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Oscillation-supported Information Processing and Transfer at the Hippocampus–Entorhinal–Neocortical Interface

György Buzsáki and Kamran Diba

Abstract

As information is propelled along the multisynaptic feedforward loops of the entorhinal–hippocampal system, each stage adds unique features to the incoming information (Figure 7.1). Such local operations require time, and are generally reflected by macroscopic oscillations. In each oscillatory cycle, recruitment of principal neurons is temporally protracted and terminated by the buildup of inhibition. In addition to providing a temporal framework in which information can be packaged, oscillatory coupling across networks can facilitate the exchange of information and determine the direction of activity flow. Potential mechanisms in the entorhinal–hippocampal system supporting these hypotheses are described.

Oscillations Provide the Structure for Information Processing in the Hippocampus

Two major network patterns dominate the hippocampal system: theta oscillations (4–10 Hz) and sharp waves with their associated ripples (140–200 Hz). Theta and sharp-wave patterns also define states of the hippocampus: the theta state is associated with exploratory ("preparatory") movement and REM sleep, whereas intermittent sharp waves mark immobility, consummatory behaviors, and slow-wave sleep. These two competing states bias the direction of information flow to a great extent, with neocortical–hippocampal transfer taking

Chapter from "Dynamic Coordination in the Brain: From Neurons to Mind," edited by C. von der Malsburg, W. A. Phillips, and W. Singer. Strüngmann Forum Report, vol. 5. ISBN 978-0-262-01471-7. Cambridge, MA: The MIT Press.

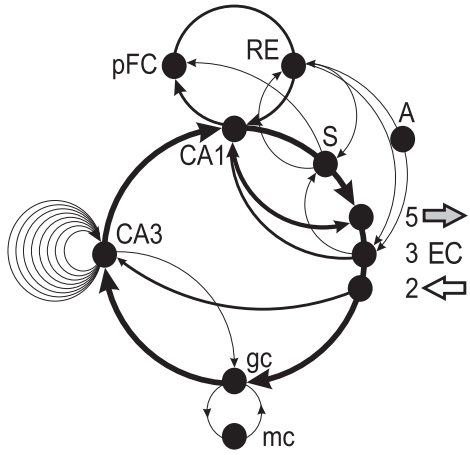

Figure 7.1 Multiple loops of the hippocampal–entorhinal circuits. The long loop connecting the layer 2 entorhinal cortex (EC), granule cells (gc), CA3, CA1, and subiculum (S) back to the layer 5 EC is supplemented by multiple shortcuts and superimposed loops. The shortest loop between the EC and hippocampus is the path from the layer 3 EC to CA1 and back to the layer 5 EC. Excitatory traffic in the multiple loops is controlled by a large family of interneurons, whose connections are not loop-like (Freund and Buzsáki 1996). mc: mossy cells of the hilus; A: amygdala; RE: nucleus reuniens of thalamus; pFC: prefrontal, anterior cingulate cortex.

place mainly during theta oscillations and hippocampal–neocortical transfer during sharp waves (Isomura et al. 2006).

The extracellularly recorded theta oscillation is the result of coherent membrane potential oscillations across neurons in all hippocampal subregions (Buzsáki 2002). Theta currents derive from multiple sources, including synaptic currents, intrinsic currents of neurons, dendritic Ca^{2+} spikes, and other voltage-dependent membrane oscillations. Theta frequency modulation of perisomatic interneurons provides an outward current in somatic layers and phase-biases the power of ongoing gamma frequency oscillations (30–100 Hz), the result of which is a theta-nested gamma burst. Excitatory afferents form active sinks (inward current) at confined dendritic domains within cytoarchitecturally organized layers in every region. Each layer-specific excitatory input is complemented by one or more families of interneurons with similar axonal projections (Freund and Buzsáki 1996; Klausberger and Somogyi 2008), forming layer-specific "theta" dipoles. The resulting rich consortium of theta generators in the hippocampal and parahippocampal regions is coordinated by the medial septum and a network of long-range interneurons. Furthermore, the power, coherence, and phase of theta oscillators can fluctuate significantly in a layer-specific manner as a function of overt behavior and/or the memory "load" to support task performance (Montgomery et al. 2009).

