EXTRACELLULAR RECORDING FROM MULTIPLE NEIGHBORING CELLS: RESPONSE PROPERTIES IN PARIETAL CORTEX

John S. Pezaris[1], Maneesh Sahani[1,2], and Richard Andersen[1,2]

[1]Computation and Neural Systems
[2]Sloan Center for Theoretical Neurobiology
California Institute of Technology
Mail Code 216-76,
Pasadena, CA, 91125

ABSTRACT

Multiple single unit extracellular recordings were made using tetrodes in macaque posterior parietal cortex while the animal was performing a visual memory saccade task. Recordings were made over a 2×2 mm area at both superficial and deep locations in one hemisphere. Signals were analyzed using an Expectation-Maximization algorithm for spike separation based on spike peak height or the first two principle components of spike shape. 27 sites were selected for analysis based on task response and clarity of separation, yielding 85 total neurons with a mode of 3 cells per site. The response criteria and stereotaxic location used were consistent with identifying neurons within the lateral intraparietal area (LIP).

For cells within the set of selected sites, responses to the task were further categorized based upon spatial characteristics (preferred direction) and temporal characteristics (time of maximal response). Neighboring cells were found to be very likely to have similar tuned direction (75% within one octant), but not comparatively likely to have similar temporal characteristics. We take this as evidence that area LIP is heterogeneous at the local level.

INTRODUCTION

Neighboring cortical cells are known to have similar inputs, often synapse locally onto each other, and yet do not necessarily compute identical outputs. By examining simultaneously recorded single-unit activity from neighboring cells, we are able to observe their response to stimuli, while also examining the level of intercell interaction, and therefore can explore the circuitry present at the local scale. Specifically, we set out to measure the spatial and temporal tuning differences between neighboring cells in area LIP.

Computational Neuroscience
edited by Bower, Plenum Press, New York, 1998

EXPERIMENTAL METHODS

We trained a rhesus monkey (*Maccaca Mulatta*) to perform the memory saccade task, monitoring his eye position using the scleral coil technique. The task, performed in a darkened room, requires the animal to fixate a centrally-presented light while a peripheral target is flashed in one of eight equally-spaced positions on a 15° radius circle about the fixation point. The animal must remember the location of the target as long as the fixation light is illuminated, delaying the instructed saccade until the fixation light is extinguished. If the saccade is performed accurately, the target is briefly reilluminated, and the animal rewarded with a drop of juice. LIP neural response to this task is characterized by three phases: a sensory response to the target flash, an elevated baseline during the delay period, and a perisaccadic burst during the cued eye motion, often combined with a second sensory response during target reillumination.

To collect neural responses, tetrodes[1] were inserted daily into cortical tissue near the intraparietal sulcus through a chronically maintained craniotomy over the lateral intraparietal sulcus (stereotaxic coordinates 6 mm anterior, 12 mm lateral), using techniques previously described[2,3]. The four tetrode voltages were filtered, digitized, and streamed to digital media while the animal performed the task. These recordings were then analyzed off-line using statistical techniques described by Sahani, *et al*[4,5], and the resulting spike trains pairwise examined for spatial tuning and temporal response profile as described in the following sections. Neurons were considered *neighbors* if they were recorded simultaneously at the same site.

Penetrations were made between 3000 and 10000 μm down from the putative cortical surface, to arbitrary depths (usually every 500 μm along a single penetration). At the sites where an on-line isolation could be made using any single channel of the four tetrode signals with traditional (single-channel) equipment, the animal was run on a block of 100 trials, and the tetrode voltages recorded for later analysis. Sites reported below were further selected for clarity of signal, multiplicity of cells, and either brisk response to the task during the memory phase, or proximity to a previously recorded site with a strong response.

RESULTS

Twenty-seven recordings were selected, with a range of 2 to 6 cells found per recording. Nine (9) sites, or 33%, carried evidence of three cells, the most commonly found number of cells per site. The median was also 3 cells per site. A histogram of the number of sites with a given cell count is shown in figure 1.

