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Assessing the Role of Feedback in Spatially Patterned Grid Cell Responses

APPROVED BY

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Dedicated to my wife Jisun.
Acknowledgments

It is my privilege to have Professor Ila Fiete as my advisor for my graduate work. Her insights regarding both scholarly and practical matters in neuroscience have always encouraged me to take the next step to becoming a scientist. I am grateful to Professor Sriram Vishwanath and Professor Jonathan Pillow for their support and helpful discussions.

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Last but not least, Jisun, you are the sunshine of my life.
We analyze the spike trains of multiple simultaneously recorded grid cells obtained in different conditions, to help determine the role of recurrent network feedback in generating grid responses.

An important class of models of grid cell activity is based on low-dimensional continuous attractor dynamics arising from recurrent connections within the grid system [1]. A necessary prediction of these models is that the strong recurrent connections force the grid responses of different cells to maintain fixed relative spatial phases over long periods of time, even if the response patterns of each neuron change. The observation that grid cells maintain their relative spatial phase relationships across different familiar environments [2] supports the presence of recurrent connections, but does not rule out the possibility that these relationships persist due to feed-forward input.

We analyze the stability of pairwise neural correlations for experiments in which the spatial responses of single neurons change over time. The first
such experiment involves resizing of a familiar enclosure, with the result that spatial grid responses rescale along the resized dimension [3]. We show that the relative spatial phase of firing between pairs of cells remains stable over time even as the absolute spatial phase of firing in these same cells changes greatly through rescaling. This result is again consistent with recurrent connectivity, but it remains possible that common external sensory cues (e.g. border information arriving from boundary cells) somehow register the rescaled grids of all cells to display the same relative phases as before rescaling.

In an attempt to address this, we analyze responses from animals first exposure to novel environments. Grid firing becomes more noisy and the spatial firing pattern expands, then relaxes back to the periodicity seen in familiar enclosures [4]. During the relaxation, external sensory cues are static and thus likely not responsible for the changing grid responses. We show that the constant phase relationships seen across familiar environments are present from first exposure as well.

Finally, we illustrate a generative model to predict grid cell spikes. The aim is to obtain the key determinants of grid cell firing, including animal location, velocity modulation, neural adaptation, and recurrent feedback in a Bayesian framework, and thus assess network contributions to grid cell activity.
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Chapter 1

Introduction

According to the continuous attractor model, topographically arranged population-level patterns or responses are driven by the animal’s velocity inputs, then the grid cell’s regular spatial response can be reproduced by translating the population pattern within the neural sheet in proportion to the animal’s movement (see Fig 1.1). Therefore, it must produce the same single neuron (SN) response up to translation, which have the same period and

![Diagram](image)

Figure 1.1: (a) Top: Recurrent connection within the grid system. Bottom: Color-coded input head-direction/velocity tuning curves. (b) A snapshot of the underlying population activity. Yellowish blobs represent coactivated grid cells in response to the animal’s movement. The green lines indicates an electrode at a fixed location. (c) Grid cell response: average firing rate of a single neuron as a function of the animal’s position within the circular enclosure.
orientation but can have different spatial phase [5].

What will the phase difference between simultaneously recorded cells be like? The recurrent network is only capable of expressing grid pattern and its translation because they are the only steady state of the continuous attractor manifold. Thus, absolute phase of the pattern in population response can drift from noise or the animal’s movement, but relative phase between neurons stays the same (see Fig 1.2). In the following chapter, it will be verified that the pairwise phase relationships are strictly preserved during major changes in SN response.

\[
\begin{align*}
\phi_1 \phi_2 \phi_3 & \quad \phi_1 \phi_2 \phi_3 & \quad \phi_1 \phi_2 \phi_3 \\
0 & \quad \pi & \quad 0 \\
\frac{\pi}{8} & \quad \frac{7\pi}{8} & \quad \frac{-\pi}{8} \\
-\pi & \quad 0 & \quad -\pi
\end{align*}
\]

\[
\begin{align*}
\Delta \phi_{12} &= \pi & \Delta \phi_{12} &= \pi & \Delta \phi_{12} &= \pi \\
\Delta \phi_{13} &= 0 & \Delta \phi_{13} &= 0 & \Delta \phi_{13} &= 0
\end{align*}
\]

Figure 1.2: Snapshots of the population activity when the network is driven by the constant velocity input in the rightward direction. Green lines represent the same electrodes at a fixed location, and the circle above them represents the neural activity of the targeted cell. (yellow=active, black=inactive) Three simultaneously recorded cells have the absolute phase ($\phi_i$) at each time step, and the values are all different across time. However, the phase difference ($\Delta \phi_{ij}$) always remains the same.

