshots whose orderly succession can create the mnemonic illusion of the flow of past time.”

The framework presented here seeks to use neural encoding and retrieval of spatio-temporal trajectories to move beyond the focus on snapshots in Tulving’s model. This focus on single snapshots is also characteristic of many neural network models that code the full viewpoint of the world as a static vector at one point in time. In contrast, the framework of episodic memory reviewed here uses models (Hasselmo, 2009, 2012; Hasselmo et al., 2010) that include encoding and retrieval of features such as speed and direction of movement on multiple different time scales. Rather than representing discrete snapshots of time, this framework represents the velocity vectors of individual agents within an episode, so that their position could be computed at different spatial and temporal scales (rather than a single frame rate). The use of velocity vectors allows continuous motion to be interpolated or extrapolated beyond individual snapshots (Figure 2) and can include encoding and retrieval of factors such as head direction and the speed and direction of movements. Consistent with this, other researchers have shown that episodic memories involve

encoding and retrieval of a perspective, either consisting of the point of view of the person retrieving the memory (a “field” perspective) or a third-person observer perspective (Conway, 2009; Robinson & Swanson, 1993; Nigro & Neisser, 1983). The description below will show how this property of episodic memory could arise from the functional role of neurons that respond on the basis of current head direction and code the position of barriers or spatial viewpoints.

A complete neural theory of episodic memory must address circuit mechanisms that could encode and retrieve the location and time of events and features on multiple scales (Howard, MacDonald, et al., 2014; Howard, Fotedar, Datey, & Hasselmo, 2004; Howard & Kahana, 2002). Episodic memories can include not only the encoding and retrieval of the place and time of an event (when John gave Mary a book) but also the location and movement of agents and objects within that event (standing by the bookshelf, John gave Mary a book that she set on the table) and the location and movement of features within individual agents and objects (the book was open in John’s right hand, and Mary closed it with the index finger of her left hand). This framework contrasts with many existing neural network models of brain function that summarize views of the world as single snapshots that are coded in large-scale vectors and processed in a feedforward manner (LeCun, Bengio, & Hinton, 2015). A complete model will require representing, interpolating, and extrapolating complex relationships between stimulus features in multiple different scales of space and time.

Episodic Memory as a Spatio-temporal Trajectory

As shown in Figure 1, many episodic memories involve encoding and retrieval of segments of continuous spatio-temporal trajectories. An example spatio-temporal trajectory is shown with lines in the figure. The trajectory includes the agent’s sense of relative location but also contains a point of view from a specific direction at each moment, and aspects of the timing of the trajectory, such as the speed of walking, and the relative timing of events at one location. Different positions along this spatio-temporal trajectory are associated with individual events involving interacting with specific people or objects.

As noted in a previous article (Hasselmo et al., 2010), this same framework could be used to encode and retrieve information on different scales for episodic memory. For example, that article notes that the appearance of each individual person or object in the episode would be associated with separate encoding of the locations and spatio-temporal trajectory of the people or objects for possible subsequent retrieval. This encoding can take place on multiple scales for both trajectory encoding and object encoding. Multiple scales of grid cell coding have been shown to be effective for encoding and

retrieval of trajectories in episodic memory (Hasselmo, 2009, 2012; Hasselmo et al., 2010) and the planning of future trajectories (Erdem & Hasselmo, 2012, 2014). Encoding can also address different object scales. Instead of encoding and retrieving only the spatio-temporal trajectory of one person, episodic memory could encode and retrieve the position of limbs on different humans or animals and the movement of these limbs to different locations. On an even smaller scale, this framework could be used to encode and retrieve the position and movement of fingers within a hand or the position and movement of eyelids and lips within a face. The accurate encoding of spatio-temporal trajectories could potentially provide a general framework for encoding and retrieval of both episodic and semantic memory on multiple different scales.

The coding of spatio-temporal trajectories was previously described in terms of coding of speed and direction at each position along a trajectory (Hasselmo, 2009, 2012; Hasselmo et al., 2010). However, extension of this work models how trajectories can also be coded in terms of complex functions such as linear dynamical systems that include both velocity and acceleration (Hasselmo, 2018) or representations such as Bezier functions, which would allow a potentially more concise representation of significant segments of a trajectory (Hasselmo, 2018). For example, as shown in Figure 2, the trajectory of a projectile such as a ball thrown through the air can be encoded and retrieved as a small dynamical matrix and initial state vector representing the full trajectory of the dynamical system rather than coding individual snapshots of the position of the ball along the trajectory.

As described previously (Hasselmo, 2018), the dynamical matrix could consist of patterns of activity in another population that interacts in a multiplicative manner on the dendritic tree. This dynamical system provides a highly accurate method for retrieval (gray dots in Figure 2) to interpolate between remembered positions or extrapolate beyond the last remembered position by replicating the application of the dynamical relationship to compute different points along the trajectory. This framework for coding of relations by complex functions could be used to code the complex relations necessary for performance of complex cognitive tasks such as Raven's progressive matrices (Hasselmo, 2018), which represents a test of general intelligence (Barrett, Hill, Santoro, Morcos, & Lillicrap, 2018; Raudies & Hasselmo, 2017; Rasmussen & Eliasmith, 2011; Carpenter, Just, & Shell, 1990).

The same technique for coding the transformation between adjacent points on a trajectory could be used for coding the uniform transformation of many points in space, for example, because of rotation of an object or an agent. If this transformation is coded as a pattern of gating activity in the network (Hasselmo, 2018), then the activity pattern replicating the transformation could then be replicated to generalize the transformation across different features. In this framework, relatively

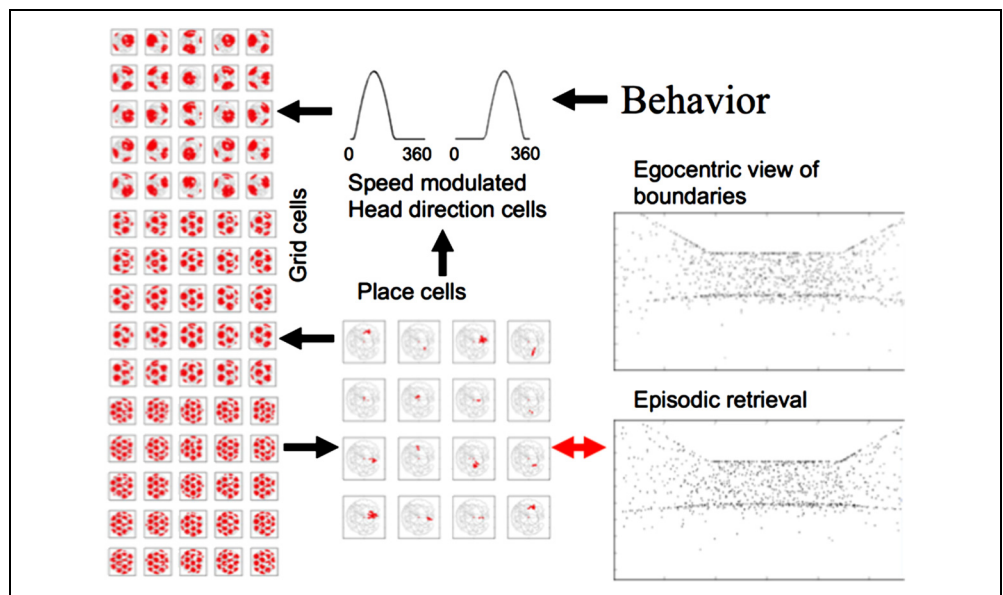
small transformation matrices could be used to compute the viewpoint of the world at any position along a trajectory. This would provide a much more efficient mechanism for encoding and retrieval of episodic memory (Hasselmo, 2018). Rather than storing a snapshot of every spatial view of the world for an agent moving around a room for several hours, instead the system can store the allocentric location and direction of the features of the room, and encode and retrieve the allocentric location and direction of a person's trajectory, and the egocentric angle of different visual features can be extracted and retrieved from the transformation of location and direction anywhere along the trajectory, as shown in Figure 3. This framework is similar to the index theory of hippocampal function presented previously (Teyler & Rudy, 2007; Teyler & DiScenna, 1986) but provides an explicit mathematical representation of how episodic memory can link to a concise semantic memory representation of functions that allows interpolation and extrapolation of more complex details of a memory in neocortical circuits.

Lesion and Imaging Data on Anatomical Circuits for Episodic Memory

Neuropsychological and fMRI studies demonstrate an important role for the hippocampus and associated structures in episodic memory. Bilateral removal of anterior hippocampus, entorhinal cortex, and parahippocampal gyrus in patient H. M. caused striking deficits for episodic memory tests (Corkin, 1984; Scoville & Milner, 1957) but sparing of working memory (Scoville & Milner, 1957). Neurophysiological data described below demonstrate that the patterns of neuronal activity in the hippocampus and entorhinal cortex are associated with encoding and retrieval of episodic memories in human participants (Rutishauser, Schuman, & Mamelak, 2008; Kreiman, 2007; Kreiman, Koch, & Fried, 2000a) and with retrieval or planning of spatio-temporal trajectories during behavioral tasks in rodents (Pfeiffer & Foster, 2013; Johnson & Redish, 2007).

Episodic memory impairments can also be caused by damage to subcortical regions including the anterior thalamus and mammillary bodies (Vann & Aggleton, 2004) and by damage to the medial septum and medial pFC caused by aneurysms of the anterior communicating artery (DeLuca, 1993; DeLuca & Cicerone, 1991). Subcortical structures contain neurons coding aspects of behavior such as head direction in the anterior thalamus (Stackman & Taube, 1998; Taube, 1995) and movement direction in the medial septum (Welday, Shlifer, Bloom, Zhang, & Blair, 2011). The medial septum and anterior thalamus also influence theta rhythm dynamics in cortical circuits that could be essential to a temporal code for episodic memory (Buzsáki, 2002; Bland &

Figure 3. Episodic memory of spatial views can involve encoding and retrieval of associations of individual spatial locations with the viewpoint from different spatial locations. In this example, the spatio-temporal trajectory is encoded and retrieved by the interaction of speed coding and direction coding that drives the firing of grid cells. The grid cells can update the firing of place cells that are associated with individual spatial views. Alternately, the individual spatial views can update the firing of place cells that drive grid cells. Hebbian modification (bidirectional red arrow) allows encoding (top) and retrieval (bottom) of associations of each place cell with a distinct spatial view, which can be represented by a single relational code of features in the environment so that neurons responding to the individual position and direction on a trajectory can encode associations that allow retrieval of the visual feature angle of specific objects in the visual environment.



Colom, 1993; Stewart & Fox, 1990; Buzsáki, Leung, & Vanderwolf, 1983).

Studies in animals demonstrate the role of the hippocampus and associated cortical regions and connections via the fornix with the medial septum and anterior thalamus. Nonhuman primates show permanent impairments of memory for trial unique objects in delayed nonmatch to sample tasks after hippocampal lesions (Zola-Morgan & Squire, 1986), and combined hippocampal, perirhinal, and parahippocampal lesions (Meunier, Bachevalier, Mishkin, & Murray, 1993; Zola-Morgan, Squire, Clower, & Rempel, 1993) and transient impairments after entorhinal lesions (Leonard, Amaral, Squire, & Zola-Morgan, 1995; Gaffan & Murray, 1992). Lesions of the fornix, which disrupt medial septum input and anterior thalamic output for the hippocampus, impair the construction of a snapshot memory for spatial location of visual features (Gaffan & Harrison, 1989) or associations with responses (Gaffan et al., 1984).

Similarly, studies in rodents showed impairments in delayed alternation caused by hippocampal lesions (Ainge, van der Meer, Langston, & Wood, 2007) or lesions of the fornix or the septum (Ennaceur, Neave, & Aggleton, 1996; Aggleton, Neave, Nagle, & Hunt, 1995; Freeman & Stanton, 1991; Stanton, Thomas, & Brito, 1984). An increase in the number of repeat visits to arms in the eight-arm radial maze occurs with hippocampal lesions (Becker, Walker, & Olton, 1980) and fornix lesions (Hudon, Doré, & Goulet, 2002; Olton, Becker, & Handelman, 1979) and by lesions (Mitchell, Rawlins, Steward, & Olton, 1982) or inactivation of the medial septum (Chrobak, Stackman, & Walsh, 1989).

Hippocampal lesions impair finding of a single fixed platform location in the Morris water maze (Morris, Anderson, Lynch, & Baudry, 1986) including in a variant

relevant to episodic memory requiring the rat to retrieve a new platform location on each day (Steele & Morris, 1999). Impairments in the Morris water maze also appear with lesions of the dorsal entorhinal cortex (Steffenach, Witter, Moser, & Moser, 2005), dorsal presubiculum (postsubiculum; Taube, Kesslak, & Cotman, 1992), and fornix (Eichenbaum, Stewart, & Morris, 1990) and also with pharmacological inactivation (Brioni, Decker, Gamboa, Izquierdo, & McGaugh, 1990) or lesions of the medial septum (Marston, Everitt, & Robbins, 1993) that will reduce theta rhythm. Performance in the Morris water maze is also impaired after lesions of the retrosplenial cortex (Czajkowski et al., 2014) and parietal lesions (Hoh, Kolb, Eppel, Vanderwolf, & Cain, 2003).