Example Spatial Profile

A typical example of spatial tuning over target location is given in figure 2. For each cell, the response is taken as the average number of spikes for the experimentally relevant period of all successful trials for each target direction, and plotted on a polar graph. Consistent with previous reports[6], we find many of the cells recorded express target selectivity within the task response.

Example Temporal Profile

A more detailed example of task response at a single site where three neurons were identifiable is shown in figure 3. The graph depicts the peristimulus time histogram (PSTH) for the target location which evoked the strongest response for this site. The

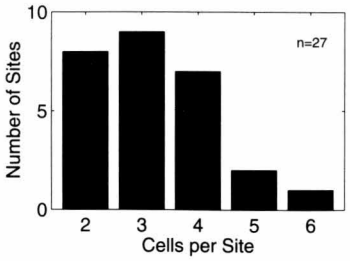

Figure 1. Tetrode recordings in posterior parietal cortex currently yield an average of three cells per tip location in our lab, when selected for task response, multiplicity of cells, and ease of signal separation.

two largest profiles (solid and dot-dashed lines) show typical LIP responses for the memory saccade task: a brief burst of activity in response to the target flash followed by a period of sustained memory activity, and a lesser perisaccadic burst. The third cell (dashed line) has a slower initial response, perhaps even lacking a distinct visual burst, followed by a decaying memory response and no perisaccadic burst.

Spatial Tuning Differences

As introduced above, we extracted the preferred direction for each cell, based on the maximum response elicited for each target location, and the time of maximum response, computed over all targets. Then, comparisons were made between these values for neighboring cells (those which were simultaneously detected in a single recording). The scattergram of preferred direction among pairs of neighboring cells is shown in figure 4. The data cluster around the unit-slope line, suggesting a tendency for neighboring cells to have similar preferred direction. Considering previous single-unit findings on the patchwork nature of LIP[7], outliers on this figure may represent recordings made when the tetrode was situated at the transition between two groups of neurons with distinct clustered preferred direction.

To quantify the similarity of tuning direction, we compute the histogram of differences between directions for neighboring cells, as shown in figure 5. The preferred direction was computed for each cell by considering the response for each target location as a vector in that direction and calculating the vector average of the eight responses. The large majority of pairs of neighboring neurons (75%) have preferred

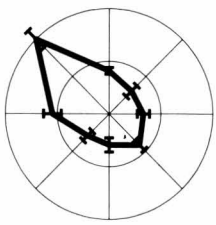

Figure 2. Example polar tuning curve. The task response is computed for a given cell for each target location and plotted in polar form where the radial excursion of the curve represents the magnitude of the response for the corresponding target direction, and error bars denote the standard error. The computed preferred direction is marked with an asterisk.

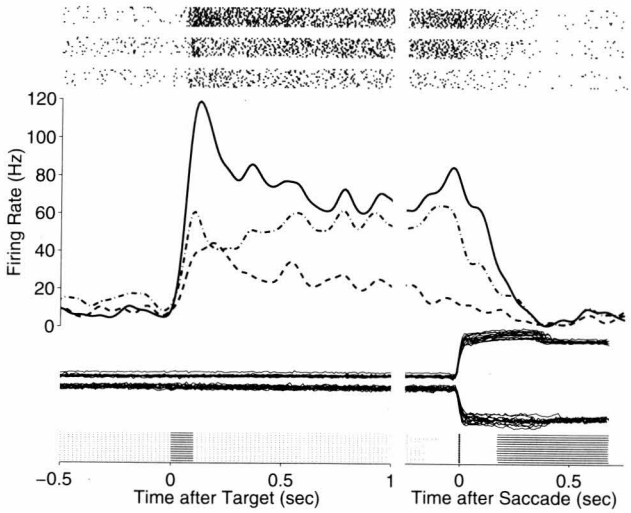

Figure 3. Example neural response to the memory saccade task. The left half of the figure is for a portion of the experimental task aligned to target presentation; the right half is aligned to the saccade. There is a small but varying amount of overlap between the two halves. At the top of the diagram are three rastergrams, separated out by cell; the corresponding rows from each group of rasters are from the same trial. In the middle are the peristimulus time histograms (PSTHs) for the same three cells, binned to 10 ms and smoothed to three bins. The solid line corresponds to the uppermost rastergram, the dash-dotted line to the middle rastergram, and the dashed line to the lower rastergram. Below the PSTHs are eye position traces, vertical position above horizontal position, with the multiple trials overlaid. At the bottom are the behavioral events. The stippled band represents the fixation point illumination, the solid band the represents the target presentation (although not apparent from this diagram, the fixation point continues to be illuminated while the target is flashed), and the sharp vertical line at $t = 0$ on the right half of the diagram represents the time of saccade. (The behavioral bands actually consist of a set of horizontal lines, one for each trial).

