

## SPONTANEOUS REPLAY OF TEMPORALLY COMPRESSED SEQUENCES BY A HIPPOCAMPAL NETWORK MODEL

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### ABSTRACT

Recent experimental evidence suggests that the hippocampus replays a temporally compressed version of recently-learned spatial sequence information during slow-wave sleep. This phase of sleep is characterized by intermittent episodes of high-frequency firing known as sharp waves. Here we partially characterize a simplified neural network model of hippocampal area CA3, based on integrate-and-fire cells, which is capable of recalling temporally compressed sequence information during brief periods of high activity.

### 1. INTRODUCTION

The hippocampus contains numerous "place cells", which fire whenever the animal is in a certain location in space [15]. Thus, spatial navigation can be thought of as a sequence learning problem, in which the animal learns a sequence of place cell firing. For some time, it has been known that place cells active during waking behavior are more likely to fire during slow-wave sleep (SWS) [16]. Recently, this finding has been extended to sequences of place cell firing. It has also been shown that the sequence replay during SWS is compressed in time [21, 18].

Accompanying slow-wave sleep are electrophysiological events in the hippocampus known as sharp waves (SPWs) [5, 19]. The most obvious feature of the SPW is a generalized increase electrical field potential, which occurs intermittently and with a variable duration and frequency [3].

Here, we show that a simplified model of hippocampal area CA3 can recall a temporally compressed sequence during a SPW-like event, and contrast these episodes of recall to the behavior of a non-learning network.

## 2. METHODS

Details of our methods appear elsewhere [1]. Briefly, the network consists of an input layer, analogous to the entorhinal cortex and dentate gyrus (EC/DG), connected one-to-one to a CA3-like layer. The CA3 layer has 1000 cells, each of which projects excitatory connections randomly and uniformly to 10% of the other units, reflecting the sparse recurrent connectivity observed in the hippocampus [7]. Each cell is modeled as an integrate-and-fire unit, with a membrane time-constant of 20 ms.

Activity is controlled by a feedback and a feedforward inhibitory interneuron. The output of the feedforward interneuron is proportional to the average EC/DG activity, and the output of the feedback interneuron is proportional to the average CA3-layer activity. We model inhibition as a shunting (divisive) effect, so that the synaptic current is the ratio of excitation to excitation plus inhibition.

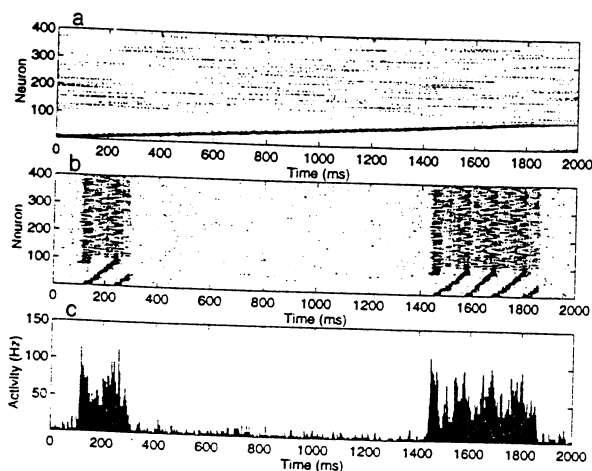
Excitatory recurrent synapses are modified by an unsupervised Hebbian rule based on physiological observations of long-term potentiation [8]. For a synapse to modify, the postsynaptic cell must fire, but the strength and sign of modification is controlled by a 150 ms running average of presynaptic activity [9].

The input to the model is a simple sequence of EC/DG cell activity, in which the first pattern activates EC/DG units 1-10, the next activates units 2-11, and so on. Each pattern lasts for 20 ms, but because of the spatial overlap between patterns, each EC/DG unit remains active for 200 ms. We simulate a sequence with 100 patterns, lasting for a total of 2000 ms. The sequence is circular, with the (nominal) first and final patterns overlapping.

