A Computationally Efficient Associative Memory Model of Hippocampus CA3 by Spiking Neurons

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Abstract—The hippocampus is involved with the storage and retrieval of short-term associative memories. In this paper, we propose a computationally efficient associative memory model of the hippocampus CA3 region by spiking neurons, and explores the storage of auto-associative memory. The spiking neural network encodes different associative memories by different subsets of the principal neurons. These memory items are activated in different gamma subcycles, and auto-associative memory is maintained by the synaptic modifications of recurrent collaterals by N-methyl-D-aspartate (NMDA) channels. Accurate formation of auto-associative memory is achievable in single presentation of memory items when synaptic modifications depend on fast NMDA channels having a deactivation time within the duration of a gamma subcycle. Simulation results also show that spike response model (SRM) improves computational efficiency over the integrate-and-fire (I&F) neuron model.

I. INTRODUCTION

The hippocampus resides within the medial temporal lobe of the brain. Many sub-regions of hippocampus have been identified. At the macroscopic level, highly processed neocortical information from all sensory inputs converges onto the medial temporal lobe [1]. These processed signals enter the hippocampus via the entorhinal cortex (EC). Within the hippocampus [2], [3], [4], there are connections from the EC to all parts of the hippocampus, including the dentate gyrus (DG), CA3 and CA1 through perforant pathway, from the DG to CA3 through mossy fibres, from CA3 to CA1 through Schaffer collaterals, and then from CA1 back to EC. There are also strong recurrent connections within the CA3 region. Figure 1(a) depicts the broad overview of hippocampus.

A key functional role of the hippocampus is the storage and recall of associative memories [5], [6]. Computational models of associative memory in the hippocampus have been actively explored in literature. A hierarchical architecture for object-place association was demonstrated by modeling the EC layer II and CA3 regions [7], [8]. A biologically realistic CA3 network which uses gamma oscillations as a means to retrieve excitatory associative memories was proposed [9]. The biophysical mechanisms to achieve the storage and recall of spatial-temporal patterns were explored using a microcircuit model of the CA1 region [10]. The anatomy of the hippocampus and surrounding regions were modeled in the Darwin X robot for a spatial memory task [11]. The mapping of sensory information was studied using a model of the medial temporal lobe and the hippocampus [12].

The CA3 region of the hippocampus was modeled with a focus on producing stable attractors in the network [13]. Mathematic models and theories about memory storage and representation have been well explored based on attractor dynamics in recent years [14], [15]. In such networks, storage of associative memory patterns is enabled by synaptic strengths that are adjusted according to some activity-dependent plas-
ticity mechanisms (of which the most widely recognized is the Hebbian rule) such that the attractors of the network dynamics represent the stored memories [16], [17], [18]. It was also shown that hippocampal region CA3, characterized by heavy recurrent connections and modifiability, could be an anatomical substrate where the attractor networks reside [19].

Dual oscillations have been recorded in hippocampus in which a low frequency theta oscillation is subdivided into about seven subcycles of high frequency gamma oscillation [20]. The theta rhythm in the hippocampus refers to the regular oscillations of the local field potential at frequencies of 4-12 Hz which has been observed in rodents [21]. In humans, the theta rhythm typically refers to oscillations in the frequencies of 4-7 Hz [22], while gamma rhythm typically refers to oscillations in the frequencies of 25-100 Hz [23]. It is thought that encoding and retrieval of information happen on different phases of a theta cycle [24]. It is also proposed that the theta rhythm could work in combination with the gamma rhythm, to actively maintain auto-associative memories [25], [26]. Theta rhythm may also have a role to play in the formation of a cognitive map in the hippocampus [27], [28].

Our work aims at investigating the storage of associative memory in hippocampus through the use of bio-realistic spiking neural networks with a focus on computational efficiency. In this paper, we propose a spike response model (SRM) based computational model of the hippocampus CA3 for the storage of associative memory. The computational model is inspired by the works of Jensen et al. [26]. Simulation results demonstrate auto-associative memory storage is achievable in single presentation of memory items when synapses are modified by fast NMDA channel, and hetero-associative memory storage by slow NMDA channel. The SRM-based model is also shown to be computationally more efficient than integrate and fire (I&F) model.

