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Neurogenesis and Multiple Plasticity Mechanisms Enhance Associative Memory Retrieval in a Spiking Network Model of the Hippocampus

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Abstract

Hippocampal CA3 is crucial for long-term associative memory. CA3 has heavily recurrent connectivity, and memories are thought to be stored as the pattern of synaptic weights in CA3. However, despite the well-known importance of the hippocampus for memory storage and retrieval, up until now, spiking neural network models of this crucial function only exist as small-scale, proof-of-concept models. Our work is the first to develop a biologically plausible spiking neural network model of hippocampus memory encoding and retrieval, with over two orders-of-magnitude as many neurons in CA3 as previous models. It is also the first to investigate the effect of neurogenesis in the dentate gyrus on a spiking model of CA3. Using this model, we first show that a recently developed plasticity rule is crucial for good encoding and retrieval. Then, we show how neural properties related to neurogenesis and neuronal death enhance storage and retrieval of associative memories in the recurrently connected CA3.

Introduction

It is well known that a brain area called the hippocampus is heavily involved in long-term memory storage and retrieval (Squire 2009). In particular, a sub-area of the hippocampus called CA3 is crucial for long-term declarative memory, which includes both spatial (Moser, Kropff, and Moser 2008) and episodic (Tulving 2002) memory. CA3 has heavily recurrent connectivity (i.e. CA3 neurons form many synapses with other CA3 neurons), more so than any other brain area (Rolls et al. 1997), and memories are thought to be stored as the pattern of synaptic weights in CA3.

However, despite the well-known importance of CA3 for memory storage and retrieval, up until now, spiking neural network models of this crucial function only exist as small-scale models. These existing models, while useful for illustrating certain computational principles, contain only up to 30 CA3 neurons (e.g. (Brijesh and Ravindran 2007; Tan et al. 2013)). Moreover, they lack biological realism. One would expect a computational model using spiking networks to be at least organized in a recurrent manner, with both excitatory and inhibitory populations forming synaptic connections, whilst the neurons are effectively in the fluctuation-driven regime, with mean membrane potential near to threshold.

Our work is the first to develop a biologically realistic spiking neural network model of hippocampus memory encoding and retrieval, with over two orders-of-magnitude as many neurons in CA3 as previous models. Before that, no plasticity mechanism exists to allow the spiking network community or hippocampal modeling community to do so in plastic spiking networks, whereby a biologically realistic spiking neural network of a credible size using spike timing dependent plasticity (STDP) has consistently failed to form long-lasting memory engrams of a reasonable number without interference (Chrol-Cannon and Jin 2015; Kunkel, Diesmann, and Morrison 2011).

While other studies have used feedforward, rate-based models of CA3, these are less realistic, and it is unclear if the findings from these simpler models also hold true for recurrent spiking networks. Such networks have very different properties from simpler networks, and one major challenge is their stability (Zenke, Agnes, and Gerstner 2015; Abbott and Nelson 2000). Neurogenesis (neuron birth) and neural apoptosis (neuron death) add extra layers of complexity, as such changes in the neural population have not been investigated in recurrent spiking CA3 networks before.

Among models of neurogenesis, all use rate-based neurons, with (Aimone, Wiles, and Gage 2009) the only exception using spiking neurons. However, they do not model CA3. In (Zenke, Agnes, and Gerstner 2015), new plasticity mechanisms are developed to enable stable encoding of memories in plastic recurrent networks that can be retrieved hours (network time) later. However, the plasticity mechanisms have yet to be shown to be reliable for memories of a realistic number. Also, it is not clear what role neurogenesis plays in enhancing memory encoding, given a plastic spiking network that can encode reasonable number of memories. Thus, our paper is the only work that investigates the effect of neurogenesis on a plastic spiking model of CA3.

Using our model, we first show that a novel plasticity rule (Zenke, Agnes, and Gerstner 2015) is crucial for good encoding and retrieval. Then, we show how properties related to neurogenesis (i.e. increased excitability of newborn neurons) and neuronal death (i.e. relative balance between birth and death) are crucial for storage and retrieval, thus explaining the functional significance of these properties.

