Forward shift from reverse replay

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Abstract In a recent experimental paper Lee et al. (Neuron 51:639–650, 2006) showed that the firing patterns of CA1 complex-spike neurons gradually shifted forward across trials toward prospective goal locations within a recording session over multiple trials. Here we propose a simple model of this result based on the phenomenon of awake sequence reverse replay (Foster and Wilson, Nature 440(7084):615–617, 2006) which occurs when the animal pauses at the reward location. The model is based on the CA3-CA1 anatomy with modulation of CA3-CA1 synaptic plasticity by feedback from CA3 projecting CA1 interneurons. Sequence replays, which are generated in CA3 by removal of subcortical inhibition on CA1 interneurons, are recoded into the synaptic weights of individual CA1 cells. This produces spatially extended CA1 firing fields, whose response provides a value function on experienced paths toward goal locations. Simulations show that the CA1 firing fields show positive movement in center of mass toward reward locations over many trials with negative shift in first few trials, and development of positive skew.

Keywords Hippocampus · Reverse replay · Place field · Forward shift · Dynamical feedback

Introduction

It is well known that the hippocampus is involved in remembering episodic events in particular environments, (Eichenbaum 2000; McClelland 1998; O’Keefe and Nadel

1978; Lee et al. 2006). The spatial information of events is represented by *place cells* which show strong firing correlations with particular locations. However, place coding in the hippocampus also interacts with non-spatial factors such as task demands and/or the reinforcement schedule, especially in complex memory tasks. It has been demonstrated that the place cells in the hippocampus are influenced by changes in the physical environmental context (Anderson and Jeffery 2003; Gothard et al. 1996; Lee et al. 2004; Leutgeb et al. 2004; O’Keefe and Nadel 1978). One important factor is the reward or goal position. Place cells change their firing characteristics when the pattern of reinforcement is altered in the same environment (Breese et al. 1989; Fyhn et al. 2002; Kobayashi et al. 1997; Markus et al. 1995). In addition, task demands modulate the place cell responses in the absence of physical changes in the environment (Bower et al. 2005; Ferbinteanu and Shapiro 2003; Wood et al. 2000). For example, Wood et al. (2000) have shown that, as a rat traverses the stem of a modified T-maze continuously while alternating between different goal locations, CA1 place cells fire more strongly in association with a particular trial type (i.e., left-to-right or right-to-left trials) of the alternation task.

A recent work which studied firing patterns over multiple trials revealed that the spatial firing correlates of CA1 place cells gradually shifted forward across trials, via the stem, toward prospective goal locations within a recording session (Lee et al. 2006). The results suggest that the shift in a reference frame bound to physical objects is not necessary to produce a systematic shift in firing locations of hippocampal neurons (Gothard et al. 1996). Instead, the results imply that a goal-oriented, cognitive reference frame can significantly influence the place cell characteristics of the hippocampal neurons, especially when animals need to divide their physical environment into multiple

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cognitive maps according to the mnemonic task demands (Lee et al. 2006).

Here we describe a simple neural network model of this forward shift phenomenon. The model is an extension of a previous modeling (Ponzi 2007, 2006b) of CA3 generated reverse sequence replay (Foster and Wilson 2006), to include a projection to CA1 to describe the forward shift phenomenon. As suggested in discussion in Lee et al. (2006), the forward shift is hypothesized to result from the reverse replay which has been observed to occur at the reward location (Foster and Wilson 2006). In the present model, replays generated in CA3 at the reward location are recoded into the CA3-CA1 synaptic weights of a CA1 cell which therefore, represents the trajectory of the animal preceeding the replay. Moreover, the replay strength of replayed place cells depends on their distance back along the animal path from the reward location so that the CA1 cell can represent a value function, whose firing rate represents the distance to the reward location. In order to ensure that, the CA1 weights reflect the replay strength we suggest that, LTP/LTD in the CA3-CA1 connections is modulated by an interneuron so that LTP occurs simultaneously to CA3 replay while LTD occurs at other times. This is regulation is hypothesised to be controlled by the CA3 projecting CA1 interneurons which are in turn regulated by GABAergic input from or brain areas and subcortical structures such as the septum (Freund and Buzsaki 1996; Sik et al. 1994; Somogyi and Klausberger 2005).

