Theta Phase Coding and Acetylcholine Modulation in a Spiking Neural Network

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Abstract. Theta frequency oscillations are a prominent feature of the hippocampal EEG during active locomotion and learning. It has also been observed that the relative timing of place cell firing recedes as its place field is traversed – a phenomena known as phase precession. This has led to the development of a theory of theta phase coding, whereby spatial sequences being encountered on a behavioural timescale are compressed into a firing sequence of place cells which is repeated in each theta cycle and stored in an autoassociative network using spike-timing dependent plasticity. This paper provides an abstract model of theta phase coding in a spiking neural network, and aims to investigate how learning and recall functions may be mediated by the neuromodulatory functions of Acetylcholine (ACh). It is demonstrated that ACh is not essential for concurrent learning and recall without interference, thanks to the robust nature of the theta phase coding implementation. However, the neuromodulation of synaptic plasticity may be essential to avoid continually consolidating false predictions when learning new routes.

Keywords: Acetylcholine, attractor network, cognitive map, Hippocampus, neuromodulation, place cells, spatial memory, STDP, theta phase coding.

1 Introduction

The hippocampus has long been identified with spatial and episodic learning and memory. This theory has been bolstered by the discovery of several distinct groups of cells throughout this brain region whose activity corresponds directly to an animal's location (place, grid and spatial view cells) or idiothetic inputs (head direction and vestibular information cells). This in turn has led to the notion that the hippocampus may function as a 'cognitive map' which integrates environmental cues, past experience and self-motion input in order to aid efficient navigation [1, 2]. The mechanisms by which the cognitive map may function have often been modelled using autoassociative memory models – recurrent neural networks with synaptic plasticity which can store input patterns and recall them from incomplete or noisy cues [3, 4, 5, 6]. These models are inspired by the presence of a large number of recurrent collaterals in various parts of the hippocampal formation, and the ease with which synaptic plasticity can be induced and observed in the region. The corresponding neural networks have been very successful in replicating the update of head direction cell activity from idiothetic cues, and path integration over a learned environment in the absence of sensory input, as well as some more abstract functions of episodic memory.

However, these networks have often utilised rate-coded neural or synaptic dynamics, while it has become clear from neurobiology that changes in the strength of synapses in the hippocampus are mediated by the temporal sequence, rather than frequency, of neuronal firing. According to this spike-timing dependent plasticity (STDP), only those pre-synaptic inputs which have been active in a short time window (~50ms) before post-synaptic spiking are potentiated, while any synapses that are active within a similar time window after post-synaptic spiking are depressed [7, 8]. In order to implement STDP within an associative network, a spiking model which can replicate the dynamics of real neurons as accurately as possible is required. Neurons in the hippocampus demonstrate one of the most well known dynamic firing patterns in the mammalian EEG. Pyramidal cells throughout the region exhibit theta (~8Hz) frequency oscillations in their local field potential whenever an animal is actively locomoting, attending to external stimuli or during REM sleep [9, 10]. Furthermore, it has been established that the firing of place cells is not simply modulated by this oscillation, but advances in phase relative to theta as their place field is traversed [9, 11, 12]. This produces a compressed temporal firing sequence within each theta cycle which corresponds directly to the current sequence of locations being navigated on a behavioural timescale – a firing sequence which is ideally suited for storage in an associative network using STDP. It has been suggested that this theta-phase coding may be the mechanism by which the hippocampus processes continuous spatial information [9, 10, 13, 14].

It has also been noted that the release of the neuromodulator Acetylcholine (ACh) is closely related to the theta oscillation [15]. ACh acts on muscarinic and nicotinic receptors within the hippocampus, and is known to be involved in learning and recall processes. This is demonstrated by experiments in which the infusion of ACh antagonists impairs performance on spatial tasks [16]. Neurobiological research has revealed several effects of ACh on neurons and synapses in this brain region, among them the enhancement of afferent input relative to excitatory feedback, and the enhancement of synaptic plasticity. These properties have led to the theory that the role of ACh is to separate phases of learning and recall within each theta cycle [9, 10]. Associative memory models can often encounter significant problems if learning and recall processes are concurrently active. During learning, for example, the activity in an autoassociative memory model must approximate external input, or the patterns which are stored will be a combination of novel experience and the recall of earlier, similar experience [4, 9, 10]. If recurrent connections are made too weak to provoke neural activity, this interference will disappear, but recall of an activity pattern from a partial cue is made impossible.