Methods

To study encoding and retrieval of associative memories in the hippocampus, we construct a three-layer spiking neuron network model of the hippocampus (Fig. 1). The three layers are the entorhinal cortex (EC), the dentate gyrus (DG) and CA3. For simplicity, we do not model CA1, which is thought to perform a simple comparator or decoding role (Tulving 2002; Rolls et al. 1997; Rolls 1987). Incoming memories are simulated by stimulating a subset of the EC neurons, which would trigger spiking activity that cascades to the other two layers via different pathways. Using three different sets of STDP models (see Section), we compare which of these would enable the stable encoding and retrieval of these memories. In this section, we describe first the hippocampal network setup, next the various plasticity rules, the different simulation settings and finally the measures to quantify memory retrieval for our study.

Network setup

The hippocampal network is made up of adaptive integrate-and-fire (AIF) neurons (Zenke, Agnes, and Gerstner 2015), of which their dynamics are described further below. The entorhinal cortex is modeled using 1024 standalone AIF neurons, which receive no other inputs other than the memory stimuli. The DG is modeled using standalone AIF neurons. Depending on the simulation settings, the size of the DG network can be 1600 or 3200 neurons. The CA3 network is a recurrent one, comprising of 3200 excitatory neurons and 800 inhibitory neurons. In the recurrent network, the neurons are connected to each other with a Gaussian connectivity profile, such that neurons that are close to each other have a higher connectivity probability. EC neurons are connected to the CA3 excitatory neurons with a connection probability of 0.15. All DG and CA3 neurons receive fluctuating Poisson inputs to achieve a low firing rate of 0.3 spikes/s and a mean membrane potential of 5 mV below spiking threshold.

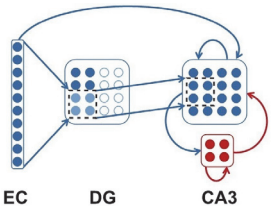

Figure 1: Network setup. Blue circles denote excitatory neurons and red circles denote inhibitory neurons. Light blue circles and unfilled circles denote newborn and yet-to-be-born DG neurons respectively. Blue arrows denote excitatory synapses and red arrows denote inhibitory synapses.

Plasticity models

We have three classes of plasticity models in our study, namely short term plasticity (Tsodyks, Uziel, and Markram 2000), STDP plasticity for excitatory synapses and STDP plasticity for inhibitory synapses impinging on excitatory neurons (Vogels et al. 2011). All three are needed for successful encoding and retrieval (Zenke, Agnes, and Gerstner 2015). There are three different types of excitatory plasticity in our study, namely pair STDP (Song, Miller, and Abbott 2000), triplet STDP (Pfister and Gerstner 2006), and unified plasticity, which is a simplified version of the plasticity model described in (Zenke, Agnes, and Gerstner 2015), which incorporates Hebbian, heterosynaptic and transmitter-induced plasticity mechanisms and was shown to reliably form memory engrams that can be retrieved with little interference.

In all network settings, the synaptic connections between EC-CA3 excitatory population and CA3-CA3 excitatory populations are plastic (using one of the three excitatory plasticity rules, plus short-term plasticity), the CA3 excitatory to CA3 inhibitory population synaptic connections are plastic (short-term plasticity) and the CA3 inhibitory to CA3 excitatory population synaptic connections are plastic (inhibitory plasticity).

The dynamics of short term plasticity has already been described in the network section; the other plasticity mechanisms are now described. The dynamics of pair STDP is described by:

$$\dot{W^{ij}} = A_+ K^i S^j(t) - A_- K^j S^i(t),$$

whereby the time evolution of the pre-synaptic variable K^i and postsynaptic variable K^j are respectively described by $\dot{K^i} = -\frac{K^i}{\tau_{K^i}} + S^i(t)$ and $\dot{K^j} = -\frac{K^j}{\tau_{K^j}} + S^j(t)$ and $A_{+/-}$ are the weight change amplitudes. The dynamics of the triplet plasticity rule is described by:

$$\dot{W^{ij}} = K_1^i A_+ (1 + K_2^j(t-\epsilon)S^j(t)) - K_1^j A_- (1 + K_2^i(t-\epsilon)S^i(t))$$