The involvement of medial temporal lobe structures in encoding and retrieval of episodic memories is consistent with fMRI data from human participants. Human participants show substantial fMRI activation associated with the encoding of new information into episodic memory (Kirchhoff, Wagner, Maril, & Stern, 2000; Wagner et al., 1998; Stern et al., 1996). Consistent with coding of a spatio-temporal trajectory, fMRI data demonstrated hippocampal and parahippocampal activity at the start of a trajectory when a participant retrieves a previously learned overlapping trajectory (Brown & Stern, 2014; Brown, Ross, Keller, Hasselmo, & Stern, 2010). Subsequent work showed that retrieval of a planned trajectory involves reactivation of intermediate locations on the trajectory (Brown et al., 2016). Studies show coding of navigationally relevant information in fMRI activity, with hippocampus coding path length and entorhinal cortex coding the Euclidean distance to the goal (Chrastil, Sherrill, Hasselmo, & Stern, 2015; Howard, Javadi, et al., 2014). Evidence also indicates that the coding of the trajectory and features along the trajectory involve an interaction of regions coding spatial

location and direction (Chrastil, Sherrill, Hasselmo, & Stern, 2016), with regions coding visual cues such as optic flow and feature angle (Chrastil et al., 2015; Sherrill et al., 2015). These fMRI data support the role of large-scale neural activity in these regions for the encoding and retrieval of spatio-temporal trajectories.

Neurophysiological Data on Coding Relevant to Episodic Memory

As noted above, research has not converged on a model for the neural coding of the broad range of events in an episodic memory. The nature of coding depends on the details of neurophysiological interactions within cortical circuits. Here, we will review evidence for functional coding by neurons in the structures implicated in episodic memory, with a focus on the open questions about coding of episodes. Electrophysiological recordings in the human hippocampus, amygdala, and entorhinal cortex demonstrate firing properties consistent with their role in the encoding and retrieval of episodic memories. Unit recordings in these structures show neural responses to highly specific categories of visual stimuli such as faces or animals (Rutishauser et al., 2011; Kreiman, Koch, & Fried, 2000b) and reveal neurons that fire during encoding of stimuli as well as during retrieval by mental imagery (Kreiman et al., 2000a). Neurons in these structures show highly detailed coding of individual identities of famous actors or famous landmarks (Quiroga, Reddy, Kreiman, Koch, & Fried, 2005) and highly selective firing during retrieval as tested by self-report of mental imagery (Ison, Quiroga, & Fried, 2015) and during recognition or recall of stimuli (Rutishauser et al., 2008). Thus, extensive data show clear responses to nonspatial stimuli in humans. In rodents, neurons show a variety of responses to the spatial and temporal dimensions of behavioral tasks but also show responses to nonspatial features such as objects or odors in the environment (Wood, Dudchenko, & Eichenbaum, 1999). Neurons also show responses suggestive of the retrieval of prior experience (Ferbinteanu & Shapiro, 2003) or the planning of future experience (Johnson & Redish, 2007). The following sections provide more details on these properties.

Theta Rhythm and Coding of Episodic Memory

The effects of fornix lesions and medial septum lesions described above highlight the potential role of theta rhythm in coding of episodic memory. These same lesions of medial septum or fornix reduce theta power in the hippocampus (Rawlins, Feldon, & Gray, 1979) and entorhinal cortex (Mitchell et al., 1982). Theta rhythm is a prominent band of rhythmic activity in the range of 6–10 Hz that appears in structures including the hippocampus, entorhinal cortex, and retrosplenial cortex during movement in a range of different species (Buzsáki, 2002; Buzsáki et al., 1983) and shows important

correlations with running speed. Theta rhythm is also associated with gamma frequency oscillations (Colgin et al., 2009; Csicsvari, Hirase, Czurkó, Mamiya, & Buzsáki, 1999; Bragin et al., 1995).

Evidence suggests that the theta rhythm could play an essential role in a temporal code for episodic and semantic memory. There have been general discussions about whether the coding of sensory input involves a code based on mean firing rate versus a temporal code based on the timing of individual spikes. The phenomenon of spiking relative to theta phase provides some of the strongest evidence for a temporal code. The field will benefit from more explicit testing of detailed codes that can address the full complexity of cognitive representations retrieved during episodic memory function.

Lesions of the medial septum cause impairments of memory encoding performance that correlate with the change in theta rhythm (Givens & Olton, 1990, 1994; Winson, 1978), and the successful learning of memory traces is accompanied by increases in theta oscillatory power (Griffin, Asaka, Darling, & Berry, 2004; Seager, Johnson, Chabot, Asaka, & Berry, 2002; Berry & Thompson, 1978). Activation of both GABAergic and cholinergic subpopulations in the medial septum enhances temporal precision of hippocampal spiking activity (Dannenberg et al., 2015), and combined lesions of both GABAergic and cholinergic subpopulations in the medial septum severely impair memory performance (Pang, Nocera, Secor, & Yoder, 2001). Activation of glutamatergic neurons in the medial septum enhances theta rhythmicity in the hippocampus via activation of cholinergic and GABAergic neurons in the medial septum (Robinson et al., 2016). Data from EEG studies indicate that theta oscillations recorded in the medial temporal lobe of human epileptic patients have been shown to increase during memory encoding and during navigation through real-world and virtual environments (Aghajan et al., 2017; Bohbot, Copara, Gotman, & Ekstrom, 2017; Ekstrom et al., 2005; Kahana, Sekuler, Caplan, Kirschen, & Madsen, 1999). Some cells in human hippocampus do not show strong theta rhythmicity in their autocorrelograms (Viskontas, Ekstrom, Wilson, & Fried, 2007), but human hippocampal neurons do show spiking that is specific to the phase of theta rhythm oscillations, and this phase specificity during stimuli predicts the subsequent ability to successfully retrieve those stimuli (Rutishauser, Ross, Mamelak, & Schuman, 2010).

Oscillatory dynamics at theta or gamma frequencies could be essential to the neural coding of episodic information. For example, as described further below, individual neurons in the hippocampus code sequences of positions along a trajectory based on the phase of firing relative to theta rhythm oscillations (O'Keefe & Recce, 1993). This phase code for position has also been demonstrated in the entorhinal cortex (Hafting, Fyhn, Bonnevie, Moser, & Moser, 2008) and the lateral septum, a hippocampal output structure where neurons do not

exhibit spatial receptive fields but instead code position solely via phase (Tingley & Buzsáki, 2018). In addition, phase coding has also been shown for the duration of time within an interval (Pastalkova, Itskov, Amarasingham, & Buzsáki, 2008) and might also exist for coding of the position of an object in a sequence or other dimensions of experience. Thus, theta rhythm might provide a substrate for a phase code of different dimensions of memory and behavior.

Phase coding might also exist for other frequencies. For example, different populations of neurons show spiking at specific phases relative to gamma frequency oscillations (Senior, Huxter, Allen, O'Neill, & Csicsvari, 2008). The duration of each gamma cycle may be too short for coding of spiking on different phases within a gamma cycle, but a binary code could be maintained by different neurons firing at either the peak or trough of individual gamma cycles. For example, firing on the peak could represent a "1" in a binary code, whereas firing on the trough could represent a "0" in a binary code. The updating of this binary code would require relatively complex patterns of synaptic connectivity to ensure that the binary code for individual neuron phase would be updated based on the update of other neuron binary codes.

Alternately, theta rhythm might play a role for the functional dynamics of cortical circuits, setting differences in dynamics for the encoding of new information on one phase of the oscillation, versus the retrieval of information at a different phase of the oscillation (Hasselmo, Bodelón, & Wyble, 2002). This is supported by empirical data on the timing of synaptic modification at different phases of theta rhythm (Hyman, Wyble, Goyal, Rossi, & Hasselmo, 2003; Huerta & Lisman, 1995), data on the effect of phase-specific manipulations that influence encoding or retrieval (Siegle & Wilson, 2014; Douchamps, Jeewajee, Blundell, Burgess, & Lever, 2013), and data on the coordination of activity in different brain regions relative to hippocampal theta (Colgin et al., 2009; Jones & Wilson, 2005; Hyman, Wyble, Rossi, & Hasselmo, 2002).

Other frequencies could be involved in similar regulation of functional gating. Neocortical regions show bursts of activity at beta and gamma frequencies associated with gating of information into working memory or top-down regulation of the flow of information into working memory (Lundqvist et al., 2016, 2018; Buschman, Denovellis, Diogo, Bullock, & Miller, 2012). Simulations have shown how bursts of gamma frequency activity could be involved in maintaining information in working memory (Lundqvist, Herman, & Lansner, 2011; Lundqvist, Compte, & Lansner, 2010; Fransén & Lansner, 1998) and how the network resonance of cortical regions at gamma and beta frequencies could be used to gate the flow of information between different cortical regions (Sherfey, Ardid, Hass, Hasselmo, & Kopell, 2018). Simulations need to explore the broad range of functional episodic memory

mechanisms that could involve network oscillatory dynamics.

Trajectory Retrieval by Place Cells

By Tulving's initial definition, episodic memory requires a code for the spatial location of a memory. As noted above, this could include the overall location of an agent during an event but could also include the location of individual agents and objects within an event or even the location of parts of objects such as a person's hand (Hasselmo et al., 2010). Encoding and retrieval of the spatio-temporal trajectory of an agent could involve neurons in the hippocampus termed "place cells," which show responses dependent on the current, spatial location of a rodent (O'Keefe, 1976; O'Keefe & Dostrovsky, 1971). Virtual navigation studies show selective responses to virtual location by hippocampal neurons in humans (Ekstrom et al., 2003).

Neuronal activity of place cells does not only represent the coding of current position but also demonstrates retrieval or planning of segments of spatio-temporal trajectories. Early studies of place cells focused on a rate code for spatial location (O'Keefe, 1976; O'Keefe & Dostrovsky, 1971), but later studies revealed a striking temporal code in which the finer-grained position of an animal relative to the position along a trajectory through a specific firing field is reflected in a shift from late to early phase of firing of place cells relative to hippocampal theta rhythm oscillations (Skaggs, McNaughton, Wilson, & Barnes, 1996; O'Keefe & Recce, 1993). On a population level, it appears that place cells fire in sequential order within a theta rhythm based on their relative coding of position (Feng, Silva, & Foster, 2015; Foster & Wilson, 2007). In addition, when animals are making a decision about future movement based on memory of the task, experimental data show place cell sequences that appear to be associated with the retrieval of prior trajectories or planning of future trajectories by the animal (Ólafsdóttir, Barry, Saleem, Hassabis, & Spiers, 2015; Pfeiffer & Foster, 2013; Johnson & Redish, 2007). Sequential firing of place cells within a theta cycle has been found to reflect future trajectories to a goal location providing one possible neural mechanism for prospective planning (Wikenheiser & Redish, 2015).

These studies provide the evidence of specific retrieval activity that could be linked to episodic memory. Related to this, neurons have also been shown to fire selectively for specific left or right trajectories in continuous spatial alternation tasks (Frank, Brown, & Wilson, 2000; Wood, Dudchenko, Robitsek, & Eichenbaum, 2000) and in a delayed nonmatch to position task (Griffin, Eichenbaum, & Hasselmo, 2007), suggesting that they may depend on the retrieval of prior trajectories or planning of future trajectories (Hasselmo & Eichenbaum, 2005). Recordings on a plus-shaped maze with different future or past arms show that some neurons selectively respond based on the prior segment of the trajectory, whereas others show selectivity for the future segment of a trajectory (Ferbinteanu &

Shapiro, 2003). Surprisingly, neurons did not show trajectory specificity in the delayed version of the spatial alternation task possibly because of difficulty in determining the time of retrieval (Ainge et al., 2007).

Thus, evidence supports the encoding and retrieval of trajectories through of a series of spatial locations by the firing rate and firing phase of place cells. However, the mechanism by which the coding of place arises is still uncertain. Neurons show changes in response to the running speed and direction (Terrazas et al., 2005; Gothard, Skaggs, Moore, & McNaughton, 1996; Muller & Kubie, 1987; McNaughton, Barnes, & O'Keefe, 1983), and models have proposed that place cells could arise from path integration in other regions that drive the hippocampal place representation (McNaughton, Battaglia, Jensen, Moser, & Moser, 2006; Redish & Touretzky, 1998; Redish & Touretzky, 1997; Samsonovich & McNaughton, 1997; Touretzky & Redish, 1996). However, path integration suffers from accumulation of error. As an alternative, other models propose that place cells could be driven by the learned response to visual features in particular configurations (Bicanski & Burgess, 2018; Byrne, Becker, & Burgess, 2007; Hetherington & Shapiro, 1993), based on a transformation of egocentric feature angle to allocentric position based on the current heading direction of the animal (Byrne et al., 2007).