The changes in neural and synaptic dynamics which are incurred by ACh suggest that it may act as a trigger to switch between functions of learning and recall. When the neuromodulator is present, afferent input dominates the dynamics of the autoassociative CA3 network, and this activity is maintained while information is stored via enhanced synaptic plasticity. When ACh is absent, feedback from recurrent collaterals dominates and plasticity is vastly reduced, allowing the network to make predictive recall without interfering with stored patterns [9, 13, 15]. This posits an elegant and biologically plausible solution to the problem of concurrent learning and recall processes which has been encountered in previous autoassociative memory models. This aim of this research is to examine an abstract model of theta phase

coding, in order to investigate the possible advantages of ACh modulation in storing and recalling temporal sequences on a behavioural time scale. To our knowledge, this is the first attempt to investigate the phenomena of both phase precession and acetycholine modulation in a spiking neural network which implements STDP. Previous research has examined theta phase coding in a similar network, but with much more simplified - and therefore, less biologically realistic - models of neural or synaptic dynamics [9, 14].

2 Methods

2.1 Network Properties and Neural Dynamics

The neural network consisted of N=20 neurons, whose activity corresponds to that of place cells in the CA3 region of the hippocampus. Each had a randomly assigned axonal delay in the range 1 : 5ms. The network was fully recurrently interconnected by excitatory synapses except for self-connections. The neurons operated according to the Izhikevich (2004) spiking model, which dynamically calculates the membrane potential (v) and a membrane recovery variable (u) based on the values of four dimensionless constants (a,b,c and d) and a dimensionless current input (I), according to Eqn. 1. This model can exhibit firing patterns of all known types of cortical neurons by variation of the magnitude of applied current and the parameters a – d [17]. The values used for tonic spiking in a standard excitatory neuron are a=0.02, b=0.2, c=-65 and d=6.

$$\begin{aligned} v' &= 0.04v^2 + 5v + 140 - u + I \\ u' &= a(bv - u) \\ \text{if } v \geq +30\,\text{mV} \text{ then } &\begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases} \end{aligned} \tag{1}$$

2.2 Synaptic Dynamics

At the beginning of each simulation, all synaptic weights were set to a value of w=0.1. Mathematically, with $s = t_{post} - t_{pre}$ being the time difference between pre- and post- synaptic spiking, the change in the weight of a synapse (Δw) due to STDP can be calculated using equation 2.

$$\Delta w = F(s) = \begin{cases} P_+ = A_+ \exp(-s/\tau_+) & \text{for s} > 0 \\ P_- = A_- \exp(-s/\tau_-) & \text{for s} < 0 \end{cases} \tag{2}$$

The parameters A_+ and A_- effectively correspond to the maximum possible change in the weight of a synapse per spike pair, while τ_+ and τ_- denote the decay constants of potentiation and depression increments respectively (see Fig. 1). Previous research suggests that the window of depression should be set larger than that of potentiation – in order to ensure that the STDP model depresses chance spike pairings and thus

operates stably [18]. This constraint was observed throughout our simulations, by setting τ_+ =20ms and τ_-=40ms while monitoring the relative size of A_+ and A_-.

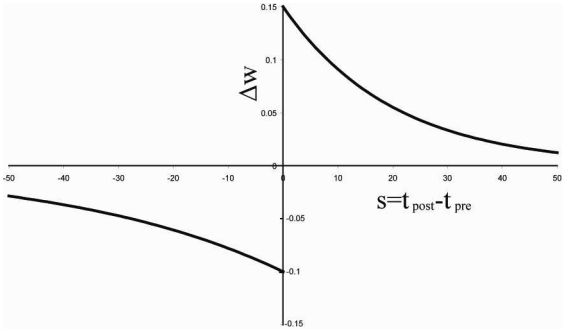

Fig. 1. The asymmetric time window of STDP.

