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Single Neuron Activity in the Monkey's Prefrontal Cortex

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Abstract. The physiology of prefrontal cortex is reviewed, emphasizing single neuron recordings from awake macaque monkeys. The functional properties of neurons from several prefrontal areas are summarized with regard to their sensory, motor, mnemonic, and behavioral aspects. A model is outlined in which an ascending efferent copy of motor behavior interacts with sensory and premovement activity in prefrontal cortex. A standing-wave hypothesis, based on the physiology and topography of the frontal eye fields, is presented as a mechanism for executing vector operations within prefrontal cortical areas.

INTRODUCTION

It is unclear how to organize a review of the physiology of the primate's prefrontal cortex (PFC) because it is unclear how to functionally characterize it. PFC has been termed association cortex as it is neither unequivocally sensory nor motor in function. However, because PFC is part of the frontal lobe, where damage is often associated with movement disorders, it has also been considered a higher-order extension of motor cortex, an idea supported by the proximity of PFC to Broca's speech center in humans and the electrical elicitation of eye movements from PFC in primates. Although a transient sensory neglect syndrome follows PFC damage, the primary and permanent disorders in humans involve behavioral deficits in executive functions, such as a loss of the ability to compose and execute plans, ranging from cooking a meal to organizing long term projects. Such complex disorders, recently reviewed by Stuss and Benson (1986), indicate that higher-order motor cortex is a valid conceptualization of PFC.

On the other hand, anatomical studies in the monkey demonstrate that several cortical areas with sensory activities project to dorsolateral PFC.

Jones and Powell's classic study (1970) indicated that PFC receives visual projections from inferotemporal cortex and auditory inputs from the superior temporal gyrus. They also found projections from posterior parietal cortex, which could provide both visual and somesthetic inputs. Subsequent anatomical studies using modern tracers have refined this basic pattern of PFC afferents (see Goldman-Rakic, this volume), and have also demonstrated projections from occipitotemporal visual areas and from polysensory cortex in the fundus of the superior temporal sulcus (Bruce et al. 1981). Thus PFC receives converging projections from higher-order, modality-specific sensory cortices and from polysensory cortex, indicating that a multimodal sensory association area is another valid conceptualization of PFC.

I will review sensory responses of PFC neurons before considering motor and cognitive aspects in accordance with the traditional stimulus-response (SR) concept of sensory inputs leading to motor responses. Even though PFC is involved in behaviors much more complex than basic SR reflexes, this is a logical order for physiological reviews (and studies as well) to proceed. One reason is that any complex behavioral situation will entail sensory stimulation, and it is imperative to know whether and how such controlling stimuli directly excite the neuron being studied. Moreover, I will organize the physiology by topics rather than strictly by cortical areas, partly to facilitate comparisons between different areas and partly because some studies lump together cells recorded from area 46, the fronted eye fields (FEF), and other prefrontal and even premotor cortical areas. I will not duplicate recent, much more focused papers and reviews concerning the physiology of the FEF (Bruce and Goldberg 1984, 1985; Bruce et al. 1985) except for the minimum necessary for motivating the models presented at the end of this paper.

LOCATION OF PREFRONTAL CORTEX

The term "prefrontal cortex" (PFC) refers to frontal lobe cortex anterior to the motor strip and adjacent premotor cortex. From a connectivity perspective, PFC is usually defined as the projection field of the mediodorsal nucleus of the thalamus. From a cytoarchitectonic perspective, PFC is homotypical isocortex of the frontal lobe with a prominent internal granular layer (layer IV), as opposed to the motor (Brodmann's area 4) and premotor areas (Brodmann's area 6) of the frontal lobe, which lack a clear internal granular layer. Whether these definitions provide accurate homologies across diverse species of mammals is unclear (Fuster 1980); however, with regard to the macaque monkey, the species emphasized in this paper, PFC simply refers to all of the frontal lobe cortical regions anterior to the arcuate sulcus (Fig. 1).

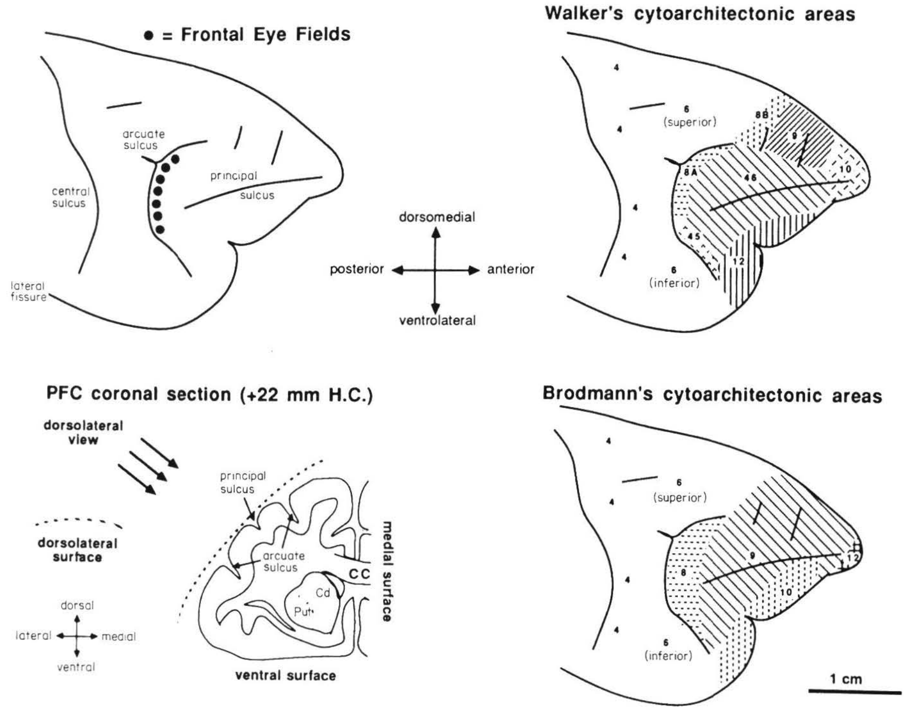


Fig. 1—Dorsolateral views of macaque frontal lobe with sulci, cytoarchitectonic areas, and frontal eye fields (FEF). TOP LEFT: The 7 dots along the arcuate sulcus mark the FEF in a particular monkey (M17, m. fascicularis) as defined by microstimulation; each electrode penetration encountered sites in the lip or anterior bank of the arcuate sulcus where saccadic eye movements were evoked with currents below 50 μA. Saccade amplitudes ranged from ~25° in the dorsomedial FEF to ~1° in the ventrolateral FEF; details of this method and case (M17) are in Bruce et al. 1985. TOP RIGHT: Walker's (1940) cytoarchitectonic parcellation of prefrontal cortex estimated for this particular case. The FEF are roughly the union of Walker's areas 8A and 45, both characterized by clusters of large pyramidal cells in layer V and a dysgranular layer IV. BOTTOM RIGHT: Brodmann's (1940) cytoarchitectonic parcellation of prefrontal cortex estimated for this particular case. Brodmann's area 8, which was often taken to be the FEF, contains Walker's areas 45 and 8A and part of area 46 posterior to the principal sulcus. Brodmann's area 9 contains Walker's area 46, 9, and 8B. Posterior to PFC, Brodmann's areas 4 and 6 denote the primary motor strip and adjacent premotor cortex. BOTTOM LEFT: Coronal section through prefrontal cortex (PFC). Note the triangular shape of the brain, with the hypotenuse being the dorsolateral surface. The arrows indicate the view of dorsolateral cortex used to trace the other panels.

Subdivisions of PFC

Given the large expanse of PFC in the primate, the next question concerns its subdivisions. Fig. 1 shows the macaque PFC and its sulci, with cytoarchitectonic areas according to Walker (1940). The tracing depicts a dorsolateral view, approximately midway between the standard dorsal view from above and the common lateral view from the side. This intermediate perspective provides an orthogonal, thereby minimally distorted, depiction of the prearcuate region of PFC, also termed the dorsolateral PFC. This paper will emphasize two parts of the dorsolateral PFC: the frontal eye fields (FEF) as defined by physiological criteria, and area 46 which lies anterior to the FEF. In Fig. 1 the dots along the arcuate sulcus indicate the FEF in this particular monkey as determined by microstimulation—each marked penetration encountered sites, either in the lip or anterior bank of the arcuate sulcus, where saccadic eye movements were evoked with currents at or below 50 μA (see Bruce et al. 1985 for details of this method and particular case—M17). These "low-threshold" FEF are roughly the union of Walker's cytoarchitectonic areas 8A and 45. Large saccades are elicited from the dorsomedial FEF penetrations (area 8A) whereas small saccades are elicited in the ventrolateral FEF (area 45). Both FEF regions are characterized by clusters of large pyramidal cells in layer V and a dysgranular layer IV. Area 45 is distinguished from area 8A by scattered clusters of large pyramidal cells in layer III of 45; however, the boundary between 45 and 8A, like most cytoarchitectonic boundaries in the frontal lobe, is not sharply defined.

Although Walker's system is used in this paper, many older studies have used Brodmann's system, so it is important to understand the relationship between Walker's and Brodmann's parcellations. Brodmann's area 8, which has often been taken as the FEF, contains not only Walker's areas 45 and 8A, but also includes considerable cortex on the surface of the prearcuate gyrus extending to nearly the posterior tip of the principal sulcus. Similarly, Brodmann's area 9 has often been used to designate recordings or lesions of the principal sulcus region, but Brodmann's 9 encompasses considerably more cortex than Walker's 46, extending to the longitudinal fissure, and thus essentially also including Walker's areas 9 and 8B. Moreover, considering the large expanse of cortex buried in the principal sulcus, Walker's area 46 is still quite large and undoubtedly has several functional subdivisions. As discussed below, both physiological and anatomical evidence indicate important distinctions between the dorsomedial region of area 46 above the principal sulcus and the ventrolateral region below. Goldman-Rakic's chapter in this volume indicates additional subdivisions of area 46 based on its connectivity with the parietal lobe.