The paper is organized as follows. Section II presents the SRM based computational model of the hippocampus CA3 region. The network consists of recurrently connected spiking neurons. The continual activation of these principal neurons alters the synaptic efficacy of synapses interconnecting these neurons. Section III discusses the synaptic learning mechanism employed that alters these synapses. Section IV presents simulation results of this network in encoding associative memories. Computational complexity of the network using SRM neurons is also compared to network using integrated and fire neurons. Section V summarizes this paper.

II. CA3 MODEL

The proposed computational model is a simplified network of the subcortical area and hippocampus that incorporates two major network components; the synaptic input from EC and DG to CA3, and CA3 itself. The network architecture and dynamics is inspired by the works of Jensen et al. [26]. An overview of the hippocampal CA3 architecture used in this paper is shown in Figure 1(b). The EC and DG are modeled as the input layer while the hippocampal CA3 region is modeled as a recurrent network. The direct perforant path input from superficial layer of EC to CA3 is quantitatively appropriate to provide cue for recall in CA3 [29], [4]. The granule cells in the DG project to the CA3 cells via the mossy fibers, which have been hypothesized to provide sparse pattern separation tasks via competitive learning [4]. The CA3 system operates as an association network and provides for the completion of stored memories during recall from a partial cue via EC [29]. All pyramidal cells in the CA3 also accept an oscillatory input that is used to model the theta rhythm. Feedback inhibitions from different interneurons are applied to the pyramidal cells and regulate interneuronal inhibition as a whole.

A. Spike Response Neurons

This paper presents the CA3 model using neurons defined by the Spike Response Model (SRM) [30]. A spike is firing at time $t_i^{(f)}$ when the membrane potential $u_i$ exceeds a threshold $V_{thres}$. The state $u_i(t)$ of neuron $i$ at time $t$ is given by (1):

$$
\begin{align*}
\dot{u}_i(t) & = \sum_{i' \in F_i} \eta_i \left( t - t_i^{(f)} \right) \\
& + \sum_{j \in \Gamma_i} w_{ij} \epsilon_{ij} \left( t - t_j^{(f)} \right) + h^{ext}(t). \tag{1}
\end{align*}
$$

The kernel $\eta_i(s)$, known as the refractory function, vanishes for $s \leq 0$ and decays to zero for $s \to \infty$. The refractory kernel defines a refractory period immediately following a spike during which the neuron will be incapable of firing another spike. After a spike has occurred at $t_i^{(f)}$, the state variable $u_i$ will be reset by adding a negative contribution $\eta_i(t - t_i^{(f)})$ to $u_i$. The kernel $\epsilon_{ij}(s)$ models the response of neuron $i$ to presynaptic spikes from neurons $j \in \Gamma_i$ and vanishes for $s \leq 0$. In addition to spike input from other neurons, a neuron may receive external input $h^{ext}$, for example from non-spiking sensory neuron. $w_{ij}$ is the synaptic strength of the connection from neuron $j$ to neuron $i$.

$F_i$ denotes the set of all firing times of neuron $i$:

$$
F_i = \left\{ t_i^{(f)} ; 1 \leq f \leq n \right\} = \left\{ t \mid u_i(t) = V_{thres} \land u_i'(t) > 0 \right\}, \tag{2}
$$

where $n$ is the length of the simulation, and $\Gamma_i$ denotes the set of presynaptic neurons which the neuron receives input from, $\Gamma_i = \left\{ j \mid j \text{ presynaptic to } i \right\}$.