directions within $\pi/4$ radians, corresponding to the central cluster of points around the unit-slope line in figure 4.

Temporal Tuning Differences

The response profile of each cell is computed by measuring the firing rate to the preferred target during each of five arbitrary but experimentally relevant epochs: *background* (250 ms before target flash), *visual* (0–250 ms after target flash), *early memory* (250–500 ms post flash), *late memory* (500–1000 ms), and *perisaccadic* (−250–250 ms about the saccade). Plotting the response versus direction for each epoch, we find that neighboring cells vary considerably in the epoch of maximal response. In the example pair shown in figure 6, the upper cell fires most vigorously in the perisaccadic epoch while the lower cell fires most vigorously in the visual epoch, despite their preferred directions (during the epochs of highest response) matching quite well.

We compared the distance in time between epochs of maximal response for neighboring cells and plot the histogram, as shown in figure 7. The temporal response for each cell was computed in five epochs as described above, and the enumerated value of the epoch with maximal response used as the index of temporal tuning. Thus, a cell

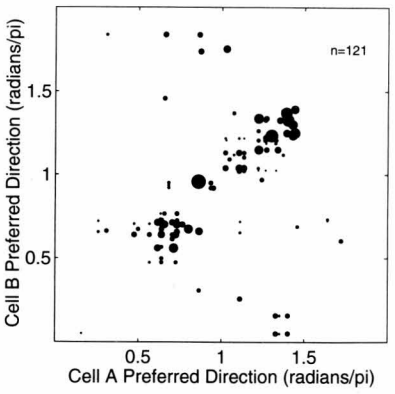

Figure 4. Scattergram of preferred directions for neighboring pairs of cells (A, B). The preferred direction was computed for each cell by taking the vector average of the response for each target direction, and pairwise plotted for neighboring cells. The diameter of each point is proportional to the square root of the product of the magnitude of the maximum responses in each neighboring pair.

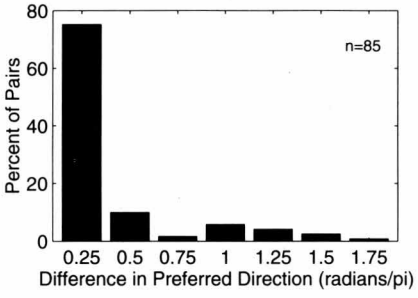

Figure 5. Histogram of differences in preferred direction. The differences in neighboring preferred direction has been binned to octants. The large majority of pairs of cells have similar preferred direction, as indicated by the large leftmost bin.

with strongest response in the visual period would have a temporal tuning of 2, one in the late memory period would have a tuning of 4. The temporal distance between tunings then was computed as the difference in tuning index. While not a rigorous metric, it does serve to show the wide distribution of temporal response peaks between neighboring cells, suggesting the cells have different computational tasks. Fully determining the exact nature of the differences between response types will require significant additional work. The metric used here intended merely to assist a gross determination of similarity among response types: as only 40% of the pairs peak in the same epoch, we conclude that the response characteristics have a broad tendency to be different among neighboring cells.

