Encoding Spatial Context: A Hypothesis on the Function of the Dentate Gyrus-Hilus System

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Abstract

There is now a very extensive body of data on the spatial correlates of neural activity in the hippocampal system of rodents. Place-specific activity is found throughout the system and lesions of various hippocampal regions cause severe deficits on spatial tasks. This has led to the hypothesis that the representation of spatial environments is a primary function of the rodent hippocampus. In this paper, we focus on a set of very interesting experimental observations which suggest that spatial representations in the hippocampus proper (CA3/1) are highly context-specific and robust to sensory changes. This suggests the existence of a context-representation system which biases the hippocampal representations. Based on experimental data from the literature, we argue that the dentate gyrus-hilus system is the locus of context processing, and present a simplified neural network model to support this hypothesis.

1. Introduction

The primary neurons of most regions in the rodent hippocampus show significantly elevated activity in localized regions of spatial environments during the performance of spatial tasks [26, 24, 29, 14]. Such cells are called place cells and the regions of high activity are termed place fields. Numerous computational models have been developed to understand the role of place cells in spatial representation and navigation [42, 36, 5, 1, 20, 30]. In this paper, we present a hypothesis that might explain some of experimental observations that are still not well-understood computationally. We believe that this somewhat speculative hypothesis can serve as an important component of an experimentally verifiable theory of spatial representations in the hippocampus.

2. Background

A partial block diagram of the hippocampus is shown in Figure 1. Sensory information comes in primarily through the *entorhinal* cortex (EC), though some processed information also enters through the subcortical and limbic projections to the *dentate gyrus* (DG) and $CA3$ regions. The output pathway of the EC, known as the *perforant path* (PP), projects to several regions of the hippocampus proper, including the dentate gyrus, CA3, and the *hilus*.
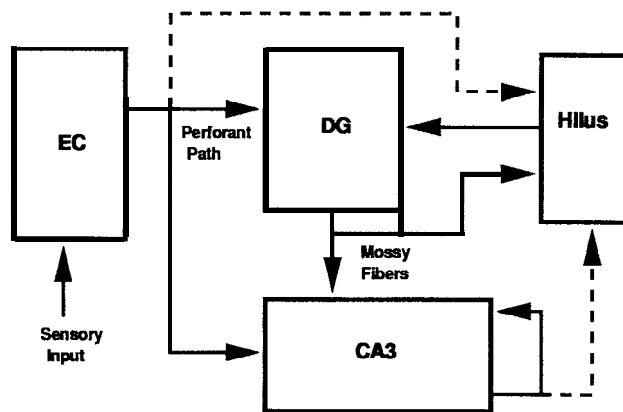

Figure 1. Architecture of the hippocampal system: Excitatory Pathways

The principal cells of the DG are *granule* cells, which are characterized by low spontaneous activity and high activity thresholds. Granule cells receive excitatory input from the entorhinal cortex and also from the *mossy cells* of the hilus [34]. They project to the *pyramidal* cells of the CA3 and to the mossy cells of the hilus [35, 33] through the *mossy fiber* (MF) connections.

The hilus contains many species of cells, but the primary excitatory neurons are the mossy cells [33].

These are characterized by high activity and a low firing threshold [35]. They receive excitatory input from the granule cells of the DG and project back to both the granule cells and inhibitory interneurons in the DG [35, 34, 4, 13]. At least five different types of interneurons bridging very specific subregions have also been identified in the DG-hilus system [9, 4], which suggests that the DG-hilus system is capable of complex information processing. Recent evidence also suggests that several pathways in the DG-hilus system might support long-term potentiation [11].

The primary cells of the CA3 region are the *pyramidal cells,* which receive stimulus from the DG via the MF projection, and from the entorhinal cortex through the perforant path. In addition, the pyramidal cells also receive excitatory connections from other pyramidal cells, creating a recurrent neural network. Place cells are often studied in CA3 or the nearby CA1 region.

There have been previous proposals that the hippocampus is important for context-dependent representation and learning [12,19] but quantitative models have focused mainly on a specific definition of context [31, 21, 16], denoting the immediate temporal antecedants of stimulus or memory patterns rather than global frames of reference. The latter notion has only recently arisen as a major issue in hippocampal research [7,30], and significant research is needed to address it.

3. Motivating Observations, Inferences, and Hypotheses

Several experimental observations regarding place representations motivate the work presented here:

1. Only a small fraction of cells in CA3 are active as place cells in any specific environment, but almost all cells act as place cells in some environment [38,39]. The set of CA3 place cells representing distinct environments appears to be chosen "randomly" for each environment [24,38].

2. Environments with similar appearance have similar place representations in the EC, but very distinct ones in CA3 [28,2].