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Theta-nested gamma oscillations are generated primarily by the interaction between interneurons and/or between principal cells and interneurons. In both scenarios, the frequency of oscillations is largely determined by the time course of $GABA_A$ receptor-mediated inhibition. Neurons that discharge within the time period of the gamma cycle (8–30 ms) define a cell assembly (Harris et al. 2003). Given that the membrane time constant of pyramidal neurons *in vivo* is also within this temporal range, recruiting neurons into this assembly time window is the most effective mechanism for discharging the downstream postsynaptic neuron(s) on which the assembly members converge. Although gamma oscillations can emerge in each hippocampal region, they can be coordinated across regions by either excitatory connections or long-range interneurons. The CA3–CA1 regions appear to form a large coherent gamma oscillator, due to the interaction between the recurrently excited CA3 pyramidal cells and their interneuron targets in both CA3 and CA1 regions. This "CA3 gamma generator" is normally under the suppressive control of the entorhinal–dentate gamma generator, and its power is enhanced severalfold when the entorhinal–dentate input is attenuated (Bragin et al. 1995). Entorhinal circuits generate their own gamma oscillations by largely similar rules, and these (generally faster) rhythms can be transferred and detected in the hippocampus.

When the subcortical modulatory inputs decrease in tone, theta oscillations are replaced by large amplitude field potentials called sharp waves (SPW). SPWs are initiated by the self-organized population bursts of the CA3 pyramidal cells (Buzsáki et al. 1983). The CA3-induced depolarization of CA1 pyramidal cell dendrites results in a prominent extracellular negative wave, from which the SPW derives its name, in the stratum radiatum. The CA1 SPWs are associated with fast-field oscillations (140–200 Hz), or "ripples" confined to the CA1 pyramidal cell layer (O'Keefe and Nadel 1978; Buzsáki et al. 1992). At least two factors contribute to the field ripples. First, the synchronous discharge of pyramidal neurons generates repetitive "mini populations spikes" that are responsible for the spike-like appearance of the troughs of ripples in the pyramidal cell layer. Second, the rhythmic positive "wave" components reflect synchronously occurring oscillating inhibitory postsynaptic potentials (IPSPs) in the pyramidal cells because the CA3–CA1 pyramidal cells strongly drive perisomatic interneurons during the SPW. In the time window of SPWs, 50,000–100,000 neurons discharge synchronously in the CA3–CA1–subicular complex–entorhinal axis. The population burst is characterized by a three- to fivefold gain of network excitability in the CA1 region, preparing the circuit for synaptic plasticity (Csicsvari et al. 1999a). SPWs have been hypothesized to play a critical role in transferring transient memories from the hippocampus to the neocortex for permanent storage (Buzsáki 1989), and this hypothesis is supported by numerous experiments demonstrating that the neuronal content of the SPW ripple is largely determined by recent waking experiences (Wilson and McNaughton 1994; Foster and Wilson 2006; Csicsvari et al. 2007).

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Reciprocal Information Transfer by Oscillations

Oscillations and neuronal synchrony create effective mechanisms for the storage, readout, and transfer of information between different structures. Oscillations impose a spatiotemporal structure on neural ensemble activity within and across different brain areas, and allow for the packaging of information in quanta of different durations. Furthermore, oscillations support the bidirectional flow of information across different structures through the changing of the temporal offset in the oscillation-related firing (Amzica and Steriade 1998; Chrobak and Buzsáki 1998b; Sirota et al. 2003; Buzsáki 2005; Siapas et al. 2005). Most importantly, exchanging information across structures by oscillations involves mechanisms different from what is usually meant by the term "information transfer."

In the usual sense, transfer of information involves two structures, or systems, which can be designated as the "source" (sender) and "target" (receiver). Typically, the information transfer process is assumed to be unidirectional and passive: the source sends the information to an ever-ready recipient. In systems coupled by oscillations, however, the method appears to be different; we refer to this process as "reciprocal information transfer" (Sirota and Buzsáki 2005; Sirota et al. 2008). The reciprocal process implies that a target structure takes the initiative by temporally biasing the activity in the sender (information source) structure (Sirota et al. 2003; Fries 2005; Sirota and Buzsáki 2005; Isomura et al. 2006; Womelsdorf et al. 2007). Biasing is achieved by the strong output ("duty cycle") of the receiver so that the information, contained in finer timescale gamma-structured spike trains, reaches the recipient structure in its most sensitive state (the "perturbation" cycle), ideal for reception. Below, we illustrate this principle using the state-dependent communication between the hippocampus and neocortex.