Furthermore, in order to stabilise activity in a recurrent network – which is effectively a positive feedback system – a system of synaptic redistribution was employed in all simulations. The amount of available neurotransmitter for each synapse was initiated at a value of 1, and decreased by a value of 0.5 with each afferent spike. The value would then recover exponentially with a time constant of 200ms. Every synaptic weight was scaled by the currently available amount of neurotransmitter upon a transmission event.

2.3 Network Input

In order to replicate the phenomena of phase precession, input to our network was formulated as a combination of theta frequency inhibition and gradually increasing excitation [19]. Every neuron in the network was fed with inhibitory input which oscillated sinusoidally between a value of I=-1nA and I=-3nA at a (theta) frequency of 8Hz. A route which consisted of a series of N=20 overlapping place fields was then traversed. Each place field was divided into seven equal segments, and each place field overlapped with five segments of those on either side. The level of excitation in the corresponding place cell would increase from a value of I=2nA as the place field was entered, by increments of I=0.25nA as each segment was traversed. This ensures that a key property of phase precession *in vivo* – that the phase of firing corresponds with distance travelled through the place field, rather than time spent within it – is replicated [2]. Once the place field is left, excitation for that place cell is reset to zero.

2.4 Acteylcholine Modulation

When neuromodulation was employed, the concentration of ACh was assumed to be uniform across the neural network, and to oscillate in the range 0 : 1 in synchrony with inhibitory input. Excitatory synaptic currents from the recurrent collaterals were inversely modulated by this concentration in the range 0 : *f*. The plasticity of recurrent synapses was also dynamically adjusted, by directly scaling each weight change by the instantaneous concentration of neuromodulator. Hence, in the presence of ACh, recurrent weights tended towards zero, eliminating excitatory feedback, while synaptic plasticity was active, in order to store incoming activity patterns without

interference. When ACh was absent, excitatory weights were enhanced and synaptic plasticity was suppressed, in order to allow predictive recall activity which would not be stored.

3 Results

3.1 Theta-Phase Coding without Acetylcholine Modulation

Initial tests of the model aimed to establish how well activity in the network approximated what is known of phase precession *in vivo*. Figure 2 illustrates the theta phase coding, whereby a section of the place field sequence is translated into a compressed sequence of place cell firing within each theta phase. Because one behavioural sequence is repeated many times on the theta temporal scale, it is possible to store a spatial route in a single trial. The learning rate in the network is effectively determined by the parameters A_+ and A_- in the STDP model. The higher these values are, the more quickly synaptic weights re-arrange to become stable and reflect the input sequence. One of the weaknesses of our model is that it does not replicate the magnitude of phase precession seen *in vivo*, which can closely approach 360 degrees [2]. However, in the absence of ACh modulation, this would provoke associations between the initial and final place cells firing in each spike sequence, creating artificial, circular associations at each stage of the route and thus corrupting the ideal weight matrix.

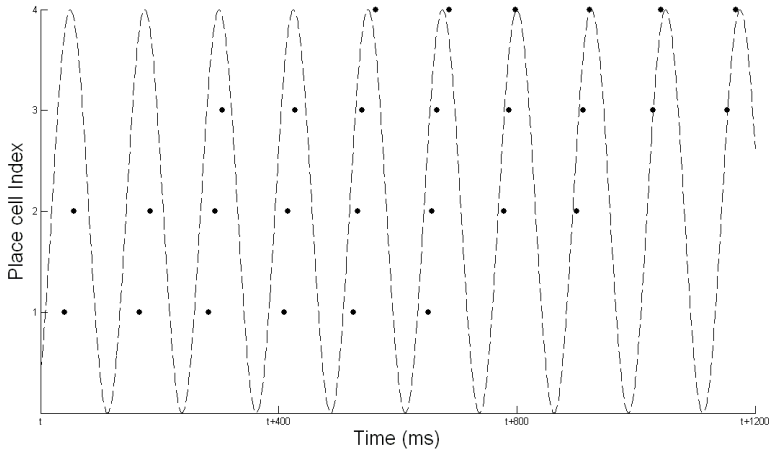

Fig. 2. The theta phase coding mechanism. As the place fields of place cells 1-4 are sequentially traversed, the phase at which the neurons fire precesses, and thus a compressed, representative firing pattern is generated in each cycle.

