Incorporating anatomically realistic cellular-level connectivity in neural network models of the rat hippocampus

Giorgio A. Ascoli*, John C. Atkeson

Krasnow Institute for Advanced Study and Psychology Department, George Mason University, MS2A1,
4400 University Dr., Fairfax, VA 22030, USA

Abstract

The specific connectivity patterns among neuronal classes can play an important role in the regulation of firing dynamics in many brain regions. Yet most neural network models are built based on vastly simplified connectivity schemes that do not accurately reflect the biological complexity. Taking the rat hippocampus as an example, we show here that enough quantitative information is available in the neuroanatomical literature to construct neural networks derived from accurate models of cellular connectivity. Computational simulations based on this approach lend themselves to a direct investigation of the potential relationship between cellular connectivity and network activity. We define a set of fundamental parameters to characterize cellular connectivity, and are collecting the related values for the rat hippocampus from published reports. Preliminary simulations based on these data uncovered a novel putative role for feedforward inhibitory neurons. In particular, "mopp" cells in the dentate gyrus are suitable to help maintain the firing rate of granule cells within physiological levels in response to a plausibly noisy input from the entorhinal cortex. The stabilizing effect of feedforward inhibition is further shown to depend on the particular ratio between the relative threshold values of the principal cells and the interneurons. We are freely distributing the connectivity data on which this study is based through a publicly accessible web archive (http://www.krasnow.gmu.edu/L-Neuron).
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1. Introduction

Classical neural network models are usually based on simple connectivity patterns (e.g., all-to-all or random sparse; layered or symmetric) and a small number of cell classes. Yet one of the most striking elements of complexity in the brain is the connectivity among neurons. In the rat hippocampus, for example, each principal cell can establish synapses with over 10,000 other neurons over a dozen of distinct cell classes. While the presence of individual connections between any two neurons is likely to be substantially stochastic, each different (sub)region of the brain is overall characterized by its own peculiar connectivity patterns. What is the role of specific connectivities in subserving network activity, coding, and function? A direct approach to address this question consists of implementing (quasi) real-scale neural network models based on plausible system-level anatomy and cellular-level connectivity.

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* Corresponding author.
E-mail address: ascoli@gmu.edu (G.A. Ascoli).

This research strategy implies the adoption of simple computational implementations of single-cell activity. A variety of efficient dynamical systems are available, including McCulloch–Pitts units augmented with electrotonic properties (Ascoli, 2003) and/or ionic channel models (Smith et al., 2000), integrate-and-fire neurons (Abbott, 1999), and low-dimension systems of differential equations (Izhikevich, 2000). Each of these models disregards important elements of single-cell behavior. However, depending on the scientific question pursued, these approximations may be preferred to drastically simplifying connectivity or scaling down the network (in the extreme, to single neurons), as becomes necessary with the more biophysically detailed models typically adopted in computational neuroscience.

Anatomically realistic neural network models of the hippocampal formation have been attempted for the dentate gyrus (Patton and McNaughton, 1995), Am-

mon's Horn (Bernard and Wheal, 1994), and area CA1 (Senft and Ascoli, 1999). However, only in one case were simulations of network dynamics actually performed (Bernard et al., 1997). The major hurdle to these efforts is the lack of complete anatomical data of connectivity among all neuronal classes, and of detailed physiological data of synaptic activity (e.g., potential amplitude, kinetics, and frequency). Nonetheless, a wealth of data has been recently accumulated on the rat hippocampus, including connectivity patterns for numerous classes of interneurons (Freund and Buzsaki, 1996) and post-synaptic potential parameters for all principal cells (e.g., Urban et al., 2001). Fig. 1 provides a simplified representation of hippocampal connectivity. The main loop goes from the entorhinal cortex (EC) to the dentate gyrus (DG), to CA3, to CA1, to the subicular complex (SC), and back to EC. This loop contains three shortcuts (the perforant pathway (PP) from EC
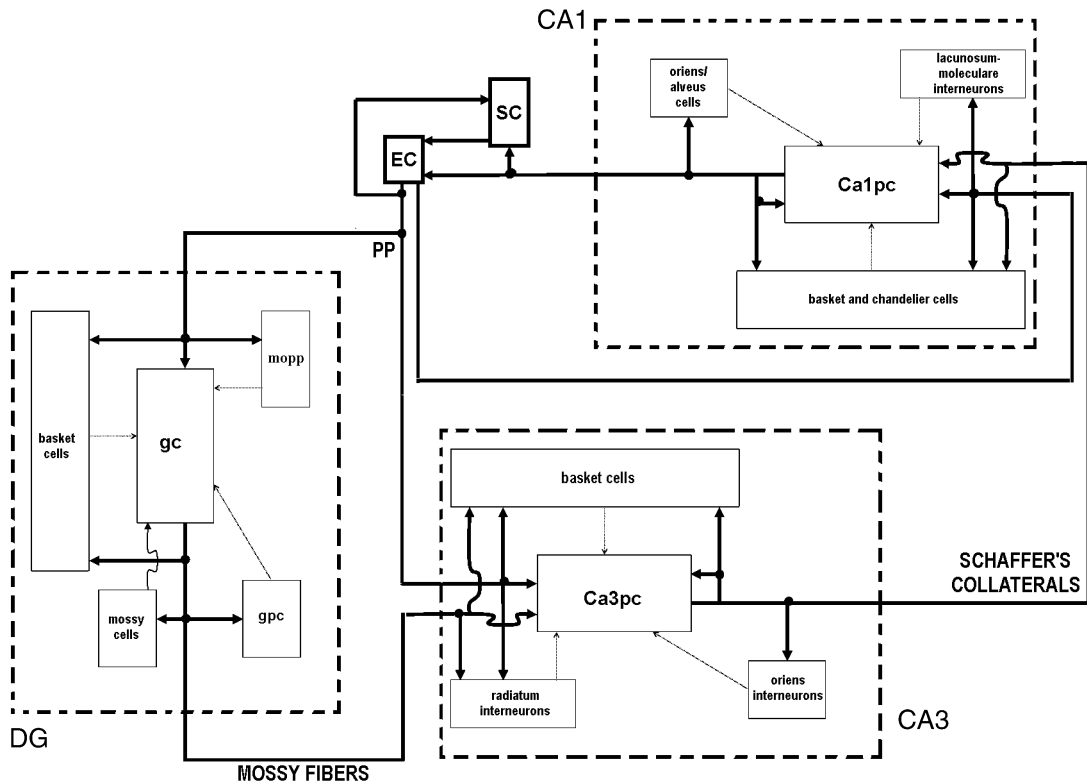

Fig. 1. Connectivity scheme of the hippocampal formation. Each box corresponds to a cellular class with the exception of EC and SC, which represent entire subregions of the network. Excitatory and inhibitory connections are represented as full and empty arrows, respectively. All abbreviations are defined in the text. Missing from this scheme is the putative connection between CA3pc and DG mossy cells.