Control of CA3 Place Fields by the Dentate Gyrus: A Neural Network Model

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Abstract

A very interesting aspect of hippocampal anatomy is the presence of two pathways projecting from the entorhinal cortex (EC) to the CA3 region — one directly via the perforant path (PP), and the other through the dentate gyrus (DG) using the mossy fibers of the granule cells. This implies that the place fields of the CA3 arise from the joint influence of EC and DG. We hypothesize that the DG plays a modulatory role in this scheme, serving to enhance discrimination during the learning of new place codes. Drawing in part on some receny experimental findings, we model a mechanism whereby DG neurons accomplish pattern separation by modulating the balance of dendritic and somatic inhibition in granule cells. Our results are consistent with a variety of observations in the literature, including the following: 1) DG lesions do not abolish CA3 place fields but disrupt spatial memory; 2) Even similar environments produce different place fields in CA3 but not in the EC. We show that DG modulation allows the model hippocampus to control spatial discrimination, and produces realistic place fields.

1 Introduction

Marr (1969) was the first to propose that the dentate gyrus might function as a pattern separator for afferent input from the entorhinal cortex, projecting it to CA3 for storage via the mossy fiber (MF) path. Following the discovery of the direct perforant path (PP) projection from EC to CA3 (Yeckel and Berger, 1990), it was suggested that this might represent a cuing input for pattern retrieval in CA3 (Rolls, 1989). Analysis of this two-path system for the storage of random patterns demonstrated its ability to handle the conflicting requirements of pattern separation (for storage) and pattern recognition (for retrieval) (Treves and Rolls, 1992; O'Reilly and McClelland, 1994). The possible role of stochastic quantal secretion for pattern separation in the DG was studied by Gibson et al. (1991), also under random pattern and connectivity assumptions. The present paper addresses the issue of DG-based pattern separation explicitly in the context of place-field type patterns, and using mechanisms suggested by recent experimental results.

The two-path projection from EC to CA3 implies that CA3 place fields are formed by a conjunction of PP and MF effects. Most of the sensory information comes via the PP input, and there is evidence that this projection alone is sometimes sufficient to maintain place-specific activity in CA3 (McNaughton et al., 1989; Knierim and McNaughton, 1995). However, the MF pathway appears to be essential for adequate spatial performance. One clue to its function comes from the report (Quirk et al., 1992) that EC place fields of the same cell in two similar environments are similar, but those of a CA3 cell are totally different. This clearly suggests context-specific recoding of EC information by the MF pathway.

The primary hypothesis studied in this paper is that the DG enhances discrimination in EC place codes by changing the balance of dendritic and somatic inhibition on the granule cells. This is based on indirect evidence (Moser, 1996) that, during exploratory behavior, there is an increase in dendritic inhibition and a decrease in somatic inhibition in the rat DG. The DG is known to have extensive and complex inhibitory subsystems (Buckmaster and Schwartzkroin, 1994), and is an ideal site for the modulation of EC information en route to CA3, functioning much like a hidden layer in a feed-forward neural network.

2 Methods

We hypothesize that the dentate gyrus operates in two modes: 1) During the *quiescent* mode — identified with retrieval—, the response of DG granule cells to stimulation from EC is very low, so that, as a whole, the signal from DG to CA3 is a low amplitude, non-specific noise-like one. Thus, CA3 neurons respond primarily to PP stimuli acting as cues for retrieval without MF influence. 2) The *alert* mode is used for the formation of new place representations (or recall of old ones from intact cues). During this mode, the DG granule cells 1) increase dendritic inhibition; and 2) decrease somatic inhibition. Thus, only those granule cells which get several simultaneously active inputs will fire, but will fire strongly. This will strongly bias *a few CA3 cells at a time*, causing the diffuse PP-based place-fields in CA3 to become localized via a competitive inhibitory mechanism. The assumption is that the DG can be switched between the two regimes based on recognition or other motivational contexts. The existence of a strong subcortical input to the DG and CA3 makes this at least plausible. There is already evidence that cholinergic influences from the septal region modulate synaptic excitability in the cortex to help in memory storage (Hasselmo et al., 1992). Such a mechanism could operate during the alert mode to increase the influence of the DG bias and preclude interference from the mnemonic system (Hasselmo, 1993).