In the waking state, transfer of neocortical information to the hippocampus can be initiated by the hippocampus via theta-phase biasing of neocortical network dynamics, as reflected in the local field potential (LFP) by transient gamma oscillations in widespread and relatively isolated neocortical areas (Sirota et al. 2008). As a result, locally generated gamma oscillations from multiple neocortical locations are time biased so that the information contained in their gamma bursts arrive back at the hippocampus at a phase of the theta cycle optimal for maximal perturbation of hippocampal networks and plasticity (Huerta and Lisman 1996; Holscher et al. 1997). In the CA1 region, this corresponds to the positive (least active, i.e., recipient) phase of the theta cycle (Csicsvari et al. 1999b). This is also the phase at which a hippocampal neuron discharges when the rat enters its place field (O'Keefe and Recce 1993). In short, through theta-phase biasing, the hippocampus can affect multiple neocortical sites so that it can effectively receive information from the resulting neocortical assemblies, by way of the entorhinal cortex (EC), at the optimal time frame.

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The direction of information transfer during slow-wave sleep at the hippocampal–neocortex axis is largely opposite to that in the waking theta state. As discussed earlier, in the absence of theta oscillations, the CA3–CA1 region gives rise to SPWs. The synchronous discharge of CA1 neurons and downstream subicular and EC neurons provides a most effective output to the neocortex (Chrobak and Buzsáki 1994). During sleep the information source (sender) is the hippocampus but, again, the transfer of information is initiated by the receiver (now the neocortex). This latter process has been hypothesized to be critical in consolidating the learned information acquired in the waking state (Buzsáki 1989).

A caveat in this two-stage model of information transfer and memory consolidation is the absence of a mechanism to coordinate and guide the hippocampal output temporally to the ongoing activity in the neocortical circuits that gave rise to the experience-dependent hippocampal input. In other words, a mechanism must exist to allow the hippocampal output during sharp wave ripples (SWRs) to address the relevant neocortical circuits. Below, we outline one such potential mechanism.

While the hippocampus is generating SPWs during slow-wave sleep, large areas of the neocortex oscillate coherently at a slow frequency (0.5–1.5 Hz) (Steriade et al. 1993a, b; Destexhe et al. 1999). During these slow oscillations, large areas of the neocortex and paleocortex (Isomura et al. 2006) toggle coherently between active (UP) and silent (DOWN) states, although isolated cortical modules can also shift between states, independent of surrounding areas (Figure 7.2). The DOWN–UP transitions can trigger K complexes and

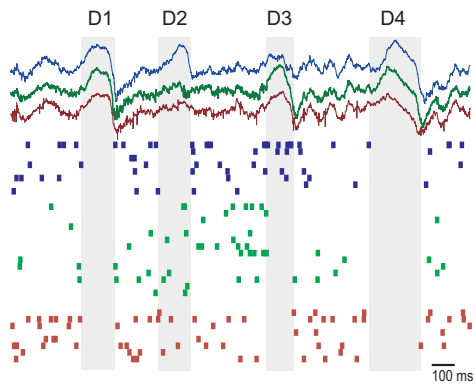

Figure 7.2 Global and local neocortical DOWN states (delta waves) during slow-wave sleep. Example of simultaneously recorded local field potentials (LFPs) and unit activity at three intracortical locations in the somatosensory area of the rat (~1 mm spaced). Note that DOWN states (shaded area) can be synchronous and global (D1, D4) or localized only to a small area (D2, D3). While the effects of global and synchronous neocortical patterns can be detected in the hippocampus by the macroscopic LFP, more localized firing patterns may exert only a subtle effect on the activity of the hippocampus. After Sirota and Buzsáki (2005).

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associated sleep spindles in the thalamocortical system (Amzica and Steriade 1997; Molle et al. 2002; Massimini et al. 2004). These same shifts also affect the timing and presumably cellular composition of the hippocampal SPWs (Siapas and Wilson 1998; Battaglia et al. 2004). The synchronous cortical unit discharges, associated with the thalamocortical spindles, can lead to an increased firing of hippocampal neurons within 30–50 ms, and this increase in activity is often coincident with SWRs. The impact of neocortical oscillations on hippocampal circuits can be demonstrated by the DOWN–UP transition-induced sinks in the hippocampus, mediated by the entorhinal input (Figure 7.3).

