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Properties of spike train spectra in two parietal reach areas

Published online: 28 August 2003
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Abstract In the lateral intraparietal area (LIP), a saccade-related region of the posterior parietal cortex (PPC), spiking activity recorded during the memory period of an instructed-delay task exhibits temporal structure that is spatially tuned. These results provide evidence for the existence of ‘dynamic memory fields’ which can be read-out by other brain areas, along with information contained in the mean firing rate, to give the direction of a planned movement. We looked for evidence of dynamic memory fields in spiking activity in two parietal reach areas, the parietal reach region (PRR) and area 5. Monkeys made center-out reaches to eight target locations in an instructed-delay task with a memory component. Neurons in both areas exhibited sustained activity during the delay period that was spatially tuned. Many single cell PRR spectra exhibited spatially tuned temporal structure, as evidenced by a significant and spatially tuned peak in the 20–50 Hz band. The PRR population spectrum of spike trains was also tuned, with the peak power centered on approximately 25 Hz. In contrast, area 5 spiking activity did not exhibit any significant temporal structure. These results suggest that different mechanisms underlie sustained delay period activity in these two areas and that dynamic memory fields, as revealed by our techniques, are more prominent in PRR than in area 5. Temporal structure in the spike train and local field potential (LFP) are related in at least one other brain area (LIP). The present results suggest then that LFP activity obtained from PRR may be better suited than area 5 LFP activity for use in neural prosthetic systems that incorporate analysis of temporal structure as part of a decode mechanism for extracting intended movement goals.

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Keywords Reaching movements · Monkey · Parietal cortex · Temporal structure

Introduction

The term ‘working memory’ refers to the ability to briefly hold and manipulate goal-related information to guide impending actions (Fuster 1980). Neural correlates of spatial working memory are revealed during so-called ‘delayed-response’ or ‘instructed-delay’ tasks in which the spatial location of a transiently presented cue is held in memory for a variable length of time and is then used to guide a particular motor action. Such tasks have shown that neurons in several regions of the brain including the prefrontal and parietal cortices exhibit cue-selective increases or decreases in their mean firing rates that are sustained during subsequent delay periods (Gnadt and Andersen 1988; Funahashi et al. 1989; Snyder et al. 1997; Rainer et al. 1998; Quintana and Fuster 1999). This tuned rate information has been referred to as a ‘memory field’ (Funahashi et al. 1989) and is believed to be important for understanding the neural basis of working memory (Goldman-Rakic 1995). However, it is presently unclear what mechanism gives rise to the selective and sustained activity that is characteristic of memory fields (Durstewitz et al. 2000) and in fact different mechanisms may underlie this activity in different regions of the brain.

Recently Pesaran et al. (2002) reported the presence of ‘dynamic memory fields’ in the PPC, defined as tuned changes in the spectrum of neural activity during a memory period. More specifically, they reported that spike train spectra in LIP exhibited spatially tuned temporal structure, as evidenced by a significant and spatially tuned peak in the gamma band at 50 Hz. Such activity could conceivably be ‘read-out’ by other brain areas, along with rate information, to give the direction of a planned saccade. The parietal cortex also contains several reach-related subdivisions (Caminiti et al. 1996; Marconi et al. 2001) and although some of these regions have been shown to exhibit rate-based memory fields

(Snyder et al. 1997; Batista et al. 1999; Buneo et al. 2002) it is presently unknown whether dynamic memory fields exist in these areas as well. Such fields could be used along with rate information to decode the direction of a planned reach.

Local field potential (LFP) activity in LIP also exhibits spatially tuned temporal structure, as evidenced by the existence of significantly elevated spectral power in the gamma frequency band (25–90 Hz). LFP activity reflects the movement of extracellular currents arising from the activation of a local neuronal ensemble and is easier to record than spiking activity, particularly over long time intervals (Mitzdorf 1985). These observations suggest that LFP activity obtained from reach-related subdivisions of the PPC, if also temporally structured and spatially tuned, could be used in neural prosthetic systems to predict the endpoint of a planned movement (Pesaran et al. 2002). LFP activity is not routinely recorded in monkey neurophysiological experiments. However, LFP activity and spiking activity are coherent in the gamma frequency band in LIP, indicating that temporal structure in spiking and LFP activity are related in this area and perhaps in other areas as well. Thus, identifying the presence or absence of spatially tuned temporal structure in spiking activity obtained from various reach-related subdivisions of the PPC may indicate which subdivisions are best suited for use in neural prosthetic systems that decode the temporal structure of LFP activity.