Spatial Coding by Grid Cells

The coding of spatial location along a spatio-temporal trajectory has been proposed to involve an interaction of both place cells and grid cells (Hasselmo, 2009, 2012; Hasselmo et al., 2010). Place cells in the hippocampus primarily code individual locations in the environment, whereas grid cells in the entorhinal cortex have been shown to fire when a foraging animal visits an array of spatial locations in the environment (Hafting, Fyhn, Molden, Moser, & Moser, 2005). The firing fields occur in a regular array of locations that can be described as falling on the vertices of tessellated equilateral triangles or in a hexagonal pattern. Different grid cells show different spatial scales (Stensola et al., 2012; Barry, Hayman, Burgess, & Jeffery, 2007; Sargolini et al., 2006; Hafting et al., 2005), allowing a population of grid cells to code individual spatial locations (Mathis, Stemmler, & Herz, 2015; Sreenivasan & Fiete, 2011; Fiete, Burak, & Brookings, 2008; Gorchetchnikov & Grossberg, 2007). Models also indicate how grid cell firing can be used to explore and find possible relational trajectories between locations (Erdem & Hasselmo, 2012, 2014) or to directly compute the relationship between different spatial locations (Bush, Barry, Manson, & Burgess, 2015). Many grid cells conjunctively code both location and current head direction of the animal (Sargolini et al., 2006).

Models of grid cell location implicitly focus on different coding principles. For example, a firing rate code for grid cells is the emphasis of models using attractor dynamics

to generate grid cell firing patterns within a population of neurons with feedback inhibition (Widloski & Fiete, 2014; Yoon et al., 2013; Giocomo, Moser, & Moser, 2011; Burak & Fiete, 2009; Fuhs & Touretzky, 2006; McNaughton et al., 2006; Conklin & Eliasmith, 2005). These models are supported by the distinct grid cell modules that share properties of spacing and orientation (Stensola et al., 2012; Barry et al., 2007) and the change in correlation with different anatomical distances between grid cells (Heys, Rangarajan, & Dombeck, 2014). These models use path integration that could accumulate errors but could be reset by sensory cues (Hardcastle, Ganguli, & Giocomo, 2015; Bush & Burgess, 2014; Touretzky & Redish, 1996).

Alternately, a temporal code model of grid cells codes location based on firing updated by shifts in frequency of input theta rhythm oscillations induced by velocity (Bush & Burgess, 2014; Hasselmo, 2008, 2014; Giocomo et al., 2011; Burgess, 2008; Burgess, Barry, & O'Keefe, 2007). These models directly replicate data on the theta phase precession firing of grid cells relative to theta rhythm oscillations (Hafting et al., 2008). Consistent with this model based on theta rhythm, experiments show a loss of grid cell spatial selectivity during loss of theta rhythm caused by inactivation of medial septum (Brandon et al., 2011; Koenig, Linder, Leutgeb, & Leutgeb, 2011), which spares the coding of head direction (Brandon et al., 2011) and place cell firing in the hippocampus (Brandon, Koenig, Leutgeb, & Leutgeb, 2014). The loss of grid cell selectivity appears to specifically depend on inactivation of GABAergic neurons in the medial septum (Robinson & Brandon, 2018). Inactivation of cholinergic neurons does not appear to alter theta rhythm or speed coding in a manner that would alter grid cells (Dannenberg, Kelley, Hoyland, Monaghan, & Hasselmo, 2019).

The role of oscillatory dynamics is further supported by changes in intrinsic rhythmicity of entorhinal neurons with spatial scale (Jeewajee, Barry, O'Keefe, & Burgess, 2008) and shifts in running speed (Hinman, Brandon, Climer, Chapman, & Hasselmo, 2016; Jeewajee et al., 2008). The influence of internal noise can be reduced by redundant coding in a population of neurons (Zilli & Hasselmo, 2010) or combining interference with attractor dynamics (Bush & Burgess, 2014; Hasselmo & Shay, 2014). The influence of external noise can be reduced by resetting location based on the angle of sensory cues (Bush & Burgess, 2014), consistent with more accurate coding near environmental boundaries than at a distance from boundaries (Hardcastle et al., 2015). The role of sensory input angle is supported by the loss of spatial coding during inactivation of regions providing head direction input (Winter, Clark, & Taube, 2015).

Another model of grid cells involves the self-organization of input from place cells (Si, Kropff, & Treves, 2012; Kropff & Treves, 2008) with spike-frequency accommodation of entorhinal neurons resulting in a time-varying response to input from place cells that self-organize into

the pattern of grid cell responses. These models (Dordek, Soudry, Meir, & Derdikman, 2016; Krupic, Bauza, Burton, Lever, & O'Keefe, 2014) are supported by evidence showing that development of place cells appears earlier than grid cells (Wills, Barry, & Cacucci, 2012; Wills, Cacucci, Burgess, & O'Keefe, 2010) and that place cell inactivation reduces grid cell firing (Bonnievie et al., 2013), whereas grid cell inactivation does not prevent place cell firing (Brandon et al., 2014), although changes in grid cell scale do influence place cell scale (Mallory, Hardcastle, Bant, & Giocomo, 2018).

Time Coding for Spatio-temporal Trajectories

As noted above, the coding of episodic memory also requires the coding of the specific time of events on multiple different scales, ranging from the time of one episode versus another episode, to the timing of different events within an episode, to the timing of specific movements during a particular event. The neural coding of time could involve the patterns of activity shown by populations of neurons referred to as time cells. This refers to neurons that respond at specific time intervals during behavioral tasks. These cells have been described as episode cells (Pastalkova et al., 2008) or time cells (MacDonald, Lepage, Eden, & Eichenbaum, 2011). They have been shown to fire during the delay period between the encounter of a cue and a delayed response (MacDonald, Carrow, Place, & Eichenbaum, 2013; MacDonald et al., 2011). These types of responses have also been shown in spatial alternation tasks, in which neurons will fire at specific intervals during running on a running wheel (Pastalkova et al., 2008) or during running on a treadmill (Kraus et al., 2015; Kraus, Robinson, White, Eichenbaum, & Hasselmo, 2013).

The coding of time in episodic memory has been proposed to occur on multiple different temporal scales (Howard, MacDonald, et al., 2014; Howard & Kahana, 2002). Consistent with this, calcium imaging data on multiple time cells in the hippocampus show that these neurons not only respond at specific time intervals within individual trials (Mau et al., 2018) but that these neurons also show changes in their response across trials within a day, and the neurons also change their population response across days (Mau et al., 2018). This provides strong empirical evidence for spatio-temporal coding across multiple scales. It is important to note that the neurons that code specific time intervals also often code specific spatial locations as place cells or grid cells (Kraus et al., 2013, 2015). Thus, the same populations of neurons can simultaneously code space and time along a spatio-temporal trajectory. The models of grid cell firing in the entorhinal cortex can account for the fact that many grid cells and place cells will also respond at specific time intervals during running (Hasselmo, 2008; Burgess et al., 2007). Consistent with the fact described above that grid cells are dependent on oscillatory input, the inactivation of medial septum also prevents the

temporal specificity of firing by time cells (Wang, Romani, Lustig, Leonardo, & Pastalkova, 2015). Alternately, both abstract models (Howard, MacDonald, et al., 2014; Howard & Kahana, 2002) and biological detailed models (Liu, Tiganj, Hasselmo, & Howard, 2019; Tiganj, Hasselmo, & Howard, 2015) show how the coding of time can arise from exponential decay of spiking rate, consistent with data from slice preparations (Tahvildari, Fransén, Alonso, & Hasselmo, 2007) and in vivo recording (Tsao et al., 2018).

Direction Coding

The memory of a spatio-temporal trajectory of an agent not only requires its location over time in the environment but also includes encoding and retrieval of its heading within the environment. In fact, the spatio-temporal trajectory includes not only the direction of overall body movement but also the moment-to-moment direction of the animal's head (Raudies, Brandon, Chapman, & Hasselmo, 2015). Consistent with this, many neurons coding the head direction of rodents were discovered, initially in the dorsal presubiculum by Ranck and Taube (Taube, Muller, & Ranck, 1990) and later in a range of structures including the anterior thalamus (Taube, 1995), the lateral mammillary nucleus (Stackman & Taube, 1998), the entorhinal cortex (Giocomo et al., 2014; Brandon, Bogaard, Schultheiss, & Hasselmo, 2013; Sargolini et al., 2006), and the retrosplenial cortex (Cho & Sharp, 2001; Chen, Lin, Green, Barnes, & McNaughton, 1994). Head direction cells respond selectively based on the current allocentric direction of the animal's head, regardless of the location of the animal in the environment and independent of the relative position of individual landmarks or features. During sleep, head direction cells appear to replay the sequence of positions encountered during behavior (Peyrache, Lacroix, Petersen, & Buzsáki, 2015). An angular velocity signal based on self-motion appears to be integrated to drive head direction neurons in structures such as the anterior thalamus, lateral mammillary nucleus, and dorsal tegmental nucleus (Clark & Taube, 2012; Taube & Bassett, 2003). As noted above, episodic memory includes specific viewpoints of an event, and head direction cells could provide an important means of remembering specific viewpoints. In addition, evidence indicates that the allocentric spatial code could arise from a transformation from egocentric viewpoints, which could use an interaction of head direction cells with egocentric viewpoint cells to create an allocentric coordinate frame (Bicanski & Burgess, 2018; Byrne et al., 2007).

The coding of direction is standard in robotics that use coding of the "pose" of the agent, which includes both location and heading direction (Milford, Wiles, & Wyeth, 2010; Milford & Wyeth, 2010). Vision-based robotics includes coding of barriers and objects and the transformation from the coordinates relative to the heading of the agent (egocentric coordinates) into coordinates of the

absolute position of the agent relative to the overall environment (allocentric coordinates; Milford et al., 2010; Milford & Wyeth, 2010; Byrne et al., 2007).

The head direction signal is not equivalent to a movement direction signal, and analysis of periods where head direction does not match movement direction shows that these cells primarily code head direction (Raudies et al., 2015), although they can code angular head motion (Clark & Taube, 2011). This supports the notion that place codes are driven more strongly by the angle of visual features dependent on head direction, rather than path integration.

Boundary Coding

As noted above and in a previous article (Hasselmo et al., 2010), the coding of episodic memory not only requires coding of the spatio-temporal trajectories of a single person but also would require the coding of the relative spatio-temporal trajectory of objects and barriers within the environment. This could include tracking of the position of environment boundaries relative to the agent. For example, your memory of walking through an apartment would include spatial viewpoints of the position of different walls of the rooms and hallways as you follow a trajectory through the environment, as shown in Figure 3.

A range of data has demonstrated the influence of environmental boundaries on coding by populations of neurons. Early data showed that place cell firing depends on the relative position of the walls of the environment (O'Keefe & Burgess, 1996), leading to the novel theoretical proposal that a specific class of neurons might code the position of an animal relative to boundaries (Hartley, Lever, Burgess, & O'Keefe, 2014; Savelli, Yoganasimha, & Knierim, 2008; Burgess, Jackson, Hartley, & O'Keefe, 2000). This modeling prediction was later supported by data showing the existence of boundary cells that respond at a specific distance and angle from boundaries in allocentric coordinates (Lever, Burton, Jeewajee, O'Keefe, & Burgess, 2009; Savelli et al., 2008; Solstad, Boccara, Kropff, Moser, & Moser, 2008). Modeling proposed that egocentric visual input about boundaries combined with head direction cells could be transformed to code allocentric spatial location (Bicanski & Burgess, 2018; Byrne et al., 2007). The egocentric coding of boundary position has been demonstrated in recent data, which shows neurons with selectivity for the distance and angle of boundaries in egocentric coordinates (Hinman, Chapman, & Hasselmo, 2017, 2019; Carstensen, Alexander, Hinman, & Hasselmo 2018), suggesting that coding of boundaries in egocentric coordinate frames could contribute to the coding of these boundaries in allocentric coordinate frames.

Object Coding

As mentioned above, the coding of an episodic memory can involve nonspatial features, such as the identity of

specific objects (Kreiman et al., 2000a). A number of studies have focused on the potential representation of objects in the hippocampus and entorhinal cortex. Recordings in the hippocampus and related cortical structures in humans show neurons with many types of nonspatial object selectivity (Rutishauser et al., 2011; Kreiman, 2007; Quiroga et al., 2005; Kreiman et al., 2000b). Similarly, many neurons in rodent hippocampus also show selective responses to nonspatial features such as specific odors or rewards (Wood et al., 1999; Otto & Eichenbaum, 1992; Wiener, Paul, & Eichenbaum, 1989). Recordings in the rodent lateral entorhinal cortex show that some neurons respond to specific objects (Keene et al., 2016; Deshmukh & Knierim, 2011) or odors (Young, Otto, Fox, & Eichenbaum, 1997), although these neurons appear less frequently than spatially coding neurons in the medial entorhinal cortex. Recordings also show object responses in the rodent perirhinal cortex (Deshmukh, Johnson, & Knierim, 2012). Responses to specific objects have been shown in the perirhinal cortex and entorhinal cortex of monkeys (Suzuki, Miller, & Desimone, 1997; Riches, Wilson, & Brown, 1991; Wilson, Riches, & Brown, 1990), along with evidence that these responses decrease or increase with repeated presentations of objects (Suzuki et al., 1997; Riches et al., 1991), consistent with models of familiarity recognition in which the responses to familiar objects increase or decrease (Bogacz & Brown, 2003; Sohal & Hasselmo, 2000).