Thus, the temporal coordination of thalamocortical sleep spindles and hippocampal SPWs (Siapas and Wilson 1998) by the slow oscillations offer a reasonable framework for hippocampal–neocortical information transfer. The DOWN–UP transitions and associated thalamocortical spindles trigger organized firing patterns of neocortical neurons which, in turn, lead to the

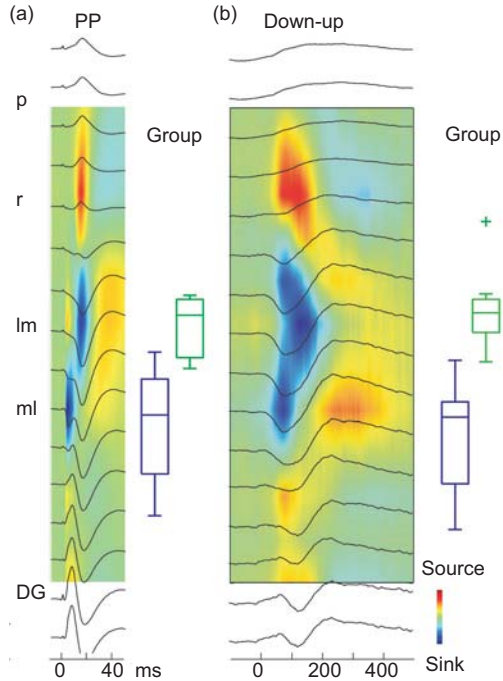

Figure 7.3 Neocortical UP state-related excitation of hippocampal neurons. (a) Perforant path (PP) stimulation-evoked LFP responses (black traces) and the derived current-source density (CSD) map. Note sinks (blue) in the dentate molecular layer (ml) and CA1 str. lacunosum-moleculare (lm). Box plots, group data of sink maxima positions (green, lm; blue, ml). (b) Averaged hippocampal LFP traces and CSD triggered by DOWN–UP transitions in an intracellularly recorded layer 3 entorhinal neuron. Box plots, group data. Similar observations were also made in the naturally sleeping rat. Modified after Isomura et al. (2006).

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activation of specific subpopulations of hippocampal neurons. These activated hippocampal neurons then give rise to SPW-related synchronous outputs and readdress the neocortex. Because the SPW is a punctuated event (~100 ms), whereas the UP state and sleep spindle are temporally protracted (~0.5–1 s), the hippocampal output can be directed to the still active neocortical assemblies. The temporal coordination of these events facilitates conditions in which unique neocortical inputs to the hippocampus and, in turn, hippocampal outputs to the neocortex might be modified selectively (Buzsáki 1989; Wilson and McNaughton 1994; Sirota et al. 2003; Steriade and Timofeev 2003). In this information transfer process, the neocortex serves as the target ("receiver") of the information from the "source" (sender), hippocampus; nevertheless, the initiator of the events is the neocortical slow oscillation.

Propagation of Activity through Multiple Stages of the Hippocampus Is State-dependent

Propagation of neuronal signals across multiple anatomical regions are frequently explained by "box-and-arrow" illustrations, where large populations of neurons in each layer or region are replaced by a single "mean neuron," representing a homogeneously behaving population (Figure 7.4). While it is tempting to designate circumscribed and specific computations for each layer or region, such a simplified view may not adequately describe information processing and propagation. Much computation can take place at the interface between layers with control being exerted on local circuit computations by the global hippocampal states. Furthermore, representation of an initiating event is not merely transferred from one layer to the next but changes progressively. Depending on the previous history of the brain and the event, each layer may add unique information to the representation.