2
Chapter 2

Phase Relationship

2.1 Experiment I: Resized Familiar Environments

The first experiment consists of a series of five separate 20 minute trials. Animals experienced a familiar environment in the first and final trial, and three intermediate trials were conducted in the enclosure resized along one or both dimensions (see Fig 2.1) [3].

![Diagram of resized environments](image)

Figure 2.1: Schematic environment across five different trials. Red arrow represents the direction of contraction or expansion of the original (familiar) environment.

2.1.1 A Description of the Experimental Results

In the resized environments, spatial periods of individual cell rescale dramatically (see Fig 2.2). To measure the inter-trial changes of the hexagonal pattern in the SN response, we computed the ratios of all the grid parame-
Figure 2.2: The SN responses across five different environments. (Horizontal Rectangle → Large Square → Vertical Rectangle → Small Square → Horizontal Rectangle.) (a) Spike locations (red) superimposed on the animal’s trajectory (black) (b) Rate map (c) Autocorrelogram (d) Grid parameters measured in the autocorrelogram: two periods $\lambda_1, \lambda_2$ and the orientation $\theta$. (see details in Methods)

The parameters (two periods and an orientation), which were estimated from the template matching algorithm (see Methods), between the first trial and the next consecutive trials. At least one of the ratios was relatively greater or less than one if there were a sizable rescaling in the SN response at that trial (see Fig 2.3 top and middle). Now if there are simultaneously recorded cells and they were recorded from the same network, then the spatial period and the orientation should be similar each other even though the SN response changes.
a lot according to the continuous attractor hypothesis. Thus, the similarity of the SN spatial responses between a pair of cells were measured from the same approach to compute the ratios of grid parameters across five successive trials, all of which were close to one (see Fig 2.3 bottom).

Figure 2.3: Top: Ratios of grid parameters of the first trial (Horizontal Rectangle) to the next trials (cell 1). Middle: The same ratios from the simultaneously recorded cell 2. Bottom: The ratio of each parameter between two cells across five different environment

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2.1.2 Relative Spatial Phase

Simultaneously recorded cells from the same network share the identical period and orientation according to the continuous attractor hypothesis. Thus it was the first step to verify the congruity of two cells’ spatial responses by comparing the estimated template parameters. The next step is to measure the “off-centeredness” of the pattern from the central point in the crosscorrelogram (see Fig. 2.4).

![Figure 2.4: Top: An autocorrelogram of a single cell’s spatial response in the original (VR) and the resized (LS) environments. Black cross lines represent the xy coordinate centered at the intersection. Middle: The same autocorrelogram of another simultaneously recorded cell. Bottom: Crosscorrelation of the above cell pair’s response. Black dashed ellipse shows the off-centeredness of the pattern.](image)
The off-centeredness is called the relative spatial phase or the phase difference between a pair of cells. The relative phase is simply represented by the vector originating from the central point and pointing toward the most nearby local peak. However, it should be reinterpreted within the frame of a grid cell’s characteristic spatial response because the same relative phases could appear in different ways in the resized environment. Thus, we defined the normalized relative phase (see Fig. 2.5). It provides us with the absolute measure of the out-of-phase between two cells’ responses regardless of their size and shape.

\[
(\phi_1, \phi_2) = \left( \frac{r_1}{\lambda_1}, \frac{r_2}{\lambda_2} \right)
\]

Figure 2.5: Given the estimated grid periodicity \((\lambda_1, \lambda_2)\) and the relative phase vector \(\vec{r}\) (blue), the normalized relative phase \((\phi_1, \phi_2)\) is the oblique projection of \(\vec{r}\) into two adjacent grid line segments (red) normalized by two periods.

Here is an example showing the normalized relative phase in two different environments, and it is the same sample in Figure 1.6. The SN response was stretched to the east and west due to the environmental resizing along the same dimension, however, the relative phase between two cells was stable across two different trials (see Fig. 2.6). In the following section, the phase
relationship will be explored through all trials as well as from different animals.

Figure 2.6: The best-fit template lattice (red circle) estimated from the grid local peaks (black asterisk) in the crosscorrelogram. The absolute phases of two cells’ spatial responses differ by the same amount of blue vector. The grid parameters \((\lambda_1, \lambda_2, \theta_1, \theta_2)\) and the normalized relative phases \((\phi_1, \phi_2)\) are specified at the bottom of each trial.
2.2 Changes in Normalized Relative Phase across Resized Environments

The normalized relative phase was measured across five consecutive trials from five distinct rats to see whether the phase differences keep constant across the rescaled enclosures. To compare distinct normalized relative phase between different cell pairs at the same time, the values were converted into the zero-mean normalized relative phase within a pair of cell. However it should be noted that zero-mean relative phase cannot be always zero even thought a cell pair has stable phase relationship due to the intrinsic noise within the network or the measurement noise. It leads to the comparison with the phase of grid local peaks relative to the template lattice because the relative phase could be varied across trials within the same range of errors, which is equivalent to the deviation of grid pattern from the template lattice (see Fig. 2.7).