A full episodic memory also requires encoding and retrieval of the location and movement of objects in addition to the interaction of agents in an episode. Neurons in the hippocampus respond to a particular orientation and distance from objects (Deshmukh & Knierim, 2013), and entorhinal neurons respond to landmark position as well as path integration (Campbell et al., 2018). Coding of objects also occurs in egocentric coordinates (Wang et al., 2018), as well as coding of the previous location of an object as trace cells in the hippocampus (O'Keefe & Nadel, 1978) and entorhinal cortex (Tsao, Moser, & Moser, 2013). Of particular interest with regard to shared mechanisms for coding agents and objects, there is new evidence that neurons that respond to the current location of a rat also respond to the location of another rat in the same environment (Danjo, Toyozumi, & Fujisawa, 2018), which includes showing theta phase coding of the position of the other rat within a firing field. These data provide important evidence of the relational coding in hippocampus of object location in egocentric coordinates relative to the agent. These mechanisms for relational coding could relate to the general coding of objects and features in a broad range of neocortical structures. There might be a general mechanism for the coding of cognitive representations within cortical regions that could be applied across sensory modalities, as supported by evidence that cortical regions can take over the function of other damaged cortical regions (Abel,

Weiller, Huber, Willmes, & Specht, 2015; Roe, Pallas, Kwon, & Sur, 1992; Roe, Pallas, Hahm, & Sur, 1990).

Speed Coding

In contrast to a snapshot view of episodic memory, the spatio-temporal trajectory view of episodic memory would code functions to allow a smooth continuous reconstruction of the elements of a trajectory. This requires coding of not only position at different time points but also the velocity and possibly even the acceleration along the trajectory. This would allow more accurate interpolation or extrapolation of the trajectory on any desired scale (Hasselmo, 2018). Consistent with this framework, neurons respond not only to the position and time during events but also to dynamical variables such as running speed. The coding of running speed has been shown in a number of different functional classes of neurons in the entorhinal cortex (Hinman, Dannenberg, Alexander, & Hasselmo, 2018; Hinman et al., 2016; Kropff, Carmichael, Moser, & Moser, 2015; Wills et al., 2012) and hippocampus (McNaughton et al., 1983).

Cells throughout the hippocampal formation spike theta rhythmically, and in addition to the firing rate speed signal in MEC, the coding of speed by the frequency of rhythmic firing has been shown experimentally in single cells in medial entorhinal cortex (MEC) (Hinman et al., 2016; Jeewajee et al., 2008). The rhythmic frequency of single cell firing usually increases as a rat runs faster, but there are also cases where the rhythmic frequency decreases as the rat runs faster (Dannenberg et al., 2019). Given that both speed signals have been identified in MEC, we investigated whether the same cells express both speed signals similarly and found that the two signals are actually independently expressed in single cells (Hinman et al., 2016). This suggests that both rate coding and temporal coding might occur for running speed. The change in coding of running speed over different time scales also suggests that neurons might be coding acceleration (Dannenberg et al., 2019). Acceleration has been used to enhance the encoding and retrieval of trajectories using dynamical matrices (Hasselmo, 2018). Another potential implication is that temporal coding of running speed not only may involve rhythmic frequency but might actually involve a phase code for running speed in terms of the timing of spikes relative to theta phase or even gamma phase for different running speeds.

Context Coding

The coding of spatio-temporal trajectories requires that different trajectories overlapping in the same location in the environment can be disambiguated. This is consistent with neurophysiological data showing that the coding of trajectories is highly context dependent. Early data showed that place cells in one environment will often turn off in a different environment and be replaced by

other place cells that were inactive in the first environment (Lever, Wills, Cacucci, Burgess, & O'Keefe, 2002; Muller & Kubie, 1987). Even within an environment, neurons will show strongly context-dependent activity. For example, when a rat runs on the stem of spatial alternation task, individual neurons will fire selectively based on the past or future turning response in the hippocampus (Ferbinteanu & Shapiro, 2003; Wood et al., 2000) and entorhinal cortex (Frank et al., 2000). Neurons also code other features of the environment such as the identity of odors or the presence of reward (Wood et al., 1999; Eichenbaum, Kuperstein, Fagan, & Nagode, 1987) and can show highly selective firing based on the influence of a spatial context on the reward valence of individual objects (McKenzie et al., 2016; Komorowski, Manns, & Eichenbaum, 2009). In some cases, the change in coding may reflect a rotation of firing fields relative to the environment (Kinsky, Sullivan, Mau, Hasselmo, & Eichenbaum, 2018). In addition, recent work has revealed that spatially specific but nongrid cells of the MEC globally remapped in response to contextual changes to an environment (Diehl, Hon, Leutgeb, & Leutgeb, 2017). Grid cells, on the other hand, have been found to exhibit either nodal rate alterations or translational shifts of the full map in response to contextual alterations to the environment (Diehl et al., 2017; Marozzi, Ginzberg, Alenda, & Jeffery, 2015). There is some evidence that contextually sensitive or nonsensitive MEC neurons actually form molecularly and anatomically distinct subpopulations within the region (Kitamura et al., 2014, 2015; Ray et al., 2014). These data are consistent with episodic coding of spatio-temporal trajectories, rather than coding only in a static spatial map.

As described here, episodic coding of an event within an episode and the more general coding of objects for cognitive processing can and should involve multiple different spatio-temporal trajectories in different coordinate systems. This is consistent with evidence from the retrosplenial cortex, which provides an important interface between sensory systems such as the visual and somatosensory system with memory-related structures such as the entorhinal cortex and hippocampus. In particular, electrophysiological data from the retrosplenial cortex demonstrate the coding of multiple different dimensions that include allocentric coding of location in space, egocentric coding of turning directions on a maze, and pathway-centric coding of position relative to the start and end of a particular path (Alexander & Nitz, 2015, 2017). This coding of multiple different coordinate systems is important for the robust and flexible coding of the environment both for coordinate transformations necessary when planning different behaviors and for the robust coding of episodic memory of a trajectory.

To account for the multiple complex representations in episodic memory and the transformations between different coordinate systems, we need more sophisticated neural representations of these types of competing production systems that can neurally represent higher order

relations within sensory input as complex functions based on dynamical matrices, which could also act as transformation matrices between different coordinate frames. The coding of complex relations can be useful both for modeling of cognitive processing (thought) and for coding the full richness of episodic memory and cognition.

Need for More Exploration of Model Space

Although we have reviewed much exciting data on the functional coding relevant to episodic memory in the hippocampus, entorhinal cortex, and related cortical structures, future progress in this field requires more extensive exploration of the full space of possible neural models. The space of possible neural models of cognition is enormous, and only a small portion of this space has been explored in research. There are many dimensions of neural function that may be relevant to cognition. Dimensions that have already been explored extensively in current models include the modifiable strength (or weight) of excitatory and inhibitory synaptic connections between neurons (Bliss & Collingridge, 1993), the magnitude of tonic depolarization of populations of neurons, and the threshold for firing of individual neurons. Synaptic dimensions of neural function that have not been explored as extensively as synaptic weight and bias include the nonlinear interactions of synapses on the dendritic tree. This could include nonlinear interactions of synapses because of N-methyl-D-aspartate receptors (Poirazi, Brannon, & Mel, 2003; Mel, 1993) or internal chemical waves (Bhalla, 2017, 2019), which have been used in sigma-Pi networks (Durbin & Rumelhart, 1989). These multiplicative interactions could play a role in gating the flow of information between populations of cortical neurons (Hasselmo & Stern, 2018). Gating of information flow can be supplemented by temporally coordinated firing of inhibitory interneurons providing cell-type- and cell-compartment-specific inhibition. Two examples of such microcircuits are axoaxonic inhibitory interneurons (Klausberger & Somogyi, 2008) targeting the axon initial segment of pyramidal neurons and the interneuron-specific vasoactive intestinal peptide-positive interneurons inhibiting parvalbumin-positive and somatostatin-positive neurons to cause disinhibition of excitatory principal neurons (Fu et al., 2014; Pi et al., 2013).

Another area that has not been explored are the intrinsic dynamics of neurons that include the spike frequency accommodation (or adaptation) caused by calcium-activated potassium currents (Barkai & Hasselmo, 1994; Connors, Gutnick, & Prince, 1982), the resonance and rebound spiking caused by hyperpolarization activated cation currents (Ferrante, Shay, Tsuno, Chapman, & Hasselmo, 2017; Klink & Alonso, 1993), and the persistent spiking caused by calcium-sensitive nonspecific cation currents (Fransén, Tahvildari, Egorov, Hasselmo, & Alonso, 2006; Fransén, Egorov, Hasselmo, & Alonso, 2003; Egorov, Hamam, Fransén, Hasselmo, & Alonso, 2002). These

dimensions of function have been effectively simulated in reduced form in single neuron models (Izhikevich, 2003), and biophysical models have explored the memory function of channels such as adaptation currents (Barkai, Bergman, Horwitz, & Hasselmo, 1994) and persistent spiking currents (Fransén, Alonso, & Hasselmo, 2002). However, implications for network dynamical function have not been fully explored.

An important step in the exploration of model space would be to systematize what we do and do not know. For example, it could be productive to characterize the functional attributes of known neural circuit models. The systemization of the properties of atomic elements provided an important framework for chemistry (Mendeleev, 1869), and mathematical systematization guided research in particle physics (Gell-Mann, 1964). As potential examples, the functional dynamics of second-order differential equations have been characterized along the dimensions of the trace and determinant of the Jacobian matrix (see page 96 of Hirsch & Smale, 1974). There have been efforts to provide a systematic categorization of an existing set of neural network architectures and their functional properties (Van Veen, 2016), but the field might benefit from a more systematic approach to understanding the large space of neural models that have not yet been explored.

SUMMARY

This article reviews a theory of episodic memory and cognitive function in which spatio-temporal trajectories are coded on multiple scales of place and time. As proposed previously (Hasselmo et al., 2010), this coding can address detailed scales of the spatio-temporal trajectories of individual features of objects (a finger or an eyelid) as well as other dimensions such as the color or size of individual features. The previous model was extended by the proposal of dynamical matrices that can code trajectories and boundaries (Hasselmo, 2018), allowing interpolation and extrapolation of not only predicted place and time but also velocity (direction and speed) and acceleration. In a hierarchical manner, this framework can also represent the spatio-temporal trajectory of overall objects, barriers, and agents observed by an agent within an event (in egocentric or allocentric coordinates) as well as the spatio-temporal trajectory and features such as egocentric direction of the individual observing the episode.