With the exception of the CA3 projection, these cross-field projecting cells are very similar to the trilaminar neurons (Freund and Buzsaki 1996). They possess a similar dendritic morphology, laminar distribution of local CA1 axons, and a projection through the fimbria. According to the laminar specificity of their dendritic tree, they are likely to be driven primarily by the local collaterals of CA1 pyramidal cells in a feedback manner. They exert their inhibitory effects on the dendritic tree of pyramidal cells in the CA1 region and also particularly in area CA3. The inhibition mediated by back-projection cells, therefore, is in a direction opposite to the excitatory dentate gyrus-CA3-CA1 axis. In fact it is suggested in Freund and Buzsaki (1996) that a cross-regional timing of action potentials by these interneurons may be important to secure population synchrony of principal cells in distributed networks and may allow a coordinated induction of synaptic plasticity (Freund and Buzsaki 1996; Sik et al. 1994; Somogyi and Klausberger 2005).

Model

The model system is depicted in Fig. 1(a). The CA3 system consists of a set of N pyramidal cells. In general each

pyramidal cell receives inhibition from the population of various types of interneuron (Freund and Buzsaki 1996), proximal excitation from the dentate gyrus (Johnston and Amaral 1998), mid-dendritic excitation from other pyramidal cells via the recurrent collaterals (Johnston and Amaral 1998), and excitation from the entorhinal cortex. Here we omit all these connections except for one-to-one excitation which carries signals generated either from dentate-gyrus or entorhinal cortex. These signals carry external environmental information such as landmarks etc., or internally generated position specific signals. The pyramidal cells are then described by activities $p_i(t)$, simply given by,

$$\frac{dp_i}{dt} = -k_1 p_i + k_2 g(e_i) f(H_X - H(t)) + k_3 I_i(x(t)) |\cos(\Theta x(t))|. \quad (1)$$

Here the activities $p_i(t)$ may represent membrane potentials or firing rates. Although we do not model spikes here explicitly the theta modulated activities $p_i(t)$ would correspond to a spike firing probability. Since we do not model spiking, the well known hippocampal theta phase precession (Skaggs et al. 1996; Jensen and Lisman

Fig. 1 **a** Anatomy of model system described in text. The solid lines denote excitatory connections, the dashed lines are inhibitory and the dot-dashed lines are modifyable excitatory connections. **b** Circular track task, animal runs clockwise. The rectangles represent the topographic place specific inputs $I_i = 0.1$ from the dentate gyrus or EC to CA3 pyramidal cells. They are overlapping in this example for generality. Replays are generated by activating the septal inhibition everytime the animal runs through the location marked R for reward

1996; Kamondi et al. 1998; Wallenstein and Hasselmo 1997) is not included, but see discussion on this point.

The $I_i(x(t))$ is one-to-one topographic input which can as explained above be either place specific input which enters the CA3 pyramidal cell via the dentate gyrus, assumed to be formed from path integration of internal motion signals on the entorhinal grid (Hafting et al. 2005). In this model each pyramidal cell i is activated by a single place specific input for simplicity. Alternatively $I_i(x(t))$ can model sensory type information from the entorhinal cortex on the perforant path. $x(t)$ is the position of the animal which fixes I_i . For completeness this signal is considered modulated by the *theta rhythm* described by the factor $\cos(\Theta x(t))$ where Θ is a constant, $x(t)$ is the position and $|x|$ denote the absolute value of x .

