

# Target Detection by Opponent Coding in Monkey Prefrontal Cortex

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## Abstract

■ The pFC plays a key role in flexible, context-specific decision making. One proposal [Machens, C. K., Romo, R., & Brody, C. D. Flexible control of mutual inhibition: A neural model of two-interval discrimination. *Science*, 307, 1121–1124, 2005] is that prefrontal cells may be dynamically organized into opponent coding circuits, with competitive groups of cells coding opposite behavioral decisions. Here, we show evidence for extensive, temporally evolving opponent organization in the monkey pFC during a cued target detection task. More than a half of all randomly selected cells discriminated stimulus category in this task. The

largest set showed target-positive activity, with the strongest responses to the current target, intermediate activity for a nontarget that was a target on other trials, and lowest activity for nontargets never associated with the target category. Second most frequent was a reverse, antitarget pattern. In the ventrolateral frontal cortex, opponent organization was strongly established in phasic responses at stimulus onset; later, such activity was widely spread across dorsolateral and ventrolateral sites. Task-specific organization into opponent cell groups may be a general feature of prefrontal decision making. ■

## INTRODUCTION

The frontal cortex plays a central role in guiding complex, flexible behavior (Miller & Cohen, 2001; Fuster, 1997; Luria, 1966; Bianchi, 1922). In the monkey, prefrontal cells code detailed information bearing on many kinds of behavioral decision (e.g., Freedman, Riesenhuber, Poggio, & Miller, 2001; Romo, Brody, Hernández, & Lemus, 1999; White & Wise, 1999; Sakagami & Niki, 1994; Funahashi, Bruce, & Goldman-Rakic, 1989; Watanabe, 1986a, 1986b).

In recent work (Machens, Romo, & Brody, 2005), opponent coding circuits have been analyzed as a plausible basis for prefrontal decision making. In such a circuit, prefrontal cells are organized into competing groups coding opposite behavioral decisions. In the work of Machens et al. (2005), the task examined was successive comparison of two vibrotactile stimuli, the monkey indicating whether a second, test stimulus was higher or lower in frequency than a first, sample stimulus. Opponent circuits were shown to provide a good account of prefrontal cell activity across the different stages of this task, including sensory responses to each stimulus, stable activity through interstimulus delays, and behavioral choices (Machens et al., 2005; Romo et al., 1999). Dynamic organization of prefrontal cells into opponent circuits may provide a general mechanism for flexible decision making in different task contexts (Machens et al., 2005), consistent with prefrontal coding of alternative behavioral categories in a wide variety of tasks (e.g., Nieder,

Freedman, & Miller, 2002; Freedman et al., 2001; Watanabe, 1986a).

In the vibrotactile comparison task (Machens et al., 2005), opponency in prefrontal coding was analyzed for the sensory continuum of vibration frequency. Evidence for opponent coding came from the finding of two groups of cells, one group with activity monotonically increasing with vibration frequency, the other with activity monotonically decreasing. For such sensory continua, opponency may be widespread in the nervous system; for example, in the same task, similar monotonic responses to stimulus frequency have been reported from secondary somatosensory cortex (Romo, Hernández, Zainos, Lemus, & Brody, 2002) to premotor cortex (Romo, Hernández, & Zainos, 2004). Here, we extended these observations to consider opponency in behavioral categories. For this purpose, we used a sequential target detection task based on previous studies of inferotemporal (Takeda, Naya, Fujimichi, Takeuchi, & Miyashita, 2005) and prefrontal (Kusunoki, Sigala, Gaffan, & Duncan, 2009) cortex. Each trial began with a cue indicating one of three pictures as the current target. The monkey then monitored a series of pictures, withholding response until the target appeared. In randomly selected cells across a large region of dorsolateral and ventrolateral pFC, we recorded responses to three kinds of pictures: current targets (T), nontargets that were targets on other trials (inconsistent nontargets,  $N_i$ ), and nontargets that never served as targets (consistent nontargets,  $N_c$ ). Although in this article we call these “stimulus categories,” they were defined by behavioral significance,

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T stimuli requiring a response on the current trial,  $N_i$  stimuli requiring a response on other trials, and  $N_c$  stimuli never requiring a response. Strong prefrontal response to target stimuli has been previously described in both human (e.g., Hampshire, Duncan, & Owen, 2007; Hon, Epstein, Owen, & Duncan, 2006; Jiang, Haxby, Martin, Ungerleider, & Parasuraman, 2000) and monkey (e.g., Everling, Tinsley, Gaffan, & Duncan, 2002, 2006; Hasegawa, Matsumoto, & Mikami, 2000) studies. In cells responding strongly to T, we predicted weakest response for  $N_c$ , the stimulus least associated to the target category. On the basis of the principle of opponent coding, we searched also for a second group of cells, responding most strongly to  $N_c$  and least strongly to T. Thus, we sought evidence for opposite, dominant patterns of event coding in the prefrontal cell population, examining the overall frequency of such patterns, and their temporal evolution in dorsal and ventral regions.