Here we present a spectral analysis of spiking activity recorded in the parietal reach region (PRR) and area 5 of the PPC during the memory period of a delayed reach task. We found that the temporal structure of the spiking activity differed between these two regions: PRR spiking activity showed a spatially tuned spectral peak, while area 5 activity did not. This suggests that different mechanisms underlie the sustained delay period activity that is observed in each area. Moreover, the presence of spatially tuned spectral peaks at both the single cell and population level in PRR and the relative lack of these in area 5, suggests that dynamic memory fields are more prominent in PRR. Lastly, the presence of spatially tuned temporal structure in PRR spiking activity suggests that LFP activity derived from PRR may be more useful than area 5 LFP activity as a source of spatial information for neural prosthetic systems.

Materials and methods

Behavioral paradigm

A schematic of the behavioral paradigm is shown in Fig. 1. Head-fixed animals sat 24 cm away from a vertically oriented board of touch sensitive buttons. These buttons were 3.7 cm in diameter and were set 7.5 cm apart. Each button contained both a red and a green light-emitting diode (LED) set behind a translucent window. The red LED instructed the animals where to direct and maintain their gaze while the green LED instructed the animals where to initially place their hands. All trials began with the illumination of the red and a green LED at the center button, located directly in front of the animals at eye level. A green (target) LED at one of the eight

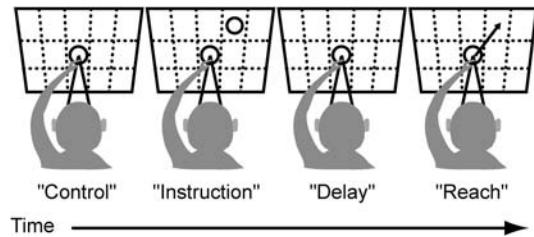


Fig. 1 Schematic of the task

peripheral locations was then briefly illuminated (300 ms duration). After a variable delay period of 600–1000 ms, the LEDs instructing the initial hand location and fixation point were turned off and the animal reached to the remembered location of the target in complete darkness while maintaining fixation. The animal was then rewarded with a small amount of juice. Five trials were performed to each target location in pseudorandom order. Eye position was monitored using the scleral search coil technique. Reaching movements were made with the contralateral (left) arm.

Neurophysiology

All experimental procedures were conducted according to the "Principles of laboratory animal care" (NIH publication no. 86-23, revised 1985) and were approved by the California Institute of Technology Institutional Animal Care and Use Committee. Single cell recordings were obtained from the right hemispheres of two adult rhesus monkeys (*Macaca mulatta*) using standard neurophysiological techniques. Activity was recorded extracellularly with varnish-coated tungsten microelectrodes (~1–2 MΩ impedance at 1 kHz, Frederick Haer & Co.). Single action potentials (spikes) were isolated from the amplified and filtered (600–6000 Hz) signal via a time-amplitude window discriminator (Bak Electronics Inc.). Spike times were sampled at 2.5 kHz.

Recordings were made in both the parietal reach region (PRR) and area 5 of the PPC. The PRR data reported on in this study ($N=87$) were obtained during the same experimental sessions as those reported in Batista et al. (1999). The area 5 data discussed here ($N=88$) were obtained during the same experimental sessions as those reported in Buneo et al. (2002).

Data analysis

Peristimulus time histograms (PSTHs) of the mean firing rate of single neurons were constructed for each target location by smoothing the spike train with a Gaussian kernel ($\sigma = 50$ ms). Population PSTHs were constructed by further averaging the spikes over all neurons and both monkeys. Confidence intervals were estimated from a distribution of PSTHs obtained by bootstrapping over trials (for single cells) or over neurons (for the population) (Efron and Tibshirani 1993).