Other regions of PFC outside the dorsolateral zone will be only briefly considered. Referring to Fig. 1, area 10 (the frontal pole) and area 12 are largely omitted, as is the cortex of the ventral surface. These regions appear to be involved in emotional, appetitive, and social behaviors (Rosenkilde 1979), and also in recognition memory (Bachevalier and Mishkin 1986).

SENSORY PHYSIOLOGY OF PREFRONTAL CORTEX

Visual Responses

Visual responses in PFC have been extensively studied. Mohler et al. (1973) first mapped visual receptive fields (RFs) in the FEF region while an awake monkey fixated a small light. Nearly 50% of the cells responded to visual probe stimuli presented in the periphery. Visual responses are also prevalent outside of the FEF, although some investigators indicate that cells anterior to the FEF are often difficult to drive using only a visual probe task and simple visual stimuli. Nevertheless, Mikami et al. (1982b) found that 69% of the cells in the posterior principal sulcal region of area 46 responded to peripheral visual stimuli presented without any behavioral significance while the monkey fixated a small central spot.

Visual Receptive Fields

Visual cells in the FEF have large contralateral receptive fields (RFs), sometimes encompassing nearly a quadrant of the monkey's visual field (Bruce and Goldberg 1985; Goldberg and Bushnell 1981; Mohler et al. 1973). Mikami et al. (1982b) found that area 46 RFs were perhaps even larger (10° to 60° square) and predominantly contralateral, although many encroached into the ipsilateral field. A related difference between the FEF and area 46 concerns encroachment of visual RFs on the foveal representation. Mikami et al. (1982b) reported that 45% of the area 46 cells with peripheral visual responses appeared to include the fovea in their RFs in that they responded to the onset or brightening of the fixation light. Other studies (e.g., Suzuki and Azuma 1977) confirm that many area 46 cells respond during visual fixation. In contrast, only 7% of FEF cells respond to visual fixation or foveal stimuli (Bruce and Goldberg 1985), and such cells are quite distinct from the more common FEF cells with peripheral visual or presaccadic movement fields.

Visual Stimulus Specificity

Mohler et al. (1973) found that small spots of light were adequate visual stimuli for mapping FEF RFs, and concluded that the FEF have little visual stimulus specificity. Mikami et al. (1982b) found a similar lack of specificity in area 46 RFs, using slit stimuli rather than spots. Few cells were sensitive to the orientation, size, or brightness of the slits. Most other reports have agreed with these conclusions (Bruce and Goldberg 1985; Goldberg and Bushnell 1981; Wurtz and Mohler 1976) but few studies have extensively tested PFC cells with visual stimuli aside from bars, spots, and very limited sets of colors or patterns. In the one study using a variety of visual stimuli, Pigarev et al. (1979), recording from anesthetized monkeys, found that whereas cells in or near the arcuate sulcus responded to simple stimuli (spots and bars), cells slightly more anterior and near the ventral bank of the principal sulcus often required complex visual stimuli, such as faces or twisted wires. More recent experiments using visual pattern discrimination (Watanabe 1986a) or matching-to-sample (Fuster et al. 1982) tasks find that a small percentage of PFC neurons respond selectively to colors per se (e.g., 6% in Fuster et al. 1982) or to other simple visual properties. It should be noted that although these paradigms insure that the monkey attends to the stimulus color or pattern, they do not systematically test different colors, patterns, or even visual field loci. The strong projections that the ventrolateral area 46 (inferior bank of the principal sulcus and prearcuate gyrus below) receives from inferotemporal cortex could provide such visual specificity, and suggests that stimulus specificity might be more prevalent than reported so far.

Visual Movement and Directional Specificity

Extant studies do not indicate much sensitivity of PFC cells to stimulus motion. Mikami et al. (1982b) did find that 10% of visually responsive cells in area 46 had a preferred direction of slit motion, but concluded that direction of motion, like slit orientation, was an unimportant parameter for PFC. We (Bruce and Goldberg 1985) found that 2% of FEF cells responded in conjunction with ocular pursuit of moving targets. However, movement sensitivity was not a central purpose of these or other PFC studies. Because PFC receives projections from several areas with motion selective neurons, including posterior parietal (PP) cortex and cortex in the superior temporal sulcus (MT, MST, and the superior temporal polysensory area, STP), stimulus motion may have more importance for PFC neurons than has thus far been observed. Perhaps complex motions such as centrifugal or centripetal motion, movement-in-depth, rotation about different axes, movements of real objects, and complex optical flow patterns must be tested as many cells in PP (Steinmetz et al. 1987), MST (Saito et al. 1986; Tanaka et al. 1986), and STP (Bruce et al. 1981), prefer such complex motions.

Visual Topography

The topography of the FEF has been studied by observing saccades evoked with microstimulation (Bruce et al. 1985). Saccade amplitude has an orderly overall representation across the FEF, with large saccades represented in the dorsomedial FEF and small saccades in the ventrolateral FEF (Fig. 1). In contrast, saccade direction lacks an overall topography, but it has a local order characterized by continuous progressions in the polar direction of electrically-evoked saccades as electrode penetrations traverse the anterior bank of the arcuate sulcus (Bruce et al. 1985). This repetitive, hypercolumnar representation of the polar direction of saccades across the FEF is discussed in more detail in conjunction with the models presented below.

Suzuki and Azuma (1983) studied the visual topography of the posterior part of area 46 and parts of the neighboring FEF by mapping visual RFs in awake fixating monkeys. RFs in the dorsomedial region (between the principal sulcus and the superior limb of the arcuate sulcus) were large and eccentric, whereas RFs in the ventrolateral region (between the principal sulcus and the inferior limb of the arcuate) were smaller and centered near the foveal representation. RFs were larger as penetrations moved anteriorly away from the arcuate and FEF (although their sample did not extend anteriorly beyond the posterior third of the principal sulcus). Thus visual RFs of cells located ventral to the posterior end of the principal sulcus encompassed the fovea and yet were quite large. Interestingly, large visual RFs that include the fovea are characteristic of inferotemporal cortex, which preferentially projects to ventrolateral parts of area 46. In contrast, large peripheral fields that spare the fovea are often found in posterior parietal cortex, which projects preferentially to dorsomedial parts of area 46. The central visual representation in ventrolateral area 46 is also consistent with the preponderance of "gaze" (or "attentive fixation") neurons there (Suzuki and Azuma 1977). Analogous to the FEF results, Suzuki and Azuma (1983) found no overall topography for visual direction (that is, the polar direction of the RF center) within area 46.

In summary, there is a general visual topography across dorsolateral PFC such that the peripheral visual field is represented in the dorsomedial part (above the principal sulcus) whereas the more central and foveal visual field is represented in ventrolateral part (below the principal sulcus). This pattern suggests a continuation into the PFC of the dorsal and ventral systems of cortical visual processing that have been previously distinguished (Ungerleider and Mishkin 1982). The dorsal system of spatial (or ambient) visual processing, epitomized by the posterior parietal cortex, appears to extend into dorsomedial parts of area 46 and the FEF, whereas the ventral cortical system of pattern (or focal) visual processing, epitomized by the inferotemporal cortex, extends into ventrolateral parts of area 46 and the FEF.

Auditory Responses

The literature on auditory responses in PFC is less extensive than the visual response literature. Because there are some substantial differences in results, I will summarize the different methodologies before reviewing the findings:

Ito (1982) studied auditory responses while the monkey detected a change in sound intensity; neither sound composition (3 KHz tone) nor location (behind the tangent screen) were varied. Azuma and Suzuki (1984) tested different sounds and speaker locations, both informally and quantitatively, in an awake monkey not doing any task. Vaadia et al. (1986) tested monkeys trained to make arm movements toward a sound (always a 100 ms noise burst) from one of an array of five speakers situated at intervals of 30° along the horizontal plane. They also tested movements to visual stimuli and two auditory control tasks: detection and passive probe. Bruce and Goldberg (1985) examined some FEF cells for responses to auditory probes presented during fixation or outside of a task. Recently, Gary Russo and I mapped auditory RFs while monkeys fixated visual targets and we also tested FEF cells during saccades directed at sounds.

Location of Auditory Activity in PFC

Although no single published study provides a comprehensive mapping of auditory activity across the entire PFC, most cells with auditory activity have been located in the superior aspect of dorsolateral PFC. Vaadia et al. (1986) found auditory activity on both sides of the superior limb of the arcuate sulcus; in fact, their recordings encompassed parts of cytoarchitectonic areas 8A, 8B, 46 and 6. Other reports are consistent with this general location. Bruce and Goldberg (1985) found auditory activity in the dorsomedial FEF; that is, area 8A. Azuma and Suzuki (1984) found auditory activity mostly in dorsomedial area 46 above the principal sulcus. Ito's (1982) auditory cells were mostly in the dorsal-posterior parts of 46 and in 8A. Overall, these physiological results agree with neuroanatomical findings that the superior region of dorsolateral PFC receives projections from both the auditory association cortex of the superior temporal gyrus (Pandya et al. 1969) and the polysensory cortex in the superior temporal sulcus (where 40% of the cells respond to auditory stimuli, Bruce et al. 1981).

