

Intention, Action Planning, and Decision Making in Parietal-Frontal Circuits

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The posterior parietal cortex and frontal cortical areas to which it connects are responsible for sensorimotor transformations. This review covers new research on four components of this transformation process: planning, decision making, forward state estimation, and relative-coordinate representations. These sensorimotor functions can be harnessed for neural prosthetic operations by decoding intended goals (planning) and trajectories (forward state estimation) of movements as well as higher cortical functions related to decision making and potentially the coordination of multiple body parts (relative-coordinate representations).

Introduction

Frontal and parietal areas are strongly interconnected and function together for many aspects of action planning. Historically, a role of frontal lobe in action has been clear (Fritsch and Hitzig, 1870; Ferrier, 1876). The primary motor cortex (M1) is a source of motor commands (Penfield and Boldrey 1937; Evarts and Thach, 1969), and more anterior regions of the frontal lobe are involved in many higher-level aspects of movement planning and decision making (Miller and Cohen, 2001; Wise, 1985). The anterior aspect of the parietal lobe is well established in the processing of somatosensory information (Mountcastle, 1957). The posterior parietal cortex (PPC) has previously been considered important for spatial attention, spatial awareness, and polysensory integration (Critchley, 1953; Ungerleider and Mishkin, 1982; Colby and Goldberg, 1999). In recent years, however, a number of studies suggest that, although the PPC is involved in these sensory functions, it has also been shown in different contexts to be important for aspects of action, including movement intention and decision making (Mountcastle et al., 1975; Andersen, 1987; Andersen and Buneo, 2002; Gold and Shadlen, 2007; Rizzolatti et al., 1997; Kalaska et al., 1997; Johnson et al., 1996; Burnod et al., 1999; Lacquaniti et al., 1995; Graziano and Gross, 1998; Desmurget et al., 2009; Rushworth et al., 2001). In this review, we refer to intention as movement planning at a cognitive level rather than at the level of movement execution (Andersen and Buneo, 2002). One example indicative of this more cognitive level is that the goals for visually guided reach movements are encoded predominantly in visual coordinates rather than muscle coordinates in the parietal reach region (PRR). Intention is not meant to refer to purpose or attitude (Schall, 2004). The strong reciprocal connections between the PPC and broad areas of the frontal lobe anterior to M1 likely comprise circuits for these action-related processes (Andersen et al., 1990a; Goldman-Rakic, 1988). The review will present PPC within the framework of its involvement with a number of functions that can be broadly classified as sensorimotor transformations (Andersen, 1987; Andersen et al., 1997; Andersen and Buneo, 2002). We will focus primarily on new research regarding four roles of PPC and associated frontal lobe areas in sensorimotor transformations related

to action, including movement planning, decision making, the formation of internal models, and coordinate transformations. The review will focus on two areas in the PPC: the lateral intraparietal area (LIP) and the parietal reach region (PRR). It will also include areas in the frontal lobe connected to PPC, particularly the dorsal premotor cortex (PMd), and other areas within the PPC, such as area 5. In the final section, we will show examples of “proof of concept” in which the action-related activity in the PPC and PMd cortex can be decoded and used to provide control signals for neural prosthetic applications.

Movement Planning

An important property of the cerebral cortex is its anatomical organization according to function. This fact is fortunate for neuroscientists, since this anatomical parcellation provides a tractable approach to understanding cortical networks by studying their component parts.

The PPC had previously been considered as a typical association cortex containing largely two areas, Brodmann's areas 5 and 7 or Von Economo's areas PF and PG, based on cytoarchitecture (Brodmann, 1909; Von Economo, 1929). As a typical association cortex, PPC's function has been thought to receive convergent multisensory inputs, form a unitary map of space, and then relay spatial information to the frontal motor areas to guide behavior. However, relatively recent neuron recording, neuroanatomical tracer, and BOLD imaging studies have revealed accumulating evidence of a variety of functional areas in the PPC (Andersen and Buneo, 2002; Mountcastle, 1998; Rizzolatti et al., 1997; Graziano and Gross, 1998), particularly areas within the intraparietal sulcus (IPS; Blatt et al., 1990). Furthermore, PPC is actively involved in movement planning (Mountcastle et al., 1975; Gnadt and Andersen, 1988). Parietal and frontal areas share similar properties and work together through their association pathways in a collective manner (Johnson et al., 1996; Burnod et al., 1999). Individual areas in the PPC have been found to encode different kinds of movements associated with different body parts. Area 5 represents spatial information for limb movement and is involved in reaching arm movements (Lacquaniti et al., 1995; Kalaska et al., 1997).