## METHODS

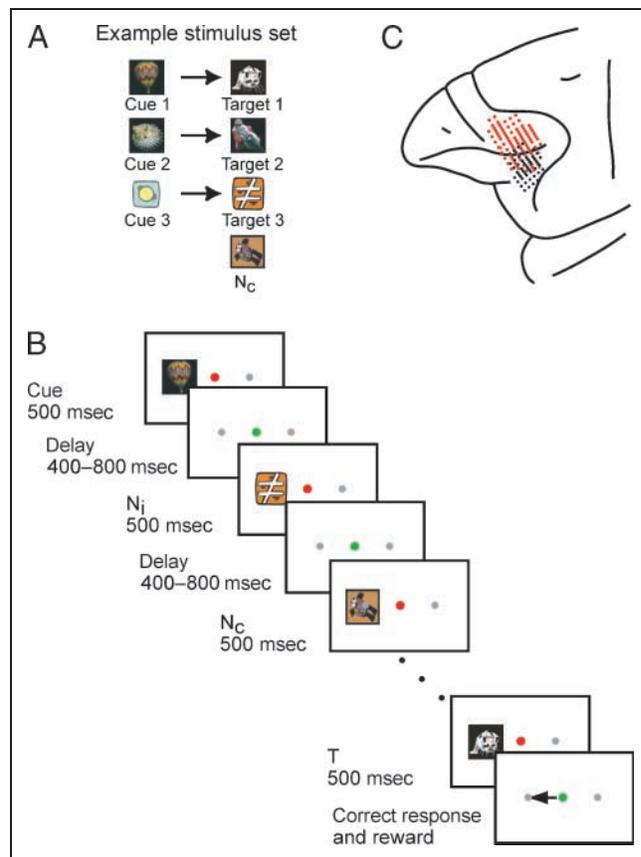
### Subjects

Subjects were two male rhesus monkeys (*Macaca mulatta*) weighing 11 and 12 kg. All experimental procedures were approved by the UK Home Office and were in compliance with the guidelines of the European Community for the care and use of laboratory animals (EUVD, European Union directive 86/609/EEC).

### Task and Stimuli

Data were recorded over a total of 55 daily sessions. For each session, the experiment involved three cue-target pairs, and a fourth picture ( $N_c$ ) never used as a target (Figure 1A). Monkeys were initially trained with a fixed set of three pairs and fixed  $N_c$  (different stimulus sets for the two animals); thereafter, new pairs and  $N_c$  pictures were occasionally introduced and maintained for a number of sessions. Here we include only data from picture sets that had become highly familiar, over at least six prior sessions, by which time monkeys' performance was at asymptote. All pictures were randomly drawn from the same set of real-life and clip-art images.

The task is illustrated in Figure 1B. Each trial began with a red central fixation point and two dim gray spots (location markers)  $6^\circ$  to left and right on the horizontal meridian. Once fixation had been held for 500 msec, a cue picture was presented, followed by zero to three nontargets and finally the cued target, all in the same location (left or right). Each picture remained for 500 msec, with random intervals of 400–800 msec between one picture and the next. During picture presentations, the fixation point remained red, and during interstimulus intervals, it changed to green. Pictures measured  $2^\circ \times 2^\circ$  of visual angle. The monkey's task was to hold fixation until the target appeared and then at its offset (fixation point change to green) to make an immediate saccade to its location for



**Figure 1.** (A) Example stimulus set. (B) Behavioral task. A central fixation point (red or green) was accompanied by gray location markers to the left and the right. On each trial, a series of stimuli (cue instructing target for current trial, 0–3 nontargets, target) appeared at the left or the right location. The fixation point remained red during stimulus presentations, changing to green during interstimulus delays. Maintained fixation was required until target offset, when a saccade to the target location brought juice reward. T = target;  $N_i$  = nontarget paired with another cue, hence serving as target on other trials;  $N_c$  = nontarget never serving as target. (C) Recording locations for monkeys A (red, transposed from right hemisphere) and B (black).

juice reward (required latency  $< 500$  msec). Target probability remained constant at 0.3 for the first three sequential positions following the cue, then if three nontargets had been presented, rose to 1.0 for the final position. Nontargets were randomly drawn with replacement from the set of two pictures serving as targets on other trials (inconsistent nontargets,  $N_i$ ) and  $N_c$ . Window size for both central fixation and end point of saccade to target location was  $\leq 3.5^\circ \times 3.5^\circ$  for 78.4% of the recorded cells and  $5^\circ \times 7^\circ$  (fixation) and  $5^\circ \times 5^\circ$  (target location) for the remainder. Cue (Cue Pictures 1–3) and side for stimulus presentation (left or right) were randomly chosen on each trial.

### Recordings

Each monkey was implanted with a custom-designed titanium head holder and recording chamber (Max Planck

Institute, Tuebingen, Germany), fixed on the skull with stainless steel screws. Chambers were placed over the lateral pFC of the right hemisphere for monkey A at anterior–posterior = 32.0, mediolateral = 22.2, and the left hemisphere for monkey B at anterior–posterior = 25.8, mediolateral = 21.2. Recording locations for each animal are shown in Figure 1C. When task training was completed, a craniotomy was made for physiological recording. All surgical procedures were aseptic and carried out under general anesthesia.

We used arrays of tungsten microelectrodes (FHC, Bowdoinham, ME) mounted on a grid (Crist Instrument Co., Hagerstown, MD) with 1-mm spacing between adjacent locations inside the recording chamber. The electrodes were independently controlled by a hydraulic, digitally controlled microdrive (Multidrive 8 Channel System; FHC). Neural activity was amplified, filtered, and stored for off-line cluster separation and analysis with the Plexon MAP system (Plexon, Dallas, TX). Eye position was sampled at 100 Hz using an infrared eye tracking system (Iscan, Boston, MA) and stored for off-line analysis. We did not preselect neurons for task-related responses; instead, we advanced microelectrodes until we could isolate neuronal activity before starting the search tasks.

At the end of the experiments, animals were deeply anesthetized with barbiturate and then perfused through the heart with heparinized saline followed by 10% formaldehyde in saline. The brains were removed for histology, and recording locations were confirmed on dorsal and ventral frontal convexities and within the principal sulcus.