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REFERENCES

- Abel, S., Weiller, C., Huber, W., Willmes, K., & Specht, K. (2015). Therapy-induced brain reorganization patterns in aphasia. *Brain*, *138*, 1097–1112.
- Aggleton, J. P., Neave, N., Nagle, S., & Hunt, P. R. (1995). A comparison of the effects of anterior thalamic, mamillary body and fornix lesions on reinforced spatial alternation. *Behavioural Brain Research*, *68*, 91–101.
- Aghajian, Z. M., Schuette, P., Fields, T. A., Tran, M. E., Siddiqui, S. M., Hasulak, N. R., et al. (2017). Theta oscillations in the human medial temporal lobe during real-world ambulatory movement. *Current Biology*, *27*, 3743.e3–3751.e3.
- 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*, 988–1002.
- Alexander, A. S., & Nitz, D. A. (2015). Retrosplenial cortex maps the conjunction of internal and external spaces. *Nature Neuroscience*, *18*, 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*, 1551.e4–1560.e4.
- Baddeley, A. D. (2001). The concept of episodic memory. In A. D. Baddeley, M. Conway, & J. P. Aggleton (Eds.), *Episodic memory: New directions in research* (pp. 1–10). Oxford: Oxford University Press.
- Badre, D., & Frank, M. J. (2012). Mechanisms of hierarchical reinforcement learning in cortico-striatal circuits 2: Evidence from fMRI. *Cerebral Cortex*, *22*, 527–536.
- Barkai, E., Bergman, R. E., Horwitz, G., & Hasselmo, M. E. (1994). Modulation of associative memory function in a biophysical simulation of rat piriform cortex. *Journal of Neurophysiology*, *72*, 659–677.
- Barkai, E., & Hasselmo, M. E. (1994). Modulation of the input/output function of rat piriform cortex pyramidal cells. *Journal of Neurophysiology*, *72*, 644–658.
- Barrett, D. G. T., Hill, F., Santoro, A., Morcos, A. S., & Lillicrap, T. (2018). Measuring abstract reasoning in neural networks. In *Proceedings of the 35th International Conference on Machine Learning*. Stockholm, Sweden.
- Barry, C., Hayman, R., Burgess, N., & Jeffery, K. J. (2007). Experience-dependent rescaling of entorhinal grids. *Nature Neuroscience*, *10*, 682–684.
- Becker, J. T., Walker, J. A., & Olton, D. S. (1980). Neuroanatomical bases of spatial memory. *Brain Research*, *200*, 307–320.
- Berry, S. D., & Thompson, R. F. (1978). Prediction of learning rate from the hippocampal electroencephalogram. *Science*, *200*, 1298–1300.
- Bhalla, U. S. (2017). Synaptic input sequence discrimination on behavioral timescales mediated by reaction-diffusion chemistry in dendrites. *eLife*, *6*, e25827.
- Bhalla, U. S. (2019). Dendrites, deep learning, and sequences in the hippocampus. *Hippocampus*, *29*, 239–251.
- Bhandari, A., & Badre, D. (2018). Learning and transfer of working memory gating policies. *Cognition*, *172*, 89–100.
- Bicanski, A., & Burgess, N. (2018). A neural-level model of spatial memory and imagery. *eLife*, *7*, e33752.
- Bland, B. H., & Colom, L. V. (1993). Extrinsic and intrinsic properties underlying oscillation and synchrony in limbic cortex. *Progress in Neurobiology*, *41*, 157–208.
- Bliss, T. V., & Collingridge, G. L. (1993). A synaptic model of memory: Long-term potentiation in the hippocampus. *Nature*, *361*, 31–39.
- Bogacz, R., & Brown, M. W. (2003). Comparison of computational models of familiarity discrimination in the perirhinal cortex. *Hippocampus*, *13*, 494–524.
- 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.
- Bonnevie, T., Dunn, B., Fyhn, M., Hafting, T., Derdikman, D., Kubie, J. L., et al. (2013). Grid cells require excitatory drive from the hippocampus. *Nature Neuroscience*, *16*, 309–317.
- Bragin, A., Jandó, G., Nádasdy, Z., Hetke, J., Wise, K., & Buzsáki, G. (1995). Gamma (40–100 Hz) oscillation in the hippocampus of the behaving rat. *Journal of Neuroscience*, *15*, 47–60.
- Brandon, M. P., Bogaard, A. R., Libby, C. P., Connerney, M. A., Gupta, K., & Hasselmo, M. E. (2011). Reduction of theta rhythm dissociates grid cell spatial periodicity from directional tuning. *Science*, *332*, 595–599.
- Brandon, M. P., Bogaard, A. R., Schultheiss, N. W., & Hasselmo, M. E. (2013). Segregation of cortical head direction cell assemblies on alternating theta cycles. *Nature Neuroscience*, *16*, 739–748.
- 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*, 789–796.
- Brioni, J. D., Decker, M. W., Gamboa, L. P., Izquierdo, I., & McGaugh, J. L. (1990). Muscimol injections in the medial septum impair spatial learning. *Brain Research*, *522*, 227–234.
- Brown, T. I., Carr, V. A., LaRocque, K. F., Favila, S. E., Gordon, A. M., Bowles, B., et al. (2016). Prospective representation of navigational goals in the human hippocampus. *Science*, *352*, 1323–1326.
- Brown, T. I., Ross, R. S., Keller, J. B., Hasselmo, M. E., & Stern, C. E. (2010). Which way was I going? Contextual retrieval supports the disambiguation of well learned overlapping navigational routes. *Journal of Neuroscience*, *30*, 7414–7422.
- Brown, T. I., & Stern, C. E. (2014). Contributions of medial temporal lobe and striatal memory systems to learning and retrieving overlapping spatial memories. *Cerebral Cortex*, *24*, 1906–1922.
- Burak, Y., & Fiete, I. R. (2009). Accurate path integration in continuous attractor network models of grid cells. *PLoS Computational Biology*, *5*, e1000291.
- Burgess, N. (2008). Grid cells and theta as oscillatory interference: Theory and predictions. *Hippocampus*, *18*, 1157–1174.
- Burgess, N., Barry, C., & O'Keefe, J. (2007). An oscillatory interference model of grid cell firing. *Hippocampus*, *17*, 801–812.
- Burgess, N., Jackson, A., Hartley, T., & O'Keefe, J. (2000). Predictions derived from modelling the hippocampal role in navigation. *Biological Cybernetics*, *83*, 301–312.
- Buschman, T. J., Denovellis, E. L., Diogo, C., Bullock, D., & Miller, E. K. (2012). Synchronous oscillatory neural ensembles for rules in the prefrontal cortex. *Neuron*, *76*, 838–846.
- Buschman, T. J., & Miller, E. K. (2014). Goal-direction and top-down control. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, *369*, 20130471.
- Bush, D., Barry, C., Manson, D., & Burgess, N. (2015). Using grid cells for navigation. *Neuron*, *87*, 507–520.
- Bush, D., & Burgess, N. (2014). A hybrid oscillatory interference/continuous attractor network model of grid cell firing. *Journal of Neuroscience*, *34*, 5065–5079.
- Buzsáki, G. (2002). Theta oscillations in the hippocampus. *Neuron*, *33*, 325–340.
- Buzsáki, G., Leung, L.-W. S., & Vanderwolf, C. H. (1983). Cellular bases of hippocampal EEG in the behaving rat. *Brain Research Reviews*, *287*, 139–171.
- Byrne, P., Becker, S., & Burgess, N. (2007). Remembering the past and imagining the future: A neural model of spatial memory and imagery. *Psychological Review*, *114*, 340–375.
- Campbell, M. G., Ocko, S. A., Mallory, C. S., Low, I. I. C., Ganguli, S., & Giocomo, L. M. (2018). Principles governing the integration of landmark and self-motion cues in

- entorhinal cortical codes for navigation. *Nature Neuroscience*, *21*, 1096–1106.
- Carpenter, P. A., Just, M. A., & Shell, P. (1990). What one intelligence test measures: A theoretical account of the processing in the Raven progressive matrices test. *Psychological Review*, *97*, 404–431.
- Carstensen, L. C., Alexander, A. S., Hinman, J. R., & Hasselmo, J. R. (2018). Spatial correlates of the retrosplenial cortex during free exploration. *Society for Neuroscience Abstract*, *44*, 508–524.
- Chen, L. L., Lin, L.-H., Green, E. J., Barnes, C. A., & McNaughton, B. L. (1994). Head-direction cells in the rat posterior cortex. I. Anatomical distribution and behavioral modulation. *Experimental Brain Research*, *101*, 8–23.
- Cho, J., & Sharp, P. E. (2001). Head direction, place, and movement correlates for cells in the rat retrosplenial cortex. *Behavioral Neuroscience*, *115*, 3–25.
- Chrastil, E. R., Sherrill, K. R., Hasselmo, M. E., & Stern, C. E. (2015). There and back again: Hippocampus and retrosplenial cortex track homing distance during human path integration. *Journal of Neuroscience*, *35*, 15442–15452.
- Chrastil, E. R., Sherrill, K. R., Hasselmo, M. E., & Stern, C. E. (2016). Which way and how far? Tracking of translation and rotation information for human path integration. *Human Brain Mapping*, *37*, 3636–3655.
- Chrobak, J. J., Stackman, R. W., & Walsh, T. J. (1989). Intraseptal administration of muscimol produces dose-dependent memory impairments in the rat. *Behavioral and Neural Biology*, *52*, 357–369.
- Clark, B. J., & Taube, J. S. (2011). Intact landmark control and angular path integration by head direction cells in the anterodorsal thalamus after lesions of the medial entorhinal cortex. *Hippocampus*, *21*, 767–782.
- Clark, B. J., & Taube, J. S. (2012). Vestibular and attractor network basis of the head direction cell signal in subcortical circuits. *Frontiers in Neural Circuits*, *6*, 7.
- Cohen, N. J., & Eichenbaum, H. (1993). *Memory, amnesia, and the hippocampal system*. Cambridge, MA: MIT Press.
- Cohen, N. J., & Squire, L. R. (1980). Preserved learning and retention of pattern-analyzing skill in amnesia: Dissociation of knowing how and knowing that. *Science*, *210*, 207–210.
- Colgin, L. L., Denninger, T., Fyhn, M., Hafting, T., Bonnevie, T., Jensen, O., et al. (2009). Frequency of gamma oscillations routes flow of information in the hippocampus. *Nature*, *462*, 353–357.
- Collins, A. M., & Quillian, M. R. (1969). Retrieval time from semantic memory. *Journal of Verbal Learning & Verbal Behavior*, *8*, 240–247.
- Conklin, J., & Eliasmith, C. (2005). A controlled attractor network model of path integration in the rat. *Journal of Computational Neuroscience*, *18*, 183–203.
- Connors, B. W., Gutnick, M. J., & Prince, D. A. (1982). Electrophysiological properties of neocortical neurons in vitro. *Journal of Neurophysiology*, *48*, 1302–1320.
- Conway, M. A. (2009). Episodic memories. *Neuropsychologia*, *47*, 2305–2313.
- Corkin, S. (1984). Lasting consequences of bilateral medial temporal lobectomy: Clinical course and experimental findings in H.M. *Seminars in Neurology*, *4*, 249–259.
- Csicsvari, J., Hirase, H., Czurkó, A., Mamiya, A., & Buzsáki, G. (1999). Fast network oscillations in the hippocampal CA1 region of the behaving rat. *Journal of Neuroscience*, *19*, RC20.
- Czajkowski, R., Jayaprakash, B., Wiltgen, B., Rogerson, T., Guzman-Karlsson, M. C., Barth, A. L., et al. (2014). Encoding and storage of spatial information in the retrosplenial cortex. *Proceedings of the National Academy of Sciences, U.S.A.*, *111*, 8661–8666.
- Danjo, T., Toyozumi, T., & Fujisawa, S. (2018). Spatial representations of self and other in the hippocampus. *Science*, *359*, 213–218.
- Dannenberg, H., Kelley, C., Hoyland, A., Monaghan, C. K., & Hasselmo, M. E. (2019). The firing rate speed code of entorhinal speed cells differs across behaviorally relevant time scales and does not depend on medial septum inputs. *Journal of Neuroscience*, *39*, 3434–3453.
- Dannenberg, H., Pabst, M., Braganza, O., Schoch, S., Niediek, J., Bayraktar, M., et al. (2015). Synergy of direct and indirect cholinergic septo-hippocampal pathways coordinates firing in hippocampal networks. *Journal of Neuroscience*, *35*, 8394–8410.
- DeLuca, J. (1993). Predicting neurobehavioral patterns following anterior communicating artery aneurysm. *Cortex*, *29*, 639–647.
- DeLuca, J., & Cicerone, K. D. (1991). Confabulation following aneurysm of the anterior communicating artery. *Cortex*, *27*, 417–423.
- Deshmukh, S. S., Johnson, J. L., & Knierim, J. J. (2012). Perirhinal cortex represents nonspatial, but not spatial, information in rats foraging in the presence of objects: Comparison with lateral entorhinal cortex. *Hippocampus*, *22*, 2045–2058.
- Deshmukh, S. S., & Knierim, J. J. (2011). Representation of non-spatial and spatial information in the lateral entorhinal cortex. *Frontiers in Behavioral Neuroscience*, *5*, 69.
- Deshmukh, S. S., & Knierim, J. J. (2013). Influence of local objects on hippocampal representations: Landmark vectors and memory. *Hippocampus*, *23*, 253–267.
- Diehl, G. W., Hon, O. J., Leutgeb, S., & Leutgeb, J. K. (2017). Grid and nongrid cells in medial entorhinal cortex represent spatial location and environmental features with complementary coding schemes. *Neuron*, *94*, 83.e6–92.e6.
- Dordek, Y., Soudry, D., Meir, R., & Derdikman, D. (2016). Extracting grid cell characteristics from place cell inputs using non-negative principal component analysis. *eLife*, *5*, e10094.
- Douchamps, V., Jeewajee, A., Blundell, P., Burgess, N., & Lever, C. (2013). Evidence for encoding versus retrieval scheduling in the hippocampus by theta phase and acetylcholine. *Journal of Neuroscience*, *33*, 8689–8704.
- Durbin, R., & Rumelhart, D. E. (1989). Product units: A computational powerful and biologically plausible extension to backpropagation networks. *Neural Computation*, *1*, 133–142.
- Egorov, A. V., Hamam, B. N., Fransén, E., Hasselmo, M. E., & Alonso, A. A. (2002). Graded persistent activity in entorhinal cortex neurons. *Nature*, *420*, 173–178.
- 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. *Journal of Neuroscience*, *7*, 716–732.
- Eichenbaum, H., Stewart, C., & Morris, R. G. (1990). Hippocampal representation in place learning. *Journal of Neuroscience*, *10*, 3531–3542.
- Ekstrom, A. D., Caplan, J. B., Ho, E., Shattuck, K., Fried, I., & Kahana, M. J. (2005). Human hippocampal theta activity during virtual navigation. *Hippocampus*, *15*, 881–889.
- Ekstrom, A. D., Kahana, M. J., Caplan, J. B., Fields, T. A., Isham, E. A., Newman, E. L., et al. (2003). Cellular networks underlying human spatial navigation. *Nature*, *425*, 184–188.
- Ennaceur, A., Neave, N., & Aggleton, J. P. (1996). Neurotoxic lesions of the perirhinal cortex do not mimic the behavioural effects of fornix transection in the rat. *Behavioural Brain Research*, *80*, 9–25.
- Erdem, U. M., & Hasselmo, M. (2012). A goal-directed spatial navigation model using forward trajectory planning based on grid cells. *European Journal of Neuroscience*, *35*, 916–931.
- Erdem, U. M., & Hasselmo, M. E. (2014). A biologically inspired hierarchical goal directed navigation model. *Journal of Physiology, Paris*, *108*, 28–37.