The simulation has two phases: training (learning), and testing (recall). During training, the input sequence arrives from the EC/DG layer, and recurrent connections can modify. Training continues until the average synaptic weight has stabilized (about 10 cycles of the input sequence). During testing, synaptic modification is switched off, inhibition is lowered by about 10-fold, and EC/DG units are activated randomly at an average rate of 1 Hz. The situation during testing is similar to SWS, during which the network may not re-experience a previously learned pattern exactly, but some amount of random activity will be present. Thus, we also refer to testing as modeled slow-wave sleep (mSWS).

## 3. RESULTS

Figure 1a and b show a network during the final cycle of learning, and during an equally long period of mSWS. The network exhibits two distinct episodes of spontaneous recall, one starting at roughly 100 ms and the other at 1400 ms. Each of the two recall episodes includes several temporally compressed repetitions of the learned sequence. Periods of recall also coincide with a substantial increase in the overall average network activity, as shown in Figure 1c. The frequency and/or duration of spontaneous recall events be changed by adjusting various network parameters. For example, lowering the amount of feedback inhibition produces longer episodes of recall, until finally, the sequence is recalled continually throughout mSWS. Raising

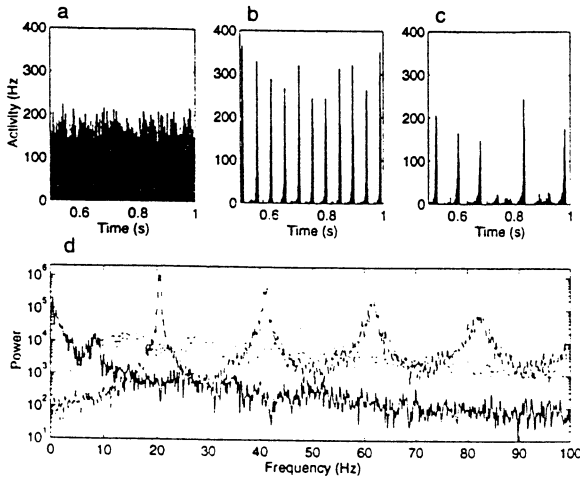


**Figure 1.** (a) *Cell firing at the end of training.* This is a rastergram of network-activity during the tenth trial of learning, by which time the average synaptic weight has stabilized. Time is along the abscissa, and neuron number is along the ordinate. Thus, each row represents the activity of one cell over time, and each dot represents one spike. This figure illustrates two distinct patterns of firing. The first 100 cells are driven directly by the input sequence from the EC/DG layer, as shown by the dark diagonal band of firing. The remaining 900 cells (of which only 300 are shown for clarity) are driven by recurrent connections from within CA3 only. These units fire over discrete episodes, spanning different portions of the sequence. We call these cells “local context units”, and hypothesize that they are roughly analogous to hippocampal place cells. (b) *Cell firing during mSWS.* Slow-wave sleep is modeled by disabling learning, lowering inhibition by approximately tenfold, and randomly activating EC/DG units at an average rate of 1 Hz. Notice the emergence of two distinct episodes of recall, each containing multiple repetitions of a temporally compressed version of the original sequence. (c) *Average network activity.* Shown here is the time course of the average network activity over all cells during the mSWS episode of (b). Although the network usually remains at low levels of activity, brief periods of high-frequency firing, reminiscent of sharp waves occur, and these are the spontaneous recall events.

inhibition produces more episodes of recall, but decreases the duration of each episode. Raising the rate of EC/DG firing has a similar effect, by virtue of the increase in feedforward inhibition.

Is learning required for the network to produce SPW-like events? We investigate this by comparing a “naive” network that has not learned a sequence to an experienced network that has been exposed to 10 cycles of the training sequence. Consistent with previous simulations [13], the naive network mostly exhibits stable non-periodic or limit cycle behavior, as shown in Figure 2a and b. However, by a change of parameters, the naive network can be made to exhibit intermittent bursts of high activity intermixed with periods of quiescence, as shown in Figure 2c. Although the time course of this pattern of firing is similar to that of spontaneous recall, its frequency profile differs considerably. As shown in Figure 2d, the power spectra of the naive networks contains multiple peaks on a relatively flat baseline while the power spectrum of activity during spontaneous recall decreases steadily with frequency.

