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Decoding Position to Analyze Spatial Information Encoding in a Large-Scale Neuronal Network Model of Rat Dentate Gyrus

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Abstract

Spatial information is encoded by the hippocampus, and the factors that contribute to the amount of information that can be encoded and the transformation of spatial information through the trisynaptic circuit remain an important issue. A large-scale neuronal network model of the rat entorhinal-dentate system was developed with multicompartamental representations of the neurons within the dentate gyrus. Spatial information was introduced to the network via grid cell activity, and the spatial information encoding capabilities of the network were assessed using a recursive decoding algorithm to estimate the position of a virtual rat using the dentate activity. To obtain a measure for the information that the network could convey, decoding error was calculated for different decoding population sizes. Decoding error decreased exponentially as a function of population size. Therefore, the time constant and the asymptote of the error curve could be used as metrics to compare the changes in encoding performance. In conjunction with the large-scale model, this paradigm can be used to characterize how neural properties, network composition, and the interactions between different subfields affect spatial information encoding.

I. Introduction

The discovery of place cells [1] within the hippocampus and grid cells [2], which provide input to the hippocampus, has provided a specific behavioral correlate by which a major aspect of hippocampal function, spatial navigation, could be explored. In rat these cell types exhibit receptive fields for specific locations within an environment called place fields. Hippocampal place cells in the CA3/4 and CA1/2 subfields mostly exhibit singular place fields while grid cells of the medial entorhinal cortex (MEC) exhibit multiple place fields that present as a repeating triangular grid.

Granule cells, the principal neurons of the dentate gyrus, have been shown to exhibit multiple place fields that are irregularly arranged across the environment [3], and experimental evidence demonstrates that the dentate gyrus significantly contributes to the encoding of spatial information [4]. By quantifying the spatial information encoded by a neural population, the transformation of spatial information as it propagates through the successive layers such as the hippocampal trisynaptic circuit (from dentate gyrus to CA3/4 to CA1/2) can be investigated, and the contributions of various neural properties (e.g. synaptic receptors, electrophysiological characteristics of neurons, feedforward and

feedback inhibition) towards the transformation could be studied. However, recording from all three regions *in vivo* is a major technical challenge.

We have been developing a large-scale neuronal network model of the rat hippocampus beginning with the entorhinal-dentate system [5–7] through which spatial information encoding and the factors that influence it can be explored. The large-scale model of the dentate gyrus included compartmental models of granule cells and basket cells and an entorhinal cortex modelled using a Poisson process. MEC grid cells provided spatially correlated activity by modulating their firing rate according to the position of a virtual rat in a square environment and the specific distribution of their spatial receptive fields. Neurons from the lateral entorhinal cortex (LEC) provided spatially uncorrelated activity with a constant mean firing rate. Granule cell rate maps were smoothed using an adaptive binning procedure and were used as the conditional intensity function in the position decoding procedure. Position was decoded using a recursive filter decoding algorithm [8]. The ability of the network to encode spatial information was then assessed by varying the number of neurons from which the decoding was performed and assessing the accuracy.

II. Methods

A. Large-Scale Model of the Entorhinal-Dentate System

The large-scale network used in this work was composed of multi-compartment neuron models that were connected based on anatomical topography, representing 1/10th of the full number of neurons in a single hemisphere of the rat entorhinal-dentate system based on the model described in [5–7]. The simulations were performed using NEURON [9] and Python. The dentate gyrus network was composed of 46,000 layer II MEC cells, 66,000 layer II lateral entorhinal cortical (LEC) cells, 120,000 granule cells and 5,600 basket cells. The models were heterogeneously distributed throughout the respective dentate gyrus and entorhinal cortical maps following anatomical data.

Granule cells were represented using 4 compartments representing a somatic compartment and 3 dendritic compartments corresponding to the dendrites in the inner, middle, and outer third of the molecular layer. Basket cells were represented using a single compartment using the parameters reported in [6]. Entorhinal neurons were represented using a Poisson process.

The entorhinal projection to the dentate gyrus was topographically structured as described in [5]. Granule cells and basket cells were probabilistically connected based on their distance between their somata and the respective axon distribution, modelled as a two-dimensional Gaussian function with anatomically constrained standard deviations. The medial and lateral entorhinal cortices provided excitatory input to both granule cells and basket cells. Granule cells further provided excitatory input to basket cells, and basket cells provided inhibitory input to granule cells. Granule cells received 1950 LEC inputs, 1685 MEC inputs, and 1100 basket cell inputs. Basket cells received 1161 LEC inputs, 871 MEC inputs, and 915 granule cell inputs.