Timing is critical to the propagation of novel information. For example, a strongly synchronous input, such as an artificial electrical pulse or an epileptic interictal spike, may propagate through multiple layers at a high speed, limited primarily by axon conduction and synaptic delays. However, physiological information rarely advances at such high speed. The fastest physiological speed of spike transmission in hippocampal networks occurs during SPW ripples. During SPWs, the CA3-initiated population burst propagates through the CA1, subiculum, entorhinal layer 5, and layers 2/3 in just 15–20 ms. While the pattern is propelled through these feedforward layers, the large SPW-related increase in excitation in the hippocampus is balanced by the progressive buildup of inhibition in successive layers. In layer 5, inhibition balances the SPW-induced excitation and inhibition in layers 2/3 overcomes the excitation. Because of the increasing inhibition in successive layers, SPW activity rarely reverberates in the hippocampal–entorhinal cortex loop, although multiple reverberations can occur in epilepsy.

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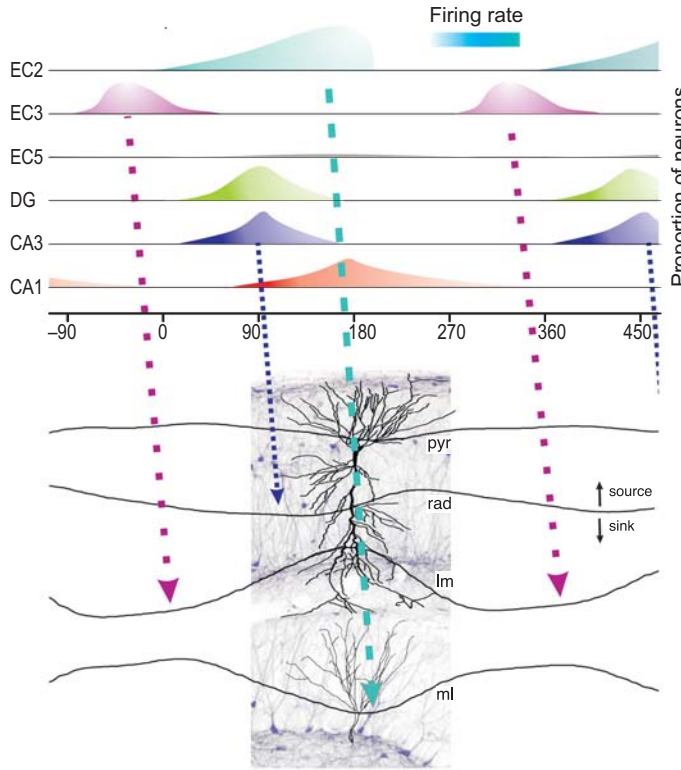

Figure 7.4 Temporal relationship between layer- or region-specific population firing patterns and theta current sinks in the hippocampus. In each region and layer, most neurons are silent or fire at low rates, with only a minority of neurons discharging at high frequency. The preferred theta phase of low and high firing neurons is different (advancing to earlier phase in EC2, DG, CA3, and CA1 neurons). Firing rate is illustrated by color intensity. The height of the histograms reflects the proportion of neurons with different discharge rates. Below: CSD theta traces are superimposed on a histological section in the CA1–dentate gyrus axis, with highlighted pyramidal cell and granule cell. Note phase-reversed sinks in CA1 str. lacunosum–moleculare (lm) and dentate molecular layers (ml) and phase-shifted sink (relative to lm sink) in str. radiatum (pyr, pyramidal layer). Tilted arrows indicate the temporal (phase) offsets between the peak of population firing in an upstream layer and the theta sinks in the target layers with the expected delays (based on axonal conduction velocity; 30° or ~ 10 ms). Note that whereas the population patterns correctly predict the timing of the dendritic sinks in their respective target layers, the propagation of spiking activity between upstream and downstream neuronal populations cannot be deduced from a simple integration of the inputs (after Mizuseki et al. 2009 and Montgomery et al. 2009).

The situation is dramatically different from SPWs in the theta state. The delay between the peak population firing rates in the entorhinal input layers (layers 2 and 3) and that of their respective target populations in dentate/CA3 and CA1 is severalfold longer during the theta state than during SPWs. Typically,

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the delays correspond to approximately half of one theta cycle (50–70 ms). Importantly, the current sinks in dentate/CA3 and CA1 pyramidal cell dendrites occur within 10–15 ms after the peak of the population activity in entorhinal layers 2 and 3, as expected by the conduction velocities of the entorhinal afferents. However, the buildup to maximum population activity in these hippocampal regions actually takes another 50 ms or so (Figure 7.4).