Because the behavior of the naive and experienced networks differ, the ability to produce SPW-like episodes of high activity must be partly due training. We therefore examine how the final distribution of synaptic weights influences this behavior by deleting different sets of synaptic weights. Removing the synaptic weights *above* a certain value makes episodes of spontaneous recall less likely although it does not diminish their quality. Deleting the weights *below* a certain value decreases both the duration and the quality of these recall events (data not shown). However, recall is still maintained even with deletion of 50% of the weaker synapses.



**Figure 2.** (a) *Stable aperiodic firing.* Shown here is the average activity of a naive network over 500 ms, during which EC/DG units fire randomly at an average rate of 1 Hz. In this case, the network exhibits stable, aperiodic firing. (b) *Oscillatory firing.* Changing one parameter (in this case, changing the time-constant of inhibition from 2 to 7 ms) switches the network into oscillatory behavior. (c) *SPIV-like activity.* When the inhibitory time-constant is further increased to 10 ms, the firing pattern becomes more complex, with brief, intermittent surges of activity, reminiscent of sharp waves. (d) *Power spectra.* Although the time course of average activity shown in (c) above bears some qualitative similarity to the time course of average activity during mSWS shown in Figure 1c, the power spectra are different. Whereas the power spectra of the naive networks in (b, dash-dot line) and (c, dotted line) are relatively flat with some peaks at their characteristic frequencies, the power spectrum of the experienced network during mSWS decays steadily with frequency (solid line).

#### 4. DISCUSSION

Because of the autoassociative nature of CA3 [11, 17], random activity can trigger the recall of stored pattern(s) of activity. The amount of activity required may be slight. When CA3 is disinhibited with picrotoxin, for example, even a *single* cell can initiate a population burst [12]. Experimental and modeling efforts have suggested that decreased levels of acetylcholine enhance synaptic transmission, thereby facilitating autoassociative recall [6]. These findings are consistent with our result that spontaneous recall occurs in the setting of random input layer activity combined with lower inhibition.

Which synapses are involved in recall? We studied this issue by deleting different subsets of synaptic weights before mSWS. The larger weights serve to trigger spontaneous recall, while the smaller weights control the quality and the duration of each episode of spontaneous recall. Thus, recall requires more than just an interconnected group of highly potentiated synapses, as might be expected. Instead, recall makes use of all manner of synapses, both strong and weak. This is consistent with the recent suggestion that synaptic modification exerts a complex, time- and activity-dependent effect, rather than a fixed gain adjustment [10].

The power spectrum of average neural activity during spontaneous recall declines exponentially at low frequencies, in contrast to the relatively flat spectra of the naive network. A similar decay (the so-called “ $1/f$ ” spectrum) has also been found in a Hopfield-type network model of neural activity during sleep [14], and in a randomly-driven network model of the cortex [20].

Memory consolidation is the process by which certain types of memory are transferred from intermediate-term storage in the hippocampus to long-term storage in the cortex [22]. The

initial phase of consolidation has been described colloquially as the hippocampus "teaching" the cortex. The data of McNaughton and colleagues [21] suggest that this teaching happens during slow-wave sleep, when sequence information is replayed. Because recall presumably occurs during SPWs, the cortex will be "taught" under conditions of high activity. This high activity is ideal for inducing long-term potentiation [4], a well-known cellular model of learning [2].

In a simplistic way, our model reproduces many of the features of the behavior of area CA3 during memory consolidation. Under the influence of spontaneous input activity, the network can repeatedly recall a temporally compressed version of a learned sequence during transient periods of increased overall activity. Such compression will facilitate associations between temporally distant events.