The $e_i(t)$ in Eq. 1 are internal ‘excitability’ variables they are simply given by,

$$\frac{de_i}{dt} = k_5 p_i - k_6 e_i. \quad (2)$$

These are the variables which generate the reverseness of the replay (Foster and Wilson 2006), as has been described in Ponzi (2007) and will be explained below. They are driven by the firing p_i and must decay slowly across the spatial environment, this decay is controlled by the parameter k_6 . Both the $p_i(t)$ and the $e_i(t)$ are necessary because the cell has localized firing given by p_i while the $e_i(t)$ reflect internal memory across the whole environment. The $e_i(t)$ are essentially a low pass filter of the firing rate $p_i(t)$. The function $g(x)$ in Eq. 1 is the sigmoidal function which is used to limit the activity of the k_2 term in Eq. 1. It is only necessary to avoid fine tuning of parameters and is set to be approximately linear in the region of $e_i(t)$ used in these simulations. Notice that, although we suggest a simpler model with topographic inputs here, it would not be problematic to replace the I_i in Eq. 1 with $\sum_j I_{ij}$ for a set of inputs j to cell i .

The term $f(H_X - H(t))$ models the modulation by the interneuron H cells, (see Fig. 1a), whose firing rate is given by $H(t)$, which will be described below. Here $f(x) = x$ is the positivity function $f(x) = x$, ($x > 0$), $f(x) = 0$, ($x < 0$). This term means that, when the H cell firing rate is above its baseline H_X the cell soma is inhibited, but when the interneuron H activity drops below its baseline activity, H_X , the soma can become activated. The strength of this *replay reactivation* depends on the the excitability $e_i(t)$ at the time of the reactivation. Therefore, the cell firing Eq. 1 can be driven by two different factors, the input $I_i(x(t))$ and a reactivation by removal of H interneuron inhibition.

Notice we do not include the CA3 recurrent collaterals. It is hypothesized that these are used to produce forward replay theta sequences encoded by time assymmetric Hebbian learning (Foster and Wilson 2007; Lisman 1999).

Since we here we only address the reverse replay here we do not require them.

Unlike the CA3 pyramidal cells the CA1 cells do not have strong recurrent collaterals and we model them as a winner-take-all (WTA) system. They are given by,

$$\frac{dq_i}{dt} = -q_i + f\left(\sum_j u_{ij} p_j - B(t) + q_i\right) \quad (3)$$

where q_i are the activities of the CA1 pyramidal cells and $u_{ij}(t)$ are modifiable weights for the all-to-all projection from CA3 to CA1. In the CA1 system we also include an inhibition from the CA1 basket cell activity which produces a WTA in the absence of strong recurrent collaterals. The basket cell is simply modeled as $B(t) = \sum_i q_i$ according to the activation from the pyramidal cell population.

We describe the projection weight $u_{ij}(t)$ update by,

$$\frac{du_{ij}}{dt} = -u_{ij}(t) + f((H_X - H(t))p_i q_j + u_{ij}(t)). \quad (4)$$

In this Eq. 4 we suggest the $u_{ij}(t)$ weights are modified by the post-synaptic q_j and pre-synaptic p_i firing rates and whether LTP or LTD occurs is modifiable by the $H(t)$ cell firing. This can occur by modification of back propagating EPSPs in the dendritic tree of the CA1 pyramidal cells. The reason for this is to ensure that LTP occurs at the same time as replay activity in CA3, while LTD occurs outside replay activity. It is this LTP modulation that allows the CA1 cells to inherit the CA3 replayed activity and produces their broad firing fields which develop over trials. Furthermore the LTD outside the replay activity produces a stabilization of the firing over many trials and a normalization over the environment. Such a modulation of learning has been included in the authors previous works (Ponzi 2006, 2006b, 2007).