The results show that the phase difference is within a margin of error, which implies that the phase relationship is stable even when the SN response changes significantly. Our results suggest the existence of recurrent connectivity, but the stable relative phase may be due to the common external sensory cues or the stabilizing feedback from the hippocampal areas (see Fig. 2.8). Thus, more constrained experiment will be explored in the following section.
Figure 2.7: Box plots show the statistical distribution of spatial phases of grid local peaks relative to the best-fit template lattice across separately recorded cell pairs from five rats (two cell pairs in rat 214). Most phases are centered at zero, and it implies that the template lattice fits to the grid pattern very well. The zero-mean relative phases are twofold ($\phi_1, \phi_2$), and they are represented by red and blue circles separately. In addition, the relative phases measured from five trials are displayed within an individual box plot. Bad recording sessions were treated as a missing value, and they are described as disconnected missing circles.

Figure 2.8: Two possible schematic systems to cause the stable phase relationship.
2.3 Experiment II: Novel Environments

The second experiment also consists of a series of five separate 20 minute trials. There is no longer resizing in all environments, but three intermediate enclosures are previously unvisited environments.

![Figure 2.9: Schematic environment across five different trials. All enclosures are the same large squares, and the first and the last trials are only recorded in the familiar environment (black). Three middle enclosures are novel to animals (red).]

2.3.1 A Description of the Experimental Results

During an animal’s first exposure to the novel environment, grid cell’s spatial response is less regular and has a larger periodicity than in a comparable familiar environment (see Fig 2.10). This increased period typically lasts for several days, but gradually contracts to the stable size of the familiar environment. In the meantime, place cells are not yet stabilized early in novel environments. Thus, they are not providing the drive to stabilize relative spatial phase (see Fig 2.11). This motivated us to investigate the relative phase again in the second experiment.
Figure 2.10: The SN responses across five consecutive trials. (Familiar → Novel → Novel → Novel → Familiar) (a) Spike locations (red) superimposed on the animal’s trajectory (black) (b) Rate map (c) Autocorrelogram (see details in Methods).

Figure 2.11: Presumably, novelty itself plays a role reducing the stabilizing inputs from the hippocampus (HPC).
Here we measured the inter-trial changes of the hexagonal pattern again in the SN response by computing the ratios of all the grid parameters between the first trial and the next trials. As we expected, the ratios of periodicity in the novel environment were relatively greater than one while the ratios in the familiar environment was close to one (see Fig 2.12 top and middle). The similarity of the SN spatial responses between a pair of cells were also measured by the same method, and it could be inferred whether two cells are recorded from the same network or not. (see Fig 2.12 bottom).
Figure 2.12: Top: Ratios of grid parameters of the first trial (FAM 1) to the next trials (cell 1). Middle: The same ratios from the simultaneously recorded cell 2. Bottom: The ratio of each parameter between two cells across five different trials.
2.4 Changes in Normalized Relative Phase in Novel Environments

In this experiment, we actually estimated the change of periodicity in the grid cell response over 8 days. To make it clear how the grid scale alters in familiar and novel environments, the period from each environment is displayed separately in the same plot (see Fig 2.13). The scale of grid pattern increased by maximally 180% when the animal was exposed to the novel enclosure in the beginning. However, the periodicity gradually relaxed back to the same scale observed in familiar enclosures at the end of the experiment.

Figure 2.13: Grid periodicity as a function of elapsed days, or the number of exposures to the environment. Blue curves represent the estimated period in novel environments, and black ones show the scale in familiar environments. Each case has two periods ($\lambda_1$: empty circle, $\lambda_2$: solid dot) because the grid parameters are twofold. The samples are all different cell pairs recorded from a rat.
We computed the zero-mean normalized relative phase again from the same samples in Figure 1.15 as well as the spatial phase of grid vertices relative to the template lattice. Even while the size of spatial field changed dramatically and the grid cell response was relatively unstable, the phase relationship was preserved from the beginning in novel environments (see Fig 2.14). High stability of relative phase despite large changes in single-neuron grid patterns even in novel environments suggests the presence of a low-dimensional continuous attractor in the dynamics.