## Data and Analysis

Physiological data were analyzed just from successfully completed trials, on average, including 25 repetitions for each combination of trial type (Cues 1–3), stimulus type, and hemifield. We excluded target data from trials with three nontargets because in this case the final target was 100% predictable. We examined just responses to choice stimuli (targets and nontargets), not cues or inter-stimulus delays. All analyses were based on smoothed spike trains (Gaussian kernel with  $\sigma = 10$  msec, width = 3  $\sigma$ ). All statistical analyses were done using MATLAB (MathWorks, Natick, MA).

## RESULTS

### Behavior

Both animals detected the great majority of targets (T), with 77.3% (monkey A) and 90.9% (monkey B) correct responses (saccade at target offset) and an additional 21.1% (monkey A) and 5.6% (monkey B) premature saccades (target still present). In both animals, correct responses occurred within 200 msec of target offset on

>95% of trials. Accuracy was also high for nontargets that were never targets ( $N_c$ ), with 98.9% correct responses (maintained fixation) for monkey A and 95.6% for monkey B. For nontargets that were targets on other trials ( $N_i$ ), the rate of correct responses was appreciably lower at 83.1% (monkey A) and 82.6% (monkey B), showing that nontarget classification was more difficult when it required reference to the preceding cue. For calculation of all these percentages, fixation breaks (saccade to location outside stimulus window) were excluded.

## Neurophysiology

### Cell Sample

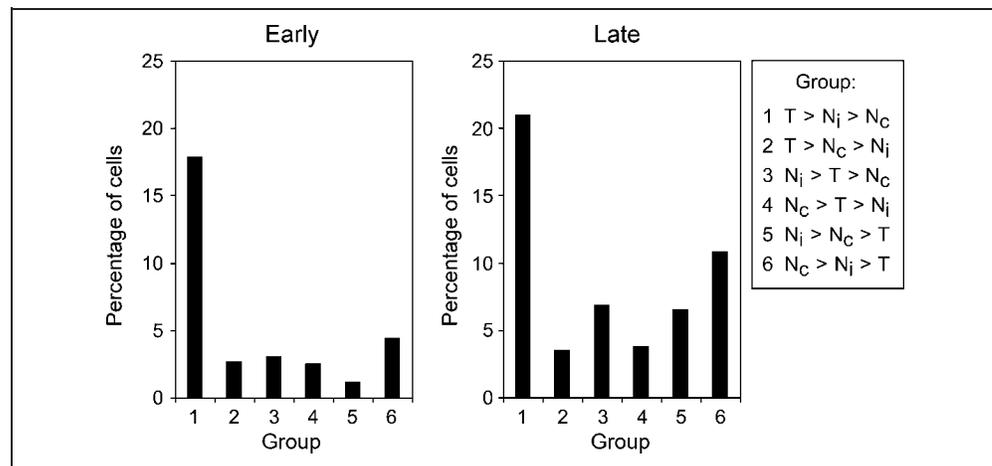
Data were recorded for 653 cells, distributed across dorsal and ventral convexities and along both banks of the principal sulcus. As described above, cells were selected without reference to activity during the task, and all analyses were based on the full cell sample. There were 342 cells from monkey A and 311 from monkey B; here we present pooled data, although all results held also in the two animals analyzed individually.

### Structured Coding of Stimulus Category

For each neuron, spike rates during each target or nontarget presentation were calculated in two analysis windows, early (50–250 msec from stimulus onset) and late (300–500 msec). Coding of stimulus category was assessed in two ANOVAs per neuron, one for each analysis window, with factors stimulus category (T,  $N_i$ ,  $N_c$ ), trial type (Cues 1–3), and hemifield (left or right). In the early window, the main effect of stimulus category was significant ( $p < .05$ ) in 210/653 cells, rising to 345/653 cells in the late window. Although randomly selected, more than 50% of all cells coded stimulus category in this task.

To search for dominant patterns of response across the cell population, category-selective neurons from each time window were sorted into six groups, determined by the six possible orders of activity for the three stimulus types. Percentages of cells in these six groups are shown in Figure 2. The resulting distributions were far from random, showing dominant patterns of stimulus coding. In line with previous reports of target selectivity in pFC (e.g., Everling et al., 2002, 2006; Hasegawa et al., 2000), there were many cells with strongest response to T. Among these target cells, by far, the most common response pattern—seen in over one sixth of all recorded neurons—was  $T > N_i > N_c$ . Dominance of this pattern was especially clear in the early window. Additional structure was seen among antitarget cells, that is, those with the weakest response to T. Among these, the most common pattern was  $N_c > N_i > T$ . As predicted by an opponent coding mechanism, the two most common patterns in the sample were complementary: In one group, strongest response to target and weakest response to a nontarget

**Figure 2.** Percentage of all recorded cells showing each possible pattern of stimulus preference. Data are shown separately for early and late analysis windows.



never associated with the target category; in the complementary group, the reverse.

Examples of these complementary patterns are shown in Figure 3. For the early analysis window, the dominant target-positive pattern is illustrated by the cell in Figure 3A. In this cell, a phasic response began around 100 msec from stimulus onset and was largely over by 200 msec. This phasic response was strongest for T, intermediate for N<sub>i</sub>, and barely visible for N<sub>c</sub>. The cell in Figure 3B shows the complementary pattern, with strong phasic response to N<sub>c</sub> and weakest to T. These transient responses, time locked to stimulus onset, suggest activity linked to initial stimulus identification. Examples of cells significant in the late window are shown in Figure 3C and D. For the cell in Figure 3C, an early response to all stimulus categories was followed by separation around 250 msec from stimulus onset, with the pattern T > N<sub>i</sub> > N<sub>c</sub>, then maintained until after stimulus offset. For the cell in Figure 3D, activity began around 200 msec from stimulus onset and was then sustained, with a strong N<sub>c</sub> > N<sub>i</sub> > T pattern, until just after stimulus offset. These late, sustained patterns suggest a role in retaining stimulus category and/or the corresponding go/no-go decision until the monkey's response at stimulus offset. Although many cells showed similar stimulus preferences in early and late periods, some did not. Figure 3E shows a cell with a strong target-positive pattern in the early period, reversing to an antitarget pattern in the period preceding the response.