The kernels $\eta_i(s)$ and $\epsilon_{ij}(s)$ fully define neuron $i$ under the SRM neuron model described in (2) to (1). The response kernels can be adapted to give rise to different neuronal characteristics. The kernels can be configured to adapt SRM to function like the I&F model. With appropriate selection of the response kernels, the SRM neuron can even approximate the Hodgkin-Huxley conductance-based neuron model [30]. Hence, the SRM offers flexibility in defining neurons with different characteristics.
B. SRM Based Pyramidal Cells and Interneurons

The SRM neuron is preferred to the integrate-and-fire (I&F) neuron due to its flexibility in defining the neuron response and the synaptic response. While the characteristics of an I&F neuron is defined by several parameters, the characteristics of a SRM neuron is defined by a continuous kernel function. The kernel function may be designed to model neurons with different characteristics like those found in a biological nervous system, such as intrinsic neuronal excitability.

Using SRM model, the dynamic of the pyramidal cells and internuron in Fig. 1(b) can be easily configured. The kernel functions used by the pyramidal cells are illustrated in Fig. 2. Figure 2(a) illustrates the refractory kernel for the pyramidal cells. Figure 2(b) illustrates the EPSP kernel function that describes the recurrent collaterals. Figure 2(c) illustrates the feedback inhibition from one internuron. Other model details are referred to our previous work [31].

III. SYNAPTIC MODIFICATION

Longer term memory storage is achieved by synaptic modifications that follow the Hebb-rule; simultaneous presynaptic and postsynaptic activity enhances synaptic efficiencies. The following equations ((3)-(5)) are defined for synaptic modifications [26]. The synaptic strength from pyramidal neuron $i$ to neuron $j$ is determined by (3).

$$\frac{\partial w_{ij}}{\partial t} = \frac{i_{\text{post}}(t-t_{ij}^{(f)}),b_{\text{glu}}(t-t_{ij}^{(f)}-t_{\text{delay}})}{\tau_{pp}}(1-w_{ij}) + \left(\frac{i_{\text{post}}(t-t_{ij}^{(f)})}{\tau_{npp}} + \frac{b_{\text{glu}}(t-t_{ij}^{(f)}-t_{\text{delay}})}{\tau_{npp}}\right)(0-w_{ij}) \\
(3)$$

where $\tau_{\text{post}} = 2.0$ ms, $\tau_{pp} = 50$ ms, $\tau_{npp} = \tau_{npp} = 250$ ms, and $t_{\text{delay}}$ is the time taken for an action potential to travel from the soma to the synapses of the recurrent collaterals, and $i_{\text{post}}(.)$ and $b_{\text{glu}}(.)$ are defined in (4) and (5) respectively.

Postsynaptic depolarization is assumed to be attributed to back-propagating action potentials or other dendritic depolarizing events that occur with a small delay relative to the spike initiation in the somatic region [32]. This postsynaptic depolarization dynamic is modeled by (4) [26].

$$i_{\text{post}}(s) = \frac{s}{\tau_{\text{post}}} \exp \left(1 - \frac{s}{\tau_{\text{post}}} \right) . \\
(4)$$

NMDA receptors are involved in potentiation and depression of synaptic efficacy by acting as a coincidence detector of the presynaptic and postsynaptic firing [33]. The kinetics of NMDA channels is modeled by the time course of the glutamate bound to NMDA receptors in (5).

$$b_{\text{glu}}(s) = \exp \left( - \frac{s}{\tau_{\text{NMDA},f}} \right) \left(1 - \exp \left( - \frac{s}{\tau_{\text{NMDA},r}} \right) \right) . \\
(5)$$

The first term in (3) simulates Hebbian LTP (long-term potentiation). Concurrent occurrence of postsynaptic depolarization $i_{\text{post}}$ and glutamate bound to NMDA receptors $b_{\text{glu}}$ will cause the synaptic weight to approach one with characteristic time $\tau_{pp}$. Partial synchrony of these events will cause the weight change to be graded with respect to the temporal separation of the events. Fully asynchronous events will decrease the synaptic weight by the second term in (3). This second term simulates LTD (long-term depression). Presynaptic event occurring without postsynaptic event will cause the synaptic weight to approach zero with characteristic time $\tau_{npp}$. Postsynaptic event occurring without presynaptic