Single cell and population spectra were calculated from data taken from the delay period of the task. More specifically, only spikes occurring within a 500-ms-long epoch beginning 100 ms after the offset of the reach target LED were considered. During this period, the rate of neural activity is approximately constant so it is reasonable to assume that the process is stationary. Methods for calculating the spectra of time series, and spike trains in particular, are described in detail elsewhere (Percival and Walden 1993; Jarvis and Mitra 2001). In brief, consider a sequence of spike arrival times $\{t_j\}$, $j = 1 \dots N$ in the interval $[0, T]$. The spectrum is evaluated by first taking the modulus squared of the Fourier transform of the data:

$$S^D(f) = \frac{\left| \sum_{j=1}^N e^{-2\pi ift_j} - N \right|^2}{T} \quad (1)$$

The subtraction of N removes the mean from the data. The result is then smoothed with a Gaussian kernel to reduce its variance:

$$S^{LW}(f) = \int_{-\infty}^{\infty} K(f - f') S^D(f') df' \quad (2)$$

This is known as a lag window spectral estimator (Percival and Walden 1993). More sophisticated spectral estimates, e.g. multitaper ones, must be used if the spectrum has a larger dynamic range. This will be the case for most continuous processes (e.g. LFP activity) as well as for some point processes. In the present study, both lag window and multitaper estimators were used but no differences were noted with regard to the main findings of this study. As a result, only lag window estimates are presented. These estimates were averaged over trials and the variance was estimated using a jackknife procedure over trials. Confidence intervals were calculated as described in Jarvis and Mitra (2001).

Results

Neurons in both PRR and area 5 exhibited sustained activity during the delay period of the task that was spatially tuned. Figure 2 shows population PSTHs based on the preferred (—) and non-preferred (···) target locations of individual neurons in PRR and area 5. Note that from 400–900 ms after cue onset (the period used to calculate single cell and population spectra), the mean rate is relatively constant. In addition, even though visual cues signaling the location of reach targets were unavailable during this period, the PSTHs in both areas display a clear spatial tuning. Sustained “memory” activity of this type has previously been observed in both PRR (Snyder et al. 1997; Batista et al. 1999) and area 5 (Buneo et al. 2002).

Figure 3A shows an example PSTH from a single PRR neuron. Spikes occurring in the delay period (indicated by the gray rectangle) were used to calculate the spectrum shown in Fig. 3B. For a Poisson process, i.e. a process in which the spike arrival times are uncorrelated, the spectrum would fluctuate around a horizontal line (λ), which has a value equal to the mean firing rate. Significant deviations from this horizontal line represent temporal structure in the spike trains. The gray lines in Fig. 3B are approximate 95% confidence intervals; thus the small peak at approximately 25 Hz in this example spectrum is indicative of temporal structure in the underlying spike trains.

Peaks in the spike train spectra were more frequently observed in PRR than in area 5. Moreover, these peaks were spatially tuned. Figures 4 and 5 show PRR and area 5 single-cell spectra calculated for the eight different target locations. For the PRR neuron (Fig. 4) there is a large peak in the spectrum in the frequency range of 20–50 Hz when the monkey reaches down and to the left. This is also the target location for which the firing rate was greatest. Another large peak in the same frequency

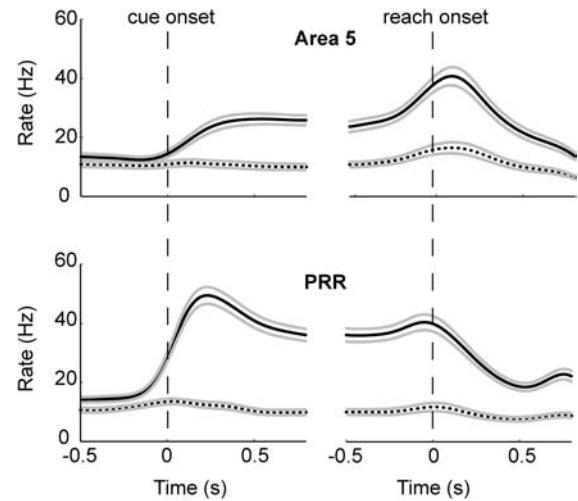


Fig. 2 Population PSTHs from area 5 (top) and PRR, for both the preferred (—) and non-preferred (···) directions. Data are aligned on cue onset (left) and reach onset (right). Gray lines are 95% confidence intervals obtained by bootstrapping over cells