Figure 2.14: The zero-mean normalized relative phases as a function of recording date. All other images are of the same representations in Figure 1.9. When there are more than one pair of cells, they are grouped together (light blue box).
2.5 Methods

**Binning and rate maps** First perform the spatial binning of the environment where a rat was foraging, given the animal’s instantaneous position sampled at 50Hz and the spike locations of the putative cells. The number of spikes assigned to a single bin (1cm × 1cm) is divided by the animal’s visiting frequency within the bin in order to compensate for the relative low visiting density as well as to obtain the normalized spike frequency. Secondly generate the smoothed rate maps of each cell from the convolution of the normalized spike frequency and the two dimensional Gaussian kernel. The size and the parameter of the kernel (standard deviation) are selected based on each cell’s spatial response. (see **Fig 2.15**)

![Figure 2.15](image)

**Figure 2.15:** (a) Spike locations (red) superimposed on the animal’s trajectory (black). (b) Gaussian kernel: size = 30cm × 30cm, s.d. = 5 cm (c) Firing rate map. Red indicates the high firing rate, and blue is the low firing rate.
**Autocorrelation and crosscorrelation**  The spatial autocorrelation is to see how regularly the multiple firing fields are formed (see *Fig 2.16*), while the crosscorrelation shows how much two cell’s spatial responses are out of phase with each other. Both spatial correlations are computed from two smoothed rate maps, $R_1$ and $R_2$ as follows:

$$
\gamma(u, v) = \frac{\sum_{x,y} [R_1(x, y) - \bar{R}_{1u,v}] [R_2(x - u, y - v) - \bar{R}_2]}{\sqrt{\sum_{x,y} [R_1(x, y) - \bar{R}_{1u,v}]^2 \sum_{x,y} [R_2(x - u, y - v) - \bar{R}_2]^2}}
$$

where $\gamma(u, v)$ is the correlation coefficient at the bin $(u, v)$, $\bar{R}_{1u,v}$ is the mean of $R_1(x, y)$ in the region under the $R_2$, and $\bar{R}_2$ is the mean of $R_2$. $R_1$ and $R_2$ are the same when computing the autocorrelation.

---

**Figure 2.16:**  (a) Firing rate map.  (b) Spatial autocorrelation generated from the rate map (a). The clear hexagonal pattern is observed.
Template matching algorithm  To estimate the correct grid period (spacing) and the orientation (angle), the best-fit template lattice must be determined in advance. The basic idea originates from the fact that any hexagonal structure can be represented by an origin, two line segments (periods), and the included angle (orientation) between them. The above elements are equivalent to two unit vectors in the vector space and it is not hard to see that the most adjacent 6 vertices around the origin can be constructed from a simple vector arithmetic of two unit vectors. Moreover the outer vertices can be generated from the linear combination of pre-determined 6 vectors as well. (see Fig. 2.17(a))

Given the autocorrelogram, it is first required to find out all the peaks that correspond to the tentative template vertices. They have a common geometric feature in that the gradient at these points is always zero. In other words, every local peak has its external boundary pixels that have a lower correlation value. Thus the local maxima can be easily discovered through the comparison of 8-connected neighborhood at each pixel. (see Fig. 2.17(b))

The template matching algorithm receives the $x$ and $y$ coordinates of the uncovered local peaks in the spatial autocorrelogram as a training data set to fit the template lattice parameters: periods and orientations of 2 unit vectors measured from a horizontal axis ($0^\circ$). (see Fig. 2.18(a)) These four parameters will always produce the hexagonal template lattice, and among them we choose the best template with the least square error. Here the cost function (1.1) measures the similarity between the template lattice and a cell’s
Figure 2.17: (a) Red circles are template vertices generated from the linear combination of two unit vectors $\vec{u}$ and $\vec{v}$. $\theta$ is the included angle. (b) Local peaks (black asterisk) superimposed on the autocorrelogram.

inherent hexagonal pattern detected in the autocorrelogram.

\[
C = \sum_{i=1}^{n} w_i \cdot \| p_i - v_i \|_2 \\
v_i \in \{ \mathbf{x} | \mathbf{x} = f(\lambda_1, \lambda_2, \theta_1, \theta_2) \}
\]

where $C$ is the cost function, $p_i$ is the local peak, $w_i$ is the correlation coefficient at $p_i$, $n$ is the total number of peaks, $(\lambda_1, \theta_1)$ and $(\lambda_2, \theta_2)$ are a pair of template parameters, $f$ is the implicit function generating a template lattice given the set of parameters, and $v_i$ is the most nearby template vertex to $p_i$. There is an additional term $w_i$ to place the relative weight on each local peak $p_i$. It helps the algorithm fit the template lattice better to the peak of higher correlation coefficient. The template matching algorithm will bring out the right spatial periodicity as well as the grid orientation which minimize the cost function (see Fig. 2.18(b)).
\[
(\lambda_1^*, \lambda_2^*, \theta_1^*, \theta_2^*) = \arg\min_{\lambda_1, \lambda_2, \theta_1, \theta_2} C
\] (2.2)