- Feng, T., Silva, D., & Foster, D. J. (2015). Dissociation between the experience-dependent development of hippocampal theta sequences and single-trial phase precession. *Journal of Neuroscience*, *35*, 4890–4902.
- Ferbinteanu, J., & Shapiro, M. L. (2003). Prospective and retrospective memory coding in the hippocampus. *Neuron*, *40*, 1227–1239.
- Ferrante, M., Shay, C. F., Tsuno, Y., William Chapman, G., & Hasselmo, M. E. (2017). Post-inhibitory rebound spikes in rat medial entorhinal layer II/III principal cells: In vivo, in vitro, and computational modeling characterization. *Cerebral Cortex*, *27*, 2111–2125.
- Fiete, I. R., Burak, Y., & Brookings, T. (2008). What grid cells convey about rat location. *Journal of Neuroscience*, *28*, 6858–6871.
- Foster, D. J., & Wilson, M. A. (2007). Hippocampal theta sequences. *Hippocampus*, *17*, 1093–1099.
- Frank, L. M., Brown, E. N., & Wilson, M. (2000). Trajectory encoding in the hippocampus and entorhinal cortex. *Neuron*, *27*, 169–178.
- Fransén, E., Alonso, A. A., & Hasselmo, M. E. (2002). Simulations of the role of the muscarinic-activated calcium-sensitive nonspecific cation current INCM in entorhinal neuronal activity during delayed matching tasks. *Journal of Neuroscience*, *22*, 1081–1097.
- Fransén, E., Egorov, A. V., Hasselmo, M., & Alonso, A. (2003). Model of graded persistent activity in entorhinal cortex neurons. *Society for Neuroscience Abstracts*, *29*, 556–557.
- Fransén, E., & Lansner, A. (1998). A model of cortical associative memory based on a horizontal network of connected columns. *Network*, *9*, 235–264.
- Fransén, E., Tahvildari, B., Egorov, A. V., Hasselmo, M. E., & Alonso, A. A. (2006). Mechanism of graded persistent cellular activity of entorhinal cortex layer v neurons. *Neuron*, *49*, 735–746.
- Freeman, J. H., Jr., & Stanton, M. E. (1991). Fimbria-fornix transections disrupt the ontogeny of delayed alternation but not position discrimination in the rat. *Behavioral Neuroscience*, *105*, 386–395.
- Fu, Y., Tucciaroni, J. M., Espinosa, J. S., Sheng, N., Darcy, D. P., Nicoll, R. A., et al. (2014). A cortical circuit for gain control by behavioral state. *Cell*, *156*, 1139–1152.
- Fuhs, M. C., & Touretzky, D. S. (2006). A spin glass model of path integration in rat medial entorhinal cortex. *Journal of Neuroscience*, *26*, 4266–4276.
- Gaffan, D., & Harrison, S. (1989). Place memory and scene memory: Effects of fornix transection in the monkey. *Experimental Brain Research*, *74*, 202–212.
- Gaffan, D., & Murray, E. A. (1992). Monkeys (Macaca fascicularis) with rhinal cortex ablations succeed in object discrimination learning despite 24-hr intertrial intervals and fail at matching to sample despite double sample presentations. *Behavioral Neuroscience*, *106*, 30–38.
- Gaffan, D., Saunders, R. C., Gaffan, E. A., Harrison, S., Shields, C., & Owen, M. J. (1984). Effects of fornix transection upon associative memory in monkeys: Role of the hippocampus in learned action. *Quarterly Journal of Experimental Psychology. B, Comparative and Physiological Psychology*, *36*, 173–221.
- Gell-Mann, M. (1964). A schematic model of Baryons and Mesons. *Physics Letters*, *8*, 214–215.
- Giocomo, L. M., Moser, M. B., & Moser, E. I. (2011). Computational models of grid cells. *Neuron*, *71*, 589–603.
- Giocomo, L. M., Stensola, T., Bonnevie, T., Van Cauter, T., Moser, M. B., & Moser, E. I. (2014). Topography of head direction cells in medial entorhinal cortex. *Current Biology*, *24*, 252–262.
- Givens, B. S., & Olton, D. S. (1990). Cholinergic and GABAergic modulation of the medial septal area: Effect on working memory. *Behavioral Neuroscience*, *104*, 849–855.
- Givens, B., & Olton, D. S. (1994). Local modulation of basal forebrain: Effects on working and reference memory. *Journal of Neuroscience*, *14*, 3578–3587.
- Gorchetchnikov, A., & Grossberg, S. (2007). Space, time and learning in the hippocampus: How fine spatial and temporal scales are expanded into population codes for behavioral control. *Neural Networks*, *20*, 182–193.
- 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*, 823–835.
- Griffin, A. L., Asaka, Y., Darling, R. D., & Berry, S. D. (2004). Theta-contingent trial presentation accelerates learning rate and enhances hippocampal plasticity during trace eyeblink conditioning. *Behavioral Neuroscience*, *118*, 403–411.
- Griffin, A. L., Eichenbaum, H., & Hasselmo, M. E. (2007). Spatial representations of hippocampal CA1 neurons are modulated by behavioral context in a hippocampus-dependent memory task. *Journal of Neuroscience*, *27*, 2416–2423.
- Hafting, T., Fyhn, M., Molden, S., Moser, M. B., & Moser, E. I. (2005). Microstructure of a spatial map in the entorhinal cortex. *Nature*, *436*, 801–806.
- Hafting, T., Fyhn, M., Bonnevie, T., Moser, M. B., & Moser, E. I. (2008). Hippocampus-independent phase precession in entorhinal grid cells. *Nature*, *453*, 1248–1252.
- Hardcastle, K., Ganguli, S., & Giocomo, L. M. (2015). Environmental boundaries as an error correction mechanism for grid cells. *Neuron*, *86*, 827–839.
- 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*, 20120510.
- Hasselmo, M. E. (2008). Grid cell mechanisms and function: contributions of entorhinal persistent spiking and phase resetting. *Hippocampus*, *18*, 1213–1229.
- Hasselmo, M. E. (2009). A model of episodic memory: Mental time travel along encoded trajectories using grid cells. *Neurobiology of Learning Memory*, *92*, 559–573.
- Hasselmo, M. E. (2012). *How we remember: Brain mechanisms of episodic memory*. Cambridge, MA: MIT Press.
- Hasselmo, M. E. (2014). Neuronal rebound spiking, resonance frequency and theta cycle skipping may contribute to grid cell firing in medial entorhinal cortex. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, *369*, 20120523.
- Hasselmo, M. E. (2018). A model of cortical cognitive function using hierarchical interactions of gating matrices in internal agents coding relational representations. ArXiv 1809.08203.
- Hasselmo, M. E., Bodelón, C., & Wyble, B. P. (2002). A proposed function for hippocampal theta rhythm: Separate phases of encoding and retrieval enhance reversal of prior learning. *Neural Computation*, *14*, 793–817.
- Hasselmo, M. E., & Eichenbaum, H. (2005). Hippocampal mechanisms for the context-dependent retrieval of episodes. *Neural Networks*, *18*, 1172–1190.
- Hasselmo, M. E., Giocomo, L. M., Brandon, M. P., & Yoshida, M. (2010). Cellular dynamical mechanisms for encoding the time and place of events along spatiotemporal trajectories in episodic memory. *Behavioural Brain Research*, *215*, 261–274.
- Hasselmo, M. E., & Shay, C. F. (2014). Grid cell firing patterns may arise from feedback interaction between intrinsic rebound spiking and transverse traveling waves with multiple heading angles. *Frontiers in Systems Neuroscience*, *8*, 201.
- Hasselmo, M. E., & Stern, C. E. (2018). A network model of behavioural performance in a rule learning task.

- Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, 373, 20170275.
- Hasselmo, M. E., & Wyble, B. P. (1997). Free recall and recognition in a network model of the hippocampus: Simulating effects of scopolamine on human memory function. *Behavioural Brain Research*, 89, 1–34.
- Hetherington, P. A., & Shapiro, M. L. (1993). A simple network model simulates hippocampal place fields: II. Computing goal-directed trajectories and memory fields. *Behavioral Neuroscience*, 107, 434–443.
- Heys, J. G., Rangarajan, K. V., & Dombeck, D. A. (2014). The functional micro-organization of grid cells revealed by cellular-resolution imaging. *Neuron*, 84, 1079–1090.
- 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, 666–679.
- Hinman, J. R., Chapman, G. W., & Hasselmo, M. E. (2017). Egocentric representation of environmental boundaries in the striatum. *Society for Neuroscience Abstracts*, 44, 710–723.
- Hinman, J. R., Chapman, G. W., & Hasselmo, M. E. (2019). Neuronal representation of environmental boundaries in egocentric coordinates. *Nature Communications*, 10, 2772.
- Hinman, J. R., Dannenberg, H., Alexander, A. S., & Hasselmo, M. E. (2018). Neural mechanisms of navigation involving interactions of cortical and subcortical structures. *Journal of Neurophysiology*, 119, 2007–2029.
- Hirsch, M. W., & Smale, S. (1974). *Differential equations, dynamical systems, and linear algebra*. Boston, MA: Academic Press.
- Hochreiter, S., & Schmidhuber, J. (1997). Long short-term memory. *Neural Computation*, 9, 1735–1780.
- Hoh, T. E., Kolb, B., Eppel, A., Vanderwolf, C. H., & Cain, D. P. (2003). Role of the neocortex in the water maze task in the rat: A detailed behavioral and Golgi-Cox analysis. *Behavioural Brain Research*, 138, 81–94.
- Howard, M. W., Fotedar, M. S., Datey, A. S., & Hasselmo, M. E. (2004). The temporal context model in spatial navigation and relational learning: Explaining medial temporal lobe function across domains. *Psychological Review*, 112, 75–116.
- Howard, L. R., Javadi, A. H., Yu, Y., Mill, R. D., Morrison, L. C., Knight, R., et al. (2014). The hippocampus and entorhinal cortex encode the path and Euclidean distances to goals during navigation. *Current Biology*, 24, 1331–1340.
- Howard, M. W., & Kahana, M. J. (2002). A distributed representation of temporal context. *Journal of Mathematical Psychology*, 46, 269–299.
- Howard, M. W., MacDonald, C. J., Tiganj, Z., Shankar, K. H., Du, Q., Hasselmo, M. E., et al. (2014). A unified mathematical framework for coding time, space, and sequences in the hippocampal region. *Journal of Neuroscience*, 34, 4692–4707.
- Hudon, C., Doré, F. Y., & Goulet, S. (2002). Spatial memory and choice behavior in the radial arm maze after fornix transection. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 26, 1113–1123.
- Huerta, P. T., & Lisman, J. E. (1995). Bidirectional synaptic plasticity induced by a single burst during cholinergic theta oscillation in CA1 in vitro. *Neuron*, 15, 1053–1063.
- Hyman, J. M., Wyble, B. P., Goyal, V., Rossi, C. A., & Hasselmo, M. E. (2003). Stimulation in hippocampal region CA1 in behaving rats yields long-term potentiation when delivered to the peak of theta and long-term depression when delivered to the trough. *Journal of Neuroscience*, 23, 11725–11731.
- Hyman, J. M., Wyble, B. P., Rossi, C. A., & Hasselmo, M. E. (2002). Coherence between theta rhythm in rat medial prefrontal cortex and hippocampus. *Society for Neuroscience Abstracts*, 28, 476–477.
- Ison, M. J., Quiñero, R., & Fried, I. (2015). Rapid encoding of new memories by individual neurons in the human brain. *Neuron*, 87, 220–230.
- Izhikevich, E. M. (2003). Simple model of spiking neurons. *IEEE Transactions on Neural Networks*, 14, 1569–1572.
- Jeewajee, A., Barry, C., O’Keefe, J., & Burgess, N. (2008). Grid cells and theta as oscillatory interference: Electrophysiological data from freely moving rats. *Hippocampus*, 18, 1175–1185.
- Johnson, A., & Redish, A. D. (2007). Neural ensembles in CA3 transiently encode paths forward of the animal at a decision point. *Journal of Neuroscience*, 27, 12176–12189.
- Jones, M. W., & Wilson, M. A. (2005). Theta rhythms coordinate hippocampal–prefrontal interactions in a spatial memory task. *PLoS Biology*, 3, e402.
- Kahana, M. J., Sekuler, R., Caplan, J. B., Kirschen, M., & Madsen, J. R. (1999). Human theta oscillations exhibit task dependence during virtual maze navigation. *Nature*, 399, 781–784.
- Keene, C. S., Bladon, J., McKenzie, S., Liu, C. D., O’Keefe, J., & Eichenbaum, H. (2016). Complementary functional organization of neuronal activity patterns in the perirhinal, lateral entorhinal, and medial entorhinal cortices. *Journal of Neuroscience*, 36, 3660–3675.
- Kinsky, N. R., Sullivan, D. W., Mau, W., Hasselmo, M. E., & Eichenbaum, H. B. (2018). Hippocampal place fields maintain a coherent and flexible map across long timescales. *Current Biology*, 28, 3578.e6–3588.e6.
- Kirchhoff, B. A., Wagner, A. D., Maril, A., & Stern, C. E. (2000). Prefrontal–temporal circuitry for episodic encoding and subsequent memory. *Journal of Neuroscience*, 20, 6173–6180.
- Kitamura, T., Pignatelli, M., Suh, J., Kohara, K., Yoshiki, A., Abe, K., et al. (2014). Island cells control temporal association memory. *Science*, 343, 896–901.
- Kitamura, T., Sun, C., Martin, J., Kitch, L. J., Schnitzer, M. J., & Tonegawa, S. (2015). Entorhinal cortical ocean cells encode specific contexts and drive context-specific fear memory. *Neuron*, 87, 1317–1331.
- Klausberger, T., & Somogyi, P. (2008). Neuronal diversity and temporal dynamics: The unity of hippocampal circuit operations. *Science*, 321, 53–57.
- Klink, R., & Alonso, A. (1993). Ionic mechanisms for the subthreshold oscillations and differential electroresponsiveness of medial entorhinal cortex layer II neurons. *Journal of Neurophysiology*, 70, 144–157.
- Koenig, J., Linder, A. N., Leutgeb, J. K., & Leutgeb, S. (2011). The spatial periodicity of grid cells is not sustained during reduced theta oscillations. *Science*, 332, 592–595.
- Komorowski, R. W., Manns, J. R., & Eichenbaum, H. (2009). Robust conjunctive item-place coding by hippocampal neurons parallels learning what happens where. *Journal of Neuroscience*, 29, 9918–9929.
- Kraus, B. J., Brandon, M. P., Robinson, R. J., II, Connerney, M. A., Hasselmo, M. E., & Eichenbaum, H. (2015). During running in place, grid cells integrate elapsed time and distance run. *Neuron*, 88, 578–589.
- Kraus, B. J., Robinson, R. J., II, White, J. A., Eichenbaum, H., & Hasselmo, M. E. (2013). Hippocampal “time cells”: Time versus path integration. *Neuron*, 78, 1090–1101.
- Kreiman, G. (2007). Single unit approaches to human vision and memory. *Current Opinion in Neurobiology*, 17, 471–475.
- Kreiman, G., Koch, C., & Fried, I. (2000a). Imagery neurons in the human brain. *Nature*, 408, 357–361.
- Kreiman, G., Koch, C., & Fried, I. (2000b). Category-specific visual responses of single neurons in the human medial temporal lobe. *Nature Neuroscience*, 3, 946–953.
- Kropff, E., Carmichael, J. E., Moser, M. B., & Moser, E. I. (2015). Speed cells in the medial entorhinal cortex. *Nature*, 523, 419–424.