Addressing the potential causes of the delayed spiking activity during theta oscillations requires a thorough understanding of the temporal evolution of spike patterns of principal cells. As described above, the hippocampal theta oscillation is not a single entity but a consortium of multiple oscillators. Hippocampal principal cells can be activated by either environmental landmarks ("place cells"; O'Keefe and Nadel 1978) or internal memory cues (Pastalkova et al. 2008). During its active state, the spike train of a principal cell oscillates faster than the LFP, and the frequency difference between the neuron and the LFP gives rise to phase interference (known as "phase precession"; O'Keefe and Recce 1993). As an example, entering the place field of a typical CA1 place cell by the rat is marked by a single spike on the peak of the locally derived theta LFP. As the animal moves into the field, the spikes occur at progressively earlier phases. The "lifetime" (i.e., the duration of activity) of pyramidal neurons in the septal part of the hippocampus corresponds to 7–9 theta cycles, during which a full wave phase advancement (360°) may take place. In addition to spike phase advancement, the number of spikes emitted by the neuron increases and decreases as well, with the maximum probability of spiking at the trough of theta, coinciding with the center of the place field (Dragoi and Buzsáki 2006). In short, spikes can occur at all phases of the theta cycle but with the highest probability at the trough. Neither the phase advancement of spikes nor the increased probability of spiking in the firing field of the CA1 pyramidal cell can be explained by simple integration of the direct entorhinal layer 3 inputs, because spikes of layer 3 pyramidal cells are phase-locked to the positive peak of the CA1 pyramidal cell layer theta (as reflected by the sink in the str. lacunosum moleculare; see Figure 7.4), which is at the theta phase with the least probability of spiking for CA1 neurons. Therefore, the entorhinal input cannot be the sole initiator of each spike, especially for those occurring in the earlier phases of the theta cycle. The situation is similar in the entorhinal layer 2–dentate granule cell/CA3 cell network because peak firing of these neuronal populations is also delayed by approximately half of one theta cycle (Mizuseki et al. 2009). It is important to emphasize that neither the evolution of spike discharge activity nor the associated theta phase precession of spikes are necessarily controlled by environmental inputs; identical patterns can also occur during memory recall, route planning, and even REM sleep (Pastalkova et al. 2008).

Although the exact source of the additional spikes at unseeded phases of the theta cycle is not known, they may derive from local circuit mechanisms, according to the following hypothesis: Hippocampal neurons, initially

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discharged by the entorhinal input, begin to interact with each other to form transient assemblies, which individually oscillate faster than the ongoing population theta, reflected in the LFP. The oscillation frequency of the active cell assembly determines the magnitude of spike phase advancement and the "life time" of the assembly (i.e., the size of the firing field in spatial metric). From this perspective, the role of the entorhinal input is to add new members to the perpetually shifting and oscillating cell assemblies rather than to "drive" each spike directly in the hippocampus. The selected assembly members then begin to interact with each other for a limited time period, which is the theta cycle, and excitation is spread to connected neurons: within each theta cycle, multiple (7 to 9) assemblies interact with each other.

What is the functional significance of these interactions? For hippocampal cell pairs with overlapping place fields, the temporal structure of spike trains within a theta cycle reflects the distances between the place field centers and their sequential activation during the run (Skaggs et al. 1996; Dragoi and Buzsáki 2006). Within the theta cycle, the relative timing of neuronal spikes reflects the upcoming sequence of locations in the path of the rat, with larger time lags representing larger distances. These cross-neuronal time delays are independent of the running speed of the rat and are not affected by other environmental manipulations (Diba and Buzsáki 2008). The cross-neuronal temporal lags are specific to theta dynamics because the same sequences can be observed during SPWs but with shorter interneuron time delays (Diba and Buzsáki 2007).