To summarize results for the cell population, Figure 4 shows mean activity histograms for two sets of cells, all target cells, that is, those with a significant effect of stimulus category and strongest response to targets (T > N<sub>i</sub> > N<sub>c</sub> or T > N<sub>c</sub> > N<sub>i</sub>; Figure 4, top), and all antitarget cells, that is, those with a significant effect of stimulus category and weakest response to targets (N<sub>c</sub> > N<sub>i</sub> > T or N<sub>i</sub> > N<sub>c</sub> > T; Figure 4, bottom). Again data are separately shown for cell groups significant in early (Figure 4, left panels; N = 135 target cells and 37 antitarget cells) and late (Figure 4, right panels; N = 160 target cells and 114 antitarget cells) windows.

For target cells in the early window (Figure 4, top left), a phasic target response began <100 msec from stimulus onset. In line with dominance of the T > N<sub>i</sub> > N<sub>c</sub> pattern, average response in these cells was weakest for N<sub>c</sub> and intermediate for N<sub>i</sub>. This result was confirmed by ANOVA across cells on mean activity in the early window, with factors nontarget type (N<sub>i</sub>, N<sub>c</sub>), trial type (Cues 1–3), and hemifield, showing a strongly significant effect of nontarget type across the whole cell sample,  $F(1,134) = 81.3, p < .001$ . Results were similar, but more sustained, for target cells significant in the late window (Figure 4, top right). Again, ANOVA across cells on mean activity in the late window showed a significant effect of nontarget type,  $F(1,159) = 73.4, p < .001$ .

For antitarget cells, there was the expected complementary pattern. Cells significant in the early window (Figure 4, bottom left) showed a phasic response to N<sub>c</sub>, with a weaker response to N<sub>i</sub> and little if any response to T. ANOVA across cells on mean activity in the early window showed a strongly significant effect of nontarget type,  $F(1,36) = 18.5, p < .001$ . Cells significant in the late window (Figure 4, bottom right) showed a small, transient-positive response to all stimulus categories. This was followed by a sustained reduction in activity for T and, again, somewhat greater sustained activity for N<sub>c</sub> than N<sub>i</sub>. Again, ANOVA across cells on mean activity in the late window showed this difference between N<sub>c</sub> and N<sub>i</sub> to be significant,  $F(1,113) = 10.8, p < .002$ .

Notably, no cell group showed phasic activity at the time of saccade production, immediately following T offset. For these cells, the results give no suggestion of activity directly linked to motor output.

Across trials, the same physical stimuli served as T and N<sub>i</sub>, whereas a different stimulus served as N<sub>c</sub>. In a further set of analyses, we examined the contribution of simple sensory preferences to opponent activity patterns. First, we considered all those cells with strongest response to N<sub>c</sub> (Figure 2, Groups 4 and 6). If these cells had a simple sensory preference for N<sub>c</sub>, then equal numbers should show the patterns N<sub>c</sub> > N<sub>i</sub> > T and N<sub>c</sub> > T > N<sub>i</sub> (again recalling

