Dynamics of Stimulus Selectivity in Inferotemporal Neurons

Lulin Dai,*, # Jun-ya Okamura,* Gang Wang*

Abstract  Neuroscientists usually investigate stimulus selectivity by using a stimulus set and identifying the stimulus that evokes the largest electrophysiological responses averaged over a certain time period. However, the visual environment, and hence the brain activity, changes all the time. A method with sufficiently high temporal resolution for the investigation of dynamic changes in stimulus selectivity is desired. Here, we propose a method by dividing the usual time window for spike rate calculation into multiple smaller time windows. We applied this method to the analysis of temporal change in stimulus selectivity of inferotemporal (IT) cells in macaque monkey recorded previously using microelectrode while they were performing an object discrimination task, in which one object had to be discriminated from others regardless of change in viewing angle. The IT cortex is located at the last stage of the ventral cortical pathway, and is important for object recognition and discrimination. The proposed method theoretically possesses temporal resolution in millisecond order. We demonstrated its ability by following the changes in stimulus selectivity with temporal resolution as high as 20 ms. Furthermore, we divided the response time window into early phase and late phase. In each phase, single cell responses to images (4 objects × 4 views; 16 images in each of the stimulus set) were compared to identify the stimulus evoking the largest response. When comparing the early and late phases, 40% of the cells showed the largest response to the same stimulus (same object and same viewing angle); 13% of the cells showed the largest response to the same object but at different viewing angles; 20% of the cells showed the largest response to different objects at the same viewing angle; and 20% of the cells showed the largest response to different objects at different viewing angles. The dynamic change of stimulus selectivity from early phase to late phase may provide important information about the underlying neuronal mechanism for object recognition. Successful application of the proposed method to the analysis of IT cell activity demonstrates the validity and usefulness of the method.

Keywords: stimulus selectivity, temporal resolution, inferotemporal neuron.

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1. Introduction
Neurons in the visual cortex which have stimulus selectivity respond more strongly to stimuli with some features than others. In the pioneer works of Hubel and Wiesel [1, 2], they investigated stimulus selectivity by identifying the stimulus that evokes the largest electrophysiological responses in a certain stimulus set. Averaged spike rate during stimulus presentation is used conventionally to evaluate the responses of the cell to the stimulus. However, such averaging is usually conducted over several hundred milliseconds, which cannot be used to follow the rapid changes in brain activity. To evaluate the dynamics of stimulus selectivity in single cells, an analysis method with higher temporal resolution is necessary.

Information on object or face shape and color is represented and processed in the ventral cortical stream that starts from the primary visual cortex extending to the inferotemporal (IT) cortex. As the temporal association area, IT cortex is the final cortical area for pure visual information representation and processing [3–5] in the monkey brain. Organization and functions of IT have been studied extensively. Compared with other cells in the early visual areas of the ventral cortical stream, IT
cells possess stimulus selectivity to relatively complex object features [5]. Before evaluation of stimulus selectivity using the averaged spike rate, the temporal property of response is first accessed by the amount of information [6]. By computing the amount of information in small time segments, several studies have examined the temporal property of information encoding. Calculation of information carried by single units every 50 ms has shown that global information is conveyed faster than fine information [7]. Information about multipart configuration is conveyed later than information about single part [8]. The information index correlations negatively with the sharpness of stimulus selectivity. They are different measures. Stimulus selectivity in the initial phase of responses of IT cells to object or face stimuli demonstrates broader tuning than that of the late phase [9]. We previously analyzed temporal change of correlation coefficient (r) between the population activities in response to two different stimulus images, and evaluated neural distance by subtracting r from 1. We found that after acquiring discrimination experience of similar objects across viewing angles, the neural distance (1 – r) of the populations of the IT cells between the same objects were significantly smaller than those between the different objects at viewing angle differences of up to 90° [10].

Our previous results depended on the counts averaged over the entire 500 ms period for stimulus presentation. However, the optimal stimulus evoking the largest spike rate among the stimulus set changed temporally. We propose here a new perspective of analyzing the dynamics of stimulus selectivity by examining the change of optimal stimulus evoking the largest spike rates among a stimulus set, in different time periods.

2. Method proposal

We investigate the dynamic change of single cell stimulus selectivity by dividing the usual time window for spike rate calculation into a combination of smaller time windows (ST windows) to increase the temporal resolution.

2.1 Approaches

After pooling all the responses of a single cell to all the stimuli in a stimulus set, we divided the procedure into two steps to evaluate the change of stimulus evoking the largest spike rates of the cell. First, we separately calculated the average spike rate in each of the ST windows. Then, the stimulus evoking the largest spike rates among the stimulus set was identified for every ST window by comparing the spike rates across all the stimuli in the stimulus set.