whereby synaptic variables $K_{1/2}^{i/j}$ evolve as per synaptic variables described for paired STDP, $A_{+/-}$ are weight change amplitudes and $t-\epsilon$ ensures that weight update is done prior to spike times. The unified plasticity model is described by:

$$\dot{W^{ij}} = K^i A_+ K_2^j(t-\epsilon)S^j(t) - K_1^j A_- S^i(t)$$
$$-\beta(W^{ij} - \tilde{W^{ij}})(K_1^j(t-\epsilon))^3 S^j(t) + \delta S^i(t),$$

whereby synaptic weight tends towards $\tilde{W^{ij}}$, and every pre-synaptic spike induces a small increase δ in synaptic weight. All synaptic variables K and weight change amplitudes A are as described earlier. The inhibitory plasticity is described by:

$$\dot{W^{ij}} = A(K^i S^j(t) + (K^j - \alpha)S^i(t)),$$

whereby α is the depressing factor.

Simulation settings

Our simulations have two phases: the encoding phase and retrieval phase. During the encoding phase, 80 out of the 1600 or 3200 DG neurons are selected to receive a new memory stimulus from the EC. In the first setting, to simulate the case whereby the stimulus can be encoded by any mature DG neuron, these 80 neurons are randomly selected. In the second setting, to simulate the case whereby newborn DG neurons are solely responsible for encoding new memory stimuli, the entire excitatory DG population is divided into blocks of 80, where one block is targeted by one memory stimulus. In addition to the above two neurogenesis (NG) settings, a third setting emulates the higher excitability of newborn DG neurons (Finnegan and Becker 2015;

Aimone, Wiles, and Gage 2009) by decreasing the spiking threshold (and hence increasing excitability) of the 80 neurons targeted by the EC for the duration of the encoding phase of each stimulus ($500\,\mathrm{ms}$). (More precisely, by "newborn neurons", we are referring to the remaining newborn DG cells after NG and subsequent cell death of a fraction of these cells due to inactivity.)

When all the available blocks of 80 DG neurons have been assigned (e.g. when there are 1600 DG neurons but 40 stimuli, requiring $40 \times 80 = 3200$ DG neurons), we "recycle" the DG neurons, under the assumption of "turnover homeostasis", whereby the rate of neuron birth and death is relatively balanced (Meltzer, Yabaluri, and Deisseroth 2005). For each new stimulus to be encoded, 80 out of all the DG neurons are randomly selected. The synaptic weights of incoming (from EC) and outgoing (to CA3) connections are then set to 0 (simulating neural death). These DG neurons are then used to encode the new stimulus (simulating NG). Hence, while EC neurons maybe involved in encoding more than one stimuli, by design, DG neurons encode only one stimulus each.

To encode a memory in the EC, 32, 96 or 160 out of the 1024 EC neurons are randomly selected at the start of each encoding phase. They are then connected to the selected DG neurons. The selected DG neurons are then randomly connected to a cluster of 100 CA3 excitatory neurons. The randomly selected EC neurons are then stimulated with 50 spikes each over a duration of $250\,\mathrm{ms}$. Spiking activities would then cascade down to the CA3 region via the EC-CA3 pathway and the newly formed EC-DG-CA3 pathway. The encoding phase involves stimulating the network with either 5, 40, or 100 stimuli, each lasting for $500\,\mathrm{ms}$ ($250\,\mathrm{ms}$ of stimulation, then letting the network activity settle for $250\,\mathrm{ms}$).

After all stimuli have been encoded, they are sequentially retrieved in chronological order. The retrieval process is very similar to encoding (e.g. same set of 32, 96 or 160 EC neurons for each memory are stimulated), except that during retrieval, only the EC-CA3 pathway is active, while the EC-DG-CA3 pathway is inactive, a phenomenon observed biologically and common in models (Becker, Macqueen, and Wojtowicz 2009; Weisz and Argibay 2009; Hasselmo and McGaughy 2004).

In all, there are two aspects in which simulation settings vary, namely 1) the different excitatory plasticity models (pair STDP, triplet STDP, unified plasticity), and 2) how DG neurons are selected to encode memories (two settings: selected randomly emulating no NG and normal excitability; selected via blocks emulating NG and increased excitability).