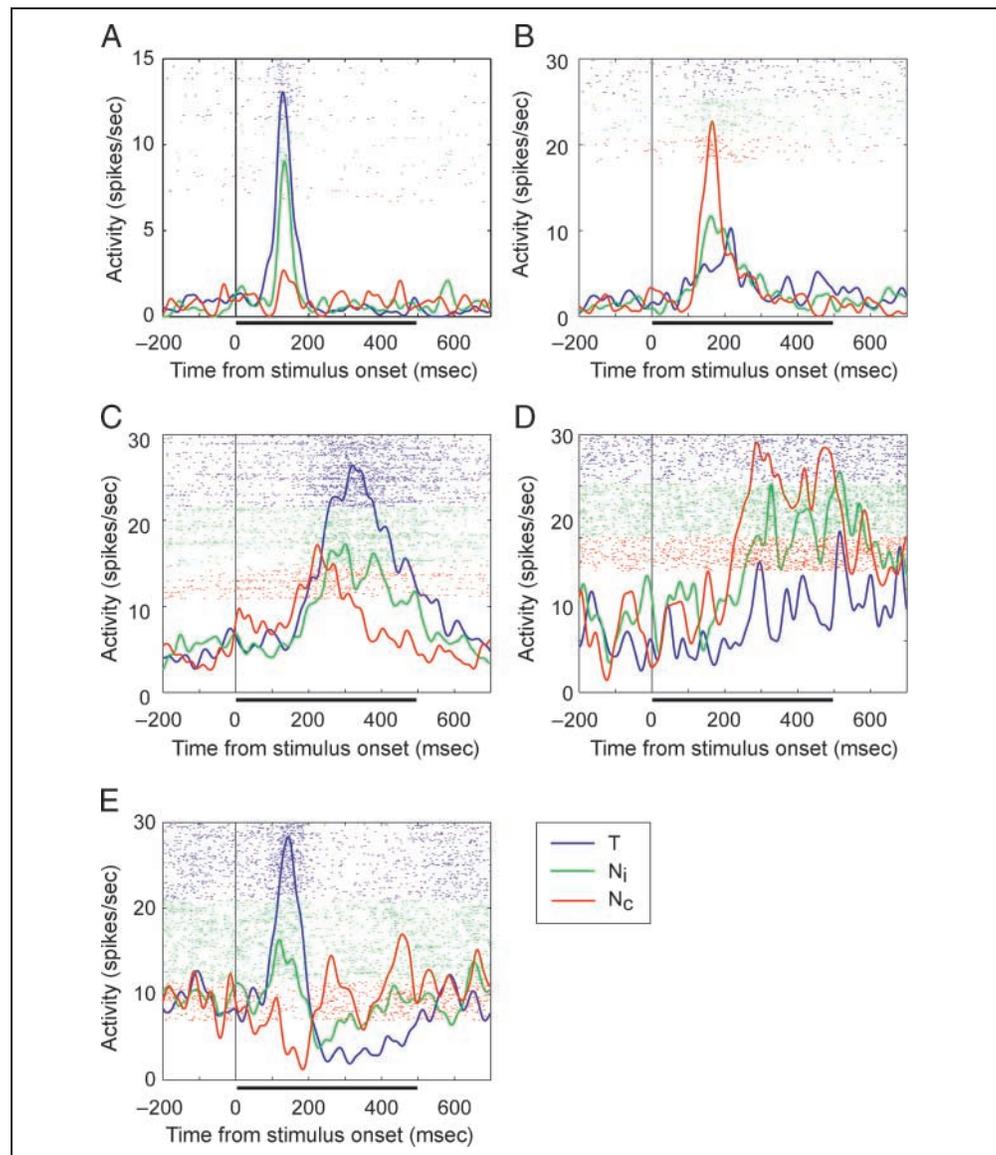
that T and  $N_i$  were actually the same stimuli on different trials). As predicted by opponent coding, in contrast, binomial tests showed greater numbers of  $N_c > N_i > T$  cells, both in early ( $p = .052$ ) and in late ( $p < .001$ ) analysis windows (both tests one-tailed). Thus, cells with the greatest response to  $N_c$  tended also to show the weakest response to T. In a second analysis, we examined cells in the two extreme opponent groups,  $T > N_i > N_c$  and  $N_c > N_i > T$ . For each cell, we calculated an index  $(T - N_i) / (T - N_c)$ . For  $N_i$  close to T, the index approaches a minimum possible value of zero, whereas for  $N_i$  close to  $N_c$ , it approaches a maximum possible value of 1. Bimodal distributions of this index might indicate some cells with activity more driven by the physical stimulus ( $N_i = T$ ), others by the behavioral category ( $N_i = N_c$ ). For neither analysis window was there a suggestion of such bimodality, either among  $T > N_i > N_c$  or  $N_c > N_i > T$  cells.

### Regional Distribution in Early and Late Windows

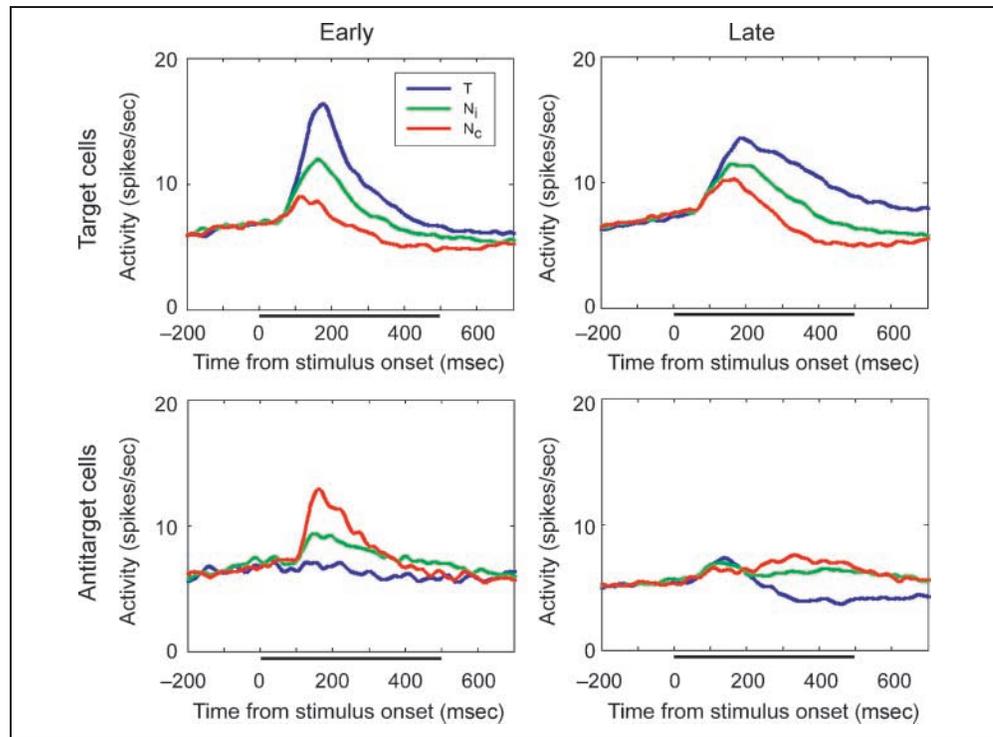
In both analysis windows, significant category selectivity was broadly distributed across the recording area in both animals. More detailed analysis, however, showed a relative preponderance of early selectivity in more ventral recording locations.