Figure 2.18: (a) Template parameters consist of 2 periods and 2 orientations, \((\lambda_1, \lambda_2, \theta_1, \theta_2)\). The grey solid line is the horizontal axis from which the orientations are measured. (b) The best-fit template lattice (red circle) and the overlaid local peaks (black asterisk). The estimated parameters from (2.2) are specified in the legend.
Chapter 3

Generative Model

3.1 Introduction

In the previous chapter, we verified the stability of phase relationships despite the dramatic rescaling in grid cell responses. However, the underlying principle of the resized spatial response was not discussed yet. According to the shift mechanism by which velocity inputs drive the population pattern flow, two possible scenarios could explain the changing phenomena. For example, if the SN response is stretched along the east and west direction it is because the amplitude of the head direction or velocity inputs for that direction is reduced relative to the other directions while the population pattern remains stable. Another plausible scenario would be stretching the population pattern while keeping the velocity gain fixed (see Fig 3.1). The latter is not consistent with the attractor hypothesis because the deformation of the population pattern does not belong to the low-dimensional attractor manifold. Therefore, one way to check another important prediction of the recurrent network will be investigating the change of velocity gain under the rescaled SN response.

Here we propose a generative model to figure out key determinants of grid cell firing, and by which to verify the new prediction of the continuous
Figure 3.1: (a) The original SN response generated from the right population network driven by the velocity inputs. (b) The expanded SN response along with two possible scenarios [5].

attractor model. The generalized linear model (GLM) is applied to model the SN response by incorporating the spatial and directional inputs, the neural adaptation, and the connectivity of simultaneously recorded cells.
3.2 Mathematical Background

A neural spike train is the set of individual spike times, and the sequence of discrete times constitutes a point process. If it is assumed that the spike trains are generated from the inhomogeneous Poisson process, the conditional probability of observing \( y_t \) spikes at time \( t \) is given by

\[
p(y_t|\vec{x}_t) = \frac{(\lambda_t \Delta t)^{y_t}}{y_t!} \exp(-\lambda_t \Delta t)
\] (3.1)

where \( \lambda_t \) is the spike rate parameter for the process at time \( t \), \( \Delta t \) is the size of time bins, and \( \vec{x}_t \) is a set of observed stimulus at time \( t \). We used \( \Delta t = 1(\text{ms}) \) to ensure that each bin has at most one spike. The likelihood of observing the entire spike responses is the product of every instantaneous conditional probability because we assumed that two separate spike responses are always independent given the observed stimulus:

\[
p(Y_{1:T}|X_{1:T}) = \prod_{t=1}^{T} \frac{(\lambda_t \Delta t)^{y_t}}{y_t!} \exp(-\lambda_t \Delta t)
\] (3.2)

where \( T \) is the total number of time bins. The spike rate \( \lambda_t \) is the key variable to make this model better predict the SN response. Therefore, we will parameterize \( \lambda_t \) as (2.3) and then fit the model parameter \( \vec{k} \) to the observed data.
\[ \lambda_t = f\left(\vec{k} \cdot g(\vec{x}_t)\right) \]  
(3.3)

\[ f(x) = \ln(1 + \exp(x)) \]  
(3.4)

\[ g(\cdot) = \text{basis function} \]  
(3.5)

The spike rate \( \lambda_t \) is determined by the linear projection of input stimulus \( \vec{x}_t \) into the kernel space \( g(\cdot) \) followed by a nonlinear link function \( f \), which generally makes the spike rate nonnegative at all times. The particular reason to select (2.4) as a nonlinearity function is because \( f \) is always differentiable as well as convex, and it plays an excellent role as a true rectifier. The parameterized likelihood of (2.2) is given by

\[ p(Y_{1:T}|X_{1:T}, \vec{k}) = \prod_{t=1}^{T} \frac{(\lambda_t(\vec{k})\Delta t)^{y_t}}{y_t!} \exp(-\lambda_t(\vec{k})\Delta t) \]  
(3.6)

and the optimal \( \vec{k}^* \) is computed by the maximum likelihood estimation (MLE). In practice, it is more convenient to work with the log-likelihood instead of (2.6) because it is often easier to compute the derivative of a sum of terms rather than the product. Also, the log-likelihood achieves its maximum at the same points as the original likelihood because the logarithm is a monotonically increasing function.
\[
\log p(Y_{1:T}|X_{1:T}, \bar{k}) = \sum_{t=1}^{T} y_t \log \lambda_t(\bar{k}) - \sum_{t=1}^{T} \lambda_t(\bar{k}) \Delta t \tag{3.7}
\]

\[
\bar{k}^* = \arg \max_{\bar{k}} \log p(Y_{1:T}|X_{1:T}, \bar{k}) \tag{3.8}
\]

The log-likelihood (2.7) has a nice property in that it is guaranteed to be a concave function of the parameter \( \bar{k} \) if the following two conditions are satisfied [6]:

- The link function \( f \) is convex.
- \( \log f \) is a concave function.