The network is simulated with a range of different learning rates on the plastic connections, EC-CA3 (feedforward) and CA3-CA3 (recurrent) to investigate robustness of results. All simulations are done on the NEST simulator (Gewaltig, Morrison, and Plesser 2012).

Measures: Signal-to-Noise Ratio (SNR)

To quantify how well each encoded memory is retrieved, a signal-to-noise ratio (SNR) measure is devised. For each simulation, we know precisely when the stimuli for each memory to be encoded is introduced into the network. Likewise for the stimuli to retrieve an encoded memory. We also know which set of CA3 excitatory neurons are stimulated during encoding in the time window of $500\,\mathrm{ms}$, which we denote as N_{enc}. For each memory retrieval, we systematically vary the size of the set of retrieved CA3 excitatory neurons N_{ret} by scanning through a range of spike counts, and compute its corresponding SNR (see 1). After this has been done for all memory retrievals, we pick the maximum SNR, and note down the corresponding spike count and mean size of all N_{ret}.

Algorithm 1 Computation of SNR

$\forall A \in N_{ret}$,
  If $A \in N_{enc}, Count_{signal} + 1$
  else, $Count_{noise} + 1$
$SNR = \frac{Count_{signal} - Count_{noise} + |N_{enc}|}{2 * |N_{enc}|}$

The SNR is normalized to an interval of $[0, 1]$, since it is highly improbable that $Count_{noise} > |N_{enc}|$ given that we select only neurons spiking more than twice in the given time window for N_{ret} and the network is in a fluctuation driven regime with low firing rate of $\approx 0.3\,\mathrm{spikes/s}$. Hence the SNR is unlikely to go below 0, which is also the case in our data collected. Therefore, a score of 0 most likely means that $N_{ret} \cap N_{enc} = \emptyset$, a score of 1 must mean that $N_{ret} = N_{enc}$, and a score of 0.5 must mean that $Count_{signal} = Count_{noise}$, whereby there are as many signal neurons as there are noise neurons in N_{ret}, one special case being $N_{ret} = \emptyset$.

Results

In this section, we present results for the comparison of all 3 plasticity rules using single memory encoding and retrieval within a certain parameter range of feedforward (FF; EC-CA3 pathway) and recurrent (REC; CA3-CA3 excitatory population) plasticity learning rates, after which we further justify that the parameter range can be further narrowed down using memory encoding and retrieval simulations of 3 stimuli. Third, using 40 stimuli (hence fully utilizing the entire dentate gyrus population), we explore the parameter space (of different learning rates, number of EC neurons per stimulus, with and without NG) and determine what parameters give the best SNR. From these set of results, we obtain for each number of EC neurons per stimulus (32, 96 and 160), a set of parameters that give the best SNR results for the case of FF plasticity only and both (FF and REC) plasticity and then use them for simulations of encoding and retrieval of 200 memories (5 times overloading of the dentate gyrus, DG). The purpose of doing so is to investigate if NG improves SNR results, and how it interacts with FF and REC plasticity. Retrieval of 200 memories is also conducted using only partial retrieval such that only a fraction of the encoding EC neurons are stimulated during retrieval.

Comparison of plasticity rules

In this first set of simulations, we investigate across a set of parameters (number of EC neurons per stimulus, with and

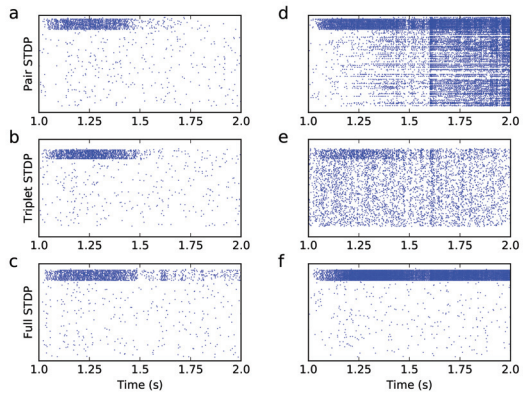

Figure 2: Raster plots for encoding (at 1 s) and retrieval (at 1.5 s) of a single stimulus. (a-c) Raster plots for simulations without NG, 32 EC neurons, and with FF and REC learning rates at 0.01. (d-f) Raster plots for simulations with NG, 160 EC neurons, and with FF and REC learning rates at 0.15.