External input corresponding to five laps of a circular route consisting of twenty overlapping place fields was then applied to the network, and the resultant weight matrix and spike raster is shown in Fig. 3. In the absence of a mechanism to differentiate between learning and recall periods, the value assigned to the maximum achievable weight of a synapse is critical. Although the synaptic weight matrix in Fig.

3 has re-arranged to reflect the behavioural sequence being learned, the recurrent connections are not powerful enough to provoke spiking activity, and so no predictive recall from these weights can occur. Hence, some separate mechanism is required to decode the weight matrix and effectively transfer it into a representative sequence of activity when cued. Similarly, the number of upcoming locations with which each place cell can associate is limited by the number of neurons which are active in each theta cycle. As the spike raster in figure 3 illustrates, only four place cells were ever concurrently active in our model, and so (without neural noise) only synaptic connections between each neuron and the three which follow or precede it can be modified.

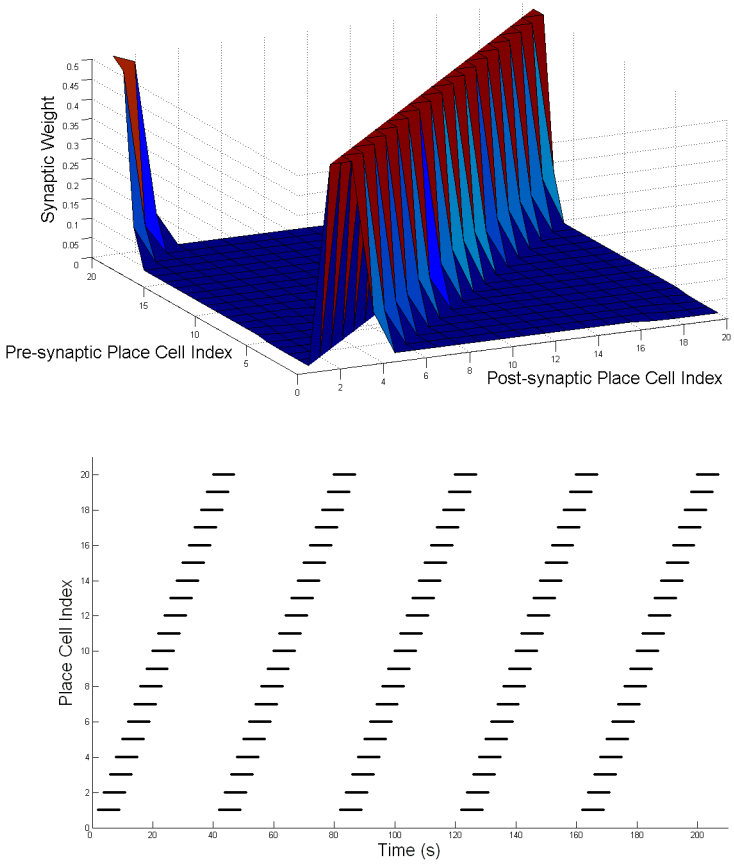

Fig. 3. Final synaptic weight matrix and overall spike raster for the network when traversing a circular route five times, with w_{max}=0.5 ; A_+=0.012 and A_-=0.01. (a) Synaptic weights from each neuron to those which follow it on the learned route have been potentiated, and to those which immediately precede it have been depressed. The majority are unchanged from their initial value, due to the absence of neural noise. (b) The spike raster illustrates the sequential firing activity, and the absence of any recall activity or experience-dependent place field expansion.

If w_{max} is increased, however, then predictive recall becomes possible, and thanks to the remarkably robust nature of this theta phase coding implementation, the recall process does not interfere with the ideal structure of the synaptic weight matrix. As Fig. 4 illustrates, the spiking dynamics, gradually increasing level of recurrent excitation from preceding place cells, and axonal delays conspire to concentrate recalled activity (in place cells 1-3) after that generated by external input (in place cells 17-20) within each theta cycle. This recall activity can be clearly seen in the overall spike raster for this simulation (Fig. 5), which also illustrates that our model replicates a well known property of phase precession *in vivo* – the experience-dependent expansion of place fields against the direction of motion [2]. The increased number of concurrently active place cells which results from this recall activity means that each neuron can alter the strength of its connections with a greater frequency of those adjacent to it on the behavioural sequence – and this is clearly illustrated by the greater spread of potentiated synapses in the weight matrix (see Fig. 5).