The concavity of log-likelihood implies that \( \hat{k} \) of (2.8) is the optimal estimate. The detailed model will be discussed in the next section.
3.3 Generalized Linear Model

The first step is to associate the grid cell response with the observable stimulus. Grid cell firings are typically modulated by the preferred locations of a single cell, and also preferred head directions especially in deeper layers of EC [7, 8]. Thus we parameterized the spatial tuning curve as a bivariate normal distribution of no correlation between $x$ and $y$ coordinates, and the directional tuning curve as a cosine function (see Figure 3.2).

![Figure 3.2: Cascade stimulus filter model. The input stimuli $X$ is projected to the stimulus filter, a series of spatial and directional tuning curves, and the grid cell response $Y$ is generated from the spike intensity ($\lambda_t$) tailored by the nonlinear function $f$.](image)

The spike rate $\lambda_t$ as a cascade sum of these stimulus filters is given by

$$
\lambda_t = f \left( \sum_\alpha k_\alpha \cdot g_\alpha(\vec{p}_t) + \sum_\beta k_\beta \cdot g_\beta(\theta_t) \right)
$$

(3.9)

$$
= f \left( \sum_\alpha k_\alpha \cdot \exp \left[ \frac{||\vec{p}_t - \vec{\mu}^*||^2}{-2\sigma^2_\alpha} \right] + \sum_\beta k_\beta \cdot ||\vec{v}_t|| \cos(\theta_t - \theta^*_\beta) \right)
$$

(3.10)

where $\vec{p}_t$ is the rat’s position at time $t$, $\theta_t$ is the head direction at time $t$, $\sigma$
represents the standard deviation of a spatial tuning curve width, $\mu^*$ is the most nearby preferred location relative to $\vec{p}$, and $\theta^*$ is the preferred head direction of a recorded cell. $\mu^*$ is predetermined by the template matching algorithm and regarded as a constant term.

This model which encodes only observable stimuli, however, is limited to accurately model the real grid cell response because neurons display a variety of nonlinear effects. Moreover, the nonlinear rectification function $f$ is not able to make the firing rate saturate at some discharge rate. Henceforth we expanded the cascade model by adding the spike history filter (see Figure 3.3). Spike history model aims to regulate the firing rate through the feedback of past spike history.

![Figure 3.3: Spike history model. Spike history filter constitutes a feedback loop to enforce the neural adaptation.](image)
The history filter can be constructed from the sum of exponential decay functions with different time constants [9], and the modified spike rate is given by

\[
\lambda_t = f \left( \vec{k}_{\{\alpha, \beta\}} \cdot g(\mathbf{x}_t)^{\{\alpha, \beta\}} + \sum_{\gamma} k_{\gamma} \cdot \left\{ \sum_{n:t^n < t} \exp \left[ -\frac{(t - t^n)}{\tau_{\gamma}} \right] \right\} \right) \tag{3.11}
\]

where \( \vec{k}_{\{\alpha, \beta\}} \) and \( g(\mathbf{x}_t)^{\{\alpha, \beta\}} \) are the integrated set of parameters and kernels from (2.10), \( t^n \) is the spike times that preceded the present time \( t \), and \( \tau_{\gamma} \) is the decay time constant. The spike rate is simplified to (2.12) and it still has the same form with (2.3), which leads to solve the original maximum likelihood (ML) problem (2.13).

\[
\lambda_t^{\{\alpha, \beta, \gamma\}} = f \left( \vec{k}^{\{\alpha, \beta, \gamma\}} \cdot g(\mathbf{x}_t)^{\{\alpha, \beta, \gamma\}} \right) \tag{3.12}
\]

\[
\mathcal{L} = \sum_t y_t \log \lambda_t^{\{\alpha, \beta, \gamma\}} - \sum_t \lambda_t^{\{\alpha, \beta, \gamma\}} \Delta t
\]

\[
\vec{k}^* = \arg \max_{\vec{k}} \mathcal{L} \tag{3.13}
\]