3. CA3 place representations in a familiar environment are remarkably robust against degradation of sensory cues (such as switching off all lights or removing most landmarks) *provided that the change occurs after the animal is introduced into the environment.* If the change occurs prior to the animal's introduction, a completely different place representation is seen, and this too remains stable *even if the environment is then returned to its original state* [27,29,2].

Taken together, these observations suggest that CA3 place fields arise from the interaction of two factors: 1) Sensory and ideothetic information; and 2) An all-or-none context-dependent selective mechanism. Observation (2) suggests that this bias arises in the DG-hilus system, since that is the only intervening structure between the EC and CA3, and observation (3) indicates that the bias too is not sustained by the direct sensory input, but is stable regardless of most sensory changes once it has been switched on.

On the basis of these implications, we hypothesize that the dentate-hilus system is the locus of context-separation within the hippocampus. Learning in the PP input to granule cells associates sensory patterns with the activation of specific granule cells, allowing the DG to recognize especially salient situations (such as the entry point to an environment). Upon entry into an environment, a *recognition* set of granule cells is activated. This, in turn, stably primes a small, environment/context-specific cohort of granule cells through granule-mossy cell interactions, and depresses the rest via feedback inhibition from the hilus — effectively creating a *latent attractor.* Only cells in this primed cohort are effectively available for the duration of the episode, and show place-specific activity as per their sensory and ideothetic input. The mossy fiber projections from this cohort then implicitly select a sub-population of CA3 cells that will represent this context/environment [38].

It is worth noting that the actual firing of granule cells is seen as being driven by sensory and path-integration information [27, 23, 40, 7, 30], but is *confined* to the primed cohort by the latent attractor set up in the DG-hilus recurrent loop. The attractor cannot express itself autonomously except under artificial disinhibition [33, 34, 4, 13]. The limiting of activity to a subgroup of DG or CA3 cells may also provide a certain degree of robustness against degraded stimuli by limiting the choice of neurons that can be fired.

We also hypothesize that the DG has (at least) two modes of operation. In the *quiescent mode,* there is little or no impact from the hilus, and DG activity consists primarily of an unstructured, noise-like response to input from the EC. In the *alert mode* — identified with locomotion, exploration, and other "active" behaviors — DG neurons become more attentive to the hilar input, which creates a primed cohort based on the DG activity distrubution at the initiation of the alert state. The existence of two or more operating modes in the DG also has experimental support [6,22].

4. Network Model

As a first step towards validating the above hypotheses, we have constructed a very simple neural network model of the EC-DG-Hilus system. It has a predetermined architecture reflecting the assumptions of our hypotheses. The aim is mainly to illustrate the gross hypothesized behavior in a hippocampus-like setting. The current model does not attempt to simulate the emergence of the required architecture via learning.
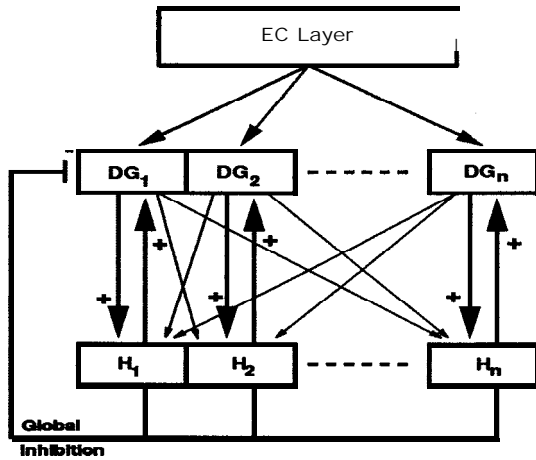

Figure 2. Network Model Architecture. Bold arrows indicate high connectivity and thin arrows weak connectivity.

The model has three layers of neurons, representing the EC, the DG, and the hilus (H). The EC layer projects randomly and diffusely to the DG layer with excitatory connections. The DG layer and the H layer are each divided into N disjoint groups, one for representing each context. Group DG_k of the dentate sends excitatory connections to group H_k of the hilus with probability γ_s, and to group $H_{j \neq k}$ with probability γ_c, where $\gamma_s > \gamma_c$. Similarly, group H_k of the hilus sends excitatory connections to group DG_k of the dentate with probability β_s, and to group $DG_{j \neq k}$ with probability β_c, where $\beta_s > \beta_c$. The hilus also sends a non-specific global inhibitory signal to all DG neurons, with a strength proportional to activity in the H layer. Thus, the hilus has a specific excitatory and global inhibitory effect on the dentate. The net effect of this is to sharpen the impact of the active H inputs on DG neurons. The whole architecture is shown in Figure 2. It should be noted that showing DG and H groups as compact divisions in the two layers is purely an il-

lustrative convenience. The hypothesis implies only a functional, and *not* a topographical organization of connectivity, though some of the latter might also exist [33, 9, 3, 4].

