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Research Report

Consequences of parameter differences in a model of short-term persistent spiking buffers provided by pyramidal cells in entorhinal cortex

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ABSTRACT

In previous simulations of hippocampus-dependent and prefrontal cortex-dependent tasks, we demonstrated the use of one-shot short-term buffering with time compression that may be achieved through persistent spiking activity during theta rhythm. A biophysically plausible implementation of such a first-in first-out buffer of short sequences of spike patterns includes noise and differences between the parameter values of individual model pyramidal cells. We show that a specific set of parameters determines model buffer capacity and buffer function, and individual differences can have consequences similar to those of noise. The set of parameters includes the frequency of network theta rhythm and the strength of recurrent inhibition (affecting capacity), as well as the time constants of the characteristic after-depolarizing response and the phase of afferent input during theta rhythm (affecting buffer function). Given a sufficient number of pyramidal cells in layer II of entorhinal cortex, and in each self-selected category of pyramidal cells with similar model parameters, buffer function within a category is reliable with category-specific properties. Properties include buffering of spikes in the order of inputs or in the reversed order. Multiple property sets may enable parallel buffers with different capacities, which may underlie differences of place field sizes and may interact with grid cell firing in a separate population of layer II stellate cells in the entorhinal cortex.

1. Introduction

Models of hippocampal and prefrontal cortex function used in simulations of many behavioral tasks need a short-term buffer that does not depend on synaptic modification. Simulated episodic encoding of spike patterns in recurrent networks often relies on spike-timing-dependent potentiation (Bi and Poo, 1998) with Hebbian learning characteristics (Hebb, 1949). Such a sequence learning protocol requires repeated and ordered presentation of successive stimuli with regular small time intervals (less than 40 ms). Short-term buffering of a sequence of input and multiple subsequent cycles of retrieved spiking activity at appropriate time intervals can provide a buffer for this synaptic encoding.

Synaptic modification is not a plausible mechanism through which to buffer a single presentation of the input, but an

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intrinsic mechanism that elicits persistent spiking in response to input is feasible. An after-depolarizing (ADP) membrane current in pyramidal cells of layer II of entorhinal cortex enables intrinsic persistent spiking (Klink and Alonso, 1997a,b; Egorov et al., 2002). The after-depolarization and persistent spiking appear to be most prominent in layer II pyramidal cells, and do not appear in layer II stellate cells (Klink and Alonso, 1997b). In contrast, layer II stellate cells exhibit subthreshold membrane potential oscillations (Klink and Alonso, 1997b) that differ in frequency along the dorsal–ventral axis and may underlie firing in a grid like pattern (Giocomo et al., 2007). Models of short-term memory based on interactions of after-depolarization and theta rhythm have been studied in simulations by Lisman and Idiart (1995) and Jensen et al. (1996), as well as in our own work (Koene et al., 2003; Koene and Hasselmo, 2005, 2007).

Our integrate-and-fire model of short-term buffering generates an asymmetric distribution of spiking activity within each cycle of the theta rhythm (Koene et al., 2003) that enables phase-locked integration of buffer intervals of acquisition and retrieval with intervals of encoding and retrieval in connected networks, as well as a plausible mechanism for the first-in first-out (FIFO) ordered replacement of items that are maintained in the buffer (Koene and Hasselmo, 2007). The model was used to simulate performance in hippocampus-dependent spatial navigation tasks (Hasselmo et al., 2002; Koene et al., 2003) and in tasks that depend on temporal context-dependent episodic memory (Koene and Hasselmo, 2006b). A limited buffer capacity and the first-in first-out replacement of items are a good fit to the recency portion of graphs of serial position data (Atkinson and Shiffrin, 1968; Kahana, 1996), and psychophysical evidence of ordered item displacement has been gathered in tests ranging from precategorical acoustic storage (Crowder and Morton, 1969) to the observed interaction between memory load and item position for semantic information (Haarmann and Usher, 2001).