The anterior intraparietal area (AIP) appears selective for grasps (Sakata et al., 1997; Baumann et al., 2009) and is interconnected with the ventral premotor cortex (PMv) (Tanne-Gariepy et al., 2002), which also has activity related to grasp movements (Rizzolatti et al., 1988). Inferior parietal lobule (IPL) neurons have been demonstrated not only to encode specific acts but also to discharge during the observation of acts done by others (Fogassi et al., 2005). Electrical stimulation of the IPL in human patients triggered strong intention and desire to move their body parts (Desmurget et al., 2009). This latter finding is very important because recording data from monkeys show neural correlates of intention (Gnadt and Andersen, 1988; Snyder et al., 1997; Andersen and Buneo, 2002), but these human experimental interventions show a role of PPC in the awareness of intention. Interestingly, stimulation of the premotor cortex produced movements, but the patients denied they had moved, indicating that increased activity in the premotor cortex did not lead to the conscious awareness of intent.

Two areas of particular interest to this review, LIP and PRR, are respectively more selective for eye movements and reaching (Andersen et al., 1987; Snyder et al., 1997; Quian Quiroga et al., 2006; Cui and Andersen, 2007). LIP is located in approximately the middle third of the lateral bank of the IPS. PRR was originally defined as an area medial and posterior to LIP (Snyder et al., 1997) and may have included more than one cortical area. Many subsequent PRR studies have largely targeted the medial bank of the IPS (Bhattacharyya et al., 2009; Baldauf et al., 2008; Pesaran et al., 2008; Cui and Andersen, 2007; Scherberger and Andersen, 2007; Pesaran et al., 2006). These areas in turn are largely connected to frontal lobe areas with similar functional selectivities—LIP to the frontal eye fields and PRR to the PMD (Andersen et al., 1985a, 1990a; Johnson et al., 1996; Tanne-Gariepy et al., 2002).

Effector Specificity

Effector specificity in general refers to activity that is specific to planning to move or to moving a particular body part. In this review, we will refer to the hand and eye preference for movement planning as effector specificity, and this term is meant to indicate relative, not absolute, specificity. For example, an area may be active for planning a reach or a saccade, but if it is significantly more active for one plan over the other, with all other variables being the same, we will label it effector specific. Since areas specific for reaching and looking are strongly interconnected within parietal and frontal cortex, no doubt for integrative purposes such as eye-hand coordination, it is not surprising to find some degree of common activation.

Early studies examining neural activity during reaching and looking found a double dissociation, with LIP more active for saccades and PRR more active for reaches (Snyder et al., 1997). A subsequent study showed that movement plans can be decoded better from populations of LIP and PRR neurons than the spatial location of the focus of attention (Quian Quiroga et al., 2006). Also, the local field potentials in PRR show distinctly different patterns for reaching compared to looking (Scherberger et al., 2005). In autonomous reach target selection tasks, PRR shows differential activity consistent with the spatial location of the chosen reach but little differential activity for saccade target selection (Scherberger and Andersen, 2007) (Figure 1).

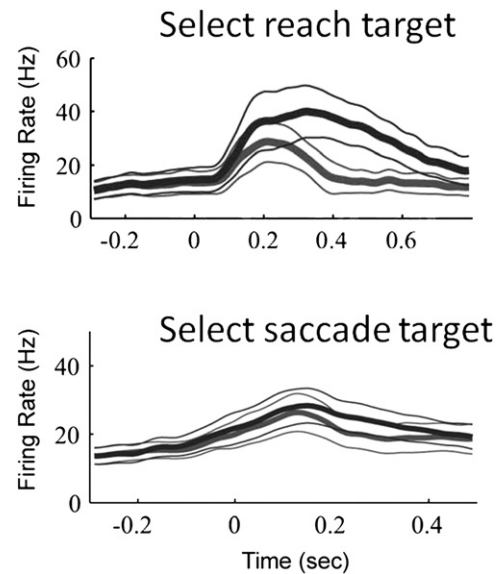


Figure 1. Population Activity of PRR Neurons during Autonomous Target Selection

The top row shows the mean firing rate (and 95% confidence limit) in the target selection for reach movements to the preferred (inside the response field, dark curve) and nonpreferred (outside the response field, light curve) target, aligned to the target onset (time 0). Bottom row shows the population activity in the saccade task. Reproduced with permission from Scherberger and Andersen (2007).