To illustrate this point, Figure 5 shows separate results for two groups of cells, those recorded on the ventral convexity ( $n = 378$ ) and the remainder ( $n = 275$ ; principal sulcus and dorsal convexity). This division into more ventral and more dorsal groups was chosen to give adequate numbers of ventral and dorsal cells in each animal individually. As in Figure 3, Figure 5 shows distributions of cells with significant stimulus selectivity and each possible order of stimulus preference. In the early window, significant stimulus coding was more common in ventral cells,

**Figure 3.** Activity as a function of time from stimulus onset in five example cells (A–E). Each panel shows a raster display (one row per stimulus presentation; spikes indicated by dots) overlaid on mean spike density functions. Blue dots and lines = T; green dots and lines =  $N_i$ ; red dots and lines =  $N_c$ . Black line below x-axis shows stimulus presentation period.



**Figure 4.** Mean activity for target ( $T > N_i > N_c$  or  $T > N_c > N_i$ ) and antitarget ( $N_c > N_i > T$  or  $N_i > N_c > T$ ) cells, separately for cells significant in early and late analysis periods. Black line below abscissa shows stimulus presentation period.

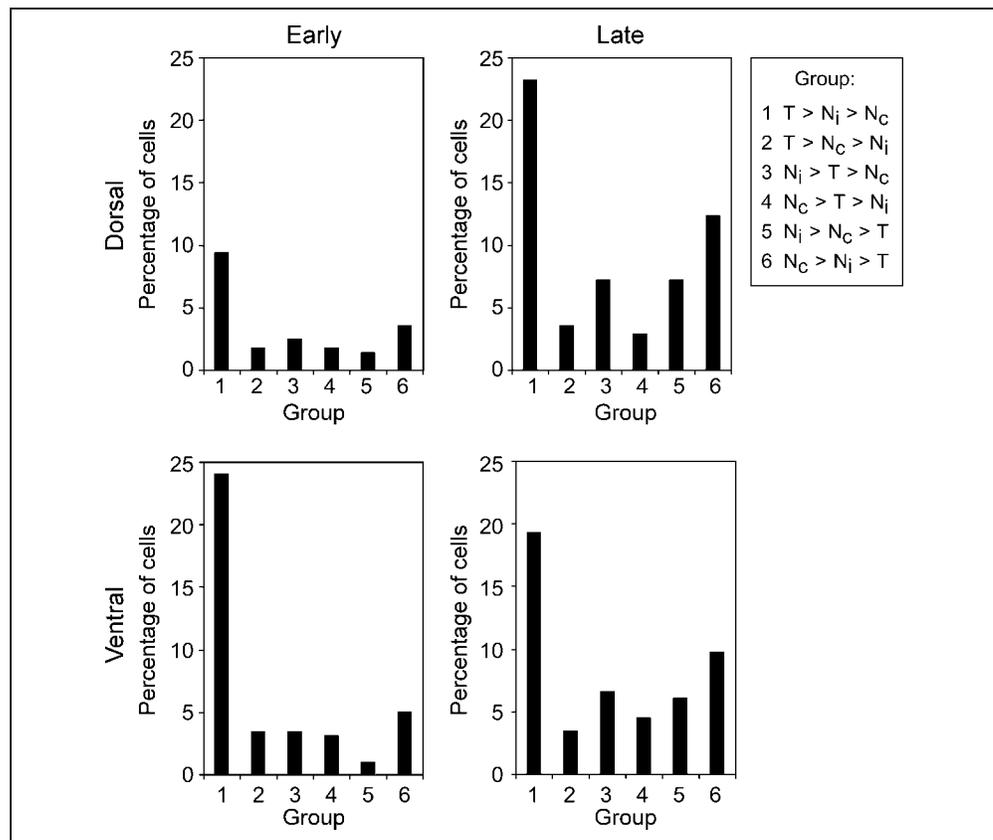


$\chi^2(1) = 26.7, p < .001$ , with an especially striking predominance of  $T > N_i > N_c$  cells. In the late window, this trend was if anything reversed, with a somewhat greater proportion of significant cells in the dorsal area. This difference in

the late window, however, fell short of significance,  $\chi^2(1) = 3.5, p < .07$ .

As Figure 5 shows, the general preponderance of  $T > N_i > N_c$  and  $N_c > N_i > T$  cells held for both recording

**Figure 5.** Percentage of all recorded cells showing each possible pattern of stimulus preference. Data are shown separately for early and late analysis windows and for cells from dorsal and ventral recording locations.



regions in both time windows. Nevertheless, early stimulus selectivity—in particular early response to targets—was most marked on the ventral convexity.

### Latency Analysis

To confirm the above results, we examined latencies for target/nontarget discrimination in individual neurons. We compared latencies for T/N<sub>i</sub> and T/N<sub>c</sub> discrimination, separately for ventral and dorsal cells.

Latency analyses for each cell were based on smoothed spike trains (see Methods). We used ANOVA to examine data for each separate 1-msec bin from -200 to +500 msec from stimulus onset. For each analysis, factors were stimulus (for one series of ANOVAs T vs. N<sub>i</sub>; for a second series T vs. N<sub>c</sub>), trial type (Cues 1–3), and hemifield. The distinction between targets and nontargets was coded as significant throughout any period of 30 msec during which the main effect passed a threshold of  $p < .05$ ; a criterion giving an acceptably low rate of false alarm in the prestimulus period. For each cell showing a period of significant discrimination, the latency of discrimination was taken as the start of the first such period.