![Fig. 2. Kernel functions. (a) The refractory function of each pyramidal cell in which AHP proceeds before ADP after each spike of pyramidal cell. (b) The response of each pyramidal cell to each spike from other presynaptic pyramidal cells. (c) The response of pyramidal cell to each spike from the inhibitory interneurons.](image-url)
Fig. 3. Synaptic weight learning window. Synaptic weight is increased when postsynaptic depolarization and glutamate bound to NMDA receptors occur concurrently. Partial synchrony of these events leads to synaptic weight loss that is graded with respect to the temporal separation of the events.

The event will decrease the weight to zero with characteristic time $\tau_{npp}$. Using the kinetics of the NMDA receptors \[34\], $\tau_{NMDA,f} = 7.0$ ms, and $\tau_{NMDA,r} = 1.0$ ms. The learning window is illustrated in Figure 3.

IV. EXPERIMENTAL RESULTS AND DISCUSSIONS

The proposed CA3 model is implemented in the MATLAB environment. Short term memory is first demonstrated by introducing seven and nine distinct memory items in sequence to the CA3 model respectively. The dynamics of the NMDA channels are varied to explore their effects on the rate of learning (i.e. ease with which memories are formed in longer term memory). Next, the network using SRM model is shown to be more computationally efficient than I&F neuron model.

A. Associative Memory Storage and Recall

We firstly conduct the experiments to elucidate the mechanism of associative memory storage and recall in the proposed model. Fig. 4 shows the repetitive firings of neurons in the network. A memory item is represented by the coincident firing of a subset of neurons within a particular gamma cycle. In Fig. 4, external input $V_{in}$ (simulation of spikes from EC and DG input layer) representing seven different memories are introduced into the network. Each of the input patterns is encoded by five pyramidal neurons ($M = 5$).

The first memory is inserted into the memory buffer at 160 ms by an external input that synchronously fires five of the pyramidal neurons. This firing triggers a short after-hyperpolarization potential (AHP) and then a slowly rising after-depolarization potential (ADP) in the neurons. This is shown by the corresponding solid red line in the $V_{refr}$ of Fig. 4A. The ADP subsequently causes the neurons to fire on next theta cycle. The firing time of each neuron is represented by a line in the membrane potential of Fig. 4B. The membrane potentials of the first group of neurons are represented by the solid red line in the membrane potential of Fig. 4C-D.

When a pyramidal neuron fires, the ADP is reset, making it possible for the same processes to occur on the next theta cycle. The second memory is inserted at 500 ms which causes the synchronous firing of another group of five neurons (represented by green line). This memory is repeated in the second gamma cycle on the subsequent theta cycle. The ADP causes persistent firing and controls the timing of the firing of each group of neurons. It can be seen that the ADP ramps for the memories are slightly offset in time. This offset causes the neurons to encode the first memory to threshold before neurons that encode the second memory and so forth for the rest of the memory items. The feedback inhibition $V_{IPSP}$ (not shown) follows each action potential from the pyramidal cells. This inhibition serves to restrict the firing of each group of neurons to discrete phases of the theta oscillation (gamma subcycles). Each memory item is repeated in the order of introduction to the network as shown in Fig. 4B.

To illustrate that the short term memory (STM) network encodes only seven patterns in each theta cycle, two more patterns are inserted. When the eighth memory is introduced to the network at 2500 ms, the last memory item of each theta
memory items 2, 3, 4, 5, 8, and 9. Neurons encoding memory item 6 are auto-associated with one another after these neurons are dropped with the introduction of the memory item 8. The neurons encoding memory item 6 are auto-associated with one another after these neurons are dropped with the introduction of the memory item 9. Neurons of memory item 6 and memory item 7 are also weakly hetero-associated. The memory items 9, 8, 1, 2, 3, 4, and 5 are sequentially repeated in the short term memory buffer after 3000 ms. The gradual build-up of hetero-associative memories is due to the deactivation kinetics of NMDA channels employed by the physiological learning rule. Fig. 3 shows that the NMDA channels still weakly span over to other gamma cycles. This results in neurons activated in adjacent gamma cycles to be more hetero-associated than neurons that are activated in more distant gamma cycles.