The demonstration of effector specificity in no way excludes attention-driven modulation in addition to this specificity (Snyder et al., 1997; Andersen et al., 1997; Quian Quiroga et al., 2006). However, the presence of planning activity in an area does caution against assuming that any increase in activity in PPC during behavior must be attention related (for instance, see “Potential Plans” section below) and emphasizes the importance of introducing controls to distinguish between attention and planning contributions to the activations.

A similar dissociation for reach and eye movements in PPC has been seen in human imaging studies. The degree of dissociation compared to overlap has varied in these studies (Connolly et al., 2003; Astafiev et al., 2003; Levy et al., 2007; Hagler et al., 2007) and likely reflects differences in the experimental design. Experiments that focused on the delay/planning period or that provided both the effector and target together rather than just the effector, or that used reaching movements instead of finger pointing movements provided the greatest degree of separation.

PPC Encodes Autonomously Chosen Motor Plans

PPC neurons can be selective for experience-dependent categorical representations (Freedman and Assad, 2006; Toth and Assad, 2002) and cognitive set regarding task rules (Stoet and Snyder, 2004). Cues are often used in these tasks and are stimuli that instruct the animals in what to do. Since earlier studies of effector specificity in LIP and PRR used red stimuli to instruct saccades and green stimuli to instruct reaches (Snyder et al., 1997; Quian Quiroga et al., 2006), it is possible that the specificity may be related to the meaning of the cue (i.e., red means saccade, green means reach) and still be sensory related rather

than reflecting actual planning. To address this possibility, a task was designed in which the stimuli were always the same and the monkeys autonomously chose whether to make a reach or a saccade (Cui and Andersen, 2007). Thus, any difference in activity cannot be attributed to sensory attributes of the stimuli but rather reflects the decisions and plans of the animals.

Figure 2 shows population activity from two animals for the autonomous choice trials, with red indicating when the monkeys chose a saccade and green a reach (Cui and Andersen, 2007). The monkeys initially fixate their hand and eyes on a fixation target located straight ahead (Figure 2A). Activity during this baseline is plotted from -0.5 to -0.2 s (Figures 2B and 2C). Next, a target appears in the response field of the neurons for 600 ms. The response field is the restricted area in space that will activate a neuron as a result of a stimulus appearing at that location or an action planned or executed to that location. This target is composed of adjacent red and green parts (Figure 2A). When the target is extinguished, the monkey chooses either a reach or a saccade. The choice bias is balanced by having the monkey play a competitive game against a computer algorithm (Barraclough et al., 2004). The effector choice trials were randomly interleaved with instructed trials in which the monkey is instructed to make a reach or a saccade by extinguishing only one of the colored components (e.g., if the red part stays on, the monkey is instructed to make a saccade) (Figure 2A). The instructed trials (data not shown) are introduced for behavioral purposes only, so the monkey does not know whether he is to make a decision or follow instructions until the target, or part of the target, goes off. After the target goes off in the decision trials, there is a 600 ms delay during which the animals decide which movement to make. At the end of this delay period, the fixation point is extinguished, providing a GO signal for the animals to make the chosen movement (Figure 2A).

During the period when the target is in the response field and the monkeys do not know whether it is a decision or instruction trial, the activity is high in both LIP and PRR (Figures 2B and 2C; 0–600 ms). When the target extinguishes, the animals know they are free to choose, but they must withhold the action until the GO signal. During this delay (600–1200 ms), the activity separates in LIP and PRR, with LIP cells differentially more active when the animals choose a saccade and PRR cells differentially more active when they choose a reach (Figures 2B and 2C).

This effector specificity reflecting the animals' choice for identical visual stimuli must be related to the decision and planning of the animals and not to the sensory meaning of the stimuli. Nor can this differential response be due to spatial attention, since the targets are always in the same location in space, and it is only the effector choice that varies. Interestingly, at the time immediately after the GO signal and before the reaching arm movement is made, the activity in LIP is statistically no different from baseline, even though attention is known to be attracted to reach targets (Baldauf et al., 2006; Deubel et al., 1998). Bisley and Goldberg (2003) have proposed that LIP forms a priority map for attention and that it is the relative amount of activation in LIP and not the absolute magnitude that indicates the location of highest priority. In this case, there is *no* premovement activity in the LIP population when the monkey is planning the reach, arguing against this priority formulation. Likewise, in this period