CA3 projecting CA1 interneuron H cells are known within the hippocampal region (Freund and Buzsaki 1996). Their cell bodies and axons rest primarily in the stratum oriens, while their dendrites may extend across the strata radiatum and stratum lacunosum-moleculare and to CA3. In addition the H cell population receives excitatory input from the active pyramidal cells and is regulated by an inhibitory GABAergic septal input, as well as by other afferents (Freund and Antal 1998). The medial septum diagonal band of Broca (MSBD) projects to the H cells and related O-LM cells in stratum radiatum and oriens of CA1 and CA3 (Johnston and Amaral 1998).

The H cells are simply modeled by a single unit,

$$\frac{dH}{dt} = -H(t) + H_X + k_6 \sum_i q_i(t) - k_S S(t). \quad (5)$$

They are activated by projection from the the CA1 pyramidal cells q_i and their firing is inhibited by activity

from the subcortical structures such as the septum $S(t)$. When the pyramidal cell input and this input $S(t)$ are zero then basket cell activity decays exponentially to its baseline level H_X .

The septal activity generates the replays as also suggested in Ponzi (2007). The septal signal itself is considered to be possibly generated by reward signals from the hypothalamus or from the thalamus. In fact, however, Eq. 5 is greatly simplified since H cells and other interneurons of the hippocampus receive projections from several cortical and other subcortical areas such as the amygdala and these are omitted. Indeed any projection which inhibits the H cells in this way would have the same effect as the term $S(t)$ here.

Results

The model is best understood by studying examples of its time series. In this paper we only consider the circular environment depicted in Fig. 1b.

The activities $p_i(t)$ and excitabilities $e_i(t)$ of the CA3 units on one pass around the track are shown in Fig. 2. In this and in all other time series figures, time is shown in arbitrary units. Furthermore in this and other figures we have chosen time series segments later in the time series to avoid effects of initial conditions of the simulated differential equations. The activities in Fig. 2a for each cell are spatially localized and modulated by the theta rhythm, as described by Eq. 1. As can be seen the firing fields are also somewhat overlapping.

Also shown in Fig. 2 is the H cell activity $H(t)$. This is above its baseline $H_X = 1$ due to its excitatory projection from the CA1 units which are in turn excited by the CA3 units in Fig. 2. At around $t = 6,650$ a *replay* reactivation is shown at the end of the circular track. This replay is generated by removal of tonic inhibition by the H cell in Eq. 1 which itself is inhibited by activation of the term $S(t)$ in Eq. 5. This is considered to occur when the rat pauses at the end of the track and consumes its food.

The excitabilities $e_i(t)$ are shown in Fig. 2b which correspond to the activities in Fig. 2a. As can be seen the excitabilities, described by Eq. 2, grow rapidly when the CA3 unit is active and decay exponentially when it is inactive. During the rapid growth period some ‘steps’ can be seen, these are due to the theta modulations in the CA3 activities. The timescale of the exponential decay given by the second term in Eq. 2 is set so that at the replay reactivation point each unit excitability $e_i(t)$ has a different magnitude. The units furthest back around the track have the lowest excitability at the replay location while the units nearest the replay location back down the path of the animal have the highest excitability levels. As can be seen the

Fig. 2 **a** Activities of the 10 CA3 pyramidal cells $p_i(t)$ on one circuit around the track. Each solid line is a different cell time series. The dashed time series at the top is the H cell activity $H(t)$. **b** CA3 pyramidal cell excitabilities $e_i(t)$ corresponding to activities in (a). Again each line is a different cell

reactivation at around $t = 6,650$ increases the excitabilities of all the cells a small amount. The excitabilities measure the distance back around the track from the animal location.