Here the dimension of the parameter space in this model is relatively high (\( \dim(\vec{k}) = n(\alpha) + n(\beta) + n(\gamma) \)). However, it should be noted that the over-fitting is more likely to occur as the dimensionality of the parameter
space increases. Moreover, sparse solution is preferable to better interpret the informative attributes. This consideration led to exploit the L1-norm regularization to automatically select the dominant basis function by penalizing every coefficient of $\vec{k}$ equally. The regularized log-likelihood function is as follows:

$$L_{\text{reg}} = \sum_t y_t \log \lambda_t - \sum_t \lambda_t \Delta t - \rho \cdot \|\vec{k}\|_1$$

(3.14)

where $\rho$ is a regularization parameter. The way to find out the optimal regularizer $\rho^*$ will be discussed in the Appendix.
3.4 Simulation I: Velocity Gain

In this section, we will investigate how the strength of velocity modulation changes when the spatial grid response is resized by fitting the regularized GLM to the simulation data set generated from the continuous attractor model.

3.4.1 Data Generation

Given the well-controlled pseudorandom velocity inputs, we simultaneously recorded four different cells that have a distinct preferred direction (W, N, S, E) from the population network of the continuous attractor model (see Figure 3.4). The preferred directions were restricted to these 4 directions in modeling. In the first trial, the gain of the velocity response was fixed with

![Figure 3.4: Schematic data generation procedure based on the continuous attractor network. Four simultaneously recorded cells are distinguished by 4 different colors (blue, green, red, yellow).](image-url)
the same value over all population neurons, while we increased the velocity gain for N and S directions in the second trial. As we expected, the grid cell’s spatial response in the second trial was contracted along the same direction of increased velocity gain.

3.4.2 GLM Analysis

Now we have two different sets of spike trains of 4 simultaneously recorded grid cells obtained in different conditions. Given the 20 minute long animal’s trajectory, the beginning 80% of data was assigned to the training set and the rest 20% to the test set.

![Figure 3.5](image)

Figure 3.5: Left: Log-likelihood score obtained from the training set as a function of the log-scaled regularization parameter (blue). Every solid dot represents the time when the number of nonzero coefficients increased. Right: The same plot computed from the test set (red). The likelihood score starts to decrease at one regularization value. It implies the over-fitting of the model and the corresponding penalty is considered to be an optimal regularization parameter.
Regularization path algorithm helps choose a penalty in (2.14) that avoids over-fitting by starting with $\rho = \rho_{\text{max}}$, which is large enough to suppress all coefficient $\vec{k}$ into zero [10]. As the regularization parameter $\rho$ is decreased, more and more non-zero coefficients will be survived, and the fitted model will start to over-fit the data from the critical point $\rho^*$ (see Figure 3.5). From the estimated $\vec{k}^*$, we could reconstruct one of the stimulus filters in the spike history model, which is the directional tuning curve. The amplitude of the estimated directional tuning curve was close to each other across all simultaneously recorded cells when the SN response is of no resizing. However, the GLM could capture the escalation of velocity gain as well in the cells showing the same preferred direction with the contracted direction (see Figure 3.6).

Figure 3.6: Estimated directional tuning curves from simultaneously recorded four distinct cells that have different directional preferences.
3.5 Simulation II : Effective coupling

In the continuous attractor model, the recurrent feedback plays the most essential role in generating regular firing pattern. Thus, we will verify whether or not any interneuronal interaction does improve the model prediction of grid cell responses.

3.5.1 Coupling Model

To take account of the interaction between simultaneously recorded cells, the coupling filter was adjoined to the previous spike history model (see Figure 3.7). It is expected to clarify how strongly two cell are connected, or whether the connectivity is excitatory or inhibitory.

Figure 3.7: Coupling model. Two cells are connected each other through the coupling filter.
The coupling filter is generated from the linear combination of exponential decay functions same as with the history filter. Thus the spike rate $\lambda_t$ is modified as follows:

$$
\lambda_t^i = f \left( \vec{\kappa}_{(\alpha,\beta,\gamma)} \cdot g(x_t^i)^{\{\alpha,\beta,\gamma\}} + \sum_{\eta} k_{\eta} \cdot \left\{ \sum_{n: t_n^j < t} \exp \left[ -\frac{(t - t_n^j)}{\tau_{\eta}} \right] \right\} \right)
$$

(3.15)

where $\lambda_t^i$ is the spike rate of $i$th neuron at time $t$, $t_n^j$ is the past spike time of $j$th (neighbor) neuron, and $\tau_{\eta}$ is the time constants for the coupling filter. Even though the additional term was added into the firing rate equation, the formula of log-likelihood function remains unchanged, which is the simple but nice property of the generalized linear model.