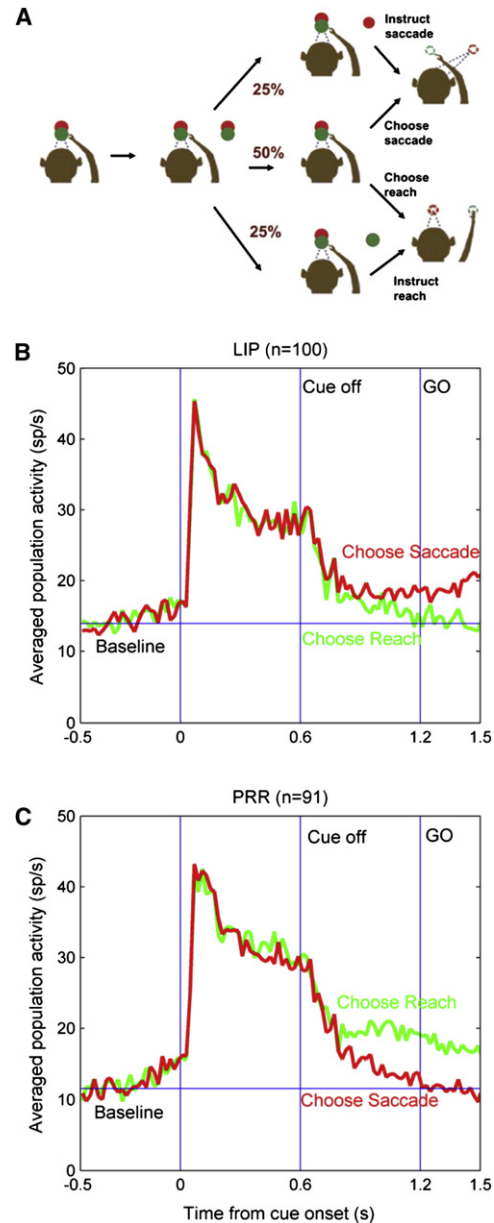


Figure 2. PPC Activity during Effector Choice Task

(A) Behavioral paradigm interleaved instructed saccade (top) and reach (bottom) and effector choice (saccade or reach) trials (middle). (B) and (C) Population histograms averaged across all isolated LIP (B, $n = 100$) and PRR (C, $n = 91$) neurons during saccade (red) and reach (green) chosen trials. The vertical thin lines indicate cue on, cue off, and central fixation off (GO signal), respectively. The horizontal thin line indicates baseline activity, which was defined by mean firing rate during the 300 ms interval beginning from 500 ms before cue onset for both saccade and reach chosen trials. Post-GO activity (0–100 ms interval after GO) of LIP population was significantly higher than the baseline ($p < 0.005$) if the monkeys decided to saccade, but dropped to baseline ($p > 0.5$) if the monkeys decided to reach. On the other hand, post-GO activity of the PRR population was significantly higher than the baseline ($p < 0.0001$) in trials in which reaches were chosen, but dropped to baseline ($p > 0.8$) in trials in which saccades were chosen. Reproduced with permission from Cui and Andersen (2007).

right after the GO signal, PRR is inactive when the monkey is choosing a saccade, even though saccades also attract attention to the target (Deubel and Schneider, 1996; Kowler et al., 1996).

Potential Plans

Both LIP and PRR showed vigorous activation during the cue period in the study of Cui and Andersen (2007) (0–600 ms epoch; Figures 2B and 2C). It could be argued that this activity reflects sensory activity and/or top-down attention. Since the monkey is not sure whether he will be instructed to make an eye or an arm movement or whether he may be free to choose an eye or arm movement, the neural activity may also reflect potential or default planning in which the monkeys form potential plans for both movements and then later select between the two. During the cue period, when a stimulus is present, the activity is higher than during the delay period in which planning and decision making take place. This additional activity may reflect the fact that there is a visual stimulus present in the cue period and not the delay period, indicating that at least a component of the activity is sensory in nature.

Default plans for spatial locations have been reported in a number of sensorimotor and motor structures (e.g., Cisek and Kalaska, 2005; Basso and Wurtz, 1998; Platt and Glimcher, 1997). It has been proposed that making decisions between two spatial locations may involve competition between potential plans (Cisek, 2006), not dissimilar to the competitive bias model for spatial attention (Desimone and Duncan, 1995). In fact, most decision-making models contain a competition between potential plans (Wang, 2008; Beck et al., 2008). Forming potential plans may not only benefit decision making but may also reduce reaction times and thus have evolutionary/survival advantage.