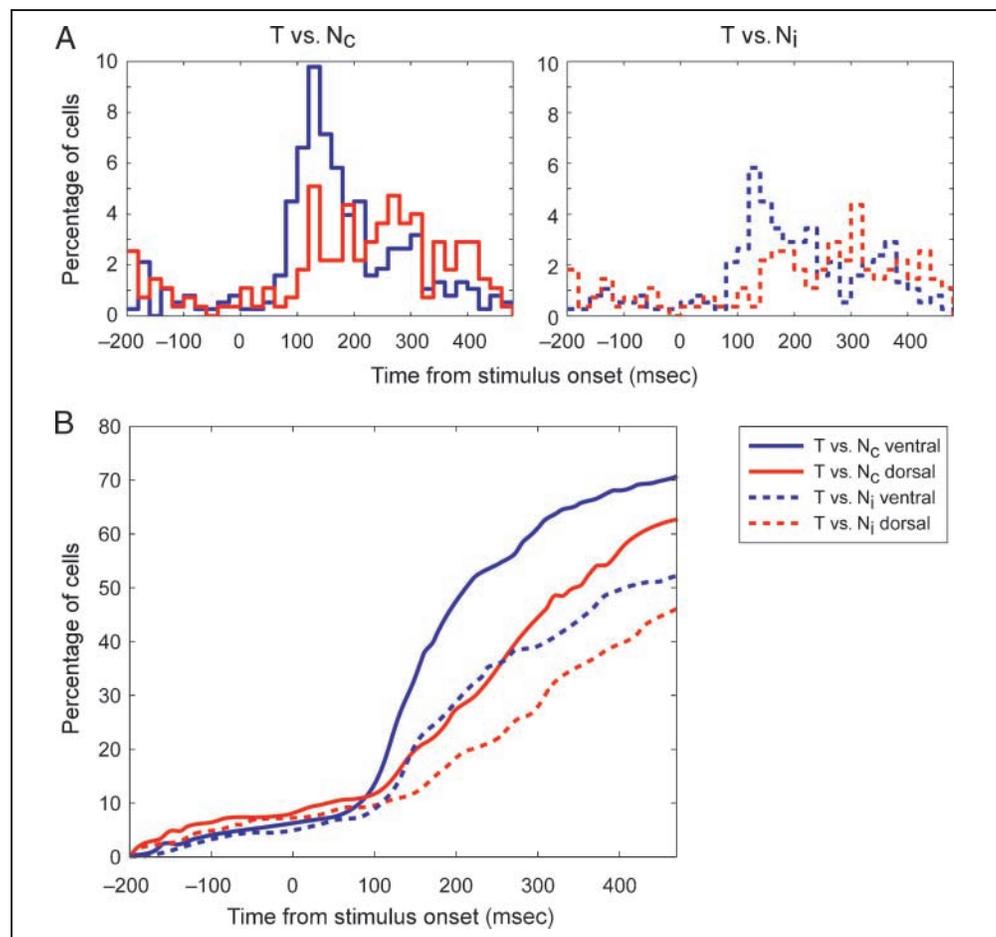
Figure 6A shows the latency distributions for T/N<sub>c</sub> (left) and T/N<sub>i</sub> (right) discriminations, separately for ventral and

dorsal cells. Cumulative distributions are shown in Figure 6B. For all curves in Figure 6B, the onset of stimulus discrimination is shown in the inflection around 100 msec from stimulus onset. Across all periods thereafter, more cells discriminated T/N<sub>c</sub> than T/N<sub>i</sub>, in line with the dominance of T > N<sub>i</sub> > N<sub>c</sub> and N<sub>c</sub> > N<sub>i</sub> > T patterns. For both types of discrimination, latencies were shorter for ventral cells, shown in the leftward shift of their latency distributions. Separately for both types of discrimination, this difference in latency between ventral and dorsal cells was strongly significant (Mann–Whitney,  $p < .001$  in each case, eliminating latencies <75 msec as false positives).

### Eye Position

A final set of analyses examined eye position within the fixation window for the three stimulus categories. Analyses were based on samples of eye position taken every 10 msec throughout the stimulus presentation. Across the stimulus period, mean deviations from prestimulus baseline were 0.34° (horizontal) and 0.27° (vertical) for T, 0.31° (horizontal) and 0.25° (vertical) for N<sub>i</sub>, and 0.31° (horizontal) and 0.25° (vertical) for N<sub>c</sub>. For all three stimulus categories, the eye remained within 1° of baseline for 95% of position samples, both horizontally and vertically. These

**Figure 6.** (A) Discrimination latency distributions for T/N<sub>c</sub> (left) and T/N<sub>i</sub> (right) discriminations. Values are percentages of all recorded cells with latency in each 20-msec bin. Blue = ventral; red = dorsal. (B) Cumulative latency distributions. Plots show proportion of all recorded cells with any period of significant discrimination (for criterion, see text) beginning at or below abscissa value.



data show good maintenance of central fixation for all stimulus categories.

## DISCUSSION

In this study, we examined prefrontal coding of stimulus category in a cued target detection task. Although randomly selected across a large region of the lateral prefrontal surface, more than 50% of all cells showed significant category discrimination. In line with previous reports (e.g., Sigala, Kusunoki, Nimmo-Smith, Gaffan, & Duncan, 2008; Asaad, Rainer, & Miller, 1998, 2000; Funahashi & Inoue, 2000; Fuster, Bodner, & Kroger, 2000), the results show large fractions of prefrontal cells coding the specific events of a well-learned task (Duncan, 2001).