2.1.1 Evaluating responses in a series of ST windows

The responsiveness of a stimulus is usually evaluated by comparing the spike rates before and after its presentation. To achieve sufficiently high temporal resolution, the time window for averaging was separated into ST windows. Depending on the experiment setting, the extracellular electrophysiological activity is usually sampled at a sampling frequency of 1 kHz or higher. Considering the time course of action potential, which usually lasts 1–2 ms, we counted the average spike rates before and after presentation of each of the stimuli in the stimulus set, for each cell in every ST window.

2.1.2 Evaluating the change of the stimulus evoking the largest spike rates within a stimulus set

Aligning the time windows with stimulus presentation, we compared the spike rates for each ST window across all stimuli in the stimulus set. In this way, we identified the maximum spike rate across all stimuli in the stimulus set, for each ST window. In some cases, the moving average could be helpful to achieve better sharpness of output. The change in the optimal stimulus could be assessed by examining the change in optimal stimulus in the series of time windows.

3. Application

The proposed method was applied to analyze the dynamics of the changes of the stimulus evoking the largest responses in single IT cells after extensive object discrimination learning. The data used here was obtained in our previous experiments [10–12], in which we created object sets and familiarized the monkeys with object images in the Object task before electrode recording.

3.1.1 Animal, stimulus image sets and task

Details of data collection have been described previously [11, 13]. Briefly, recording was conducted on two male macaque monkeys (Macaca fuscata). All procedures were performed in accordance with the National Institute of Health Guide for the Care and Use of Laboratory Animals. The experimental protocols were approved by the Ethics Committee of Laboratory Animal Care and Welfare, Kagoshima University.

Details for object creation have been described in detail previously [13]. Briefly, for each object image set, four objects were created from a three dimensional prototype by changing the parameters defining the shape of the object in different ways using three-dimensional graphics software (Shade 9; e-frontier, Tokyo, Japan). Four views of each object were obtained by rotating the object at 30° intervals around an axis perpendicular to the visual axis between the viewer’s eyes and the object. Each object set consisted of 16 images (4 views × 4 ob-
An example is shown in Fig. 1a. Different object sets were generated from distinctly different prototypes. The average size of the object image was 6.5° of visual angle.

We trained the monkeys to perform the Object task (Fig. 1b) so that they acquire prior experience with the object images before electrophysiological recording. In the task, the monkey started a trial by pressing a lever placed in front of it. After continuously pressing the lever and fixating at a fixation spot for 500 ms, image of the first object appeared, followed by two to five images of the same object in different view angles in random order. Then, a different object was presented. Both stimulus presentation time and inter-stimulus interval were 500 ms. The monkey had to signal the change in object by releasing the lever and ignore the changes in view of the same object by keeping the lever pressed. The task required the association across different views of each object.

Electrophysiological recording of the IT cortex using tungsten electrodes (FHC, Bowdoinham, ME, USA) was conducted after the monkey’s performance plateaued. The recording sites were determined with reference to MRI images. The sites were the ventrolateral regions of the IT cortex, lateral to the anterior middle temporal sulcus. The sites were located 16 to 19 mm anterior to the ear canal in one animal, and 15 to 17 mm in the other. Peri-stimulus time histograms (PSTH) averaged over stimulus repetitions for each stimulus image in an object set are shown in Fig. 2. Responses of a total of 942 cells recorded from four hemispheres of two monkeys were used for analyses.

### 3.1.2 Evaluating change of stimulus selectivity

Figure 3a demonstrates PSTH averaged over all cells from one monkey. In response to the presentation of stimulus, spike rate started to increase at 100 ms, and peaked at 150 ms. We plotted the differences between the spike rates in two consecutive bins (Fig. 3b). The spike rates decreased after the peak, and increased again at 280 ms. In the current study, to quantitatively evaluate the change in stimulus selectivity, we divided the response period into an early phase of 100 to 280 ms and a late phase of 280 to 660 ms. We also conducted analysis in ST windows of 20 ms each. The response magnitude was determined as mean spike rate for each time window minus the spontaneous spike rate measured over a 400-ms period immediately preceding the stimulus onset. Only neurons showing significant difference ($p < 0.05$, Wilcoxon signed-rank test) in spike rate were included in the present study.

### 4. Results

#### 4.1 Electrophysiological responses of single cells to the stimulus images in a stimulus set

Each IT cell usually responded differently to the 16 images in an object set. Responses of one IT cell are shown
in Fig. 2. The responses demonstrated large differences between the 16 stimulus images. View 0 of object 3 evoked the largest response. The responses to some images of objects 2 and 4 remained relatively significant, but there was almost no response to some other images; for example, all views of object 1. In addition to the difference across the responses to different stimulus images, we also observed a change in spike rate in response to the same image along the time axis. We usually observed a rapid increase in spike rate from 100 ms after stimulus onset, which peaked at about 150 ms. After a rapid decrease thereafter, the spike rate remained relatively high until about several hundred milliseconds after the end of stimulus.