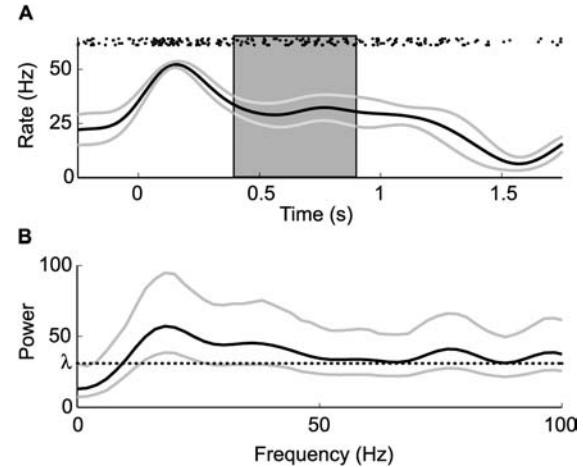


Fig. 3 **A** PSTH from a single PRR neuron for a single target location. Data are plotted from the time of target onset. Spikes occurring during the delay period (indicated by the gray box) were used to calculate the spectrum shown in **B**. **B** Single cell spectrum (—) for the same neuron in **A**. Gray lines are 95% confidence intervals obtained via a jackknife method. λ (···) represents the spectrum that would be obtained if spike arrival times were uncorrelated (i.e. a Poisson process) and has a value equal to the mean rate

band can be seen for a neighboring target location, i.e. when the monkey reaches straight down. No peaks are observed for the remaining six directions. Thus, this neuron exhibited spatially tuned spectral power in the 20–50 Hz band. In contrast, the area 5 neuron (Fig. 5) exhibits spectra for different target locations that do not show any significant deviations from the spectrum expected for a Poisson process. In other words, this neuron did not exhibit spatially tuned power in any frequency band.

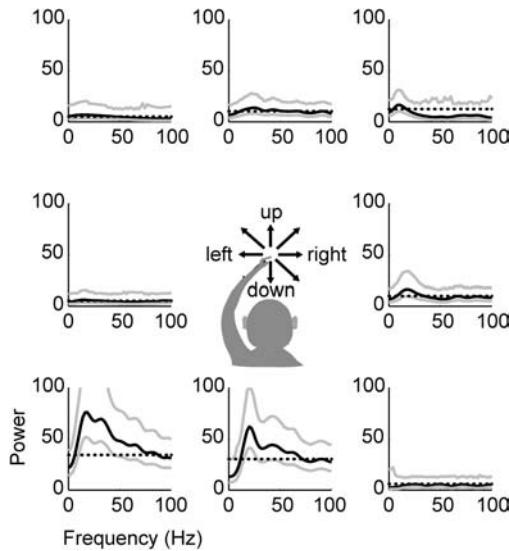


Fig. 4 PRR single cell spectra for eight different target locations. Plot conventions as in Fig. 3B

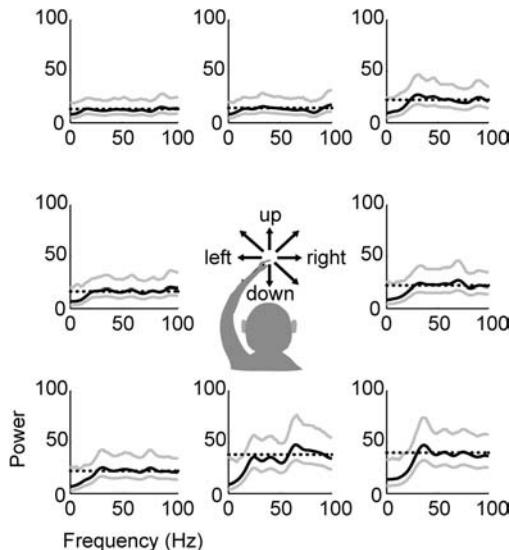


Fig. 5 Area 5 single cell spectra for eight different target locations. Plot conventions as in Fig. 3B