Potential movement plans toward multiple *spatial* targets coexist in virtually the entire parietal-frontal network, even including primary motor cortex (Bastian et al., 2003). It would be interesting to determine whether there are regions of the posterior parietal and frontal cortex that do not reflect potential plans and only code the decision outcome in *effector* choice tasks. If such areas exist, it would suggest that PRR and LIP carry signals related to both the potential plans and outcomes of the effector decision process, while other areas within parietal and frontal cortex carry only the outcome of the decision. Such a distinction would be consistent with the decision process occurring within a parietal-frontal circuit that includes PRR and LIP, with competition between potential plans and the outcome being computed within that circuit. Areas that only represent the outcome could be downstream of this effector decision process and receive information conveying results of deliberation from the decision network. However, it is also possible that the decision process occurs entirely outside of PRR and LIP and these regions reflect only the potential plans but are kept updated; that is, these areas are coding decision outcomes because there is only one plan after the decision is made.

Antimovements

Not all movements are oriented toward a visible goal. For instance, one might wish to reach to a soda can but reach away from a bee. In the latter case, the visual stimulus and the goal of the movement are not congruent. This discordance has

been used to separate sensory goals from movement plans in antisaccade and antireach tasks. In some studies, monkeys have been trained to move in the opposite direction to the appearance of a stimulus. It is reasoned that if the cells *only* encode the location of the stimulus, they are sensory related, and if they *only* encode the location of the goal, they are movement related.

Antisaccade tasks with recordings in LIP have yielded mixed results with respect to this sensory-motor dissociation, with one report indicating largely sensory encoding (Gottlieb and Goldberg, 1999) and another indicating largely movement encoding (Zhang and Barash, 2000, 2004). Differences in the details of the behavioral tasks may account for these different findings. In reach tasks, antireaches produce brief activation for the cue in area 5 of posterior parietal cortex and PMd, followed by activity coding the intended direction of the reach movement (Kalaska, 1996).

Antireach experiments in PRR (Gail and Andersen, 2006) produced results similar to those of Zhang and Barash (2000, 2004) and Kalaska (1996). The task for the PRR experiments used four different directions for pro- and antimovements so that the spatial tuning of the cells for both rules could be determined. Briefly flashed targets were used, and variable delays were interposed before the GO signal to target planning activity. Finally, the task rule to be applied was provided each time at the beginning of the trial, prior to the presentation of the target cue. Most cells showed tuning only to the planned reach direction (45%). A smaller proportion, termed “visuomotor cells,” showed brief tuning to the target location followed by tuning to the movement direction (7%). The number of cells tuned to only the target location was statistically insignificant. The fact that most of the cells encoded *only* the movement direction rules out attention as a major contributing factor for these neurons. An attention explanation also does not appear to apply to the visuomotor cells. The time of the GO signal was not predictable, and it would be expected that the monkeys shift spatial attention at least partially toward the fixation point where the GO signal occurred. Instead, the movement goal tuning in the visuomotor tuned neurons persisted throughout the delay period and at the population level became strongest toward the end of the delay period.

Subsequent modeling studies (Brozovic et al., 2007) have examined how this context information might be integrated in PRR with the target-stimulus location provided later in the trial, similar to the task parameters in the study by Gail and Andersen (2006). The networks integrated the target location and context through a classic gain field mechanism (Zipser and Andersen, 1988; Brozovic et al., 2007, 2008). The modeling studies showed that the context could originate from feedback from the output (motor) layer of the network, consistent with feedback from frontal lobe structures, or from input to the middle layer, which represents PRR. Thus, the context information could originate either from top-down (e.g., from frontal cortex or other parietal areas) or bottom-up (e.g., from extrastriate visual areas) sources, although the authors suggested that the former route is more likely. A more recent study has shown that individual neurons in PRR and PMd are gain modulated by context information (Gail et al., 2009), consistent with the neural network models (Brozovic et al., 2007).

Sequential Reach Movements

Many natural reach behaviors entail sequences of movements. Frontal cortical areas have been shown to encode information including subsequent movement parts, directions, and temporal organization (Tanji and Shima, 1994; Shima and Tanji, 1998; Ninokura et al., 2003; Fujii and Graybiel, 2003; Ohbayashi et al., 2003; Lu and Ashe, 2005; Mushiake et al., 2006; Histed and Miller, 2006; Averbeck et al., 2006; Shima et al., 2007). However, the first sequential movement study of PRR showed activity only for the movement that was next in the sequence (Batista and Andersen, 2001). This study used a complicated task that likely resulted in the animals planning only one movement at a time. Recently, these experiments have been repeated with a simpler paradigm that promotes planning two movements simultaneously. In this newer paradigm, both movement plans are simultaneously represented in the activity of PRR neurons (Baldauf et al., 2008).