SUMMARY

We have presented a count of cells recovered per tetrode recording made at arbitrary penetration depths in parietal cortex. Our findings suggest that the tetrode

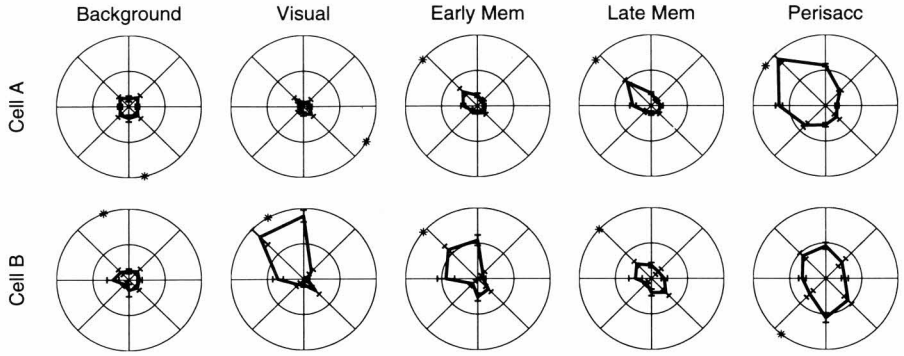

Figure 6. Neighboring cells tend to have less similar response dynamics. Here are normalized tuning curves versus target location for each of the five arbitrarily defined experimental epochs (see main text) for two simultaneously recorded cells. The vertical direction on the polar plots corresponds to the upper target location; the value along each radial arm indicates the neural response to the corresponding target location. Asterisks indicate the computed preferred direction for each tuning curve.

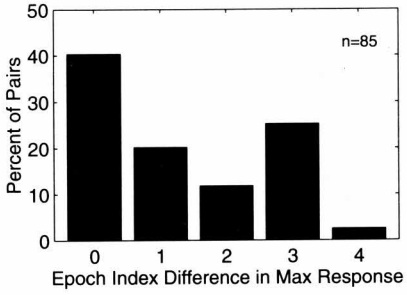

Figure 7. Using the arbitrary segments defined in the text, we determined the epoch of maximal response for each cell, and then measured the difference in epoch index for neighboring cells. The wide distribution of index differences indicates the responses for neighboring cells are not typically identical.

recording technology makes it easy to detect multiple cells per site in monkey cortex. We further examined the spatial and temporal tuning for simultaneously recorded cells and found that such neighboring neurons tended to have similarity in spatial tuning, but dissimilarity in temporal response. We take these results to be evidence for locally heterogeneous circuitry within parietal cortex, specifically area LIP, that carries locally homogeneous spatial selectivity.

ACKNOWLEDGMENTS

This work was generously supported by the Keck Foundation, the Sloan Center for Theoretical Neuroscience at Caltech, the Center for Neuromorphic Systems Engineering at Caltech, the Office of Naval Research, and the National Institutes of Health. The experiments would not have been possible without the assistance of B. Gillikin.

REFERENCES

1. M.L. Recce, and J. O'Keefe, The tetrode: an improved technique for multi-unit extracellular recording, *Society for Neuroscience Abstracts*, 15(2):1250 (1989).
2. J.S. Pezaris, M. Sahani, and R.A. Andersen, Tetrodes for monkeys, *Computational Neuroscience: Trends in Research 1997*, J.M. Bower, ed., Plenum Press, New York (1997).
3. J.S. Pezaris, M. Sahani, and R.A. Andersen, Multiple single unit recording using tetrodes in macaque visual cortex: electrode design and spike identification, *Society for Neuroscience Abstracts*, 21(2):905 (1995).
4. M. Sahani, J.S. Pezaris, and R.A. Andersen, Extracellular recording from multiple neighboring cells in primate cortex, *Neural Networks: from Biology to Hardware Implementations*, Chia, Italy, September 23–27, 1996.
5. M. Sahani, J.S. Pezaris, and R.A. Andersen, Extracellular recording from multiple neighboring cells: a maximum-likelihood solution to the spike-separation problem, *Computational Neuroscience: Trends in Research 1998*, J.M. Bower, ed., Plenum Press, New York (1998).
6. S. Barash, R.M. Bracewell, L. Fogassi, J.W. Gnadt, and R.A. Andersen, Saccade-Related Activity in the Lateral Intraparietal Area II. Spatial Properties, *J. Neurophysiology*, 66(3), (1991).
7. G.J. Blatt, R.A. Andersen, and G.R. Stoner, Visual receptive field organization and cortico-cortical connections of the lateral intraparietal area (area LIP) in the macaque, *J. Comparative Neurology*, 299:421-445 (1990).