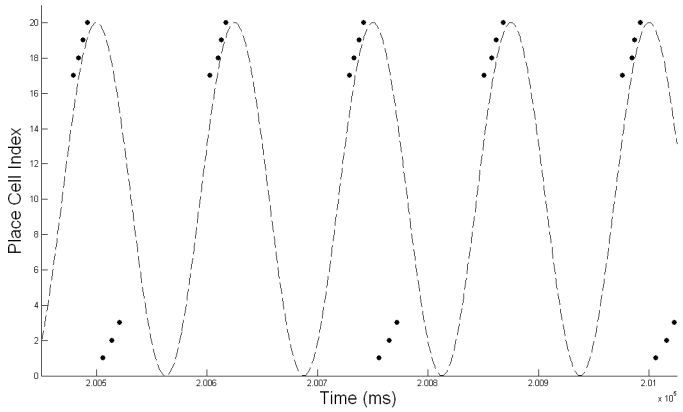

Fig.4. Recall activity in the network with w_{max}=5, A_+=0.12 and A_-=-0.1. Place cells 17 – 20 were being stimulated sequentially by external input, and activity in place cells 1-3 being recalled immediately after this activity had terminated. The sequence of firing is maintained during recall by the increasing level of recurrent synaptic input from activity in the preceding neurons, and axonal delays.

3.2 Phase precession with Acetylcholine modulation

When ACh modulation is introduced into the network, the value of the maximum synaptic weight becomes less important (unless it is set trivially low), and predictive recall and the experience-dependent expansion of place fields become present in all incarnations of the network. The final weight matrix and spike raster for a typical simulation using an identical route to that examined above are shown in Fig. 6. These are remarkably similar to that produced by the model in the absence of neuromodulation, with a large maximum weight limit (see Fig. 5). The one key difference lies in the spread of the peak in the weight matrix. Because plasticity in absent during recall when ACh is present in the network, no associations are generated between those neurons which are active due to external input, and those which are concurrently active due to recurrent input.

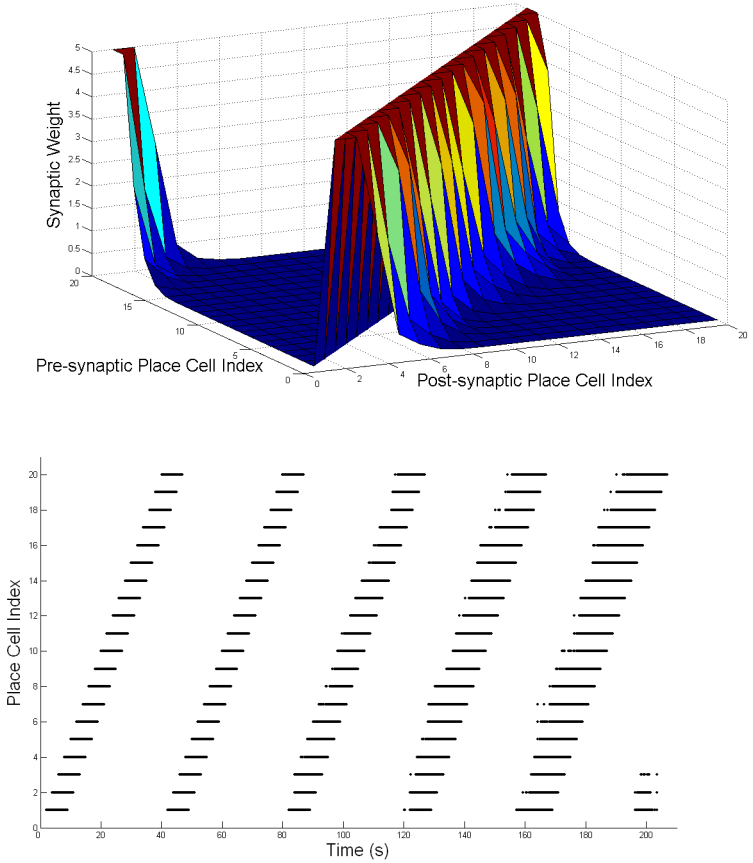

Fig. 5. Final synaptic weight matrix and overall spike raster for the network when traversing a circular route five times, with w_{max}=5 ; A_+=0.12 and A_-=0.1. (a) A comparison with the weight matrix in Fig.3 illustrates how each place cell has become associated with a greater number ahead of it on the route, due to the concurrent learning and recall activity. (b) The experience dependent expansion of place fields against the direction of travel, and predictive recall are also clearly visible in the spike raster (the activity corresponding to the beginning of the sixth run was not externally applied).