2.1 Entorhinal Cortex (EC)

The model for EC place fields is purely phenomenological, based on the known characteristics of these fields (broad spatial coverage, noisiness, dependence on sensory cues, etc.) Thus, the response of EC cells is modeled with broadly tuned, noisy place fields centered at random coordinates in the environment. Each EC cell, i, is assigned a center, $\bar{c} = (c_i^x, c_i^y)$. The output of cell i at time t is defined by the following stochastic prescription:

$$\begin{aligned} z_i(t) = & \\ & exp(-a_i(x(t) - c_i^x + q_x)^2 - b_i(y(t) - c_i^y + q_y)^2 + \\ & d_i\sqrt{a_i}(x(t) - c_i^x)\sqrt{b_i}(y(t) - c_i^y)) \end{aligned} \tag{1}$$

where $x(t)$ and $y(t)$ are the animal's coordinates at time t, a_i and b_i are parameters which control the size and shape of the elliptical place field, d_i is an orientation parameter with values between 1 and -1, and q_x, q_y are 0-mean uniform random variables with variance σ_q, which essentially controls the accuracy with which an EC cell discerns the animal's location. Usually, σ_q will be small.

2.2 Dentate Gyrus (DG)

The activation to DG granule cell i is given by:

$$y_i(t) = \sum_{j \in EC} w_{ij} f(z_j(t) - \phi\theta_i) \tag{2}$$

where w_{ij} is the synaptic weight from EC cell j to cell i, $z_j(t)$ is the output of j at time t, θ_i is a synaptic threshold representing dendritic inhibition, and ϕ is an indicator variable for the alert mode. The output is then calculated as

$$z_i(t) = f\left(tanh((G_{DG} + \phi g_{DG}) y_i(t))\right) \tag{3}$$

where G_{DG} is a small fixed gain parameter and g_{DG} a much larger gain increment representing the decrease in somatic inhibition during the alert mode. $f()$ is a rectifier function: $f(x) = x$ if $x > 0$ and 0 otherwise.

2.3 CA3

Only the extrinsic afferents to CA3 are included in this model, since it focuses on pattern formation. The activation of CA3 pyramidal cell, i, is modeled as:

$$y_i(t) = \sum_{j \in EC} w_{ij} z_j(t) + \sum_{j \in DG} w_{ij} z_j(t) + \sum_{j \in CA3} w_{ij} z_j(t-1) \tag{4}$$

where w_{ij} are synaptic weights and $z_j(t)$ presynaptic cell outputs. The output is then calculated as

$$z_i(t) = f\left(tanh(G_{CA3}(y_i(t) - \alpha(t)\theta_i))\right) \tag{5}$$

where G_{CA3} is a fixed gain parameter and θ_i is the firing threshold. The $\alpha(t)$ parameter, which models normalizing inhibition, is defined as:

$$\alpha(t) = \frac{1}{N_{CA3}} \sum_{i \in CA3} y_i(t) \tag{6}$$

Simulations were carried out in $L \times L$ square environments. All place fields were systematically mapped out at all L^2 locations. Parameters were set to reasonable values without any explicit optimization.

3 Results

The results demonstrate that modulating the balance of inhibition can significantly enhance place discrimination both within and across similar environments. Figure 1 shows the effect of mode switching on the similarity of place codes in a simulated 40×40 grid environment with random EC fields and a 200/1000/200 network. It plots the similarity between CA3 place codes for 1000 randomly chosen pairs of locations (out of a possible $2,558,400$ pairs). Similarity between two place code vectors is measured by the cosine of the angle between them:

$$s(A, B) = \frac{A.B}{|A||B|} \tag{7}$$

where A and B are place code vectors. This precludes a globally attenuated version of code A as being considered different from A.

In the quiescent mode, with the dentate gyrus effectively out of the loop, similarity values are roughly a linear function of distance between locations. In the alert mode, however, there is a clear thresholding effect, indicating that the environment is divided up into well differentiated local neighborhoods. The overall distribution of similarity also changes from a broad one centered around 0.5 to one skewed strongly towards low similarity — again indicating an increase in spatial discrimination on average.