The "fixed" temporal delays driven by theta dynamics have consequences for mechanisms of hippocampal coding. The first is a sigmoid relationship between within-theta time lags and distance representations, because the natural upper limit of distance coding by theta-scale time lags is the duration of the theta cycle (120–150 ms). As a result, upcoming locations that are more proximal are given better representation, with poorer resolution of locations in the distant future; distances larger than 50 cm are poorly resolved by neurons in the dorsal hippocampus because their expected temporal lags would otherwise exceed the duration of the theta cycle. Therefore, they fall on the plateau part of the sigmoid. Another consequence is that temporal resolution scales with the size of the place field; smaller place fields provide temporal lags, which represent very fine spatial resolution, whereas larger place fields that encompass the enclosure simultaneously provide a much coarser distance representations (Figure 7.5). These multiscale representations take place simultaneously, and possibly scale along the septotemporal axis of the hippocampus (Maurer et al. 2005; Kjelstrup et al. 2008). Assuming that locations can be regarded as analogous to individual items in a memory buffer (Lisman and Idiart 1995; Dragoi and Buzsáki 2006), this temporal compression mechanism limits the "register capacity" for the number of items that can be stored within a single theta cycle "memory buffer." By the same analogy, the sigmoid relationship suggests that episodic recall is high for the spatiotemporal conditions that surround a

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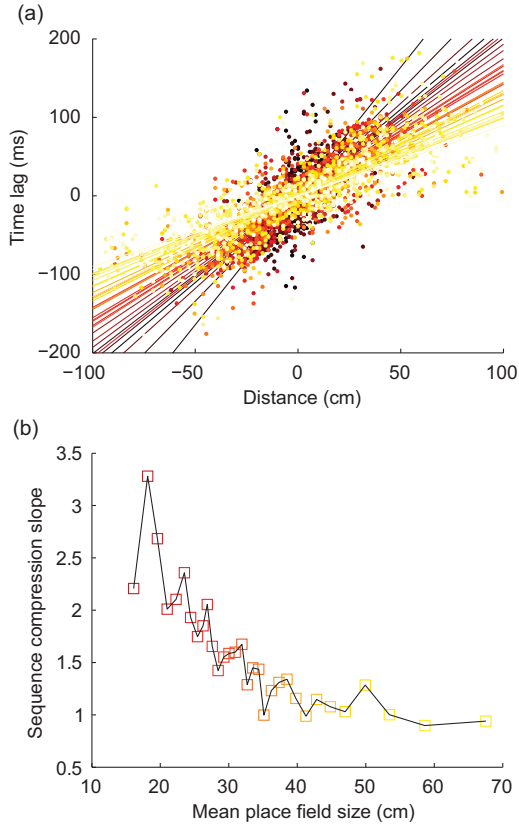

Figure 7.5 Sequence compression scales with place-field size. (a) Cell pairs are shown in groups of 100 (3200 pairs in total) with colors linked to the mean place-field size for the pairs; cf. (b) for corresponding values. Best linear fit is also depicted, illustrating that a smaller place field shows finer resolution but lower distance compression. Similarly, larger place fields provide the majority of points representing larger distances. (b) The slope of the best-fit line ("sequence compression slope") decreases with increasing field-size.

recalled event, whereas the relationships among items representing the far past or far future, relative to the recalled event, are progressively less resolved.

How can the mechanism responsible for maintaining theta-scale time delays be protected from firing rate changes, environmental modifications, and other factors that constantly affect hippocampal neurons? A working model is illustrated in Figure 7.6. The simple hypothesis is that interneuron-mediated inhibition provides a "window of opportunity" during which a postsynaptic neuron may spike, according to its excitatory inputs. The timing of this window may be established by the combined effect of presynaptic excitatory activity and inhibition. Through recurrent and feedforward connections, the spiking

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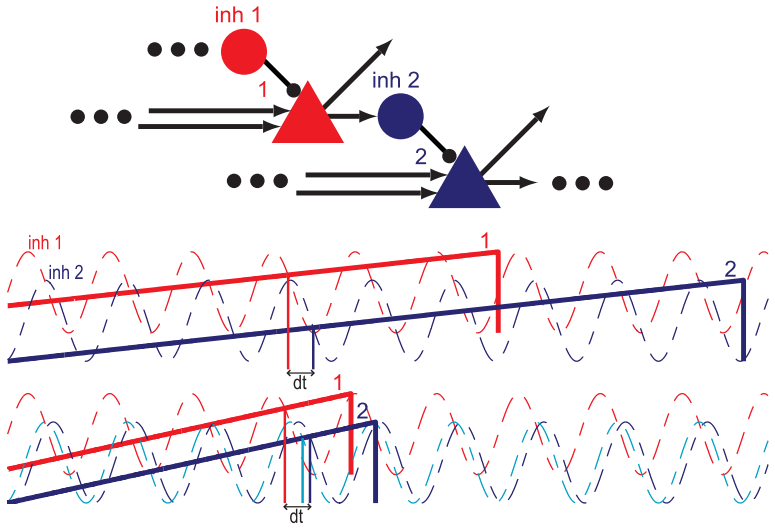