Evidences show that NMDA receptors are involved in the long term plastic changes in synaptic transmission [35], [36]. Molecular and functional evidence further indicates that different NMDA receptors have significant different properties and kinetics [34]. In hippocampus, pyramidal cells express NR2A and NR2B mRNAs, and that the expression of NR2A increases throughout postnatal development [34]. NR2A-mediated receptor channels have considerably shorter offset deactivation time (of the order of tens of milliseconds) than other channel subtypes [34]. Evidences also show that the adult pyramidal cells (> 5 weeks old) have excitatory postsynaptic current (EPSC) amplitude 4-fold larger than in very young (up to 2 weeks old) neurons, and both the EPSC rise time (up to 70%) and fast (up to 70%) and slow (up to 90%) decay time constants decreased with age [37]. These age-related developmental changes in NMDA receptor subunit composition can alter the kinetics of NMDA channels.

Fig. 6(b) illustrates the resulting synaptic matrix when the deactivation kinetics of NMDA channels are reduced accordingly. Here, it is shown that different memory items are less hetero-associated. This suggests that older animals are better in forming auto-associative memory than younger animals. Fig. 6(c) illustrates the resulting synaptic matrix when the EPSC amplitude and deactivation kinetics of NMDA channels are respectively increased and reduced accordingly. Here, it is shown that formation of auto-associative memory by hippocampal CA3 can be achieved even when the memory items are presented once to the network. Fig. 6(c) illustrates the resulting synaptic matrix when the EPSC amplitude and deactivation kinetics of NMDA channels are respectively increased and reduced accordingly.

B. Computational Efficiency

The integrate-and-fire (I&F) neuron model is one of the most widely used models for the simulation of spiking neural
systems. Burkitt has provided a thorough review of I&F neuron models and its variations for homogeneous [38] and inhomogeneous synaptic inputs [39]. A key reason for its popularity is its efficiency in terms of implementation cost. For comparison, the leaky I&F neuron takes 5 FLOPS (floating point operations) to compute compared to 1200 FLOPS for the Hodgkin-Huxley model [40]. This difference becomes a consideration when simulating a network of neurons.

The SRM neuron has the potential to be even more computationally efficient compared to the I&F neuron, by means of a lookup table (LUT). A lookup table is a data structure that saves processing time by retrieving a value from memory rather than actually performing the floating point operations as is usually done in spiking neuron simulations. The tables are usually pre-calculated and stored in memory during the initialization phase of the algorithm.

The use of lookup tables in spiking neural networks simulations had been explored by Ros et al. using ED-LUT [41]. However, ED-LUT focused on improving the efficiency of computationally expensive compartmental conductance-based neuron models. Instead, we demonstrate that SRM with lookup table can also improve the efficiency of computationally cheap I&F neuron models. To illustrate this, the I&F neuron model is defined in (6).

\[
\tau_m \frac{du}{dt} = -u(t) + RI(t)
\]

where \(\tau_m\) is the membrane time constant, \(u(t)\) is the membrane potential, \(R\) is the membrane resistance, and \(I(t)\) is the input current.

In the case of a time dependent stimulus \(I(t)\), the membrane potential \(u(t)\) is given by (7).

\[
u(t) = u_i \exp\left(-\frac{t - \tau_m}{\tau_m}\right) + \frac{1}{C} \int_0^{t-i} \exp\left(-\frac{s}{\tau_m}\right) I(t-s) \, ds
\]

where \(u_i\) is the initial condition of the membrane potential, and \(i\) is the time that the last spike occurred.