Auditory Receptive Fields

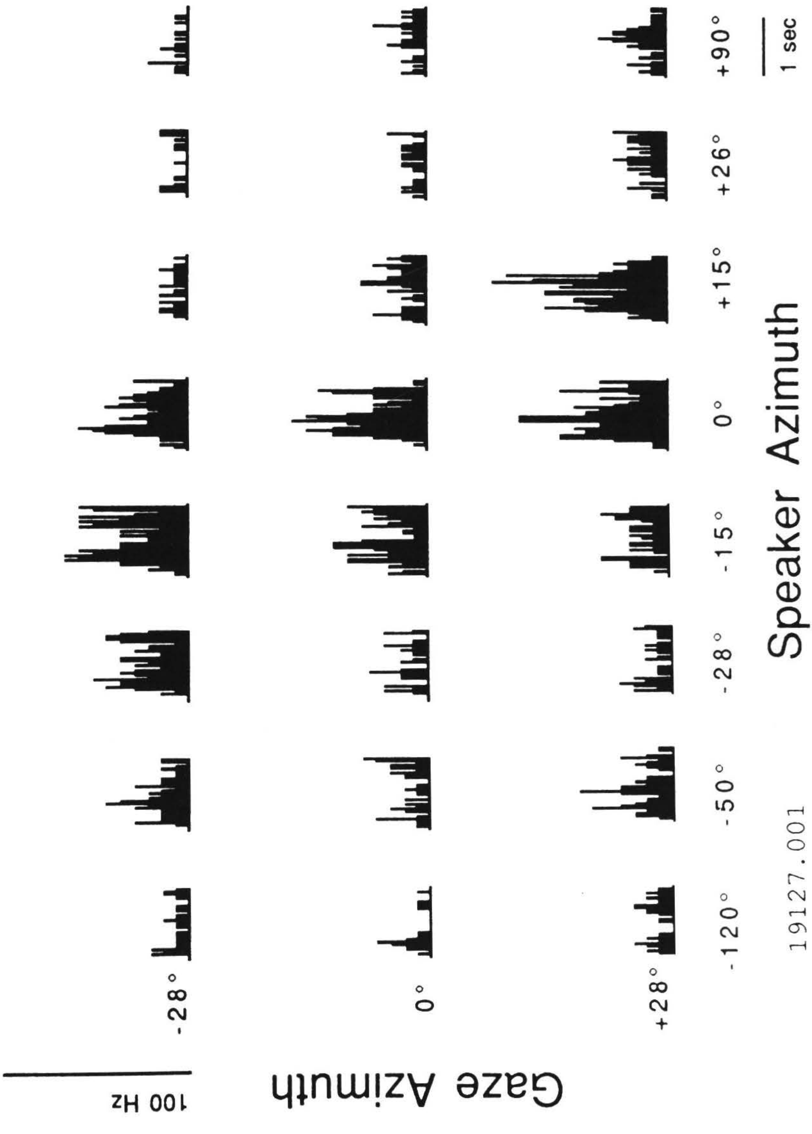
Auditory fields are best mapped in the awake macaque monkey by using arrays of speakers or by moving single speakers along the azimuth (as opposed to dichotic stimulation traditionally used in auditory investigations of anesthetized subjects). Most cells in monkey PFC with auditory responses have definite RFs in space. There is agreement that these auditory fields are large (perhaps 30°–90° in width), but disagreement regarding the locations of auditory field centers. Azuma and Suzuki (1984) mapped the auditory fields of 14 cells. Nearly all preferred contralateral stimuli and the median field *center* was beyond the far visual field border (~90°); they suggested that auditory cells may process the parts of the environment where the monkey cannot see. Vaadia et al. (1986) obtained quite different results. Although for most of their cells the best speaker location was contralateral, the median best speaker was just 30° eccentric. Furthermore, a sizable proportion of cells (~25%, estimated from their Fig. 11) had best locations in the ipsilateral visual field, and many (~15%) preferred the speaker situated directly in front (0°). They did not test locations beyond 60° eccentricity, but it is hard to see how this could affect their general conclusions. Our (Bruce and Goldberg 1985) FEF results fit Azuma and Suzuki's somewhat better than Vaadia's, in that all FEF cells with auditory activity responded solely or optimally to a speaker in the contralateral field. My recent data also indicates that most auditory fields are centered in the contralateral visual field and only rarely are ipsilaterally centered; however, we find, unlike Azuma and Suzuki, that most auditory fields are centered within the visual field of view. Moreover, we find that auditory field centers are strongly affected by the monkey's direction of gaze (Fig. 2), in a manner analogous to that which Jay and Sparks (1984) reported for auditory fields of cells in the intermediate layers of the monkey superior colliculus. A comprehensive mapping study of PFC could reveal an auditory topography that resolves these differences inasmuch as the recordings were all from different areas; however, differences in experimental testing methods appear to be more important because the recording sites overlap more than the results.

Auditory Stimulus Specificities

Thus far auditory responses in macaque PFC appear to be unselective for particular sounds; however, most studies have emphasized selectivity for a sound's location or its behavioral significance, not its composition. In the squirrel monkey the opposite has been the case; sound compositions, especially intraspecific calls, have been emphasized and localization has been informally noted. Newman and Lindsley (1976) found that monkey calls, particularly "noisy" vocalizations, excited cells more than tones, clicks, and other artificial sounds. Wollberg and Sela (1980) also found that calls, particularly cackles, were most effective, and that 50% of the cells responded to only one or two calls whereas only 3% responded to all seven calls tested.

Auditory-visual Convergence

Most studies of auditory responses also tested visual stimuli, and hence afford a measure of auditory-visual convergence in PFC at the single neuron level. Again there is substantial disagreement. Azuma and Suzuki (1984) found no cells that responded to both visual and auditory stimuli. Likewise,


Gaze Azimuth
-28°
0°
+28°
Speaker Azimuth
-120°
-50°
-28°
-15°
0°
+15°
+26°
+90°
100 Hz
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almost all of Ito's "phasic" cells responded exclusively to either auditory or visual stimuli. At the other extreme, 88% of Vaadia et al.'s (1986) cells with "early responses" during the auditory localization task also responded during visual localization. We (Bruce and Goldberg 1985) found an intermediate result: of 30 FEF cells with auditory responses, 14 also responded to visual stimuli. My more recent unpublished data also indicate substantial populations of both bimodal and purely auditory cells both within and surrounding the dorsomedial part of the low-threshold FEF.

Summary of Auditory Activity

Overall, both the location of auditory responses in PFC and the auditory field locations are consistent with the visual topography. In particular, auditory responses are found in dorsomedial parts of lateral PFC where visual RFs are eccentric, and most auditory RFs are eccentric in comparison to visual fields in ventromedial area 46 and FEF. Auditory responses probably guide orientation to objects in the periphery via arm movements, saccadic eye movements, and covert attention. In this regard, it is likely that auditory activity, particularly activity representing space within the visual field, converges with visual activity and creates a multimodal (or supramodal) representation of extrapersonal space. Much more research is needed in this regard.

The apparent lack of auditory specificity in the macaque PFC may be misleading, just as I suggested that its apparent lack of visual specificity may be. One possibility is that cells in ventrolateral area 46 respond selectively to natural calls, as some squirrel monkey frontal cells do, whereas cells in dorsomedial PFC, as Vaadia's results suggest, primarily serve stimulus localization and consequently respond independently of sound composition per se. In other words, the auditory organization of PFC may parallel its visual-saccadic organization.

Fig. 2—Auditory receptive field of a cortical neuron recorded near the dorsomedial region of the Frontal Eye Fields (FEF). Each histogram represents summed activity of ten trials with 1.5 sec of white noise delivered at 24 different combinations of speaker and gaze azimuth. The three rows of histograms show that its auditory field was strongly affected by the monkey's direction of gaze. The speaker locations yielding the strongest responses shifted systematically as a function of gaze, in the same direction that a classic *visual* receptive field would shift. However, the magnitude of the auditory field shifts is less than the magnitude of the gaze shifts. The prestimulus-baseline portion of the histograms was omitted in order to have a more manageable figure; typical baseline activity of the unit was comparable to the nonresponse in the top-right condition and there was no obvious suppression below baseline for any condition.

Somatosensory Responses

Somatosensory responses of PFC neurons have not been studied in awake macaque monkeys; however, there is evidence for such activity from early studies using anesthetized, paralyzed recording preparations. Bignall and Imbert (1969) found evoked responses to contralateral forelimb stimulation over much of the dorsal prefrontal cortex of squirrel monkeys; Schechter and Murphy (1975) found somatosensory responses of single cells there. Finally, some of the cells in the macaque's periarcuate region with somatosensory responses (Rizzolatti et al. 1981) may lie anterior to the arcuate fundus and hence in PFC, although most were postarcuate; that is, in area 6.

BEHAVIORAL PHYSIOLOGY OF PREFRONTAL CORTEX

Enhancement of Sensory Responses

The concept of behavioral enhancement of sensory responses has been tested by Wurtz and his colleagues in many areas of the brain. Basically, their concept is that intrinsic sensory-evoked responses of neurons may be "enhanced" when the eliciting stimulus has particular behavioral significance. Usually enhancement is reported as an increase in either the discharge frequency or duration relative to a situation where the exact same physical stimulus lacks behavioral significance to the subject. Enhancement is postulated to highlight activity elicited by stimuli that serve to guide behavior.