Conclusions

We have demonstrated a simple, abstract model of theta-phase coding in place cells within the autoassociative CA3 network of the hippocampus. This implementation of theta-phase coding is remarkably robust, and can function effectively even in the presence of significant recall activity without interference. Concurrent learning and recall activity is possible both with and without Acetylcholine modulation, provided that the maximum weight limit is set sufficiently high. This result leaves us with the

question of what significance this form of neuromodulation may have *in vivo*. Previous research has suggested that the main role of ACh may be to allow the elimination of redundant learned spatial sequences, and their subsequent replacement with new navigational routes which make use of the same place fields. This makes intuitive sense, as synaptic plasticity is only absent during the recall phase when ACh is present, and hence the predictions of future location which are made are not stored in the recurrent weights. This is illustrated by the narrower peak of potentiation in the synaptic weight matrix of Fig. 6. Without the damping of synaptic plasticity, redundant sequences will be continually recalled and consolidated. Although the ACh modulated network may still predict future locations based on past experience, new associations (and thus new predictions) will be rapidly acquired. The next step in this research, therefore, is to assess how incarnations of the network with and without neuromodulation can learn, recall, un-learn and re-learn a wider variety of complex behavioural sequences.

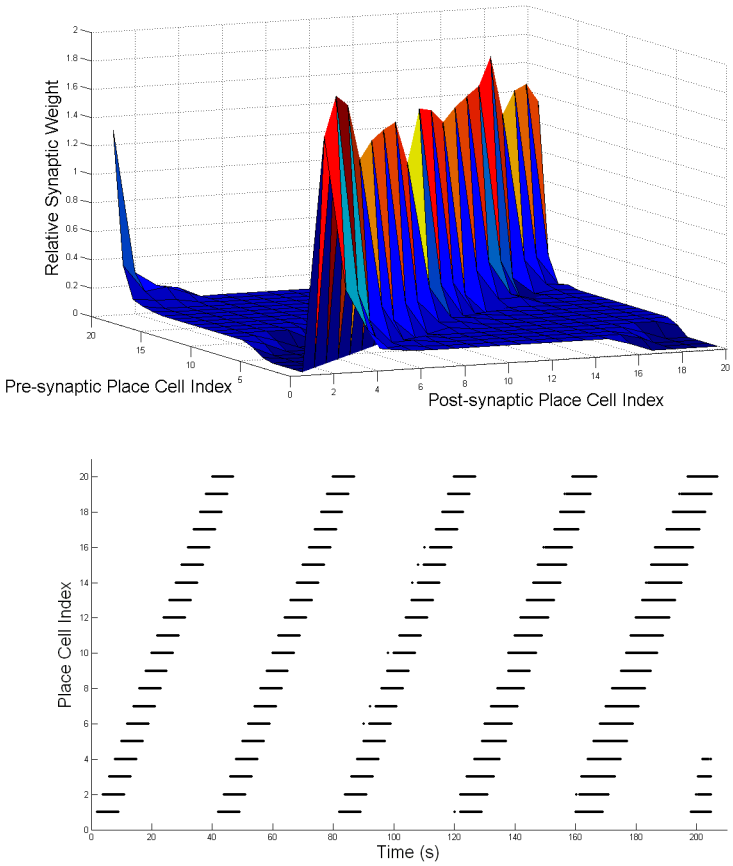

Fig. 6. Spike raster and final synaptic weight matrix for theta phase coding simulations with ACh modulation. Recall activity (place cells 1-4 were not receiving any external input at the end of the stimulation) and the experience-dependent expansion of place fields are clearly visible in the spike raster. The weight matrix retains its ideal structure, but has a narrower

spread, and plasticity is absent during the recall phase, and hence external input is not associated with recurrent activity.

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