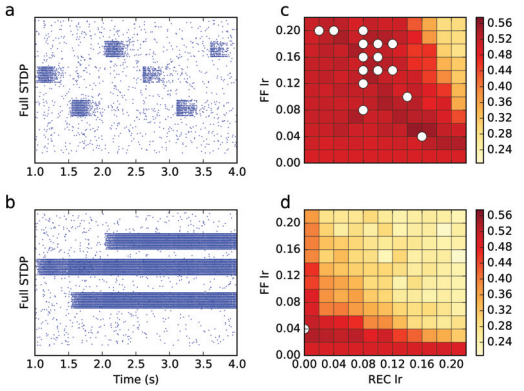

Figure 3: Raster plots for encoding (at 1 s) and retrieval (at 2.5 s) of 3 stimuli, and colormaps for SNR given range of FF and REC learning rates. (a) Raster plot for simulation with NG, 32 EC neurons, and FF and REC learning rates at 0.06. (b) Raster plot for simulation with NG, 160 EC neurons, and FF and REC learning rates at 0.16. (c) Colormap for SNR with given range of FF and REC learning rates, for simulations with NG and 32 EC neurons. White markers denote learning rates with SNR values above 90 percentile of the maximum SNR value. (d) Colormap for SNR with NG and 160 EC neurons. White markers as above.

without NG, range of FF and REC learning rates), how the 3 different plasticity rules compare using SNR as a metric. We use a range of learning rates, from 0.0 to 0.2, with an interval of 0.01. From Figure 2 on page 4, we observe that the full plasticity model, at low learning rates and 32 EC neurons per stimulus, is able to trigger sufficient spiking activities during retrieval Figure 2 on page 4c, as opposed to the other 2 plasticity models 2(a,b). At higher learning rates and 160 EC neurons per stimulus, the pair and triplet plasticity models are also able to retrieve the memory encoded to some extent but in the process generate considerable amount of background noise such that their SNR suffer (see Figure 2 on page 4d,e). On the other hand, the full plasticity model is able to retrieve the encoded memory without generating much background noise (see Figure 2 on page 4f). This demonstrates how the homeostatic terms in the model help to balance network activities. However, spiking activities from memory encoding last beyond the usual time window of 500 ms and into the retrieval time window. Hence, from this set of simulations of the 3 different plasticity models, we confirm that the full plasticity models outperform the other 2 models in memory encoding and retrieval across the broad range of parameters (SNR colormaps not shown), but persistent activities at high learning rates can become a problem for simulation with multiple memories. We investigate this in the next simulation with 3 stimuli, whilst using the same parameters.

Defining parameter space for learning rates

Here, by increasing the number of stimuli to 3, we further investigate how the full plasticity model would perform given the same set of parameters as in . As expected, in the setting of low learning rates, retrieval of memories encoded achieves good SNR (see Figure 3 on page 4a). However, at high learning rates, spiking activities from memory encoding phase persist into the retrieval phase, adversely affecting the SNR (see Figure 3 on page 4b). This observation can be made in the SNR colormaps for the learning rates under different parameter settings. The space of learning rates with relatively better retrieval is larger in the case of 32 EC neurons per stimulus as compared to larger (96 and 160) number of EC neurons per stimulus (see Figure 3 on page 4c,d). This is mainly due to the fact that with more EC neurons per stimulus, there are more synaptic connections on the EC-CA3 pathway potentiated which increase overall excitation of the CA3 population, leading to poorer SNR overall. Hence, to discover what the optimal set of parameters are for memory encoding and retrieval, we repeat the above simulations using 40 stimuli (fully utilizing the whole DG network), but with a narrower range of learning rates.