Visual responses of cells in the FEF are often enhanced when the visual stimulus is the target for a saccadic eye movement (Bruce and Goldberg 1985; Goldberg and Bushnell 1981; Wurtz and Mohler 1976). Furthermore, Goldberg and Bushnell (1981) quantitatively determined that enhancement of visually-evoked activity in the FEF only occurred during a saccade task, and not when the task called for the monkey to detect the dimming of the peripheral target while maintaining fixation. They defined an "enhancement index" as the ratio of the discharge in the experimental task to the discharge in the control task. Whereas 50% of FEF visual responses had an enhancement index greater than 1.5 in the saccade task, only 5% were enhanced to that degree in the peripheral dim paradigm. They also found that saccadic enhancement in the FEF was spatially selective: when two stimuli were simultaneously presented, one in the cell's RF and one outside it, enhancement was obtained only when the saccade was to the RF stimulus. Overall, the study of Goldberg and Bushnell indicates that FEF enhancement is very well suited for a role in the selection of targets for saccadic eye movements.

Mikami et al. (1982a) tested area 46 neurons for enhancement with a slightly different task: the monkey had to maintain fixation of a central spot throughout each trial, and then press the left lever if a peripheral target had briefly appeared during the trial or press the right lever if no target had been shown. Their results were negatve in that only a few cells had slightly larger visually evoked responses in their detection-memory paradigm when compared to responses to the same stimuli tested in the standard fixation task. Perhaps enhancement of stimulus activity in area 46 is specific for tasks involving spatial memory, such as the spatial delay tasks used in many of the studies reviewed below.

Movement-related Activity in PFC

Bizzi (1968) was the first to observe cells in the FEF region of PFC that consistently discharged during and after particular (albeit large) ranges of spontaneous saccadic eye movements made in the dark. Thus, these cells had motor-related activity in the absence of both sensory stimuli and task contingencies. In later studies of the FEF (Bruce and Goldberg 1985) we estimated that 25% of the cells in the FEF have such postsaccadic activation. However, we discovered that another 25% of FEF cells responded *before* particular saccadic eye movements (Fig. 4, bottom row) even in the absence of overt visual targets. Such presaccadic responses were usually restricted to the situation of motivated, purposive eye movements and less evident before spontaneous saccades in the dark. Most of these "presaccadic" cells respond to visual stimuli as well. Electrically elicited saccades are closely related to this presaccadic neural activity (Bruce et al. 1985), supporting the hypothesis that presaccadic activity in the FEF is an important part of the brain's system for initiating saccades.

Other motor-related activity is evident in PFC. For example, the postsaccadic type of activity is also found in PFC outside the FEF (Bizzi 1968; Bruce and Goldberg 1985; Goldberg and Bushnell 1981), although its full extent has not been mapped. Moreover, the behavioral studies to be discussed below find substantial numbers of cells that respond in relation to the skeletal responses the monkeys are asked to perform. Often this activity precedes the movement, but sometimes it follows. Sometimes it is specific for particular movement directions, but sometimes it precedes all responses. For example, Watanabe (1986b) found a variety of relationships between PFC cell activity and key press behavior in the context of a go/no-go discrimination. Many cells responded before the presses (go trials) although some cells responded only when the animal had to withhold responding (no-go trials). Many "go" cells also responded when the monkey pressed the panel to initiate trials, indicative of a simple motor-related activity.

Spatial Memory-related Activity in PFC

Much physiological investigation of PFC has been motivated by the finding that monkeys with lesions of PFC, most especially cortex in and around the

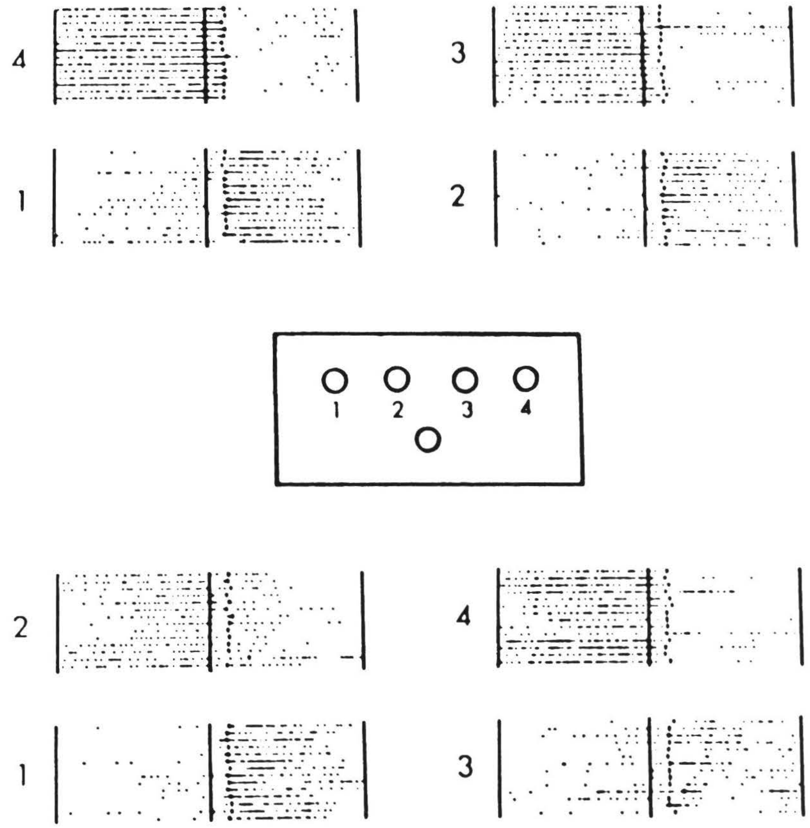


Fig. 3—PFC cell studied by Niki (1974c) with directionally selective activity during delay period of delayed alternation (DA) task. Rasters are aligned on the onset of the choice light (signal to respond) and the heavy dots indicate the key depressions. The four sets of rasters correspond to four separate experiments, each using a particular pair of the 4 choice keys. In each case this unit discharged before responses to the right key and not before responses to the left key. Therefore the unit's activity was a function of the relative, not absolute, key position. For example, examine activity for key 2 when paired with 3 versus when paired with 1, or for key 3 when paired with 4 versus when paired with 2.

principal sulcus (area 46), have a severe and specific difficulty with tasks that necessitate a short-term memory for spatial locations. After behavioral investigations over several decades into the nature of this deficit, studies of single cell activity in area 46 during delay tasks in the late 1960s by Joaquin Fuster at UCLA, and Hiroaki Niki were begun in Japan and at NIMH.

Both adopted the technique of single neuron recording in behaving monkeys that had just been developed by Ed Evarts for studying motor cortex cells, and both devised automated versions of the delay tasks that had previously been used to study the deficits of monkeys with experimental lesions. Niki (1974a) began with the delayed alternation (DA) task, whereas Fuster (1980, 1985) used the delayed response (DR) task. Both tasks tell the monkey the spatial location for the next response: the DR by an explicit visual cue, the DA implicitly by the location of the previous response. Then, both tasks impose a delay (e.g., 10–30 sec) before giving a signal to respond, and so the monkey must remember the upcoming correct direction over the delay period.

All studies found that different PFC cells respond during the different parts of the delay tasks. Thus some cells are activated by the cue, some cells are activated immediately before the response, and some cells are more or less continuously active throughout the delay. The most intriguing cells are those with differential delay activity, first reported by Niki (1974b). These cells respond throughout the delay, but only when the cued response will be in one direction, i.e., left or right. According to Niki, about 5% of PFC cells have such differential (or directional) delay (DD) activity. Subsequent studies have focused on these DD cells because their activity may represent, or indeed may help provide, the short-term memory needed to correctly perform the DR and DA tasks.

One basic question regarding DD cells is whether they code in terms of sensory cues or motor responses. In other words, is their discharge during the delay coding the location of the previous cue stimulus or the direction of the next movement? Niki and Watanabe (1976) investigated this issue by training monkeys to do three types of DR tasks: (a) conventional left-right; (b) up-down DR tasks; and (c) a conditional DR task in which the monkeys responded *right* following the up cue and *left* following the down cue. The data indicated two types of DD cells: DD-*cue* cells (~75%) responded as a function of the cue location whereas DD-*response* cells (~25%) responded as a function of the response direction. The temporal pattern of the histograms was generally consistent with this typology because the discharge of DD-cue cells appeared to begin with the cue's appearance, whereas DD-response cells appeared to increase their discharge gradually over the delay. Furthermore, the activity of the response type was predictive of errors whereas the activity of the cue type was not. Some cells could not be thus classified: perhaps they required a finer set of target locations that include oblique directions; the "memory fields" of DD neurons have not been studied quantitatively (but see Funahasi et al. 1986).

Another basic question concerns the coordinate system of DD activity. Niki (1974c) tested the relative versus absolute coding of PFC cells during the DA task. Figure 3 illustrates his task and results for one cell. Any pair of the four response keys could be designated as active for the left-right alternation task. Therefore the two inner keys, 2 and 3, could be the left hand key in one pairing and the right hand key in another. Niki found that all DD cells coded *relative*, rather than absolute, key locations. The cell in Fig. 3 discharged before responses to key 2 when key 2 was paired with key 1 and thus constituted the right-hand member of the pair, but was suppressed during the delay before responses to key 2 when it was paired with key 3 and thus was the left-hand member of the pair. Similarly, the cell discharged before responses to key 3 when it was paired with key 2, but was silent preceding responses to key 3 when it was paired with key 4. Because the monkey's head was fixed during these studies (like most other PFC recording experiments) it also follows that whatever DD activity is coding (previous stimulus or next response), the underlying coordinate system cannot be craniotopic. However, because the direction of gaze was not monitored in these and most other experiments, we cannot yet judge if a retinotopic coordinate system is consistent with Niki's findings.