The CA3 activities $p_i(t)$ time series at a replay event similar to the one shown in Fig. 2a is shown magnified in Fig. 3. Notice the replay timescale is much smaller than the track timescale in Fig. 2a. Also notice that, the activities are several times larger than during the theta periods shown in Fig. 2. The CA3 unit nearest the replay location has the strongest reactivation while the unit furthest away has the weakest reactivation. The H cell activity $H(t)$ is also shown. It is now below baseline $H_X = 1$ in contrast to the theta period in Fig. 2a when it was above baseline. It is below baseline because it is inhibited by the septal term in Eq. 5 as described above. Notice that, the H cell is ‘in phase’ with the CA3 units during theta activity while the rat is moving around the track, but ‘in anti-phase’ with the

Fig. 3 Time series of activity of CA3 cells $p_i(t)$ at replay event. Each CA3 cell activity $p_i(t)$ is shown as solid line with the order the same as those in Fig. 2. Also shown is the H cell time series as dashed line

CA3 units during the replay event while the rat is paused at the end location.

The activation of a CA1 cell around the track for a successive pair of trials early in learning is shown in Fig. 4a for repeated traversals around the track shown in Fig. 1b. The firing rate is quite flat throughout a whole trial. The periodic modulations are due to the periodic theta driving of inputs $I_i(t)$ in Eq. 1 shown in Fig. 2a while the periodic peaks are due to overlapping activations from different CA3 layer cells as can also be seen in Fig. 2a. The large activation at the end of each trial is caused by the replay reactivation event in CA3. The same cell for a pair of later trials is shown in Fig. 4b. Here the firing rate clearly increases across the trial and this produces the forward shift toward reward location in the center of mass. Further the increase in skew in the direction of motion toward reward is clear.

How this occurs is very easy to understand. As shown in Fig. 3 the replay reactivates the most recently experienced place cells which strongest magnitude. This creates a kind of reverseness. According to the model design described in Eqs. 1, 5 the replay occurs when the H interneuron is inhibited by the activation of the septum $S(t)$. This is also when LTP occurs at the CA3-CA1 synapses according to Eq. 4. Indeed the total amount of the LTP synaptic modification is given by the product of the CA3 cell activation and displacement of the H cell below its baseline integrated across the period where the H cell is inhibited by the septum during the replay. Due to the fact the LTP is designed to occur during a CA3 replay event, and not during theta activity outside a replay event, where LTD occurs in fact, the replay is *recoded* into a CA1 cell. The synaptic weights u_{ij} of the CA1 cell now represent the replay strength. This CA1 cell can be said to provide a *value function* along the trajectory leading to the reward

Fig. 4 **a** Activity of a CA1 pyramidal cell on an early trial. **b** Activity of same CA1 pyramidal cell as (a) on a successive pair of trials late in learning. In (b) the arrows mark the end of the preceding trial and start of the succeeding trial

location since its firing rate on subsequent traversals of the same track provides a signal proportional to the distance to the reward location ahead of the animal.

How the center of mass (COM) of this CA1 cell varies across trials is shown in Fig. 5a. The center of mass for each trial is calculated according to,

$$COM = \frac{\sum_i^N q(t_i)x(t_i)}{Q} \quad (6)$$

where,

$$Q = \sum_i^N q(t_i). \quad (7)$$

In these equations t_i is the time of the i -th iteration of the runge kutta integrator, and there are N iterations each trial. Therefore, Q is the total firing rate for each trial while COM is the total firing rate weighted by the position $x(t_i)$ of the animal on the track at time t_i each trial. As shown in Fig. 5a the COM initially decreases rapidly and then slowly increases. We also show the change in total firing rate Q for

Fig. 5 **a** Variation of center of mass of CA1 cells versus trial number. **b** Variation of total firing rate of CA1 cell versus trial number

each trial in Fig. 5b which increases across trials and then slowly stabilizes later. Notice that, firing rates are always stable and bounded no matter how many times the track is traversed and reward is found.