In the Baldauf et al. (2008) study, visual stimuli instructing a reach location produced a huge response in PRR, but when the same stimulus was used as a timing cue and not a reach target it produced almost no response. This context-dependent gating for PRR is similar to that seen for cue targets in antireach tasks mentioned above (Gail and Andersen, 2006). These findings contrast with much larger responses seen in LIP for flashed irrelevant cues (Bisley and Goldberg, 2003; Powell and Goldberg, 2000) or timing cues (Campos et al., 2009). The difference in degree of visual response between LIP and PRR may indicate that (especially flashed) stimuli tend to form automatic potential eye movement plans but not reach plans. This is plausible behaviorally, considering the much greater frequency of saccades compared to reaches. Interestingly pop-out distracters (made salient by their physical properties) produce less activity than non-pop-out targets when monkeys are performing visual search with eye movements (Ipata et al., 2006). The authors proposed that this modulation was due to top-down modulation of salience in LIP. However, it is also possible that top-down influences may regulate the level of activity of potential eye movement plans represented in LIP. Another possibility is that there is a stronger coupling of sensory signals with movement planning in LIP compared to PRR.

In rapid hand-movement sequences, attention in humans has been shown to be distributed among target locations (Baldauf et al., 2006), similar to the activity in PRR. As discussed above, the findings of effector specificity, the coding of mostly reach goals in antireach tasks, and the lack of evoked activity to flashed timing cues strongly suggest that PRR codes reach plans. It is possible that PRR has a top-down influence on extrastriate areas and biases the processing of sensory stimuli. This effect would be similar to the effect of frontal eye field (FEF) activity on the modulation of attention in V4 (Moore and Armstrong, 2002) and could be accomplished by directing attention to reach goals through its feedback projections to visual areas. Such a mechanism would indicate at least partially separate top-down control of attention for stimuli that are targets for reaches and saccades.

Decision Making: Action Selection in Parietal-Frontal Circuits

Decision processes range from those that are largely externally driven (e.g., stop when the light is red) to internally driven (e.g.,

take route A rather than route B to the lab today). An example of the external variety is a perceptual decision, in which the subject views a noisy or ambiguous display and makes a choice based on the subject's percept (Newsome et al., 1989; Bradley et al., 1998; Dodd et al., 2001). Studies of area MT show that trial-to-trial variation in neural firing can affect the perceptual choice of animals in deciding which direction they perceive motion at low thresholds (Britten et al., 1996). In this type of experiment, the direction of the perceived motion is indicated by eye movements, and area LIP integrates perceptual evidence for making the decision (Shadlen and Newsome, 1996).

Internal (autonomous) decisions (Coe et al., 2002; Barraclough et al., 2004; Cui and Andersen, 2007) are sometimes referred to as "free choice" in which selections are made concerning "where, when, or how" (Haggard, 2008). The example in Figure 1 shows selection of "where" by PRR neurons (Scherberger and Andersen, 2007). The effector choice task in Figure 2 uses a "how" decision (Cui and Andersen, 2007). An advantage of using a "how" decision task for neurophysiological study is that the locus of attention covaries in space with the "where" decisions but does not with the "how" decisions, and thus two sources of potential activation, spatial attention and planning, can be more easily separated for effector decisions.

Additional evidence for a role of LIP and PRR in decision making is the finding that they encode the expected value of the reward for a movement (Platt and Glimcher, 1999; Sugrue et al., 2004; Musallam et al., 2004; Yang and Shadlen, 2007) (Figure 7). Neurons in the putamen and caudate nucleus have been shown to encode action value (Samejima et al., 2005). Action value is the value that a potential action would produce, regardless of which action is chosen. It can be used to bias selection of a particular action. In the oculomotor region of the caudate, cells are found that code action value, chosen value, and the choice of the saccade (Lau and Glimcher, 2008). Chosen value refers to the value that a chosen action really produces, and it can be used for reinforcement learning. It is not currently clear whether LIP and PRR neurons encode action value or chosen value (Rangel, 2009).