Synopsis of PFC Activity during Delay Tasks

The results of the physiological investigations of cell activity during the DA, DR, and related tasks indicate a possible physiological basis for the importance of PFC in short-term spatial memory tasks. One processing model is that sensory responses in PFC are coded as short-term memories represented by the cue type of DD cell. As the monkey anticipates the time to respond, (see Niki and Watanabe 1979 and below) cue-based DD activity feeds the response-type DD cells. As discussed above, both types of DD cells appear to code in a relative rather than absolute manner, possibly divorced both from the specifics of the stimulus that gave rise to the activity and from the exact movement that the monkey will eventually perform because of it (although inappropriate DD activity in the second type of cell predicts an incorrect response). When the trigger to respond is received, directional information coded by DD-response type cells is passed to cells with differential movement-related activity. Perhaps these cells are one class of projection neurons of PFC, sending axons to premotor (PM) and supplemental motor cortex (SMA) as well as to subcortical structures in order to effect a movement. As elaborated below, another important element in this picture may involve PFC activity arising from an efferent copy of the movement actually made. It should also be noted that these delay types of activity are probably related to Walter's contingent negative variation (CNV). CNV is a slow negative potential recorded from the anterior regions of the scalp that occurs between a preliminary conditioned stimulus (CS) and the motor imperative stimulus. CNV appears shortly after the CS (after

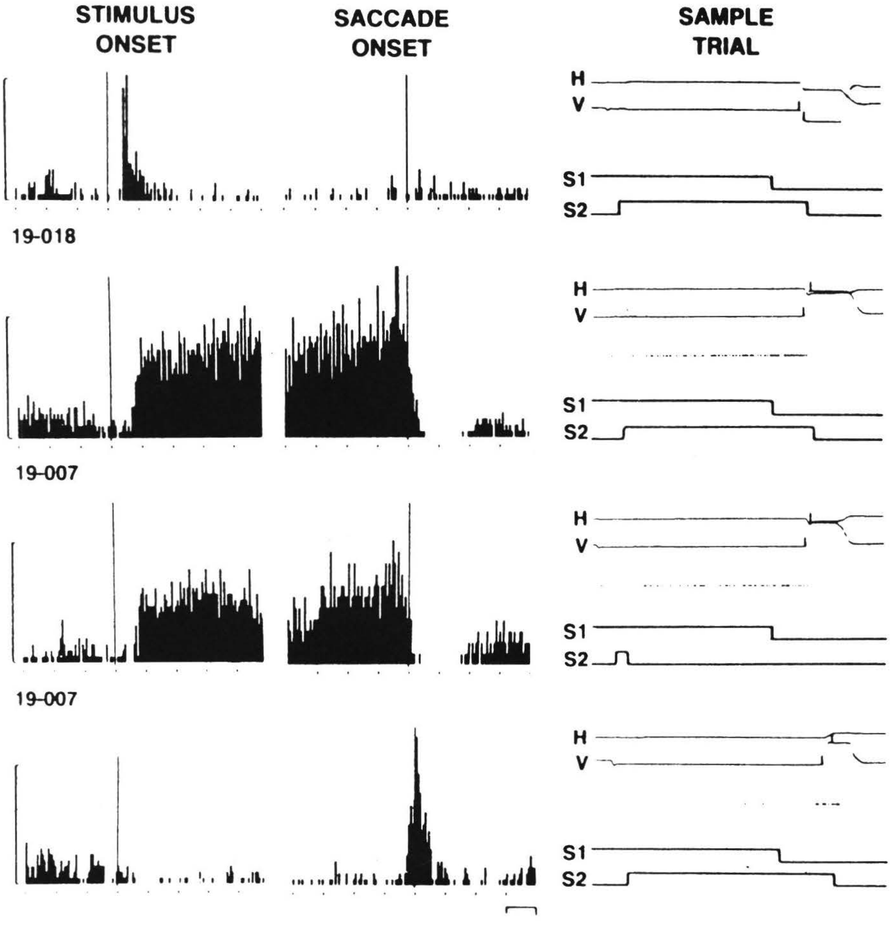


Fig. 4—Basic types of presaccadic activity in the frontal eye fields during a delayed saccade task. Each row has a histogram aligned on stimulus (saccade target) onset, a histogram of the same trials aligned on saccade onsets, and a representative trial with eye traces (Horizontal & Vertical), stimulus traces (S1 = fixation light, S2 = saccade target), and unit discharges (dots between eye and stimulus traces). Offset of S1 was the cue to saccade. Histograms all sum 16 trials. Histogram calibration lines are 100 Hz. ROW 1: *Visual cell* discharged phasically in response to stimulus onset, but was silent preceding saccades. ROW 2: *Visuomovement cell* discharged tonically from when target appeared until saccades were made. ROW 3: *Same visuomovement cell* as row 2 in a delay task: the target appeared for only 50 ms, but the cell still discharged until the saccades were made over 1 sec later. ROW 4: *Movement cell* discharged immediately before saccades but did not respond to the target's appearance. (Bruce & Goldberg 1985) a number of conditioning trials), fills the delay, and ends upon execution of the motor response.

Spatial Memory Related to Eye Movements

Mnemonic activity similar to that of the DD cells can also be demonstrated in an oculomotor version of the DR task, both in the FEF and in neighboring area 46. FEF cells with both visuomovement activity and purely visual activity may continue to respond for several seconds following the presentation of a brief saccadic target in their RF (Bruce and Goldberg 1985). Figure 4 shows that this mnemonic type of activity (3rd row) is almost indistinguishable from the activity of the same cell during a task in which the target was continuously present, but the monkey must also delay its saccade (2nd row). Thus the FEF have cue, movement, and mnemonic types of activities analogous to those described in PFC using skeletal DR tasks (Fuster 1985). Recently, we have discovered that many area 46 cells have an analogous DD type of activity in conjunction with oculomotor delay tasks (Funahashi et al. 1986), and are now testing whether or not DD activity of area 46 cells is specific for the modality of stimulus and type of motor response.

Anticipatory Neuronal Activity in PFC

For about 20% of the movement and visuomovement types of presaccadic cells in the FEF (Bruce and Goldberg 1985; Goldberg and Bruce 1985), an anticipatory activity that precedes the appearance of the target becomes evident after the monkey has made saccades into a cell's movement field in several successive trials. Similarly, Niki and Watanabe (1979) noted cells with anticipatory discharges in DA and DR and also demonstrated anticipatory activity during an explicit timing task. They found many response anticipation cells in both PFC and the neighboring anterior cingulate area. As was the case in the FEF, response anticipation cells were sharply silenced following execution of the motor response.

EFFERENT COPY AND VECTOR OPERATIONS IN PFC

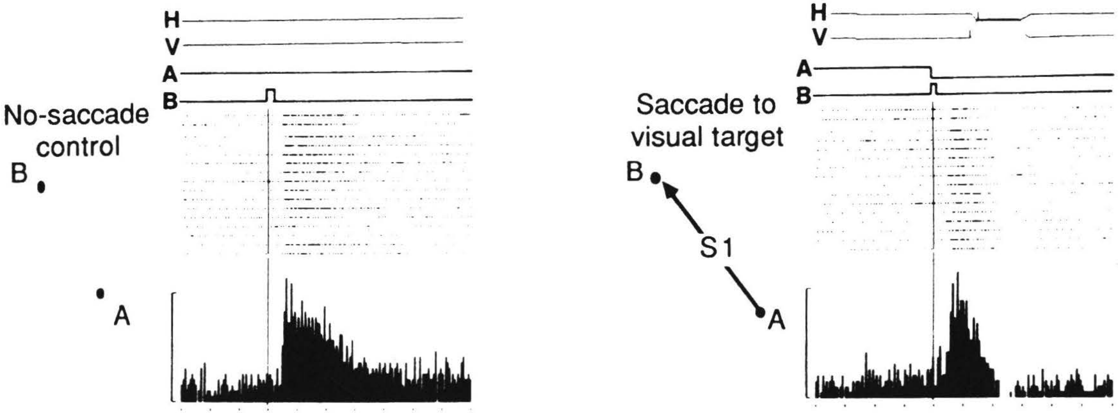
This section outlines an efferent-copy/vector-subtraction hypothesis which is motivated by recent physiological studies of the FEF (Bruce and Goldberg 1985; Bruce et al. 1985). The model emphasizes that the FEF receive an efferent copy of each saccadic eye movement made, and postulates that this postsaccadic activity is vectorially substracted from ongoing presaccadic FEF activity that may or may not have provoked that saccadic eye movement in the first place. I will (a) review the physiological evidence for an efferent copy subtraction in the FEF; (b) present a block model for this subtraction in the context of the overall saccadic system; and (c) propose a neural mechanism for efferent copy subtraction based on the topography of population activities across the FEF.