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## REFERENCES

- [1] D A August and W B Levy. Temporal sequence compression by a hippocampal network model. In *INNS World Congress on Neural Networks*, pages 1299–1303. Mahwah, NJ, 1996. Lawrence Erlbaum.
- [2] T V P Bliss and T Lomo. Long-lasting potentiation of synaptic transmission in the dentate area of the anaesthetized rabbit following stimulation of the perforant path. *J. Physiol.*, 232:331–356, 1973.
- [3] G Buzsaki. Hippocampal sharp waves: Their origin and significance. *Brain Res.*, 398:242–252, 1986.
- [4] G Buzsaki. Two-stage model of memory trace formation: A role for 'noisy' brain states. *Neuroscience*, 31(3):551–570, 1989.
- [5] G Buzsaki, Z Horvath, R Urioste, J Hetke, and K Wise. High-frequency network oscillation in the hippocampus. *Science*, 256:1025–1027, 1992.
- [6] M E Hasselmo, E Schnell, and E Barkai. Dynamics of learning and recall at excitatory recurrent synapses and cholinergic modulation in rat hippocampal region CA3. *J. Neurosci.*, 15(7):5249–5262, 1995.
- [7] N Ishizuka, J Weber, and D G Amaral. Organization of intrahippocampal projections originating from CA3 pyramidal cells in the rat. *J. Comp. Neurol.*, 295:580–623, 1990.
- [8] W B Levy and O Steward. Synapses as associative memory elements in the hippocampal formation. *Brain Res.*, 175:233–245, 1979.
- [9] W B Levy and O Steward. Temporal contiguity requirements for long-term associative potentiation/depression in the hippocampus. *Neuroscience*, 8(4):791–797, 1983.
- [10] H Markram and M V Tsodyks. Redistribution of synaptic efficacy between neocortical pyramidal cells. *Nature*, 382:807–810, 1996.
- [11] D Marr. Simple memory: a theory for archicortex. *Phil. Trans. Royal. Soc. Lond.*, 262:23–81, 1971.
- [12] R Miles and R K S Wong. Single neurones can initiate synchronized population discharge in the hippocampus. *Nature*, 306:371–373, 1983.
- [13] A A Minai and W B Levy. The dynamics of sparse random networks. *Biol. Cybern.*, 70:177–187, 1993.
- [14] M Nakao, K Watanabe, T Takahashi, Y Mizutani, and M Yamamoto. Structural properties of network attractor associated with neuronal dynamics transition. In *Proceedings of the International Joint Conference of Neural Networks*, volume 3, pages 529–534. Inst. of Electrical and Electronic Engineers, 1992.
- [15] J O'Keefe and L Nadel. *The Hippocampus as a Cognitive Map*. Oxford: Clarendon Press, London, 1978.
- [16] C Pavlides and J Winson. Influences of hippocampal place cell firing in the awake state on the activity of these cells during subsequent sleep episodes. *J. Neurosci.*, 9(8):2907–2918, 1989.
- [17] E T Rolls. Functions of neuronal networks in the hippocampus and cerebral cortex in memory. In R M J Cotterill, editor. *Models of Brain Function*, pages 15–33. Cambridge Univ. Press, 1989.

- [18] W E Skaggs and B L McNaughton. Replay of neuronal firing sequences in rat hippocampus during sleep following spatial experience. *Science*. 271:1870–1873. 1996.
- [19] S S Suzuki and G K Smith. Spontaneous EEG spikes in the normal hippocampus. I. Behavioral correlates, laminar profiles and bilateral synchrony. *Electroenceph. Clin. Neurophys.*, 67(4):348–359. 1987.
- [20] M Usher, M Stemmler, C Koch, and Z Olami. Network amplification of local fluctuations causes high spike rate variability, fractal firing patterns and oscillatory local field potentials. *Neural Computation*, 6(5):795–836, 1994.
- [21] M A Wilson and B L McNaughton. Reactivation of hippocampal ensemble memories during sleep. *Science*, 265:676–679, 1994.
- [22] S Zola-Morgan and L R Squire. The primate hippocampal formation: Evidence for a time-limited role in memory storage. *Science*. 250:288–290. 1990.