Entorhinal cortex layer II (ECII) is the major source of input to the hippocampal system. Pyramidal neurons in ECII exhibit after-depolarization (ADP) following spikes (Klink and Alonso, 1997b), and membrane potentials in both the entorhinal cortex and hippocampus are modulated at theta rhythm, due to input from the medial septum. Combined rhythmic modulation and ADP may be used in a mechanism that sustains regular persistent spiking, a sequence buffer first proposed by Lisman and Idiart (1995). In prior work, we demonstrated an integrate-and-fire model of a short-term spike buffer in ECII that is based on these properties (Koene and Hasselmo, 2007). If short sequences of spiking patterns are sustained in ECII then these time-compressed and repeated representations of a behavioral episode can elicit significant synaptic potentiation in hippocampal recurrent networks (Koene et al., 2003).

A constrained set of biophysical requirements follows from the general principles of the working buffer:

- ADP rise and fall time constants ($\tau_{\text{rise,ADP}}$, $\tau_{\text{fall,ADP}}$) must be (a) sufficiently large so that the ADP manages to return a neuron's membrane potential to threshold on the rising flank of depolarization by theta rhythm, and (b) small enough to allow persistent spiking to be terminated by a limited interval of inhibitory input. Ideally, rise and fall time constants are each similar to the duration of a theta cycle. Experimental results by Klink and Alonso (1997b) and simulation studies by Fransén et al. (2002) suggest time constants that differ significantly from initial versions of our model. We attempt a first analysis of the effect of this difference here.
- Afferent input must appear within specific phase intervals of the theta cycle, which enables ADP to achieve the first repetition of new item spiking either (a) within the same theta cycle for a forward-order buffer, or (b) as the first item reactivation on the depolarizing flank of the next theta cycle for an order reversing buffer. These input intervals must be separated from the theta interval in which sustained buffer activity reappears to avoid interference between buffered spike patterns and novel input.
- A network of interneurons must supply adequate recurrent inhibition to neurons in the buffer in response to buffered item spikes, so that a minimum time interval between the spikes of successive item representations is enforced. The inhibitory mechanism of item separation also supports continued temporal coherence between the spikes of neurons that represent one item without relying on strengthened connections between those neurons.

We hypothesize that natural conditions of short-term buffering in ECII include variations of the values of this set of critical model parameters in individual neurons, as well as additive noise (White et al., 2000). Here we demonstrate first-in-first-out buffer function in the noisy case, at different frequencies of the network theta rhythm or of network-wide recurrent inhibition, and in cases of individual differences between parameter values for (i) the characteristic amplitude and time-constant of after-depolarization (ADP) and (ii) the neuron-specific strength of recurrent inhibitory input.

Within the neural circuitry of the buffer, model parameters of the neurons and their connections must fall within a similar range that allows them to function together to hold one item in the persistent spiking buffer. This is a general principle of self-selection during one-shot acquisition of a novel item input with a representative pattern of spiking buffer neurons. Where there are differences between the parameters of pyramidal neurons in ECII, we show that those may affect reliable buffer function and may affect the capacity of the buffer. Differences between individual neurons have two main consequences: (1) Neurons with similar model parameter values form subsets or categories. Within a subset, neurons can function as successful components of a persistent firing buffer with characteristics specific to the subset of neurons. (2) A persistent spiking neuron can drop out of the representation of a specific buffered item, thereby reducing the ensemble size of the neural representation. This second consequence is also a common outcome of significant noise. Parameter and noise related consequences are mitigated when large ensemble sizes are used to represent each buffered item. We speculate that the existence of different subsets may lead to effective buffering of sequence input in multiple buffers with different characteristics, such as buffering with repetition in the same order as input is received or with repetition in the reversed order.

2. The model

In a previous work, we demonstrated the usefulness of our working buffer model in simulations of hippocampus guided