Background for the Model

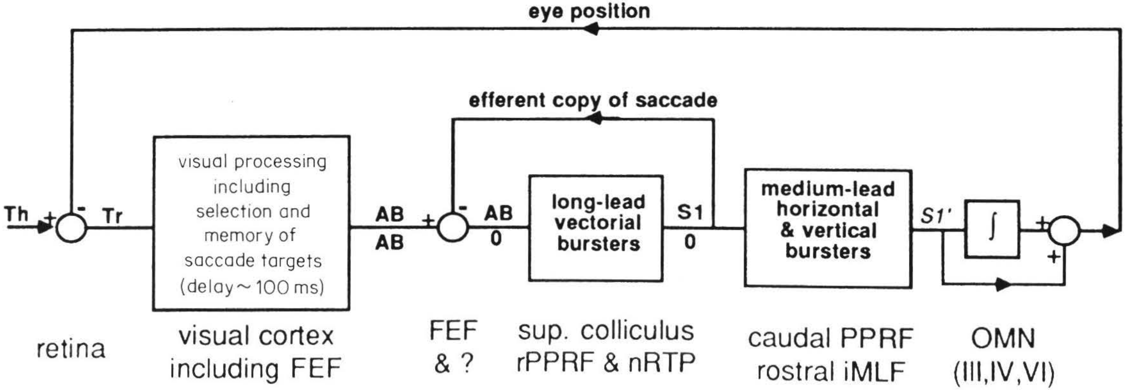
Many investigators have emphasized sensory or other premovement activities of PFC cells because premovement activity provides a neural mechanism for initiating behavior. For example, studies in area 46 emphasize how differential neural activity during the delay (DD activity) could be a mechanism for correct DR behavior. Similarly, the FEF have distinct types of presaccadic activity (anticipatory, visual, and movement) (Bruce and Goldberg 1985), which help provide adaptive control of saccadic eye movements. However, a ubiquitous aspect of premovement activity in prefrontal cortex is that it ceases when the response is executed. Perhaps this aspect holds less interest because there are sometimes trivial reasons for why a cell's response ceases. For example, a discharge may end because the response is inherently phasic in nature or because the eliciting stimulus was removed from the receptive field, either by the experimenter or by an eye movement of the subject. Therefore, it may seem that these reasons would explain why, in standard visually guided saccade tasks, most presaccadic activity in the FEF stops in conjunction with the execution of the saccadic eye movements. However, Fig. 5a shows an experiment demonstrating that the ending of presaccadic activity in the FEF is an active consequence of saccadic eye movements (Bruce and Goldberg 1985), not just a passive waning of the elicited visual response. This cell had tonic responses to brief visual stimuli in the fixation task, yet responses to the same physical stimulus were truncated in the saccade task. As is evident by examining several histograms in published studies (Bruce and Goldberg 1985; Bruce et al. 1985; Goldberg and Bruce 1985; Goldberg and Bushnell 1981) this postsaccadic cessation of activity was usually sharp, complete, and in a consistent temporal alignment with the saccadic movement, even when monkeys naturally varied their saccade latencies (e.g., Fig. 4 and Fig. 9 in Bruce and Goldberg 1985) or when arbitrary delays were imposed (e.g., Fig. 4). Usually the spike rate following saccades fell below the baseline rate, and often cells were briefly silent in marked contrast to their robust activity preceding the saccade. The exact onset of suppression of presaccadic activity varied from cell to cell, ranging from approximately the start of the saccade (see Fig. 7 in Goldberg and Bruce 1985) to nearly 100 ms after the saccade ended.

Area 46 neurons have a similar pattern of suppression, evident in published examples showing cells that discharged either throughout the delay interval

A


H
V
A
B
No-saccade control
B
A
H
V
A
B
Saccade to visual target
B
S1
A

B


eye position
Th
+
-
Tr
visual processing including selection and memory of saccade targets (delay ~ 100 ms)
AB
AB
+
-
AB
0
efferent copy of saccade
long-lead vectorial bursters
S1
0
medium-lead horizontal & vertical bursters
S1'
∫
+
+
retina
visual cortex including FEF
FEF & ?
sup. colliculus rPPRF & nRTP
caudal PPRF rostral iMLF
OMN (III,IV,VI)

or immediately before the end of the delay, but ceased discharging upon the monkey's behavioral action (Fig. 3). The exact temporal relation of the arm movement to the suppression is not evident in these studies because the rasters are aligned on either the response key closure or the cue to move. Dramatic cessation of premovement activity following the movement is also seen in premotor cortex (Brodmann's area 6, behind PFC; see Fig. 7 in Evarts et al. 1984).

Source of Movement-related Suppression

This suppression of presaccadic activity might be effected via the postsaccadic activity in the FEF originally seen by Bizzi (1968). The source for both the suppression and the postsaccadic activity is probably an efferent copy of saccadic eye movements from premotor centers in the brain stem (e.g., burst neurons of deeper intermediate layers of the superior colliculus or similar vectorial bursters in the different parts of the brain stem saccade generator – see Fig. 5b). Postsaccadic activity in the FEF behaves like an efferent copy in that it reliably follows each saccade the monkey makes into its movement field, even spontaneous saccades made in the dark or rapid phases of nystagmus (Bizzi 1968; Bruce and Goldberg 1985; Bruce et al. 1985). Explicit postsaccadic activity could mediate the suppression via local inhibition.

Fig. 5A—Suppression of visual activity in the frontal eye fields by saccadic eye movement. *LEFT*: Raster-histogram showing tonic discharge of FEF neuron (#13–370, Bruce and Goldberg 1985) to a brief (50 ms) visual stimulus in its receptive field. Calibration lines on the ordinate are 100 Hz; tics along the abscissa are spaced every 200 ms. *RIGHT*: Rasters-histogram showing a visually-guided saccade to the same RF stimulus. Visual responses were tonic in the fixation task; however, in the saccade task the discharge quickly declined and went below baseline @ 400–600 ms post-stimulus. Histograms based on eye records showed that this cell was completely suppressed for approximately 100 ms beginning 100 ms after the saccade ended.

Fig. 5B—Model of efferent copy feedback to cancel presaccadic FEF activity. Visual processing box encompasses several areas (prestriate areas, post. parietal cortex, superficial sup. colliculus, etc.) as well as FEF, that participate in the target selection process as well as memory for targets. Brain stem saccade generator has an early stage coded vectorially (by cells with arbitrary movement fields) by long-lead bursters in the intermediate layers of superior colliculus, rostral paramedian pontine reticular formation (rPPRF), and nucleus reticularis tegmentus pontis (nRTP), and a later stage coded for primary actions of eye muscles via medium-lead bursters that discharge in proportion to a saccade's horizontal (caudal PPRF) and vertical (rostral iMLF) components. Th and Tr are targets in head and retinal coordinates. Details of the saccade generator such as the pause cells are omitted, as is a mechanism to convert its vector-coded inputs into frequency-coded bursts for the particular oculomotor nuclei (OMN).

In contrast to postsaccadic activity, presaccadic activity in the FEF is an unreliable index of saccades in several ways. First, much presaccadic activity in the FEF requires visual targets and is absent in conjunction with spontaneous saccades in the dark. Second, even those cells discharging before purposive saccades made without visual targets respond less if at all when the same saccades are made spontaneously in the dark (Bruce and Goldberg 1985). Lending strong support to the efferent copy hypothesis, a suppression below baseline follows spontaneous saccades in the dark even when the presaccadic activity is missing (Figs 6 and 7 in Bruce and Goldberg 1985). Third, during difficult paradigms such as the two-step saccade paradigm described below, FEF movement cells may burst in the absence of an actual saccade (Goldberg and Bruce 1981), as if their signal for a saccade was ignored by the brain stem. Again consistent with the efferent copy/cancellation hypothesis, such inconsequent "presaccadic" activity is prolonged relative to trials having saccades.

Model for the Role of Efferent Copy in the FEF

Figure 5B has a block diagram of an efferent copy model for suppression of presaccadic FEF activity. The main sequence has target signals being selected and passed to the saccade generator downstream; however, the model hypothesizes that when a saccadic eye movement is programmed, an efferent copy of that movement is sent to the FEF and effectively cancels ongoing presaccadic activity there that may have helped elicit the movement. Notice that presaccardic signals are never coded in craniotopic (often called "spatial") coordinates until they reach the neural integrator immediately before the extraocular motor neurons. Thus for the saccadic system, visual signals remain retinotopic and presaccadic signals are coded as movement vectors, not as orbital goals. The saccade generator is not delineated here; some models use an additional neural integrator to sum the output of a pulse generator and reset it after each saccade. However, most extant models operate in the spike frequency domain whereas signals in the FEF, superior colliculus, and elsewhere prior to the saccade generator follow a place code. The problem of converting the place code of the retina and most of the visual system to the frequency code required by oculomotor neurons is not solved by my model either, although it acknowledges this problem by splitting the saccade generator into "place" and "frequency" stages (Henn et al. 1982).

Functional Implications of the Model: One-step Task

This model provides a mechanism whereby the FEF can prolong visual activity indefinitely and yet provoke only one saccade in response to a particular visual target. Prolonged electrical stimulation of the FEF, like the superior colliculus, elicits a staircase of saccades, each saccadic "step" having a similar size and direction with brief refractory periods of ~100 ms separating successive saccades. Because electrical thresholds for eliciting saccades are lowest near FEF cells with presaccadic activity and the size and direction of elicited saccades matches the movement field for presaccadic activity (Bruce et al. 1985), it follows that prolonged activity of presaccadic cells risks a similar consequence: repeated elicitation of a particular saccade. In the model, an efferent copy feedback ends presaccadic activity before the refractory period of the brain stem saccade generator elapses, thus preventing the FEF from triggering an erroneous additional saccade.

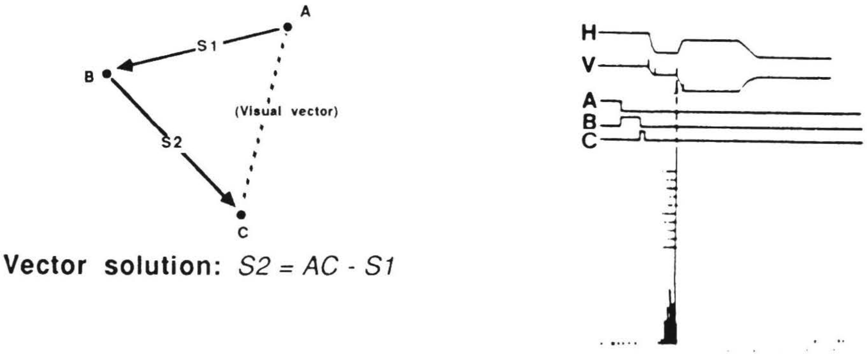
Further Implications of the Model: Two-step Task

When cancellation via efferent copy is formulated as a vector subtraction, then additional implications are evident. Consider the two-step saccade task (Hallet and Lightstone 1976) illustrated in Fig. 5. After the monkey obtains fixation of target A, A is extinguished and two successive targets are flashed at B and then at C. Presentations are sufficiently brief so that C is extinguished before any saccade begins. As shown, the monkey first saccades to location B and then makes a second accade from B to C.