Differences in the spectra of single PRR and area 5 neurons were reflected in the population as well. Figure 6 shows PRR and area 5 population spectra for both the preferred and non-preferred target locations. Two key features can be observed. First, in both areas there is a suppression of the spectrum (below that expected for a Poisson process) at low frequencies. This can be seen in the spectra for both the preferred and non-preferred locations. Assuming renewal, this suppression is consistent with an effective refractory period, one that is slightly longer in timescale than the biophysical one, and corresponds to spike firing being less likely during an interval of about 10–20 ms. Second, in PRR there is a broadband peak in the spectrum for the preferred target

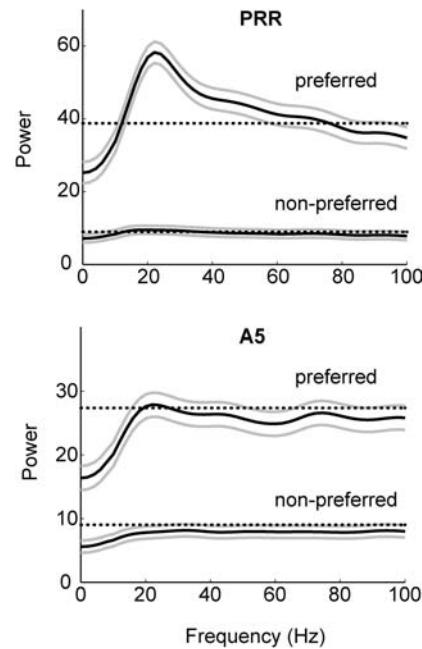


Fig. 6 PRR and area 5 population spectra for both preferred and non-preferred target locations. Plot conventions are otherwise as in Fig. 3B

location that is centered on about 25 Hz. No such peak can be seen in the spectrum for the non-preferred target location. Thus, at the population level PRR exhibited significantly tuned power in the 20–50 Hz band. In contrast, no peaks can be seen in the population spectra for area 5 for either the preferred or non-preferred locations. Thus, spectral power in area 5 is not spatially tuned.

Discussion

The present study demonstrates that spiking activity in PRR, but not area 5, exhibits spatially tuned temporal structure. These results may indicate that different mechanisms underlie the sustained delay period activity that is observed in these areas. The present results also suggest that dynamic memory fields, defined as tuned changes in the spectrum of neural activity during the memory period, are more prominent in PRR than in area 5. Lastly, the presence of spatially tuned temporal structure in PRR spiking activity suggests that LFP activity derived from PRR may be more useful than area 5 LFP activity as a source of input for neural prosthetic systems.

It should be noted that the peaks observed in the spike train spectra in PRR are present regardless of how the spectrum is estimated. As stated in “Materials and methods,” we have used both lag window and multitaper spectral estimators and have observed the same results. In addition, the frequencies of the observed peaks do not appear to be related to the firing rates of the cells. Spectral

peaks are visible in cells with very different firing rates, and are absent in some cells in the non-preferred direction even when the rate is relatively high in that direction. Moreover, the peaks are also observed in the population for PRR when the individual spectra are divided by their mean rates before averaging. These observations indicate that the spatially tuned spectral peaks are a property of spiking activity in PRR.