In fact on the first replay event all the synaptic weights of CA1 cells have weights given by previous experience which has no relevance to the track in the simulation. The first replay event causes positive learning at these synapses and then they are slowly adjusted over trials to reflect the replayed strengths measuring the distance to the reward location in the current context and specific environment. This is what causes the drop in the COM on the first few trials and then increase after. Indeed this is as observed in Lee et al. (2006) when tasks are switched. The fact that, the weights are adjusted slowly over several trials provides an averaging over multiple trials which gives a robustness against fluctuations in path to the reward location.

Figure 5a also reveals a small roughly six trial backwards and forwards periodic variation in the center of mass. This is a quasiperiodicity induced by the non-integral ratio of track length, which determines the reward replay location, and the imposed theta oscillation period in Eq. 1.

Although small it may be relevant to real animal behavior by providing a signal which counts laps around the track, see discussion.

Discussion

We have presented a simple model of the forward shift in COM of CA1 place fields based on sequence replay at the reward location.

This work includes modeling of reverse replay of which a more detailed explanation is given in Ponzi (2007). The sequence replay is robust and will occur in reverse even on a circular track without an endpoint, since the replay mechanism does not require associative connections between place cells. Therefore, there is no necessity for the forward connections to place cells ahead of the rat's replay location to happen to be zero or weak, as required by models where reverse replay occurs through activation of a connection matrix. The associative connections between CA3 cells can then be used to produce the forward replay over future trajectories often observed during theta periods. Indeed this is reasonable since forward replay over a future path from an arbitrary location is a much more difficult thing to produce by a neural network than simply replaying where one has recently been.

Phase precession of spikes with respect to the theta rhythm of the local field potential is well known to occur in the hippocampus, CA3 and CA1 (Skaggs et al. 1996; Jensen and Lisman 1996; Kamondi et al. 1998; Wallenstein and Hasselmo 1997). Since we are not modeling spikes, phase precession is not explicitly represented in this model as mentioned above. Modulation by theta rhythm itself is not in fact necessary in this model but included in Eq. 1 for completeness through the term $|\cos(\Theta x(t))|$, to illustrate the phase relationship the H cell has with the CA3 pyramidal cells and the theta rhythm. If phase precession had been included the modulation by constant frequency Θ would have to be replaced by a non-constant frequency $\Theta(x)$ increasing with position x . This is not at all problematic for the model, but not necessary here. In fact phase precession has been hypothesized to have a variety of functions. It has been suggested that, location information can be obtained from the phase of spiking with respect to the LFP theta rhythm (Skaggs et al. 1996). However, it is also known that, location information is also contained in the changing firing rate as the rat crosses the place field (Skaggs et al. 1996). Since we are here only interested in location information it is justified in the interests of model simplicity to leave out phase precession. Furthermore, the location information necessary here pertains only to whether the animal is in the place field or not, its more accurate position within the field. Indeed we suspect phase

precession plays more complex role outside the scope of this model, for example it may be employed in the embedding of current location into future and past path sequences (Jensen and Lisman 1996; Lisman and Otmakhova 2001).

The model makes various testable predictions. For example the model predicts that the inhibitory *H* cell is in phase with CA3 during motion, but in anti-phase during replay. Furthermore, as explained, *H* cell firing is suppressed below baseline during replays. In principle it would be possible to check this. For example, Somogyi and Klausberger (2005) describe how some of the different cells of the hippocampus, pyramidal cells, O-LM cells, basket cells etc., modulate their firing rates with respect to the theta rhythm and sharp wave ripple events. Cells can be distinguished by a preferred spiking phase with respect to theta and a preference to fire during ripples or not. O-LM cells and axo-axonic cells are similar to the *H* cell here and have suppressed firing during ripple events, while bistratified, basket cells and pyramidal cells have enhanced firing during ripples, like our pyramidal cells (CA3 and CA1) here. The relevance of phasic inhibition by the hippocampal interneurons to the phenomenon of phase precession in CA3 pyramidal cells has been studied by model simulation by Baker and Olds (2007).