The environment is modeled simply as an $M \times M$ grid on which the simulated animal moves by continuing its previous direction (with 50% probability) or randomly choosing one of eight possible directions to the cells abutting its current location (with 50% probability). If it encounters a wall, it bounces off in a random direction into the environment. The switching between the quiescent and alert modes is modeled by a binary variable, ϕ, which is set to 0 during the quiescent phase and to 1 in the alert phase. The equations for each layer are given below:

EC *Layer:* The EC layer is modeled at a purely phenomenological level, based on the known characteristics of EC place fields [28]. Each cell is given a broad, Gaussian place field with a randomly chosen center and random shape and orientation. As the animal moves on the grid, each EC cell's activity just reflects its place field. This method bypasses the many difficulties associated with generating EC activity from simulated environmental cues or landmarks [42, 36]. Each EC cell, i, is assigned a center, $\bar{c}_i = (c_i^x, c_i^y)$. The output of cell i at time t is defined by the following equation:

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

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 O-mean uniform random variables with variance σ_q, which controls the accuracy with which an EC cell discerns the animal's location.

DG Layer: The DG layer receives excitatory input from EC and focused excitaory as well as global inhibitory input from H. Since the input from H represents a feedback, it has a delay of 1 time step. The effect of going from the quiescent to the alert mode is to increase the gain for both excitatory and inhibitory input from H. The activation to DG granule cell i is given by:

$$
\begin{aligned}
y_i(t) = \\
SEC \sum_{j \in EC} w_{ij} z_j\,(t) \\
+ \,(g_H + \phi \delta_g) \sum_{j \in H} w_{ij} z_j(t-1)
\end{aligned}
$$

$$-(G_H + \phi\delta_G)\sum_{j \in H} z_j(t-1) \qquad (2)$$

where w_{ij} is the synaptic weight from cell j to cell i, z_j (t) is the output of j at time t, g_{EC} and g_H are quiescent mode excitatory gains for EC and H inputs, respectively, G_H is the baseline inhibitory gain from H, δ_g and δ_G are changes in excitatory and inhibitory gains during the alert mode, and ϕ is the indicator variable described earlier. The output of i is calculated by setting the k_{DG} most excited DG cells to 1 and the rest to 0, simulating competitive firing mediated by feed-forward inhibition from EC and local-circuit inhibition within the DG. In the simulation, we set g_H and G_H to 0 for clarity.

H Layer: The H layer simply provides feedback to the DG layer, as described above. We do not model any inhibitory mechanisms in the H layer, since most inhibition originating in the hilus appears to be directed at the DG [9] (though see [4]). The activation for H cell i is given by:

$$y_i(t) = g_{DG}\sum_{j \in DG} w_{ij}z_j(t) \qquad (3)$$

where g_{DG} is a gain. Firing is by simple thresholding, so that $z_i(t) = 1$ if $y_i(t) > \theta_H$, where θ_H is the common threshold for all H cells.

5. Simulation Results

To illustrate the hypothesized mechanisms, the model described above was simulated as a small neural network with 40 EC cells, 150 DG cells, and 30 H cells. The network had three cell groups, so each DG group had 50 cells and each hilus group 10. Two "similar" 40 x 40 environments, ENV_1 and ENV_2, were simulated by generating EC fields for one environment randomly, and then producing those for the second by a small (variance = 0.1) random perturbation of the first environment's field centers.

The simulation had four phases, each lasting 2000 time steps (Figure 3). In the first phase — representing the quiescent mode — the EC output was driven by randomly generated position inputs with O-mean unit variance Gaussian noise added to the output in an attempt to simulate spatially random activity in otherwise spatially tuned units. The ϕ parameter was set to 0. As shown in the first 2000 steps of Figure 3, the DG activity, driven by the EC input, was spread throughout the layer. At step 2001, we introduced a "recognition event", which corresponded to the activity in the DG concentrating almost entirely in group DG_1, and a simultaneous switch of ϕ to 1. This simulated
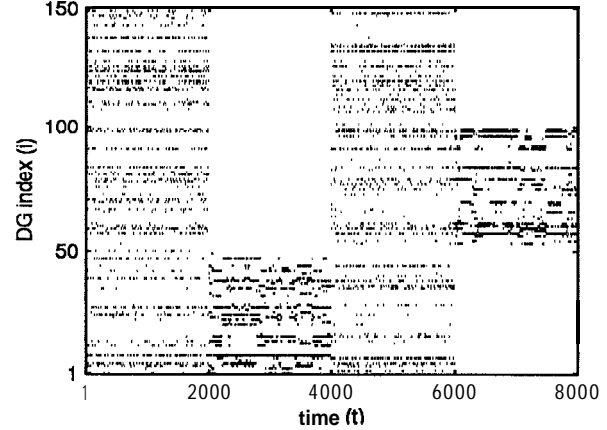

Figure 3. DG activity for two environments

the recognition of ENV_1 by the animal. As the figure shows, subsequent DG activity — as the simulated animal moved about — was concentrated in DG_1, which would create CA3 place fields specific to the ENV_1 context.