The spatially tuned spectral peaks observed in PRR can be interpreted as dynamic memory fields (Pesaran et al. 2002). This activity can conceivably be read-out by other brain areas, along with rate information, to give the direction of a planned reach. Areas that might make use of such information include the premotor cortex and primary motor cortex. Both areas receive projections from reach-related areas of the parietal lobe including those in the bank of the intraparietal sulcus (Johnson et al. 1996), where PRR resides. Interestingly, in these areas spiking activity associated with arm movements does exhibit temporal structure under certain conditions (Murthy and Fetz 1996; Donoghue et al. 1998; Lebedev and Wise 2000) and the observed oscillations are in approximately the same frequency band as those observed in PRR (16–50 Hz). In primary motor cortex temporal structure is not consistently related to motor behavior (Murthy and Fetz 1996; Donoghue et al. 1998) and its relation to specific aspects of movement planning such as direction is unclear. However, in premotor cortex temporal structure is present during the performance of instructed-delay reaching tasks and is in fact spatially tuned (Lebedev and Wise 2000). These observations and the results of the present study, which employed an instructed-delay task with a memory component, suggest that spatially tuned temporal structure in spike trains may be a common feature of areas involved in planning arm movements to seen or unseen (i.e. memorized) visual target locations (PRR and premotor cortex), but may be less common in areas more closely tied to movement execution (primary motor cortex, area 5).

Several mechanisms have been proposed to underlie the persistent delay period activity observed in area 5, PRR and other cortical areas including recurrent excitatory connections within a neural network, synfire chains, and intrinsic cellular mechanisms (Hebb 1949; Abeles 1991; Goldman-Rakic 1995; Marder et al. 1996; Wang 2001). The differences in the PRR and area 5 spike train spectra reported here may indicate that a different mechanism gives rise to sustained activity in each area. For example, the observed temporal structure in PRR may indicate that delay period activity in this area arises from a recurrent network phenomenon. Alternatively, the temporal structure could reflect a tendency for PRR neurons to simply fire in bursts (Bair et al. 1994). Evaluation of LFP activity in PRR, presently underway, should shed light on which mechanism gives rise to temporal structure in PRR and in so doing clarify our understanding of sustained delay period activity in this area.

There have been many recent advances in the field of cortical neural prosthetics (Chapin et al. 1999; Fetz 1999; Isaacs et al. 2000; Wessberg et al. 2000; Serruya et al. 2002; Taylor et al. 2002; Shenoy et al. 2003). Although neural activity from a number of cortical regions could potentially serve as a source of input for neural prosthetic systems, several properties of the posterior parietal cortex (PPC) make it a particularly attractive candidate. For example, the PPC is believed to play an important role in visuomotor adaptation (Clower et al. 1996), which could be advantageous for overall system performance by continually adjusting for visual-prosthetic misalignments and counteracting neural sampling biases (Meeker et al. 2002). However, the PPC contains several reach-related subdivisions (Caminiti et al. 1996; Marconi et al. 2001) and it is currently unclear which subdivisions are best suited for use in neural prosthetic systems.

It was recently suggested that using LFP activity rather than spiking activity could accelerate the development of such systems, as LFP activity is easier to record than spiking activity over long time intervals and can be used to decode an intended movement direction with approximately the same accuracy as the spike rate (Pesaran et al. 2002). Since temporal structure in spiking and LFP activity have been shown to be related in at least one cortical area (LIP), the presence of tuned temporal structure in PRR spike train spectra suggests that LFP activity obtained from this area could prove to be a useful source of input for a cortically based neural prosthesis. It should be mentioned that although area 5 spiking activity did not show strong evidence of tuned temporal structure, it is still possible that area 5 LFP activity will show structure, as temporal structure in LFP and spiking activity are not always strictly related (Murthy and Fetz 1996; Donoghue et al. 1998; Frien et al. 2000). Evaluation of LFP activity in area 5 and PRR, presently underway, should provide additional information on the usefulness of both regions as sources of input for neural prosthetic systems.

Acknowledgements This study was supported by the Sloan-Swartz Center for Theoretical Neurobiology, the National Eye Institute, and the Defense Advanced Research Projects Agency (DARPA). We thank Bijan Pesaran and Hansjörg Scherberger for helpful comments. We also thank Betty Gillikin and Viktor Shcherbatyuk for technical assistance, Janet Baer and Janna Wynne for veterinary care and Cierina Marks for administrative assistance.

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