B. Generating Grid Cell Activity

Grid cell activity was generated using the following equation developed by Blair *et al.* [10]:

$$G(r, \lambda, \theta, c) = g\left(\sum_{k=1}^3 \cos\left(\frac{4\pi}{\sqrt{3}\lambda} u(\theta_k + \theta) \cdot (r - c)\right)\right). \quad (1)$$

The angle θ defines the global orientation of the rate map while $\theta_1, \theta_2, \theta_3, (-30^\circ, +30^\circ, +90^\circ)$ create the triangular structure of the rate map and $u(\theta_k) = (\cos(\theta_k), \sin(\theta_k))$. The spatial offset is defined by $c = (x_0, y_0)$, and λ controls intervertex distance. The gain function was $g(x) = \exp(a(x - b)) - 1$ with $b = -\frac{3}{2}$ and a controlling the size of the place fields. The sizes and distances between the place fields were constrained by values reported in [11].

The movement of a virtual rat within an 80 cm $\times$ 80 cm square environment was simulated to provide the input to equation (1) resulting in a firing rate time series that would be used to generate spiking activity using an inhomogeneous Poisson process. Each grid cell had a unique set of parameters resulting in different firing rates and spike times. LEC spike times were generated using a homogeneous Poisson process with a mean firing rate of 3 Hz.

C. Constructing Spatial Rate Maps

Granule cell spikes were sorted into square bins with side lengths of 2 cm based on the time of the spike and the position of the rat at that time. The rate map was smoothed using the adaptive binning procedure developed by Skaggs *et al.* [12] which involved iterating through each bin and expanding a circle centered at each bin until the following criterion was met:

$$N_{spikes} > \frac{\alpha}{N_{occ}^2 r^2}, \quad (2)$$

where N_{spikes} is the number of spikes within the circle, N_{occ} is the number of samples during which the rat occupied the circle, r is the radius of the circle in bins, and α is a scaling parameter, set to 1.0×10^{13} . The value within the bin is then set to $r_s \cdot \frac{N_{spikes}}{N_{occ}}$ with r_s denoting the temporal sampling rate.

The spatial information score of the rate maps was computed using the following equation reported in Skaggs *et al.* [12]:

$$SI = \sum_i p_i \cdot \frac{\lambda_i}{\lambda} \cdot \log \frac{\lambda_i}{\lambda}, \quad (3)$$

in which λ_i corresponds to the firing rate in the i^{th} bin, λ is the mean firing rate, and p_i is the probability that the rat is in the i^{th} bin. Equation (3) only resembles the calculation for the mutual information between firing rate and position as it replaces the proper terms for the joint and marginal probabilities by the normalized firing rate. Furthermore, the metric is restricted to characterizing single neurons; the sum of this metric across a population will

not indicate the spatial information of the population. However, it has validation potential as it has been used to quantify spatial information for neurons recorded *in vivo* [12–15].

D. Position Decoding Using Point Process Filtering

Using the smoothed rate maps, the point process filtering technique developed by Brown *et al* [8] was used to estimate the position of the rat based on the spiking activity of a population of granule cells using the following equations: One-Step Prediction

$$x_{k|k-1} = x_{k-1|k-1} + Fx_{k-1|k-1} \quad (4)$$

One-Step Prediction Variance

$$W_{k|k-1} = FW_{k-1|k-1}F^T + RW_e \quad (5)$$

Posterior Variance

$$W_{k|k}^{-1} = W_{k|k-1}^{-1} + \sum_{c=1}^c [[\nabla \log(\lambda_{k\Delta}^c)[\lambda_{k\Delta}^c \Delta]^T] \quad (6)$$

$$- \nabla^2 \log(\lambda_{k\Delta}^c)[n_{k\Delta}^c - \lambda_{k\Delta}^c \Delta]]$$

Posterior Mode

$$x_{k|k} = x_{k|k-1} + W_{k|k-1} \sum_{c=1}^c \nabla \log(\lambda_{k\Delta}^c)[n_{k\Delta}^c - \lambda_{k\Delta}^c \Delta]. \quad (7)$$

The variable k corresponds to the sample number, and Δ is the temporal step size which was 1 ms. The firing rate due to the position of the rat at time k is obtained from the smoothed rate map and is denoted by $\lambda_{k\Delta}^c$ where each c denotes a different neuron, and the number of spikes generated by the neuron is indicated by $n_{k\Delta}^c$. The firing rate multiplied by the temporal step size, $\lambda_{k\Delta}^c \Delta$, computes the probability that the neuron would generate a spike. The ∇ and ∇^2 symbols denote the first and second derivatives with respect to position, respectively.