- Kropff, E., & Treves, A. (2008). The emergence of grid cells: Intelligent design or just adaptation? *Hippocampus*, *18*, 1256–1269.
- Krupic, J., Bauza, M., Burton, S., Lever, C., & O'Keefe, J. (2014). How environment geometry affects grid cell symmetry and what we can learn from it. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, *369*, 20130188.
- LeCun, Y., Bengio, Y., & Hinton, G. (2015). Deep learning. *Nature*, *521*, 436–444.
- Leonard, B. W., Amaral, D. G., Squire, L. R., & Zola-Morgan, S. (1995). Transient memory impairment in monkeys with bilateral lesions of the entorhinal cortex. *Journal of Neuroscience*, *15*, 5637–5659.
- Lever, C., Burton, S., Jeewajee, A., O'Keefe, J., & Burgess, N. (2009). Boundary vector cells in the subiculum of the hippocampal formation. *Journal of Neuroscience*, *29*, 9771–9777.
- Lever, C., Wills, T., Cacucci, F., Burgess, N., & O'Keefe, J. (2002). Long-term plasticity in hippocampal place-cell representation of environmental geometry. *Nature*, *416*, 90–94.
- Liu, Y., Tiganj, Z., Hasselmo, M. E., & Howard, M. W. (2019). A neural microcircuit model for a scalable scale-invariant representation of time. *Hippocampus*, *29*, 260–274.
- Lundqvist, M., Compte, A., & Lansner, A. (2010). Bistable, irregular firing and population oscillations in a modular attractor memory network. *PLoS Computational Biology*, *6*, e1000803.
- Lundqvist, M., Herman, P., & Lansner, A. (2011). Theta and gamma power increases and alpha/beta power decreases with memory load in an attractor network model. *Journal of Cognitive Neuroscience*, *23*, 3008–3020.
- Lundqvist, M., Herman, P., Warden, M. R., Brincat, S. L., & Miller, E. K. (2018). Gamma and beta bursts during working memory readout suggest roles in its volitional control. *Nature Communications*, *9*, 394.
- Lundqvist, M., Rose, J., Herman, P., Brincat, S. L., Buschman, T. J., & Miller, E. K. (2016). Gamma and beta bursts underlie working memory. *Neuron*, *90*, 152–164.
- MacDonald, C. J., Carrow, S., Place, R., & Eichenbaum, H. (2013). Distinct hippocampal time cell sequences represent odor memories in immobilized rats. *Journal of Neuroscience*, *33*, 14607–14616.
- MacDonald, C. J., Lepage, K. Q., Eden, U. T., & Eichenbaum, H. (2011). Hippocampal “time cells” bridge the gap in memory for discontinuous events. *Neuron*, *71*, 737–749.
- Mallory, C. S., Hardcastle, K., Bant, J. S., & Giocomo, L. M. (2018). Grid scale drives the scale and long-term stability of place maps. *Nature Neuroscience*, *21*, 270–282.
- Marozzi, E., Ginzberg, L. L., Alenda, A., & Jeffery, K. J. (2015). Purely translational realignment in grid cell firing patterns following nonmetric context change. *Cerebral Cortex*, *25*, 4619–4627.
- Marston, H. M., Everitt, B. J., & Robbins, T. W. (1993). Comparative effects of excitotoxic lesions of the hippocampus and septum diagonal band on conditional visual-discrimination and spatial-learning. *Neuropsychologia*, *31*, 1099–1118.
- Mathis, A., Stemmler, M. B., & Herz, A. V. (2015). Probable nature of higher-dimensional symmetries underlying mammalian grid-cell activity patterns. *eLife*, *4*.
- Mau, W., Sullivan, D. W., Kinsky, N. R., Hasselmo, M. E., Howard, M. W., & Eichenbaum, H. (2018). The same hippocampal CA1 population simultaneously codes temporal information over multiple timescales. *Current Biology*, *28*, 1499.e4–1508.e4.
- McKenzie, S., Keene, C. S., Farovik, A., Bladon, J., Place, R., Komorowski, R., et al. (2016). Representation of memories in the cortical–hippocampal system: Results from the application of population similarity analyses. *Neurobiology of Learning and Memory*, *134*, Pt. A, 178–191.
- 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*, 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*, 663–678.
- McNaughton, B. L., & Morris, R. G. M. (1987). Hippocampal synaptic enhancement and information storage within a distributed memory system. *Trends in Neurosciences*, *10*, 408–415.
- Mel, B. W. (1993). Synaptic integration in an excitable dendritic tree. *Journal of Neurophysiology*, *70*, 1086–1101.
- Mendeleeev, D. (1869). On the relations of element's properties to their atomic weights (translated from German). *Zeitschrift für Chemie*, *12*, 405–406.
- Meunier, M., Bachevalier, J., Mishkin, M., & Murray, E. A. (1993). Effects on visual recognition of combined and separate ablations of the entorhinal and perirhinal cortex in rhesus monkeys. *Journal of Neuroscience*, *13*, 5418–5432.
- Milford, M. J., Wiles, J., & Wyeth, G. F. (2010). Solving navigational uncertainty using grid cells on robots. *PLoS Computational Biology*, *6*, e1000995.
- Milford, M. J., & Wyeth, G. (2010). Persistent navigation and mapping using a biologically inspired SLAM system. *International Journal of Robotics Research*, *29*, 1131–1153.
- Misra, P., Marconi, A., Peterson, M., & Kreiman, G. (2018). Minimal memory for details in real life events. *Scientific Reports*, *8*, 16701.
- Mitchell, S. J., Rawlins, J. N., Steward, O., & Olton, D. S. (1982). Medial septal area lesions disrupt theta rhythm and cholinergic staining in medial entorhinal cortex and produce impaired radial arm maze behavior in rats. *Journal of Neuroscience*, *2*, 292–302.
- Morris, R. G., Anderson, E., Lynch, G. S., & Baudry, M. (1986). Selective impairment of learning and blockade of long-term potentiation by an N-methyl-D-aspartate receptor antagonist, AP5. *Nature*, *319*, 774–776.
- Muller, R. U., & Kubie, J. L. (1987). The effects of changes in the environment on the spatial firing of hippocampal complex-spike cells. *Journal of Neuroscience*, *7*, 1951–1968.
- Nigro, G., & Neisser, U. (1983). Point of view in personal memories. *Cognitive Psychology*, *15*, 467–482.
- Norman, K. A., & O'Reilly, R. C. (2003). Modeling hippocampal and neocortical contributions to recognition memory: A complementary-learning-systems approach. *Psychological Review*, *110*, 611–646.
- O'Keefe, J. (1976). Place units in the hippocampus of the freely moving rat. *Experimental Neurology*, *51*, 78–109.
- O'Keefe, J., & Burgess, N. (1996). Geometric determinants of the place fields of hippocampal neurons. *Nature*, *381*, 425–428.
- 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*, 171–175.
- O'Keefe, J., & Nadel, L. (1978). *The hippocampus as a cognitive map*. New York, NY: Oxford University Press.
- O'Keefe, J., & Recce, M. L. (1993). Phase relationship between hippocampal place units and the EEG theta rhythm. *Hippocampus*, *3*, 317–330.
- Ólafsdóttir, H. F., Barry, C., Saleem, A. B., Hassabis, D., & Spiers, H. J. (2015). Hippocampal place cells construct reward related sequences through unexplored space. *eLife*, *4*, e06063.
- Olton, D. S., Becker, J. T., & Handelmann, G. E. (1979). Hippocampus, space and memory. *Behavioral and Brain Sciences*, *2*, 313–365.
- Otto, T., & Eichenbaum, H. (1992). Neuronal activity in the hippocampus during delayed non-match to sample performance in rats: Evidence for hippocampal processing in recognition memory. *Hippocampus*, *2*, 323–334.