Determining the best parameters

In this set of simulations, the learning rates used are $\{0.0, 0.001, 0.01, 0.1\}$. As shown in Figure 4 on page 5a-c, increased number of EC neurons per stimulus not only increase background activities, but is also more prone to triggering spiking activities in other CA3 memory engrams. This is because the EC neurons are randomly picked. Hence, during retrieval, the increased overlap of EC neurons across memories would also trigger spiking activities in the other memory engrams. The SNR would deteriorate with the number of stimuli. The SNR colormaps for the different number of EC neurons with NG are shown in Figure 4 on page 5d-f. We further notice that memory retrieval is consistently better for the case of NG than without and that memory retrieval is better for less EC neurons (see Table 1 on page 6). For the case of 32 EC neurons per stimulus, FF and REC plasticity give better SNR than just FF

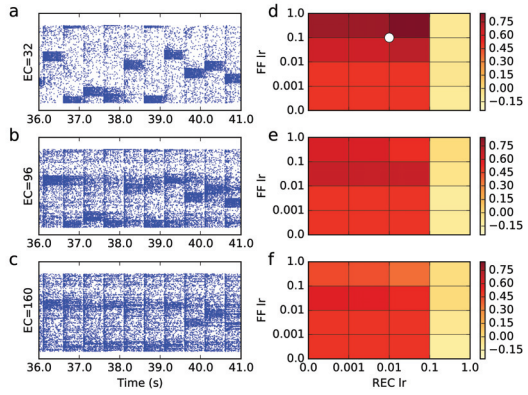

Figure 4: Raster plots for simulation for encoding and retrieval of 40 stimuli (retrieval of last 10 stimuli shown), and colormaps for SNR with given range of FF and REC learning rates. (a) Raster plot for simulation with 32 EC neurons, NG and with FF and REC learning rates at 0.1 and 0.01 respectively. (b) Raster plot as above, for 96 EC neurons. (c) Raster plot as above, for 160 EC neurons. (d) Colormap for SNR with given range of FF and REC learning rates, for simulations with NG and 32 EC neurons. White markers denote learning rates with SNR values above 95 percentile of the maximum SNR value. (e) Colormap as above, for 96 EC neurons. (f) Colormap as above, for 160 EC neurons.

alone. But these two modes of plasticity give similar SNR results for more EC neurons per stimulus. This could be due to the fact that with more EC neurons per stimulus, a larger spike count is required to give the optimal SNR. This results in drop in both signal and noise. While previously, with 32 EC neurons, both signal and noise neurons are more numerous in the FF+REC case than the FF case, resulting in a higher SNR, this effect is drowned out by the increased background noise (96 and 160 EC neurons per stimulus). We further note that a lower learning rate is required to give the maximum SNR for more EC neurons. We have also run further simulations such that 1) FF learning rate $= \{1.0\}$ and REC learning rate $= \{0.0, 0.001, 0.01, 0.1\}$ and 2) FF learning rate $= \{0.0\}$ and REC learning rate $= \{0.001, 0.01, 0.1, 1.0\}$. Both set of simulation do not yield better SNR than those above. In particular, for the second set of simulations, whereby FF learning rate $= 0.0$, persistent spiking activities such as those in Figure 3 on page 4b occur at large REC learning rates, effectively drowning out spiking activities of retrieved memories. The learning rates (both FF and FF+REC) for maximum SNR are used next for simulations of up to 200 stimuli, loading the DG up to $5x$ its designated capacity.

Robustness of results in DG overloading

For this set of simulations, we select simulation settings in Table 1 on page 6 with red color font for overloading. Firstly, We tried simulations each with 80, 120, 160 or 200 numbers of stimuli and then retrieved the last 40 encoded memories. Next, we tried encoding 200 memories and then retrieved them in batches of 40 memories each: $\{1-40\}, \{41-80\}, \{81-120\}, \{121-160\}, \{161-200\}$. Third, the second set of simulation are repeated with partial retrieval such that only 0.25, 0.5 or 0.75 of encoding EC neurons are stimulated during retrieval. In general, the observations made agree with those made in . In the first simulations, more memories result in poorer retrieval. For example, for 32 EC neurons and FF+REC plasticity, the SNR for 80, 120, 160 or 200 numbers of stimuli are respectively 0.86, 0.84, 0.81 and 0.76. The SNR for the retrieved memory batches in the second simulations ($\{1-40\}, \{41-80\}, \{81-120\}, \{121-160\}, \{161-200\}$, same parameters) are respectively 0.51, 0.57, 0.63, 0.71 and 0.76. Hence, older memories are "forgotten". The SNR for the third simulations (partial retrieval of last 40 encoded memories, same parameters) are respectively 0.72, 0.66 and 0.55 for 0.75, 0.5 and 0.25 of encoding EC neurons stimulated during retrieval. The SNR for the partial retrieval of encoded memories $\{41-80\}$ are respectively 0.55, 0.51 and 0.5 for 0.75, 0.5 and 0.25 of encoding EC neurons stimulated during retrieval. Hence, partial retrieval can be achieved but only for the more recent memories. In the above simulations, 32 stimulating EC neurons give better SNR results compared to 96 EC neurons, and FF+REC plasticity perform better than just FF plasticity alone.