Figure 7.6 Microcircuit for temporal lag stability. While receiving excitatory input from unspecified sources, pyramidal cells (e.g., cell 1, red) are effectively inhibited by circuit interneurons (inh 1, red) and, in turn, drive other interneurons (inh 2, blue) that inhibit additional cells (e.g., cell 2), etc. In this figure, the synaptic efficacy of the individual components is inversely proportional to the length of the connection arrow. For example, to produce an action potential, pyramidal cells integrate excitatory input over many sources, whereas a small amount of excitatory input is sufficient to trigger a spike in an interneuron. Cells fire when excitation exceeds inhibition. The middle panel depicts the excitatory drives for the two interdependent place cells 1 and 2 (colors correspond) on a 2-m long track, with inhibition for each superimposed with a dashed line. Excitatory and inhibitory input to cell 2 are delayed relative to excitatory and inhibitory input to cell 1, resulting in net time lag dt. When the track length is shortened (1 m-long; bottom), the rise in excitatory drives occurs over a shorter duration (i.e., fewer theta cycles), and the place fields are shifted relative to each other. Inhibition to cell 2 (e.g., inh 2) is strongly coupled to the spiking of the earlier firing place-cell (1), and in our model, oscillates at this cell's frequency (and shows phase-precession). Hence the time lag of the trailing cell (2) is maintained relative to that of the leading cell (1), with the consequence that distance representations of the two neurons scale with the size of the apparatus (Diba and Buzsáki 2008). A similar mechanism may be responsible for the stable time lags across neurons at different travel velocities.

of interneurons (e.g., inh 2 in Figure 7.6) is tightly coupled to changes in the drive from the leading assembly (e.g., by neuron 1 in Figure 7.6), thus effectively determining timing for the trailing assembly (represented by neuron 2), which is in turn coupled to other inhibitory partners, and so on. In short, the stability of time lags between neurons arises from the theta network dynamics.

Using this hypothetical mechanism, let us consider the following paradox: Since nearly every place cell in the hippocampus oscillates faster than the ongoing LFP, how does the combined population generate a slower frequency output than its constituents? The answer lies in the strict temporal delays between active neurons. Consider 100 identical, partially overlapping, place cell

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assemblies that evolve while the rat navigates. With zero time delays between the neurons, the population frequency would have to be identical to the frequency of place cells. However, the insertion of temporal lags between cell pairs, in proportion to their distance representations of the environment, can slow the momentary population firing frequency. In this scenario, it turns out that the mean population frequency, also reflected by the LFP, is equal to the mean of the oscillation frequencies of the individual neurons plus the mean time lag (Geisler and Buzsáki, unpublished). In summary, the period of theta oscillations is largely determined by the time lags between active neuron pairs. Conversely, the ensuing theta dynamics constrains the propagation of activity across neurons. Such "bidirectional causation" is the essence of emerging dynamics of interacting neurons, and these constraints determine the speed of state-dependent computations in hippocampal circuits.

Conclusion

Our discussion on the temporal dynamics of networks was largely confined to hippocampal networks, which reside in the dorsal (septal) part of the structure. Although recent findings point to quantitative differences in place representations of more ventral hippocampal neurons (Maurer et al. 2005; Kjelstrup et al. 2008), the mechanisms discussed above may apply to the entire hippocampus. Since the hippocampal theta oscillations are coherent along the entire septotemporal axis of the hippocampus, they may serve as a temporal integration mechanism for combining local computations taking place at all segments and representing both spatial and nonspatial information. Furthermore, the computational principles discussed for the operations of the hippocampal circuits likely apply to other systems with similar forms of oscillatory dynamics.

Chapter from "Dynamic Coordination in the Brain: From Neurons to Mind," edited by C. von der Malsburg, W. A. Phillips, and W. Singer. Strüngmann Forum Report, vol. 5. ISBN 978-0-262-01471-7. Cambridge, MA: The MIT Press.