- Pang, K. C., Nocera, R., Secor, A. J., & Yoder, R. M. (2001). GABAergic septohippocampal neurons are not necessary for spatial memory. *Hippocampus*, *11*, 814–827.
- Pastalkova, E., Itskov, V., Amarasingham, A., & Buzsáki, G. (2008). Internally generated cell assembly sequences in the rat hippocampus. *Science*, *321*, 1322–1327.
- Peyrache, A., Lacroix, M. M., Petersen, P. C., & Buzsáki, G. (2015). Internally organized mechanisms of the head direction sense. *Nature Neuroscience*, *18*, 569–575.
- Pfeiffer, B. E., & Foster, D. J. (2013). Hippocampal place-cell sequences depict future paths to remembered goals. *Nature*, *497*, 74–79.
- 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*, 521–524.
- Poirazi, P., Brannon, T., & Mel, B. W. (2003). Arithmetic of subthreshold synaptic summation in a model CA1 pyramidal cell. *Neuron*, *37*, 977–987.
- Quiroga, R. Q., Reddy, L., Kreiman, G., Koch, C., & Fried, I. (2005). Invariant visual representation by single neurons in the human brain. *Nature*, *435*, 1102–1107.
- Rasmussen, D., & Eliasmith, C. (2011). A neural model of rule generation in inductive reasoning. *Topics in Cognitive Science*, *3*, 140–153.
- Raudies, F., Brandon, M. P., Chapman, G. W., & Hasselmo, M. E. (2015). Head direction is coded more strongly than movement direction in a population of entorhinal neurons. *Brain Research*, *1621*, 355–367.
- Raudies, F., & Hasselmo, M. E. (2017). A model of symbolic processing in Raven's progressive matrices. *Biologically Inspired Cognitive Architectures*, *21*, 47–58.
- Rawlins, J. N., Feldon, J., & Gray, J. A. (1979). Septo-hippocampal connections and the hippocampal theta rhythm. *Experimental Brain Research*, *37*, 49–63.
- Ray, S., Naumann, R., Burgalossi, A., Tang, Q., Schmidt, H., & Brecht, M. (2014). Grid-layout and theta-modulation of layer 2 pyramidal neurons in medial entorhinal cortex. *Science*, *343*, 891–896.
- Redish, A. D., & Touretzky, D. S. (1997). Cognitive maps beyond the hippocampus. *Hippocampus*, *7*, 15–35.
- Redish, A. D., & Touretzky, D. S. (1998). The role of the hippocampus in solving the Morris water maze. *Neural Computation*, *10*, 73–111.
- Riches, I. P., Wilson, F. A., & Brown, M. W. (1991). The effects of visual stimulation and memory on neurons of the hippocampal formation and the neighboring parahippocampal gyrus and inferior temporal cortex of the primate. *Journal of Neuroscience*, *11*, 1763–1779.
- Robinson, J. C., & Brandon, M. P. (2018). Disentangling the role of medial septal cell types in grid cell generation. *Society for Neuroscience*, *44*, 508–526.
- Robinson, J., Manseau, F., Ducharme, G., Amilhon, B., Vigneault, E., El Mestikawy, S., et al. (2016). Optogenetic activation of septal glutamatergic neurons drive hippocampal theta rhythms. *Journal of Neuroscience*, *36*, 3016–3023.
- Robinson, J. A., & Swanson, K. L. (1993). Field and observer modes of remembering. *Memory*, *1*, 169–184.
- Roe, A. W., Pallas, S. L., Hahm, J. O., & Sur, M. (1990). A map of visual space induced in primary auditory cortex. *Science*, *250*, 818–820.
- Roe, A. W., Pallas, S. L., Kwon, Y. H., & Sur, M. (1992). Visual projections routed to the auditory pathway in ferrets: Receptive fields of visual neurons in primary auditory cortex. *Journal of Neuroscience*, *12*, 3651–3664.
- Rutishauser, U., Ross, I. B., Mamelak, A. N., & Schuman, E. M. (2010). Human memory strength is predicted by theta-frequency phase-locking of single neurons. *Nature*, *464*, 903–907.
- Rutishauser, U., Schuman, E. M., & Mamelak, A. N. (2008). Activity of human hippocampal and amygdala neurons during retrieval of declarative memories. *Proceedings of the National Academy of Sciences, U.S.A.*, *105*, 329–334.
- Rutishauser, U., Tudusciuc, O., Neumann, D., Mamelak, A. N., Heller, A. C., Ross, I. B., et al. (2011). Single-unit responses selective for whole faces in the human amygdala. *Current Biology*, *21*, 1654–1660.
- Samsonovich, A., & McNaughton, B. L. (1997). Path integration and cognitive mapping in a continuous attractor neural network model. *Journal of Neuroscience*, *17*, 5900–5920.
- Sargolini, F., Fyhn, M., Hafting, T., McNaughton, B. L., Witter, M. P., Moser, M. B., et al. (2006). Conjunctive representation of position, direction, and velocity in entorhinal cortex. *Science*, *312*, 758–762.
- Savelli, F., Yoganarasimha, D., & Knierim, J. J. (2008). Influence of boundary removal on the spatial representations of the medial entorhinal cortex. *Hippocampus*, *18*, 1270–1282.
- Scoville, W. B., & Milner, B. (1957). Loss of recent memory after bilateral hippocampal lesions. *Journal of Neurology, Neurosurgery and Psychiatry*, *20*, 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, U.S.A.*, *99*, 1616–1620.
- 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*, 2274–2286.
- Sherfey, J. S., Ardid, S., Hass, J., Hasselmo, M. E., & Kopell, N. J. (2018). Flexible resonance in prefrontal networks with strong feedback inhibition. *PLoS Computational Biology*, *14*, e1006357.
- Sherrill, K. R., Chrastil, E. R., Ross, R. S., Erdem, U. M., Hasselmo, M. E., & Stern, C. E. (2015). Functional connections between optic flow areas and navigationally responsive brain regions during goal-directed navigation. *Neuroimage*, *118*, 386–396.
- Si, B., Kropff, E., & Treves, A. (2012). Grid alignment in entorhinal cortex. *Biological Cybernetics*, *106*, 483–506.
- Siegle, J. H., & Wilson, M. A. (2014). Enhancement of encoding and retrieval functions through theta phase-specific manipulation of hippocampus. *eLife*, *3*, e03061.
- 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*, 149–172.
- Sohal, V. S., & Hasselmo, M. E. (2000). A model for experience-dependent changes in the responses of inferotemporal neurons. *Network*, *11*, 169–190.
- Solstad, T., Boccara, C. N., Kropff, E., Moser, M. B., & Moser, E. I. (2008). Representation of geometric borders in the entorhinal cortex. *Science*, *322*, 1865–1868.
- Sreenivasan, S., & Fiete, I. (2011). Grid cells generate an analog error-correcting code for singularly precise neural computation. *Nature Neuroscience*, *14*, 1330–1337.
- Stackman, R. W., & Taube, J. S. (1998). Firing properties of rat lateral mammillary single units: Head direction, head pitch, and angular head velocity. *Journal of Neuroscience*, *18*, 9020–9037.
- Stanton, M. E., Thomas, G. J., & Brito, G. N. (1984). Posterodorsal septal lesions impair performance on both shift and stay working memory tasks. *Behavioral Neuroscience*, *98*, 405–415.
- Steele, R. J., & Morris, R. G. (1999). Delay-dependent impairment of a matching-to-place task with chronic and intrahippocampal infusion of the NMDA-antagonist D-AP5. *Hippocampus*, *9*, 118–136.

- Steffenach, H. A., Witter, M., Moser, M. B., & Moser, E. I. (2005). Spatial memory in the rat requires the dorsolateral band of the entorhinal cortex. *Neuron*, *45*, 301–313.
- Stensola, H., Stensola, T., Solstad, T., Froland, K., Moser, M. B., & Moser, E. I. (2012). The entorhinal grid map is discretized. *Nature*, *492*, 72–78.
- Stern, C. E., Corkin, S., Gonzalez, R. G., Guimaraes, A. R., Baker, J. R., Jennings, P. J., et al. (1996). The hippocampal formation participates in novel picture encoding: Evidence from functional magnetic resonance imaging. *Proceedings of the National Academy of Sciences, U.S.A.*, *93*, 8660–8665.
- Stewart, M., & Fox, S. E. (1990). Do septal neurons pace the hippocampal theta rhythm? *Trends Neurosciences*, *13*, 163–168.
- Suzuki, W. A., Miller, E. K., & Desimone, R. (1997). Object and place memory in the macaque entorhinal cortex. *Journal of Neurophysiology*, *78*, 1062–1081.
- Tahvildari, B., Fransén, E., Alonso, A. A., & Hasselmo, M. E. (2007). Switching between “on” and “off” states of persistent activity in lateral entorhinal layer III neurons. *Hippocampus*, *17*, 257–263.
- Taube, J. S. (1995). Head direction cells recorded in the anterior thalamic nuclei of freely moving rats. *Journal of Neuroscience*, *15*, 70–86.
- Taube, J. S., & Bassett, J. P. (2003). Persistent neural activity in head direction cells. *Cerebral Cortex*, *13*, 1162–1172.
- Taube, J. S., Kesslak, J. P., & Cotman, C. W. (1992). Lesions of the rat postsubiculum impair performance on spatial tasks. *Behavioral and Neural Biology*, *57*, 131–143.
- 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*, 420–435.
- Terrazas, A., Krause, M., Lipa, P., Gothard, K. M., Barnes, C. A., & McNaughton, B. L. (2005). Self-motion and the hippocampal spatial metric. *Journal of Neuroscience*, *25*, 8085–8096.
- Teyler, T. J., & DiScenna, P. (1986). The hippocampal memory indexing theory. *Behavioral Neuroscience*, *100*, 147–154.
- Teyler, T. J., & Rudy, J. W. (2007). The hippocampal indexing theory and episodic memory: Updating the index. *Hippocampus*, *17*, 1158–1169.
- Tiganj, Z., Hasselmo, M. E., & Howard, M. W. (2015). A simple biophysically plausible model for long time constants in single neurons. *Hippocampus*, *25*, 27–37.
- Tingley, D., & Buzsáki, G. (2018). Transformation of a spatial map across the hippocampal–lateral septal circuit. *Neuron*, *98*, 1229.e5–1242.e5.
- Touretzky, D. S., & Redish, A. D. (1996). Theory of rodent navigation based on interacting representations of space. *Hippocampus*, *6*, 247–270.
- Treves, A., & Rolls, E. T. (1994). Computational analysis of the role of the hippocampus in memory. *Hippocampus*, *4*, 374–391.
- Tsao, A., Moser, M. B., & Moser, E. I. (2013). Traces of experience in the lateral entorhinal cortex. *Current Biology*, *23*, 399–405.
- Tsao, A., Sugar, J., Lu, L., Wang, C., Knierim, J. J., Moser, M. B., et al. (2018). Integrating time from experience in the lateral entorhinal cortex. *Nature*, *561*, 57–62.
- Tulving, E. (1972). Episodic and semantic memory. In E. Tulving, & W. Donaldson (Eds.), *Organization of memory* (pp. 382–402). New York: Academic Press.
- Tulving, E. (1984). Précis of elements of episodic memory. *Behavioral and Brain Sciences*, *7*, 223–268.
- Tulving, E. (2001). Episodic memory and common sense: How far apart? *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences*, *356*, 1505–1515.
- Vann, S. D., & Aggleton, J. P. (2004). The mammillary bodies: Two memory systems in one? *Nature Reviews Neuroscience*, *5*, 35–44.
- Van Veen, F. (2016). *The neural network zoo*. Retrieved from <http://www.asimovinstitute.org/neural-network-zoo>.
- Viskontas, I. V., Ekstrom, A. D., Wilson, C. L., & Fried, I. (2007). Characterizing interneuron and pyramidal cells in the human medial temporal lobe in vivo using extracellular recordings. *Hippocampus*, *17*, 49–57.
- Wagner, A. D., Schacter, D. L., Rotte, M., Koutstaal, W., Maril, A., Dale, A. M., et al. (1998). Building memories: Remembering and forgetting of verbal experiences as predicted by brain activity. *Science*, *281*, 1188–1191.
- Wang, C., Chen, X., Lee, H., Deshmukh, S. S., Yoganarasimha, D., Savelli, F., et al. (2018). Egocentric coding of external items in the lateral entorhinal cortex. *Science*, *362*, 945–949.
- Wang, Y., Romani, S., Lustig, B., Leonardo, A., & Pastalkova, E. (2015). Theta sequences are essential for internally generated hippocampal firing fields. *Nature Neuroscience*, *18*, 282–288.
- Welday, A. C., Shlifer, I. G., Bloom, M. L., Zhang, K., & Blair, H. T. (2011). Cosine directional tuning of theta cell burst frequencies: Evidence for spatial coding by oscillatory interference. *Journal of Neuroscience*, *31*, 16157–16176.
- Widloski, J., & Fiete, I. R. (2014). A model of grid cell development through spatial exploration and spike time-dependent plasticity. *Neuron*, *83*, 481–495.
- Wiener, S. I., Paul, C. A., & Eichenbaum, H. (1989). Spatial and behavioral correlates of hippocampal neuronal activity. *Journal of Neuroscience*, *9*, 2737–2763.
- Wikenheiser, A. M., & Redish, A. D. (2015). Hippocampal theta sequences reflect current goals. *Nature Neuroscience*, *18*, s289–s294.
- Wills, T. J., Barry, C., & Cacucci, F. (2012). The abrupt development of adult-like grid cell firing in the medial entorhinal cortex. *Frontiers in Neural Circuits*, *6*, 21.
- Wills, T. J., Cacucci, F., Burgess, N., & O’Keefe, J. (2010). Development of the hippocampal cognitive map in preweanling rats. *Science*, *328*, 1573–1576.
- Wilson, F. A., Riches, I. P., & Brown, M. W. (1990). Hippocampus and medial temporal cortex: Neuronal activity related to behavioural responses during the performance of memory tasks by primates. *Behavioural Brain Research*, *40*, 7–28.
- Winson, J. (1978). Loss of hippocampal theta rhythm results in spatial memory deficit in the rat. *Science*, *201*, 160–163.
- Winter, S. S., Clark, B. J., & Taube, J. S. (2015). Spatial navigation. Disruption of the head direction cell network impairs the parahippocampal grid cell signal. *Science*, *347*, 870–874.
- Wood, E. R., Dudchenko, P. A., & Eichenbaum, H. (1999). The global record of memory in hippocampal neuronal activity. *Nature*, *397*, 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*, 623–633.
- Yoon, K., Buice, M. A., Barry, C., Hayman, R., Burgess, N., & Fiete, I. R. (2013). Specific evidence of low-dimensional continuous attractor dynamics in grid cells. *Nature Neuroscience*, *16*, 1077–1084.
- Young, B. J., Otto, T., Fox, G. D., & Eichenbaum, H. (1997). Memory representation within the parahippocampal region. *Journal of Neuroscience*, *17*, 5183–5195.
- Zilli, E. A., & Hasselmo, M. E. (2010). Coupled noisy spiking neurons as velocity-controlled oscillators in a model of grid cell spatial firing. *Journal of Neuroscience*, *30*, 13850–13860.
- Zola-Morgan, S., & Squire, L. R. (1986). Memory impairment in monkeys following lesions limited to the hippocampus. *Behavioral Neuroscience*, *100*, 155–160.
- Zola-Morgan, S., Squire, L. R., Clower, R. P., & Rempel, N. L. (1993). Damage to the perirhinal cortex exacerbates memory impairment following lesions to the hippocampal formation. *Journal of Neuroscience*, *13*, 251–265.