In this cell population, the pattern of stimulus preferences was well matched to the predictions of an opponent coding model (Machens et al., 2005). Two complementary patterns were dominant. Most common was the pattern  $T > N_i > N_c$ ; that is, cells responding most strongly to the current target and most weakly to a nontarget never associated with the target category. This result matches previous reports of target-selective activity in monkey pFC (e.g., Everling et al., 2002, 2006; Hasegawa et al., 2000) and strong frontal response to targets in human neuroimaging (e.g., Hampshire et al., 2007; Hon et al., 2006; Jiang et al., 2000). Next most common, however, was a complementary pattern, with weakest response to targets and strongest response to nontargets never serving as targets. Although much less common than  $T > N_i > N_c$  cells,  $N_c > N_i > T$  cells were still about twice as common as the average for remaining cell groups (Figure 2). The dominance of  $T > N_i > N_c$  and  $N_c > N_i > T$  patterns in prefrontal neurons matched the monkeys' behavior, with best discrimination between T and  $N_c$ , and reduced accuracy for  $N_i$ . The results suggest that, in a well-trained task, large sets of prefrontal cells are organized into groups coding for opposing behavioral decisions, with extreme responses for the stimuli that are most easily classified, and intermediate activity for stimuli with greater behavioral uncertainty. They extend the idea of prefrontal opponent coding from sensory (Machens et al., 2005) to behavioral continua.

Our results show temporal evolution of this opponent organization. In the early analysis window, activity was characterized by many cells with phasic responses, strongest either for T or  $N_c$ . Although widely distributed across our recording area, these early responses were most common on the ventral surface. Correspondingly, it is the ventrolateral frontal cortex that receives direct input from the temporal lobe, bringing shape and object identity from the ventral visual stream (e.g., Ungerleider, Gaffan, & Pelak, 1989). In the late analysis window, many cells showed sustained coding of stimulus category lasting up to or beyond the response. This late, sustained activity was at least as common in dorsal as in ventral regions. One possible route for this ventral to dorsal expansion is the widespread

connection within pFC (Pucak, Levitt, Lund, & Lewis, 1996). A plausible suggestion is that phasic cells, predominantly ventral, fed into sustained cells coding the decision until responses were made. Another possible route is parallel input to dorsal regions from other response selection systems (Rushworth, 2000). Whatever the route, our results show that, by the end of the stimulus period, opponent coding of target–nontarget category was widespread throughout large regions of pFC.

Previous modeling work (Machens et al., 2005) has emphasized how the same opponent circuits can dynamically adapt to create the different phases of complex behavior, for example, stimulus encoding, preservation in working memory, and response decision. Although broadly consistent with this principle, our results also suggest a degree of separation in active cell populations early and late in the choice process.

Notably, neither early nor late cells showed phasic activity after target offset, at the time saccades were made. Elsewhere we have shown that target-selective cells in this task show little activity in standard delayed-saccade tests (Kusunoki et al., 2009) with the same saccade parameters. It is unlikely that target-related activity, either early or late, is closely associated with motor output.

A simple opponent circuit model might predict roughly equal numbers of cells associated with opposite behavioral decisions. Especially in the early period after stimulus onset, in contrast, we observed strong asymmetry of the two dominant activity patterns, with many more target than anti-target cells. Asymmetries of this sort have sometimes been described in other go/no-go tasks, with many more cells responding to go than to no-go stimuli (Sakagami & Niki, 1994; for a contrary case, see Watanabe, 1986a). A variety of asymmetries in our task could account for the results. It is the target that is associated with both the go response and the reward. On each trial, there is only a single possible target picture but several different nontargets, making it economical to describe the task as “target” versus “other.” Perhaps of most significance, monkeys watched a series of nontargets in our task, awaiting the final target. Under these circumstances, it is plausible to suppose that, for this task, “nontarget” was a default decision overturned on final target appearance. In any task, pFC will doubtlessly act in tandem with other neural systems that also contribute to the behavioral decision; quite possibly, its input is especially important when a default decision must be overturned (cf. Norman & Shallice, 1980). Perhaps for this reason, our task required a stronger prefrontal signal for target than for nontarget, unbalancing the number of cells coding for these behavioral alternatives.

The asymmetry, meanwhile, is reminiscent of high attentional demands for target stimuli in human behavioral studies. Commonly, subjects can monitor many nontargets in parallel but are severely restricted in detecting simultaneous targets (Duncan, 1980). Asymmetric target/nontarget representation in prefrontal cells could provide one basis for this result.

In a parallel report, we describe high behavioral accuracy and strong target/nontarget discrimination in prefrontal cells for a task with entirely fixed stimulus categories; that is, fixed target never serving as nontarget and fixed nontargets never serving as targets (Kusunoki et al., 2009). In line with the present finding of good behavioral accuracy for  $N_c$ , linked to good neuronal discrimination from  $T$ , these results confirm the benefit of consistent stimulus–response association in target detection tasks (Schneider & Shiffrin, 1977).

Our results leave several open questions. Although decision making may be controlled by mutual inhibition between target and antitarget cell groups, as proposed in opponent coding models (Machens et al., 2005), our results give no direct evidence for such inhibition. A second question is how far opponent coding of behavioral categories extends beyond pFC into earlier sensory and later motor regions (cf. Romo et al., 2002, 2004).

pFC is essential to the flexibility of human and animal behavior (Miller & Cohen, 2001). Prefrontal cells have a corresponding flexibility of function, adapting to code the specific information that a current task requires (Duncan, 2001; Freedman et al., 2001; Rainer, Asaad, & Miller, 1998; Sakagami & Niki, 1994). In the current task, over one half of all recorded cells coded relevant distinctions between target and nontarget categories. The same stimulus, furthermore, could serve as target on one trial but nontarget on the next, requiring reorganization of behavioral categories with each new trial and cue. Our data suggest that, in pFC, flexible assembly of opponent coding circuits may provide a general mechanism for adaptive programming of complex behavior.

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