### 3.5.2 GLM Analysis

In this simulation, we fixed and recorded a single cell as an input $X_1$ in the model while simultaneously recording neighboring cells as an input $X_2$, of which preferred directions are equal to each other, but phases in the cortical sheet are all different (see Figure 3.8 left). After fitting the coupling model into the all cell pairs, we could obtain the shape of estimated coupling filters. Interestingly, most of the coupled neurons provided the main cell with the inhibitory inputs, which is consistent with the synaptic weight used in the original continuous attractor model. Furthermore, we could imagine the
shape of connectivity strength looks like a Mexican hat function that was also included in the attractor model (see Figure 3.8 right).

![Figure 3.8](image)

Figure 3.8: Left: Simultaneously recorded cells (red and blue squares) from the simplified population network (grey lattice). Middle: Coupling model. Right top: The estimated coupling filters from different cell pairs that are distinguished by the color. Right bottom: Connectivity strength as a function of the phase of neighboring cells relative to the main cell.

We also compared the predictability of coupling model (CM) with the simple cascade stimulus model (CSM). The estimated spatial response of the test set from CM (Fig 3.9-A2) was reasonably similar to the original grid cell response (Fig 3.9-A3), while the predicted SN response from CSM (Fig 3.9-B1) showed more diffusive spatial fields (Fig 3.9-A1). The better prediction of the coupling model could be confirmed by the comparison of log-likelihood scores between two models (Fig 3.9-C). These results imply that the statistical
correlation between neurons strongly contributes to generate the regular grid cell response.

Figure 3.9: (A1-A2) Predictions of grid cell response from two different models (B1 and B2). (A3) The real grid cell’s spatial response. (B1) Cascade stimulus model (CSM). A stimulus filter consists of the cascade sum of spatial and directional tuning curves. It is followed by the nonlinear function which tailors the spike rate. (B2) Coupling model (CM). The expanded model by employing effect of the neural adaptation and the interaction of neighbored cells. (C) Maximum likelihood scores of two models (B1 and B2).
Chapter 4

Conclusion and Future Work

We analyzed the spike trains of multiple simultaneously recorded grid cells obtained in resized familiar environments and the novel environment so as to assess the role of recurrent network feedback and continuous attractor dynamics in generating grid responses. High stability of relative phase despite the large changes in single-neuron grid patterns in both experiments strongly suggests the presence of a low-dimensional continuous attractor in the dynamics.

We also proposed more active strategy to figure out the main determinants of grid cell responses, and to verify the mechanism of deformation in grid cell spatial responses through the generalized linear model (GLM). The generative model demonstrated its capability to correctly estimate the spatial and directional tuning curve as well as the unobserved physiological characteristics, therefore, we will apply the proposed GLM to the real experimental data explored in the first chapter so as to verify the relationship between the velocity gain and the expansion or contraction of the SN response.
Appendix
Appendix 1

Coordinate Descent Algorithm

Here is the mathematical details to solve the L1-regularized GLM problem. The ordinary log-likelihood $L$ as a function of the parameter vector $\Theta$ is given by

$$L = \sum_t y_t \log \lambda_t - \sum_t \lambda_t \Delta t \quad (1.1)$$

The goal is to minimize the negative L1-regularized log-likelihood $R$

$$R = -L + \rho ||\Theta||_1 \quad (1.2)$$

We approximate $R$ with $R_Q$, the quadratic Taylor expansion of $R$ to apply Newton’s method in optimization

$$R_Q = -L_Q + \rho ||\Theta||_1 \quad (1.3)$$

The gradient of $R_Q$ with regard to the coordinate $j$ is given by

$$\frac{\partial R_Q}{\partial \theta_j} = -L'(\tilde{\Theta}) - L''(\tilde{\Theta})(\theta_j - \tilde{\theta}_j) \pm \rho$$

$$= -\sum_t x_j^t e^{\tilde{\Theta}x^t} \left( \frac{y_t}{\lambda_t} - \Delta t \right) - \sum_t \frac{(x_j^t)^2 e^{\tilde{\Theta}x^t}}{(1 + e^{\tilde{\Theta}x^t})^2} \left( \frac{y_t (1 - e^{\tilde{\Theta}x^t})}{\lambda_t^2} - \Delta t \right) (\theta_j - \tilde{\theta}_j) \pm \rho$$

$$= s_j \theta_j + w_j \pm \rho \quad (1.4)$$
This is a linear function with positive slope, and a discontinuity at $\theta_j = 0$. Therefore, we can update each coordinate by the following three decision rules. We repeat this update step on all parameters until convergence.

Figure A1. The next estimate of parameter $\theta_j$ is determined by the above three criteria.
Bibliography


Vita

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