Simulation of single unit recording data in a neural simulation guiding movement of a virtual rat in a virtual environment

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Abstract

The Catacomb software package was used to develop a hippocampal simulation with interacting populations of spiking neurons, which guides the movements of a virtual rat in a virtual environment. This helps define specific functional problems and find specific solutions constrained by the physiological data. The network spiking activity can be observed in the same format as unit data obtained when a rat performs a spatial navigation task, including representation of the location of the rat when a cell fires (to create place field maps), and the timing of spikes relative to the local field potential (to analyze theta phase precession).

Many neural simulations do not explicitly address the movements of an agent in an environment, making it difficult to relate the activity of the simulation to electrophysiological data from awake behaving animals. The hippocampal simulation described here uses interacting populations of spiking neurons, which guide the movements of a virtual rat in a virtual environment. This proves useful in defining specific functional problems and in finding specific solutions constrained by the physiologically realistic structure of the model. Simulations demonstrate specific dynamical requirements necessary to obtain these functions in a biologically realistic representation of the hippocampal formation, allowing explicit simulation of previous theoretical work from this laboratory. 1.) Encoding of new information without interference from previously encoded information requires transitions between encoding and retrieval states, 2.) Selection of the shortest pathway to the closest goal location or the best match to a retrieval cue requires mechanisms for timing and synchronization of retrieval activity (Hasselmo et al., 2002b), and 3.) Encoding of a pathway or an episodic memory requires buffering of information to allow strengthening of synapses between sequentially activated place cells (Fransen et al., 2002). The activity of the network can be

observed in exactly the same format as the unit data obtained when a rat performs a spatial navigation task, including representation of the location of the rat when a cell fires (to create place field maps), and the timing of spikes relative to theta rhythm in the local field potential (to analyze theta phase precession). We focused on modeling the behavior of a rat in a T-maze reversal task (M'Harzi et al., 1987). The Catacomb system describes the environment of this T-maze in terms of solid walls and reward locations.

A virtual food-reward is placed at the end of one arm of the T-maze. The virtual rat encodes the environment and the location of the food during initial exploration. When the rat is subsequently placed into the stem of the virtual T-maze, the simulated network output can guide it up the stem, make the correct turning choice and go to the food reward (Hasselmo et al.,in press, 2002b). Sensory input for proximity to objects activates a unit representing the ventral tegmental area (VTA) response to food reward. Input from VTA enters prefrontal cortex (PFC) units along with subthreshold place input that represents the location of the virtual rat and causes spiking and activation of intrinsic cellular mechanisms which maintain working memory for reward location. Region CA3 and entorhinal cortex (EC) layer III receive buffered sequences of place input representations from EC layer II. Their output converges in region CA1. The spiking output of CA1 can guide the movements of the virtual rat.

The advantage of using a spiking simulation to guide a virtual rat is that simulation units can be analyzed in exactly the same manner as neurons recorded in the hippocampus in awake behaving rats. The place fields of units can be evaluated by plotting the location of the virtual rat at the time of each spike. The broader spread of activity in EC of the simulation causes larger place fields in EC versus CA1, consistent with experimental data (Barnes et al., 1990; Quirk et al., 1992; Frank et al., 2000). The firing of units can be evaluated relative to the phase of theta rhythm. Neurons in the simulation have properties similar to theta phase precession (Skaggs et al., 1996), with predictive firing appearing at later phases of theta when the rat is first entering the place field of a region CA1 place cell. This corresponds to activity driven by the retrieval activity in region CA3. Then, as the virtual rat moves further into the place field, this predictive firing does not occur, and firing appears at earlier phases of theta dependent upon direct input from EC layer III, bearing information about the current location. These separate phases of sensory input versus predictive retrieval could underlie the biphasic nature of theta phase precession, in which a strong correlation with position only appears in late phases of theta (Mehta et al., 2000, 2001).

This talk will focus on how these processes may occur during theta rhythm oscillations in the rat hippocampal formation, which have been observed in rats during active exploration and in humans during performance of a virtual maze task. These theta rhythm oscillations depend upon cholinergic and GABAergic input from the medial septum. Modeling and analysis demonstrates that the timing of excitatory and inhibitory currents during the theta rhythm (Wyble et al., 2000) could allow separate phases of encoding and retrieval (Hasselmo, Bodelon and Wyble, 2001). This would enhance the encoding of new sequences for navigation (Wallenstein and Hasselmo,

1997), as well as the retrieval of previously encoded sequences (Sohal and Hasselmo, 1998). During encoding phase, synaptic currents arising from EC are strong (Brankack et al., 1993; Bragin et al., 1995). Transmission from CA3 is weak, preventing retrieval, but LTP at these synapses is very strong (Holscher et al., 1997; Wyble et al., 2001), allowing encoding of the associations between entorhinal inputs. During retrieval phase, synaptic currents arising from EC are weak, but synaptic currents arising from CA3 are strong (Rudell et al., 1980; Brankack et al., 1993; Bragin et al., 1995; Wyble et al., 2000), allowing effective retrieval of previously encoded sequences. However, during this phase these synapses do not encode the retrieval because they do not show LTP (Holscher et al., 1997; Wyble et al., 2001), instead they show LTD or depotentiation.

The selection of the shortest path to the goal can be guided by the coincidence of backward spread of activity from goal representations in EC with forward spread of activity from current location in hippocampus (Hasselmo, Wyble and Cannon, 2001). Prior simulations using continuous firing rate neurons rather than spiking neurons have successfully demonstrated this mechanism (Gorchetchnikov and Hasselmo, 2001). Simulations of EC illustrate how it may buffer information about slow transitions through the environment, so that sequences representing specific pathways can be encoded (Fransen et al., 1999; Hasselmo et al., 2000). In the absence of theta oscillations, cholinergic modulation decreases and synaptic potentials increase in magnitude (Hasselmo, 1999). These changes in dynamics could contribute to generation of sharp wave events and the consolidation of information previously encoded in the hippocampus.

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