Using a first-order autoregressive model of the path of the rat, the state evolution matrix F and covariance matrix W_e were calculated. During One-Step Prediction, the position $x_{k|k-1}$, is estimated using the autoregressive model parameters and the previous position estimate $x_{k-1|k-1}$, which incorporates the spiking history within the interval $(0, (k-1) \Delta)$. Similarly, One-Step Prediction Variance estimates the covariance matrix of the One-Step Prediction position based on the autoregressive model parameters.

The Posterior Mode and Variance use the neuron firing probabilities based on their conditional intensity functions and the actual spike times to update the one-step estimates and obtain the estimate of the current position, $x_{k|k}$, and the covariance matrix of the posterior, $W_{k|k}$, under the assumption that the neurons are conditionally independent. These estimates incorporate the spiking history within the interval $(0, k)$. The derivatives of the log of the firing rates are weighted by the firing probabilities and spike counts to compute these estimates. The derivation of equations (4–7) are detailed by Barbieri *et al.* in [18].

III. Results

A. Emergence of Place Fields

The large-scale network was driven by spatially correlated and uncorrelated activity through the MEC and LEC, respectively for a simulation length of 2000 seconds. Rate maps were constructed based on the granule cell activity and smoothed using the adaptive binning process. Example rate maps are shown in Fig. 1. The rate maps exhibit irregularly spaced and multiple place fields as has been reported in the literature [3]. The spatial information score of the simulated granule cells was 0.87 ± 0.02 bits/spike which is comparable to the experimentally recorded value of 1.1 ± 0.56 bits/spike as reported in [13].

B. Decoding Analysis

To investigate the effect of the number of neurons on the accuracy of the estimates, neurons were randomly selected from the total population for use in the decoding for populations of 100, 200, 500, 1000, 2000, 5000, and 10000 neurons. The decoding error was computed as the Euclidean distance between the true and predicted positions. Decoding was performed based on the last 20 seconds of the simulation. Fig. 2 depicts example estimated positions due to different population sizes, and Fig. 3 plots the mean error. It is evident in Fig. 3 that the error decreased exponentially as population size increased which also indicates that more spatial information was encoded by the ensemble activity. Fig. 2 shows that there is a delay between the actual position and the estimated position, suggesting that the network encodes the past history. The delay, regardless of population size, was approximately 200 ms.

IV. Discussion

As a potential procedure to quantify spatial information encoding in a network, the exponential relationship between error and population size offers two metrics: the time constant and the asymptote. The rate at which error decreases may indicate how sensitive spatial information encoding is to a property, which in this work was the amount of information each neuron contributed to the ensemble encoding. The exponential relation suggests an initial superlinear summation of spatial information followed by a sublinear summation. The asymptote indicates that there is a limit to the maximum performance of the population. Identifying the neural properties that then determine the values for these metrics would offer insight into how encoding is performed.

Using the large-scale model, the contributions of many properties towards spatial information encoding could be investigated in the dentate gyrus such as the biophysical properties of the neurons, feedforward and feedback inhibition, and the associational mossy

cell system. As the large-scale model is developed further to include the CA3/4 and CA1/2 subfields, the influence of the dentate gyrus' ability to encode spatial information on subsequent areas can be explored. The general method of analysis could also be applied beyond that of spatial information as additional types of information (e.g., multisensory information from the LEC [17]) are identified and included in the model.

V. Conclusion

Currently, the neuronal model used in this work represents one of the largest and most comprehensive models of the rat hippocampus (see also Bezaire *et al.* [18]) but also one of the few models that is beginning to incorporate behaviorally relevant input at this scale. As such, the model can be used to explore higher-level consequences to the synaptic, neuronal, or network dynamics beyond intermediate-level phenomena such as oscillations or spatiotemporal firing properties. Behaviorally relevant input further allows the intermediate level properties to be interpreted against a higher-level context such as spatial encoding and decoding. The large-scale nature of the model also allows a means through which the analysis of large neural datasets can be developed. The metrics reported in this manuscript are simply tools by which such analyses can be performed.

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Figure 1.

Rate maps generated by simulated granule cells. The rate maps were smoothed using adaptive binning. The red areas represent areas of higher firing rate while blue areas represent lower firing rate. Multiple place fields can be seen, and they are arranged irregularly throughout the environment.

Figure 2.

Estimated position based on different population sizes of neurons over a 20 second period. Each subplot shows the actual x and y coordinates of the virtual rat (black). The estimated position is overlaid in red. As the number of neurons used during decoding increases, the estimate becomes more accurate. A lag can be seen between the actual position and estimated position. This lag is 356 ms.

Figure 3.

Mean error plotted against population size. As population size increases, error decreases exponentially. An asymptotic value of 1.5 predicts the minimum error that can be achieved by the network at a population size of infinity.