Selection of an Action in Parietal-Frontal Circuits: Integrated and Serial Models

Decision making traditionally has been considered a separate process from action planning (Tversky and Kahneman, 1981), as illustrated in Figure 3A. However, recent neurophysiological studies suggest that potential plans for movements to multiple target locations are simultaneously represented in a collection of motor-related areas (e.g., Shadlen and Newsome, 2001; Cisek and Kalaska, 2005; Basso and Wurtz, 1998; Platt and Glimcher, 1997). Thus, target selection and movement preparation may involve the same brain circuits and are performed in an integrated manner as diagrammed in Figure 3B (Shadlen and Newsome, 2001; Fagg and Arbib, 1998; Cisek, 2006, 2007; Wang, 2008;), as opposed to a serial model in which decision making occurs before action planning (Schall, 2002). Nevertheless, this idea has only been tested for spatial target selection, which involves spatial attention, which in turn engages numerous brain areas. It remains unknown whether plan selection and movement preparation are represented in segregated brain areas for other kinds of decision making. In the nonspatial

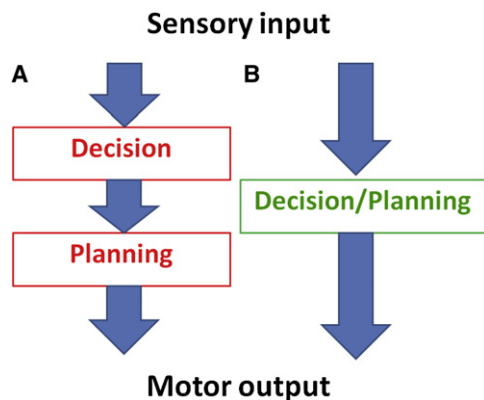


Figure 3. Illustrations of Two Theoretical Frameworks of Decision Making and Action Planning

(A) Traditional serial model in which decision making is considered a process separated from action planning.

(B) Recent integrated model. Neurophysiological evidence suggests that potential plans for movements to multiple target locations are simultaneously represented in a collection of parietal and frontal areas, as opposed to a serial model in which decision making occurs before action planning.

effector choice, PRR and LIP are found to represent both potential plans and the outcome of the decision, and thus potentially participate in the decision circuit and contribute to the deliberation. It will be interesting to determine if effector decisions also follow this integrated model or if they have an additional hierarchical component that codes only the selected plan downstream of decision circuits.

In effector choice, if the deliberation is carried out by a competition between potential saccade and reach plans, this competition may be at least partially carried out between LIP and PRR within the parietal lobe. From a theoretical point of view, LIP and PRR share the same (predominantly eye-centered) reference frame, which would benefit such a competitive computation.

Corticocortical Communication

Local field potentials (LFPs) are oscillations in the electrical field within a few hundreds to thousands of microns of the recording microelectrode tip driven largely by synchronous activity of synaptic potentials, but action potentials also contribute when they are sufficiently synchronous (Mitzdorf, 1987; Logothetis and Wandell, 2004). Using combined optical and electrical recording in V1 cortex, it has recently been estimated that the spread of the LFP is very local, with greater than 95% of the signal originating from within 250 μm of the recording electrode (Katzner et al., 2009). Spikes of individual neurons occur largely on the negative peaks of the oscillations, suggesting that during this phase of the LFP oscillation the membrane potentials are closest to threshold for spiking. The magnitudes of the oscillations in certain frequency bands are modulated with attention and motor preparation in the parietal, occipital, and frontal lobe areas (Fries et al., 2001; Pesaran et al., 2002; Scherberger et al., 2005; Murthy and Fetz, 1996; Sanes and Donoghue, 1993; Mehring et al., 2003). It has been proposed that these oscillations may synchronize with inputs to an area, increasing communication between regions of the brain (Mishra et al.,

2006; Sejnowski and Paulsen, 2006; Salinas and Sejnowski, 2000). In other words, if cortical area A projects to cortical area B, and the phase of the spikes from cortical area A are in phase with the membrane oscillations of cortical area B, and this phase is such that spikes arrive at the low threshold phase of the oscillations, then spikes from area A are more likely to produce spikes in area B. During these periods, there would be greater communication or influence of area A on B. An experimental prediction suggests that during periods of greater communication there will be greater coherence between the phase of spiking in one area and the LFP in another (if in fact the phase of the incoming spikes and the membrane oscillations are at the low threshold periods of the oscillations). Changes in spike-field coherence may be a useful signature for tracing the dynamics of communication between cortical areas (Pesaran et al., 2008; Gregoriou et al., 2009).