Another prediction is that of the periodicity that results from the rat regular motion and theta, and its possible role for lap counting. Although this is a small effect it could in principle be measured for animals on very short tracks with very precisely restricted movement trajectories and velocities.

The model relies on a coordination between replays and LTP at the CA3-CA1 synapses which is proposed to be provided by the CA3 projecting CA1 interneurons (Freund and Buzsaki 1996; Sik et al. 1994). In this work we hypothesized that this learning is further regulated by the septum. Indeed Schroeder et al. (2001) describe lateral septal activation in a nicotine-association experiment and activation of a specific dorsal lateral region of the septum in a chocolate-conditioning experiment (Schroeder et al. 2001). They point out that the septum does receive projections from dopamine neurons in the ventral tegmental area and has been implicated in feeding behavior (Stanley et al. 1988; Oliveira et al. 1990). Furthermore, as mentioned above several other cortical and subcortical structures project to the hippocampus, including to the interneurons, and these may all also be involved in the regulation of hippocampal learning. This regulation would depend on task demands and other factors, and may also involve various neuromodulators besides GABA such as dopamine and acetylcholine etc., as also described in the authors previous works (Ponzi 2006a, b).

LTP itself has been directly associated with sharp wave ripple events (Behrens et al. 2005; Buzsaki and Chrobak

2005). Buzsaki (1989) proposed a two-stage model of memory encoding: during theta, information about the current environment reaches the hippocampus via the entorhinal cortex; during sharp waves, population bursts in CA3 may lead to LTP induction in CA1. In this model sharp waves reflect the summed post-synaptic depolarization of large numbers of pyramidal cells in the CA1 and subiculum as a consequence of synchronous discharge of bursting CA3 pyramidal neurons. The trigger for the population burst in the CA3 region is the temporary release from subcortical tonic inhibition. The author describes experimental evidence that shows that population bursts in CA3 may lead to long-term potentiation in their post-synaptic CA1 targets and that activity patterns of the neocortical input to the hippocampus determine which subgroup of CA3 neurons will trigger the subsequently occurring population bursts. The author outlines a model of memory trace formation where during exploratory theta behaviors neocortical information is transmitted to the hippocampus via the dentate gyrus. Weakly potentiated CA3 neurons then initiate sharp wave population bursts upon the termination of exploratory activity. It is suggested that, the strong excitatory drive brought about by the sharp waves during consummatory behaviors and immobility may be sufficient for the induction of long-term synaptic modification both in the initiator neurons of the CA3 region and in their targets in CA1.

Indeed a recent in vitro experimental study by Behrens et al. (2005) shows that, stimuli that induce LTP can lead to the generation of sharp-wave ripples in rat hippocampal slices. The authors demonstrate that sharp-wave ripples induce synaptic change among pyramidal cells and therefore, demonstrate a link between the induction of LTP and this physiological network pattern. Furthermore, in the hippocampus in vivo, both synaptic plasticity and network activity are known to be closely interdependent. Bikbaev and Manahan-Vaughan (2008) found that, changes in theta and gamma activity correlate tightly with the occurrence of LTP. In support of the two-stage model (Buzsaki 1989) they suggest that, tetanisation-driven activation of sensory inputs synchronizes the activity of granule cells and interneurons and thus facilitates the encoding of acquired stimuli. As in other brain areas frequency dependent LTP/LTD is also known in the hippocampus. For example, Dunwiddie and Lynch (1978) show that, high frequency stimulation of CA1 cells (as occurs during sharp-wave ripples) can result in LTP while very low frequency stimulation can result in LTD.

The model presented here reproduces the gradual positive shift in *COM* in a simple and transparent way. Similar modeling may also be applied to other areas “downstream” of the hippocampus, for example, pFC or the ventral striatum where replays occurring in the hippocampus may

produce extended firing fields as value functions on experienced trajectories in these brain areas too.

In future work we will address how the model behaves under task switching, for example from the circular track to the alternation task or T-Maze.

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