At step 6001, the ϕ variable was reset to 0, switching out the context bias from the H layer, and EC activity once again became random, leading to broad, sparse activity in the DG. At step 8001, the system was switched back into the alert mode, this time with an ENV_2 recognition event, and DG activity became concentrated in DG_2 for the duration of the episode. It is clear from the figure that the DG representation for this case is totally different than the representation for ENV_1. Figure 4 shows the empirically reconstructed activity of four representative DG cells in ENV_2. Despite the extreme simplicity of the model, it is clear that a reasonable set of place fields is obtained (see [14] for characteristics of DG place fields.)

6. Discussion

The results described in the previous section are not surprising, since the system was effectively designed to produce them. However, they do show how a plausible set of assumptions about DG-hilus architecture and activity could lead to the hypothesized context-dependent spatial coding.

Previous proposals about DG function [18, 41, 20, 30] have all focused on the notion that it "orthogonalizes" the PP input, thus allowing discriminations between similar sensory situations. This might well be a function of the DG, but it is clearly not enough to
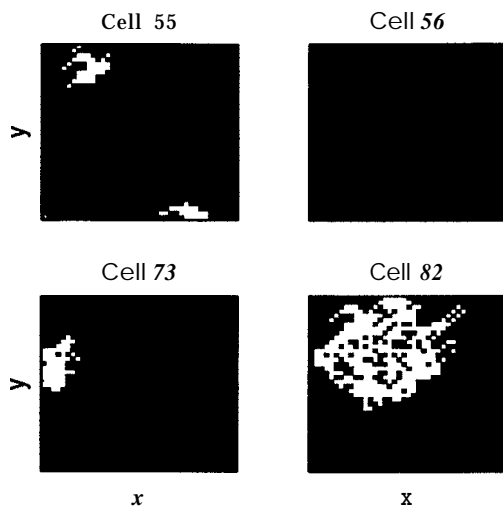
Cell 55   Cell 56

Cell 73   Cell 82

Figure 4. Activity of four DG_2 *cells* **in** ENV_2

explain the observations cited above. The critical requirement is for a *sustained* selective bias throughout an episode. This clearly requires some type of reverberatory mechanism to set up an attractor dynamics. It has been proposed [25] that the recurrent system in CA3 might prime a cohort of pyramidal cells in a given context. However, the CA3 is also hypothesized to be the locus of memory retrieval and pattern completion [18, 41, 10], spatial distance coding [25], temporal information processing [15, 21, 16], and several other related functions. It is highly unlikely that the CA3 can serve these retrieval functions and maintain primed cohorts (unless its architecture is more complex than is generally believed), and the DG-hilus system offers a logical and more reasonable alternative. Simpler types of context representations (such as those needed to disambiguate similar stimulus sequences [31, 21, 16] during path integration) may well exist in CA3. Interestingly, there has also been speculation that the DG-hilus recurrent system might be an associative memory system as CA3 is hypothesized to be [35, 3]. Once again, though, the logic of information flow suggests that the context separation system be an afferent for the recall system, which the DG is for CA3. Our model is closely related to the recently proposed "chart hypothesis" [32] for context-dependence in the hippocampus. However, we place the system in DG-hilus rather than CA3 and use a disynaptic (DG-H-DG) rather than monosynaptic recurrence, which provides the possibility of delicate modulation and control within the recurrent loop. Support for the DG-hilus location comes from the evidence

of attractor dynamics [37] and context-dependence [17] in the DG. The network we describe also has strong similarities to adaptive resonance theory (ART) models [8].

The central dilemma that the hippocampal system must confront is the conflict between sensitivity and robustness. The system must be sensitive to small differences in distinguishing between similar distinct situations, but robust against changes within the same situation. A stable context representation is a temporally logical solution to this. The system is sensitive at the beginning of an episode so it can recognize the correct context. Once this has been done, the context pins the system down, making it robust against changing stimulus, until there is a stimulus disruptive enough to jolt the system into a new context. This is logical because true changes in spatial context (change of environment) require very specific events (e.g., entry into a room or maze), and do not happen spontaneously regardless of how much sensory stimuli might change. In the absence of a reset event, it is logical for an animal to assume a stable context once one has been identified.

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