Comparing (1) and (7), it can be observed that the membrane potential \(u(t)\) in the SRM neuron is a closed form expression while the I&F neuron is not because the latter expression involved an integral term. The advantage of having a closed form expression is that it may be implemented in the form of a lookup table.

A comparative study was conducted to examine the difference in computational efficiency between the SRM neuron and I&F neuron. The effects of varying network size, for \(M = 1\) to

Fig. 6. Synaptic weights between pyramidal cells represented in a grey scaled colour weight matrix. Numbers in both axes identify the neuron in the network. Colour of the square at location \(i, j\) denotes the synaptic weight of the connection from neuron \(j\) (y-axis) to neuron \(i\) (x-axis). These figures show the effect on synaptic weights by different deactivation kinetics of NMDA channels on synaptic modification. (a) Memory items are more hetero-associated with longer deactivation kinetics of NMDA channels. (b) Memory items are less hetero-associated with shorter deactivation kinetics of NMDA channels. (c) Faster acquisition of auto-associative memory when EPSC amplitude is four times larger.
**TABLE I**

Comparative Results of Mean Simulation Times (Standard Deviation in Parentheses) in Seconds Between SRM Neuron and I&F Neuron over 20 Trials.

<table>
<thead>
<tr>
<th>M</th>
<th>SRM</th>
<th>I&amp;F</th>
<th>Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32.337 (0.212)</td>
<td>61.320 (0.294)</td>
<td>47.26%</td>
</tr>
<tr>
<td>3</td>
<td>259.083 (1.962)</td>
<td>488.203 (4.126)</td>
<td>46.93%</td>
</tr>
<tr>
<td>5</td>
<td>688.748 (12.218)</td>
<td>1314.946 (11.947)</td>
<td>47.62%</td>
</tr>
<tr>
<td>7</td>
<td>1307.845 (12.386)</td>
<td>2545.041 (16.937)</td>
<td>48.61%</td>
</tr>
<tr>
<td>9</td>
<td>2179.592 (34.509)</td>
<td>4225.119 (71.486)</td>
<td>48.41%</td>
</tr>
</tbody>
</table>

Fig. 7. Boxplot of log (simulation times in seconds) for varying network size, $M = 1$ to $M = 9$, between the SRM neuron and I&F neuron over 20 trials. On each box, the central mark is the median, the edges of the box are the 25th and 75th percentiles, the whiskers extend to the most extreme data points not considered outliers, and outliers are plotted individually. However, due to the wide range of simulation time values, the edges of the box and the extreme whiskers are compressed and not clearly visible. Nonetheless, this figure illustrates that the SRM neuron model is computationally more efficient than the I&F neuron. The lines across the boxplots connect the mean simulation times.

$M = 9$, were also examined. The simulations were conducted using MATLAB on a Intel i7 2.8GHz machine over 20 trials, each for 6 seconds in simulation time with a time step of 0.1 ms. The results are summarized in Fig. 7 and Table I.

It is readily observed from Fig. 7 and Table I that the SRM neuron is approximately 2 times more efficient than the I&F neuron. This demonstrates that the SRM neuron implemented by a lookup table is more computationally efficient than the I&F neuron. In addition, it is observed that the improvement over the I&F neuron remains consistent with increasing network size (see Fig. 8). Hence, this makes the SRM neuron a suitable choice for implementing large neural networks in comparison to I&F neuron model.

**V. CONCLUSION**

The simulation results showed that the proposed CA3 model can capture multiple memory items in real time and incorporate them into memory. The dynamics of ADP in pyramidal cells led to the sustained firing of memory items. This mechanism produced a repetition of each memory item once every theta cycle. Consequently, the repeated firing of memory items led to the gradual incorporation of each item in memory via modification of the synaptic strengths between groups of neurons. Simulations showed that auto-associative memory is acquired in single presentation of memory items through the use of fast NMDA channels. The simulation results also showed age-related development changes in NMDA receptors can affect the formation of auto-associative memory. In addition, the result showed network using SRM neurons can be simulated in a shorter time than network using I&F neurons.

**REFERENCES**