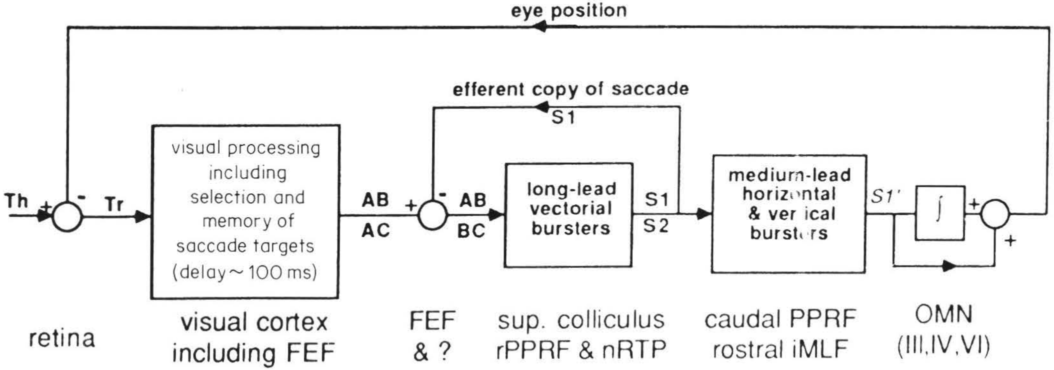
Although this is a contrived situation, humans naturally perform this two-saccade response when simply instructed to follow the light, as do monkeys who have been previously trained to saccade to briefly illuminated targets. Actually, the essence of the task is not a planned, voluntary chain of saccades, but rather that after a saccade to target B is programmed and passes a "point of no return", the subject realizes that B is incorrect and that C is the correct target. The saccade to B cannot be stopped, but immediately (~100 ms) after it ends the subject fashions a second saccade that foveates C, or rather where C had been flashed on the screen. The intriguing aspect of this phenomenon, and the reason why variants of this task have been intensively studied in man and monkeys for the past two decades, is that the peripheral retinal locus corresponding to the second saccade is never stimulated. Thus, the brain fashions a saccade that is visually guided yet quite different from the retinal vector provided. For example, this phenomenon has been exploited to show that the activity of movement cells in the intermediate layers of the superior colliculus cannot be simply imposed by the visual map of the superficial layers (Sparks and Porter 1983).

The "solution" most often proposed for this two-step task involves translating target C into craniotopic space by adding a gaze vector to its retinal coordinate, with the implication that saccades are made in a craniotopic, not retinotopic manner. Rather than considering the pros and

A


A
S 1
B
(Visual vector)
S 2
C
Vector solution: S2 = AC - S1
H
V
A
B
C

B


eye position
efferent copy of saccade
S1
Th
+
-
Tr
visual processing including selection and memory of saccade targets (delay ~ 100 ms)
AB
AC
+
-
AB
BC
long-lead vectorial bursters
S1
S2
medium-lead horizontal & vertical bursters
S1'
∫
+
+
retina
visual cortex including FEF
FEF & ?
sup. colliculus rPPRF & nRTP
caudal PPRF rostral iMLF
OMN (III,IV,VI)

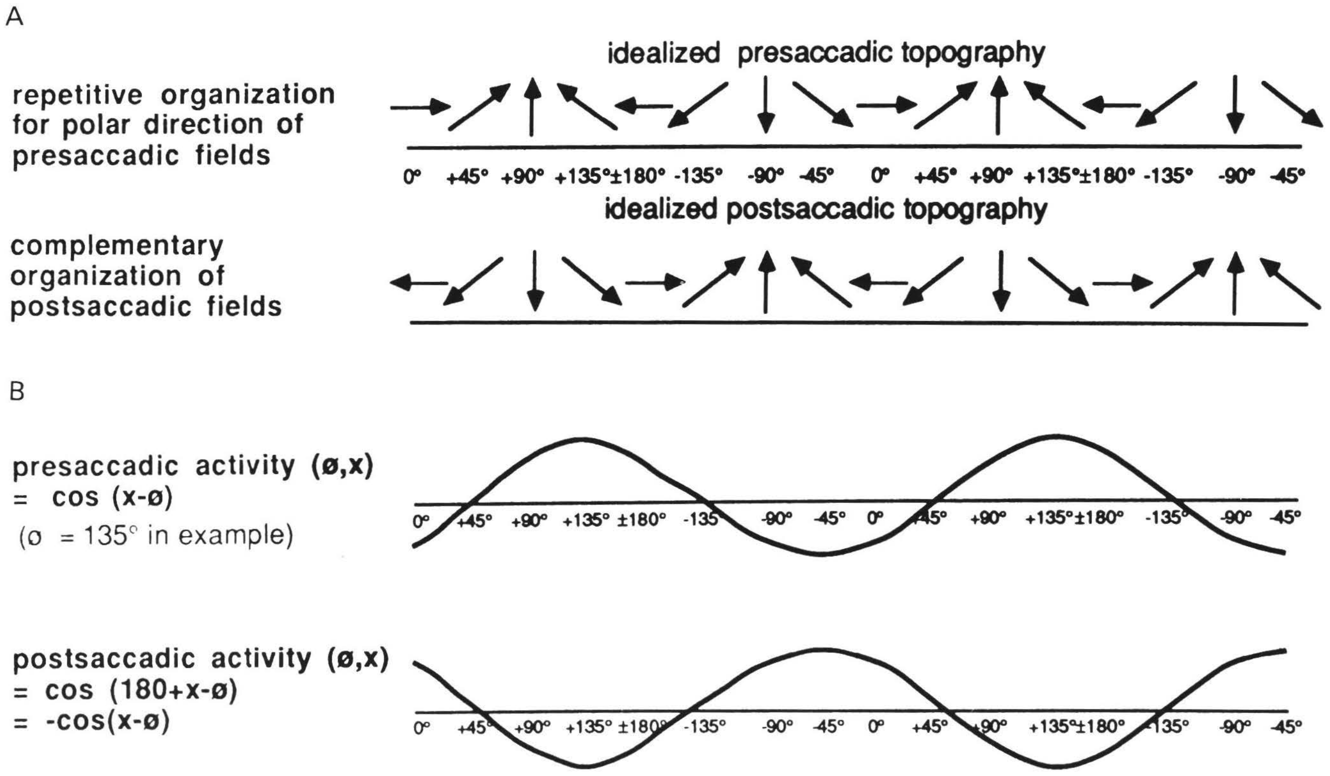
cons of this approach, I want to show how the vector subtraction of efferent copy model, which serves to cancel presaccadic activity for simple visually guided saccades, also solves this two-step task. As shown in Fig. 6, this vector arithmetic approach is simple: the saccade from B to C is retinotopic vector AC minus the initial saccade S1 (vector AB).

Thus, the saccade system can solve the two-step task by this simple vector subtraction. It appears that the FEF may do just that (Goldberg and Bruce 1981). After the movement field of each presaccadic FEF neuron was mapped with a standard visual saccade task, the two-step task was arranged so that the second saccade vector corresponded to the cell's best saccade. Nearly all FEF cells with presaccadic movement activity, like the one shown in Fig. 6A, discharged before this saccade into their field even though visual stimuli never appeared there. Their activity began immediately after the first saccade was made and stopped when the second saccade was made.

This vector arithmetic operation could be done in the FEF because all three necessary pieces of information are found there: the minuend, carried by retinotopic visual activity; the subtrahend, carried by postsaccadic activity; and the difference, that is the premovement activity that "solves" the two-step task. This scheme is outlined in the same block model given in the previous figure, but now applied to the two-step task. In the first time frame (above the main line), retinotopic vector AB exits the selection box indicating the subject's initial selection of target B. There is nothing to subtract because the subject has been fixating, and hence signal AB passes to the saccade generator which programs saccade vector S1 (from A to B). In the second time frame (below the main line) target C (retinotopic vector AC) is selected; however, before the refractory period of the saccade generator

Fig. 6A—Vectorial diagram of two-step saccade task (*LEFT*), and responses of a frontal eye field visuomovement neuron in this task (*RIGHT*). Monkey first fixates light A, then A is extinguished and lights B and C are sequentially flashed, with light C extinguished before saccade S1 begins. Times of the flashes are adjusted to obtain successive saccades to B, and then from B to C. Equation shows that saccade vector S2 equals visual vector AC less saccade vector S1. *RIGHT*: Visuomovement FEF neuron (Goldberg and Bruce, unpublished) tested in a two-step task contrived to have saccade S2 match the cell's movement field. The cell responded immediately after the first saccade, but did not respond to either the first saccade or the second target when tested separately in control tasks.

Fig. 6B—Block model of previous figure applied to the two-step task. The signals passed between the blocks during two successive time frames are indicated above and below the main path. Target B (retinal vector AB) is selected in the first time frame, and then target C (retinal vector AC) is selected for the second time frame. When the saccade generator exits its refractory state following saccade S1 and is ready to process the second target selection (AC), an efferent copy of saccade S1 has arrived over the feedback path, producing the difference vector BC for the saccade generator, which then generates saccade S2.