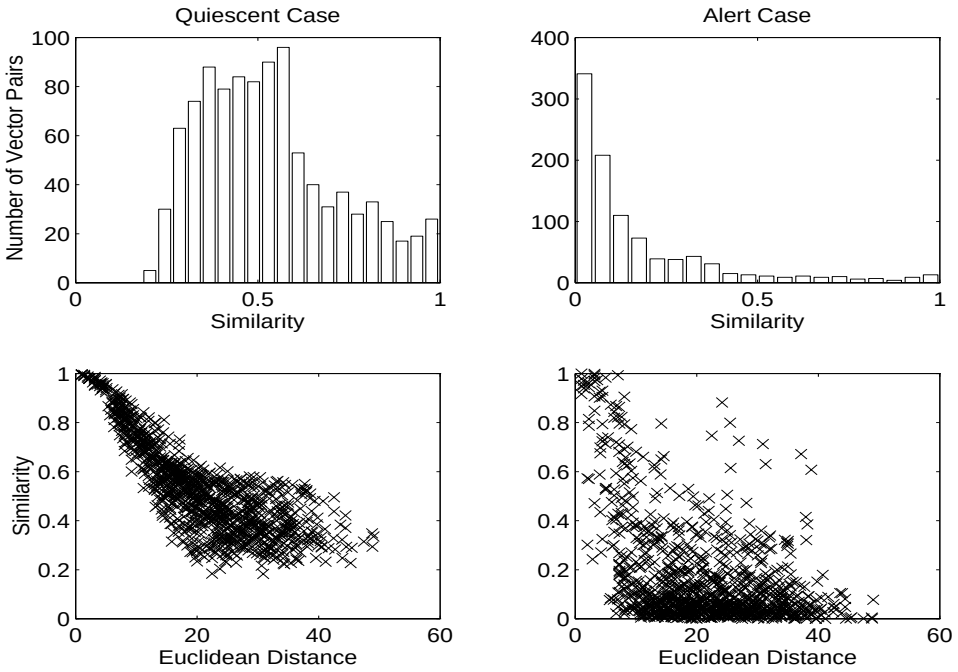

Figure 1: The top two graphs show the distribution of similarity values between 1000 pairs of CA3 place code vectors in the quiescent and alert modes. The lower two graphs plot these similarities as a function of euclidean distance between the locations in each pair. A thresholding effect is clear in the bottom right graph.

Figure 2 shows how the hypothesized mechanism can enhance discrimination of similar environments. Similar environments are produced by first generating a random 40×40 environment and then perturbing its EC place field centers to produce another. The similarity of the two environments is quantified by the variance of the applied perturbation. Similarity values are then calculated for the corresponding locations in the environments, and averaged to give the overall similarity of the CA3 place representation. It can be seen that, in the quiescent mode, discrimination in CA3 is very similar to that in the EC as a function of environment similarity. In the alert mode, however, discrimination between similar environments is enhanced greatly.

4 Summary

This paper has presented a simple neural network model of how changing the degree of dendritic and somatic thresholds in the dentate gyrus can lead to the enhancement of spatial discrimination in the hippocampus. Clearly, however, this simplistic mechanism needs to be augmented in complex ways to account for the experimental data on place code stability and plasticity in response to cue manipulation, etc. In particular, the issues of context-dependent discrimination and path integration need to be addressed. Interesting ideas on these are now beginning to emerge in the literature (Touretzky and Redish, 1996; McNaughton et al., 1996).

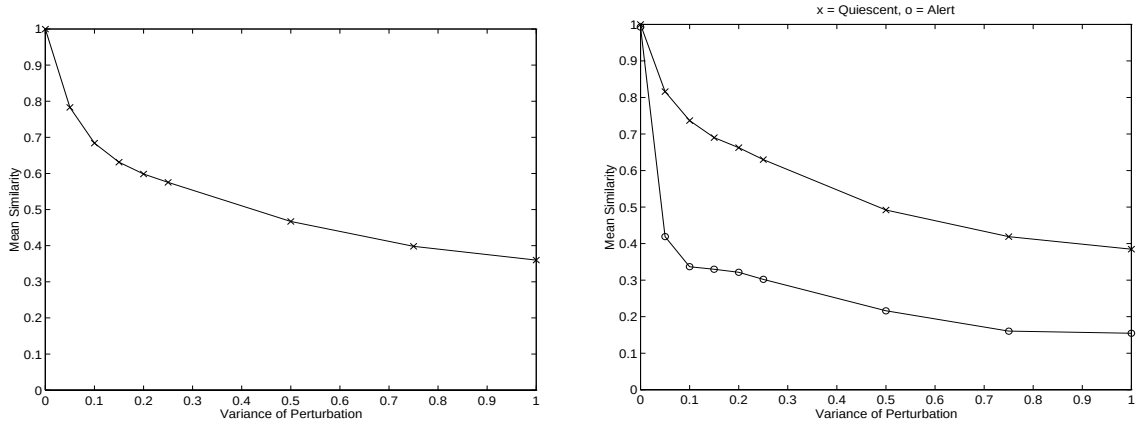

Figure 2: The graph on the left shows average similarity between EC representations of two environments as a function of their (simulated) sensory similarity. The graph on the right shows the corresponding CA3 similarities between environment pairs in the quiescent and alert modes. Note how alertness increases discrimination between very similar environments.

5 References

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