4.2 Changes of the stimulus evoking the largest responses

We divided the response period into an early phase of 100 to 280 ms and a late phase of 280 to 660 ms. The stimulus evoking the largest response among the stimulus set was evaluated in early and late phases separately.

According to the difference in stimuli evoking the largest response among the stimulus set between the early and late phases, we classified the cells into four types (Fig. 4). Type I is defined as a cell showing the largest responses to the same images in the early and late phases. Type II cells showed the largest responses to the same objects but in different views between the early and late phases. Type III cells showed the largest responses to the same views but in different objects between the early and late phases. Type IV cells showed the largest responses to different objects in different views between the early and late phases.

Figure 5 shows the distribution of the cells. Type I cells constituted 40% of all cells. Type II cells constituted 13%. Type III and type IV cells constituted 20% and 27%, respectively.

4.3 Analysis of the dynamics in changes of the stimulus evoking the largest responses with higher temporal resolution

The stimulus evoking the largest response among the stimulus set was assessed for every 20 ms bin (Fig. 6). As shown in the example in Fig. 6, the type I cell showed the largest response to the same stimulus across almost
all time periods. Even in the 20-ms time window, the stimulus evoking the largest response (30-degree view of object 4) among the stimulus set remained almost unchanged. The type II cell showed the largest responses to different views of the same object (object 1) in most time periods after reaching a peak in spike rate. The type III cell showed the largest responses to the 90-degree views of different objects in most bins. Type IV cells showed the largest responses to different objects and different views.

5. Discussion

In the present study, we propose a perspective that provides higher temporal resolution to evaluate the dynamics of the changes in the stimulus evoking the largest response among the stimulus set. To demonstrate its use, we applied this method to the analysis of the change in the stimulus evoking the largest response in IT cells. We separated the time period into an early phase of 100 to 280 ms and a late phase of 280 to 660 ms. As demonstrated in Fig. 5, this method provides a tool to measure the dynamics of the changes in the stimulus evoking the largest response in a series of ST windows.

We applied this method to the analysis of IT cell activity in the current study. The stimulus set consists of different views of different objects. Visualization of the change in the stimulus evoking the largest response may be applicable to other studies in which it is necessary to evaluate the dynamics of the changes in the stimulus evoking the largest response among the stimulus set. Comparisons between the signals in different time periods of the responses have been discussed previously [7–9, 14, 15]. Global categorical information such as monkey faces, human faces, or shapes was conveyed in the early time period, while fine information such as identity or facial expression was conveyed in the late time period [7, 14]. For shape, information about individual parts is integrated in the early time period, while information about specific multipart configurations is integrated in the late time period [8, 15]. By following the stimulus evoking the largest response among the stimulus set, the current study provides a perspective to study dynamic changes of the optimal stimulus in the response time course of IT cells.

Type I cells constitute the largest percentage of all the IT cells. A large percentage of cells retained similar stimulus selectivity over the whole response time course. Interestingly, we also identified type II and type III cells.
The stimulus selectivity of type II cells changed but the change was limited to the views of the same object. On the other hand, the stimulus selectivity of type III cells changed for different objects of the same view. The difference in property of type II cells from that of type III cells should be important in the establishment of view-invariant object recognition, since object discrimination across views requires generalization across views of the same object, and at the same time differentiation across objects.

Although artificial intelligence has advanced rapidly, the brain works much smarter than “machines”. Yet, despite the impressive knowledge for other aspects of the human body, the brain remains largely unknown. One of the most difficult and challenging aspects is to understand the meaning of activity dynamics. Our method demonstrates a way to observe one aspect of dynamics at the level of single cell stimulus selectivity. It should be helpful to build a complete picture of the neural mechanisms of object recognition, which is expected to contribute to the development of new machine learning algorithms or techniques in computer vision.

6. Conclusion

Understanding the neuronal basis of brain functions such as visual object recognition is one of the goals for neuroscience researchers. In most cases, scientists investigate the response selectivity of cells to determine their involvement in information processing when presented with an external stimulus. In the present study, we proposed a method to demonstrate dynamic changes in stimulus selectivity, and successfully applied it to the analysis of IT cell activity, which is a promising novel tool in the research of neuronal activity.

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Lulin Dai
Ms. Lulin Dai received her MS degree from Graduate School of Medicine, Central South University, China, in 2013. She is currently a student pursuing a PhD degree in Faculty of Engineering, Kagoshima University. Her research interests include biological psychiatry, neural information processing and deep brain stimulation.

Jun-ya Okamura
Dr. Jun-ya Okamura received his PhD. from Kyushu University, Japan. He is currently an assistant professor in Department of Information Science and Biomedical Engineering, Kagoshima University. His research interests include biomedical engineering, neuroscience, and neural information processing.
Gang Wang
Dr. Gang Wang received his PhD degree from Graduate School of Medicine, Kagoshima University, Japan, in 1993. He is currently a professor in Faculty of Engineering, Kagoshima University. His research interests include bio-signal processing, neural information processing and modeling.