A
idealized presaccadic topography
repetitive organization for polar direction of presaccadic fields
0° +45° +90° +135° ±180° -135° -90° -45° 0° +45° +90° +135° ±180° -135° -90° -45°
idealized postsaccadic topography
complementary organization of postsaccadic fields
B
presaccadic activity (ø,x) = cos (x-ø)
(ø = 135° in example)
0° +45° +90° +135° ±180° -135° -90° -45° 0° +45° +90° +135° ±180° -135° -90° -45°
postsaccadic activity (ø,x) = cos (180+x-ø) = -cos(x-ø)
0° +45° +90° +135° ±180° -135° -90° -45° 0° +45° +90° +135° ±180° -135° -90° -45°

elapses an efferent copy of S1 is subtracted from AC. This means that vector BC, not AC, is sent to the saccade generator, which programs S2, the correct second saccade.

POPULATION MECHANISMS FOR VECTOR OPERATIONS IN CORTEX

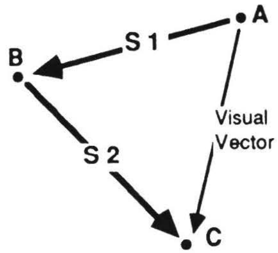
To complement the block model, a standing wave hypothesis of how the cortex of the FEF might compute the vector subtraction just discussed is presented in Figs. 7 and 8. The hypothesis is based on three particular aspects of FEF physiology:

1) *Repetitive organization of saccade direction across the FEF as mapped by microstimulation.* As mentioned earlier, the FEF have a global topography for saccade amplitude, but not for saccade direction. Instead, electrode penetrations down the bank of the arcuate sulcus indicate that saccade direction is represented in a repetitive manner (Bruce et al. 1985), resembling the organization of stimulus orientation preferences across striate cortex or stimulus motion preferences across area MT (Albright et al. 1984). The top row in Fig. 7 shows an idealized mapping of saccade direction across the FEF.

2) *Complementary postsaccadic activity*. The model postulates that postsaccadic activity is mapped across the FEF in a topography that complements the mapping of presaccadic activity. In addition to the purely postsaccadic cells, a number of FEF cells combine pre-and postsaccadic activities. In such cells the movement field for these two types of responses are opposite; that is, if there is activity before saccades in one direction then the activity following saccades is maximal for saccades directly opposite the presaccadic field (e.g., Fig. 20 in Bruce and Goldberg 1985, Fig. 6 in Bruce et al. 1985).

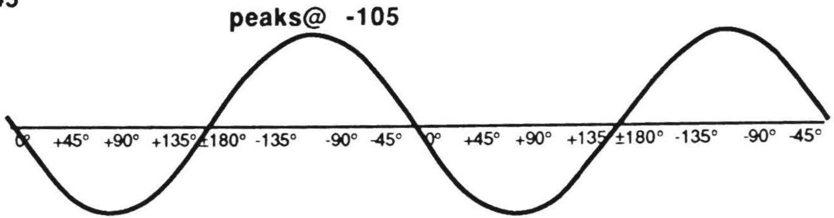
Fig. 7A—Idealized organization of polar direction topography (visual or movement) across the frontal eye fields (FEF). Presaccadic field local topography (*TOP*) based on mapping the FEF with microstimulation (Bruce et al. 1985). *Below* is complementary postsaccadic local topography based on the finding that FEF cells that have both presaccadic and postsaccadic activity have pre- and postsaccadic movement fields with opposite directions (Bruce and Goldberg 1985).

Fig. 7B—Idealized standing wave pattern of activity across the FEF in response to a particular saccade. *TOP*: Activity preceding saccade of direction $\emptyset$ is maximal at points representing $\emptyset$ (in the example $\emptyset = 135°$). Sinusoidal functions analytically represent the broad tuning of FEF visual and movement fields (Bruce and Goldberg 1985) and the multiple representations of each direction. *BOTTOM*: Inverse pattern of postsaccadic activity following saccade direction $\emptyset$. Pre- and postsaccadic activity associated with the same polar angle will destructively add, providing a mechanism for the efferent copy subtraction hypothesized in the block model of the previous figure.

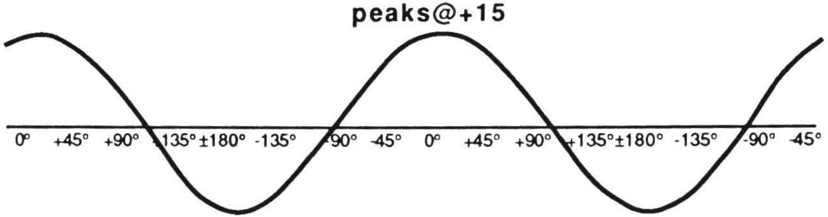


$\O\,(AC) = -105°$
$\O\,(S1) = -165°$
$\O\,(S2) = -45°$

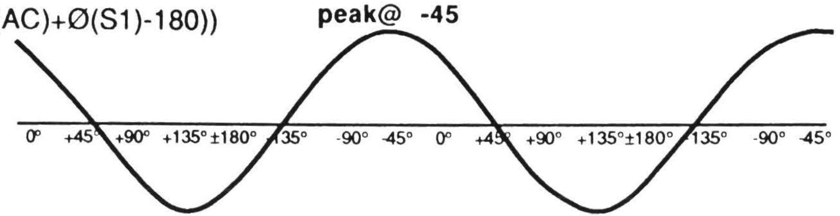
presaccadic activity(AC)
$= \cos(x - \O\,(AC))$
$= \cos(x - (-105))$



postsaccadic activity (S1)
$= \cos(x - \O\,(S1) + 180)$
$= \cos(x - 15)$



sum = presaccadic activity(S2)
$= 2\sin(1/2\,(\O(AC) - \O(S1))) \cdot \cos(x - 1/2(\O(AC) + \O(S1) - 180))$
$= 2\sin(30) \cdot \cos(x + 45)$
$= \cos(x - (-45))$
$\rightarrow \O(S2) = -45°$



3) *Broad movement fields*. FEF presaccadic and postsaccadic fields all have broad tuning for polar direction (Bruce and Goldberg 1985), so the postulated vector operations must act on population activity that codes spatial information with activity across many individual neurons.

The standing wave hypothesis is diagrammed in Fig. 7b. It assumes that the intrinsic circuitry of the cerebral cortex coerces it toward activity patterns of standing waves of a standard amplitude and periodicity, phase being the only continuously adjustable parameter. Sinusoidal functions are used to represent the population responses to a single stimulus or movement. The sinusoid fit is satisfactory if tuning curves of individual cells had a half width of ±45° and a full width of ±90°; we (Bruce and Goldberg 1985) fit FEF fields with Gaussian distributions for polar direction and found comparable tuning. Determination of the precise function will require empirical and theoretical analysis.

The model postulates that postsaccadic activity merges with the ongoing presaccadic activity in an additive manner. In Fig. 7, notice that the presaccadic standing wave corresponding to a direction $\emptyset$ will be perfectly cancelled by adding the postsaccadic standing wave that follows the saccade made in direction $\emptyset$.

Figure 8 examines the model in the context of the two-step task. Here the presaccadic standing wave corresponding to the direction of the second visual target is transformed, rather than cancelled, by the first saccade, yielding a new standing wave that corresponds to the correct second saccade. This case is also solved analytically in the left-hand equations, under the assumption that the standing waves are sinusoids. The two-step case introduces the additional assumption that new target selections can sometimes simply replace (rather than add to) ongoing presaccadic activity. In fact, recent studies indicate that when two targets are presented simultaneously, saccades are directed at their average location if the targets are close together, but to one or the other target location (i.e., bistable) if the targets are spatially separate. In polar coordinates the critical difference is about 30° (Ottes et al. 1984).

The model has problems that can only be alluded to in this short paper. First, it is undefined with respect to saccade amplitude; even when the minuend and subtrahend are the same size the difference amplitude may

Fig. 8—Standing wave hypothesis (see previous figure) yields analytical and graphical solutions of two-step saccades, suggesting a population mechanism for the vector subtraction model. *LEFT*-hand equations show sum of two cosines analytically derived via trigonometric identities. Addition of the two cosine functions yields a cosine of the same period, but with a different phase, corresponding to a different polar direction. The sum also has a different amplitude, equal to 1.0 in this particular example, but ranging from 0.0 (destructive cancellation) to 2.0 (constructive addition).

be different. However, this omission could be taken as predicting that vector operations between saccades of widely differing amplitudes would be poorly done, just as the smooth pursuit and saccadic systems fail to communicate well in variants of the two-step task. Another important problem concerns joining ipsilateral and contralateral fields because the FEF, like most other visual and oculomotor structures, represents only the contralateral field in each hemisphere. The corpus callosum may help solve this problem by joining the two FEF at their vertical saccade representations (Bruce and Goldman-Rakic 1984). However, despite all of these issues, this standing wave model is basically correct in that it is more a synthetic description of FEF physiology (Bruce and Goldberg 1984, 1985; Bruce et al. 1985) than an independent theory derived from mathematical considerations.

GENERAL IMPLICATIONS FOR FRONTAL LOBE FUNCTIONS

The two-step saccade task is essentially a convenient way of reliably having the subject select a particular goal and then execute a movement that fails to achieve that goal. In the oculomotor sphere an efferent copy of the saccade actually made, correct or erroneous, is used to compute the remaining vectorial error and the physiological activity of the FEF reflects such a subtraction mechanism, in both simple visually-guided and two-step saccade situations. An important issue for future studies involves what types of efferent feedback in other areas of PFC have as the type of feedback must match the functions of each area. In general, prefrontal cortex appears crucial for maintaining behavorial goals while processing ongoing information, actions, and thoughts directed at achieving them. My hypothesis is that such "efferent feedback" is essential for stepping PFC through different patterns of activity in accord with external and internal events that govern its goals, in the same way that FEF activity can sustain a saccadic goal for several seconds, yet its pattern of activity changes within a fraction of a second in response to feedback from oculomotor behavior.

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