Discussion

From our results, memory retrieval for up to 200 encoded stimuli is achieved even when the plasticity is kept on during the retrieval phase, despite using a simplified version of the plasticity models in (Zenke, Agnes, and Gerstner 2015). While acknowledging that the network has not been simulated for hours to make conclusions about stability of the simplified plasticity model, we think that the network architecture also plays a role in preserving encoded memories. Specifically, memory encoding is done via both the EC-CA3 pathway (plastic) and EC-DG-CA3 pathway (static), while memory retrieval is done via the EC-CA3 pathway only. For the case of both FF+REC plasticity, memory engrams formed using both the EC-CA3 pathways and REC CA3 connections. This gives better SNR than just FF plasticity alone. While REC plasticity alone may also encode memories, this occurs at high REC learning rates, which persistent spiking activities dominate the network. The highly REC CA3 network hence operate best as an associative memory by sharing the task of encoding memory engrams between both FF and REC synaptic connections.

Memory retrieval deteriorates with increased encoded memories. This is primarily due to noise in the network, which can be attributed to 3 main sources: 1) during encoding, DG neurons other than those assigned may spike even if they are less excitable, 2) CA3 neurons are randomly assigned during encoding and hence some may already be encoding for an earlier stimulus, 3) EC neurons are randomly selected for each memory and hence may already be used for an earlier stimulus. For the second and third source of noise, it can be observed from Table 1 on page 6 how noise neurons are generally more for the FF+REC case as compared to just the FF case. We systematically remove the above sources of

	With NG						Without NG					
	FF			FF+REC			FF			FF+REC		
32	0.83	75, 10(3)	0.1, 0.0	0.87*	96, 21(3)	0.1, 0.01	0.80	75, 15(3)	0.1, 0.0	0.82	85, 21(3)	0.1, 0.01
96	0.68	54, 18(4)	0.01, 0.0	0.68	60, 23(4)	0.01, 0.01	0.59	34, 15(4)	0.01, 0.0	0.59	33, 14(4)	0.01, 0.001
160	0.60	43, 23(6)	0.01, 0.0	0.59	42, 24(6)	0.01, 0.001	0.54	25, 17(7)	0.01, 0.0	0.53	21, 15(8)	0.01, 0.001

Table 1: Maximum SNR for simulations with 40 stimuli. The results are tabulated for the different number of EC neurons, and the case of with and without NG. A maximum SNR (first column) is chosen for the case of FF (EC-CA3) plasticity only, and FF+REC (CA3-CA3) plasticity. In the second column $(x, y(z))$, x denotes the number of CA3 neurons spiking during retrieval that are in the set of stimulated CA3 neurons during encoding (signal), while y denotes the number of CA3 neurons spiking not in the set of stimulated neurons (noise) and z denotes the spike count used to calculate the optimal SNR. In the third column (x, y), x denotes the learning rate for FF plasticity, while y denotes the learning rate for the REC plasticity. * denotes the maximum SNR.

noise in one simulation of 40 stimuli, by 1) setting threshold for un-assigned DG neurons to some arbitrary high values, 2) CA3 neurons are assigned in block, hence there are no overlap, and 3) EC neurons are selected in blocks, hence there are no overlap. This results in perfect retrieval with 40 stimuli (no overloading). However, 1) and 3) are biologically unrealistic while 2) would imply that there must be at least as many CA3 neurons as there are memories.

In reality, forgetting of older memories is natural. Also, spiking of other CA3 neurons other than those encoding the particular memory during retrieval may help to associate several related memories in downstream networks. Memories in the hippocampus are also further consolidated in the cortex, of which how they function as a complete system is still an active field of research. The model we have studied set up a framework for further computational studies in such a direction.

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