Increases in spike-field coherence have been recorded between PRR and PMd while monkeys select between reach targets (Pesaran et al., 2008). In some trials, the selection was instructed, and in others the monkeys chose the targets. In the autonomous decision tasks, the PMd-PRR and PRR-PMd spike-field coherences were greater for choice than for instructed trials (Figure 4). As mentioned above, it is possible that the increased coherence may represent differences in communication between the two cortical areas during autonomous choice and instruction. Interestingly, only about a quarter of the paired recordings showed significant spike-field coherence, and these pairs indicated the decision of the animal earlier than pairs that did not have significant coherence. These results suggest that there may be a subset of cells connecting these two areas that coordinates the decision process.

Timing in the Circuit

Timing within the parietal-frontal decision circuits provides insight into which areas may encode the decision earlier. These experiments require simultaneous recordings from the same animals in order to keep constant such factors as level of training, performance, and other experimental variables that might influence timing comparisons (Miller and Wilson, 2008).

One would normally expect that decision-related activity begins earlier in frontal lobe areas and passes back to parietal areas (Monosov et al., 2008). This seems to be the case with instructed and autonomous decisions for selecting spatial locations. Spike activity appears first in PMd and later in PRR for the onset of the target stimuli (Pesaran et al., 2008). This result is a bit surprising since it suggests that a route other than through PRR, perhaps subcortical, produces this very early activation of PMd. As shown in Figure 4, spike-field coherence timing also suggests that the PMd to PRR link of the circuit is activated first followed within a few milliseconds by a hand-shake back from PRR to PMd. For this measure, absolute timing cannot be determined because the coherence is estimated using an analysis window of ± 150 ms stepped in 10 ms increments; however, relative timing between the PMd-to-PRR and PRR-to-PMd spike-field coherences can be determined because they are obtained with the same analysis methods. Similar results of frontal areas leading parietal areas have been found in eye movement tasks in which the supplementary eye fields (SEF) lead LIP (Coe et al., 2002).

Population magnitude differences

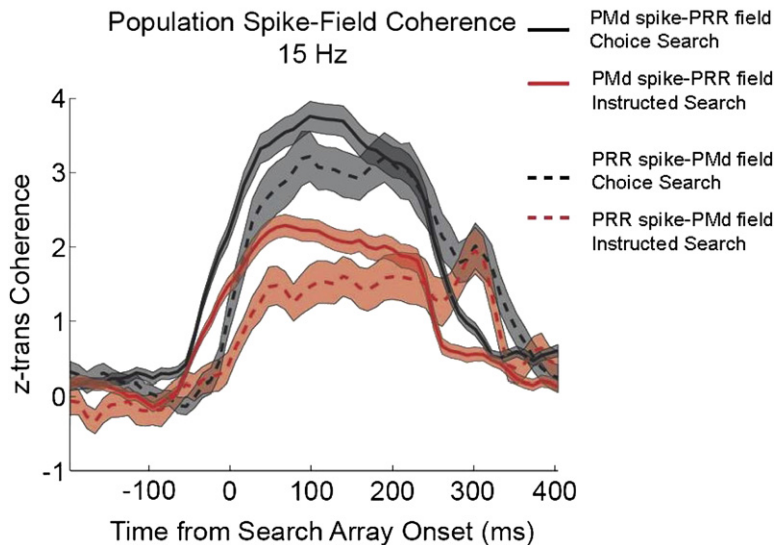


Figure 4. PMd-PRR Spike-Field Coherence Is Stronger in the Trials in which the Target Was Autonomously Selected

Population average 15 Hz PMd-PRR spike-field coherence is plotted every 10 ms: PMd spike-PRR field coherence (solid); PRR spike-PMd field coherence (dashed). Free search (black); instructed search (red). Coherence is z transformed before averaging; 95% confidence intervals, Bonferroni corrected (shaded). Reproduced with permission from Pesaran et al. (2008).

However, the timing within this circuit may depend on the task at hand. For instance, the more conventional center-out reach task produces approximately simultaneous activation in PRR and PMd (Pesaran et al., 2008). In attention tasks, FEF is active first for visual search tasks that are believed to rely on top-down attention, but LIP is active first for pop-out stimuli that are considered indicative of bottom-up attention (Buschman and Miller, 2007; but see Schall et al., 2007). It will be important to determine the timing of effector choice in the parietal-frontal circuit. Interestingly, in trials where the effector is instructed before the target, effector-specific activity diverges in parietal cortex earlier than in frontal cortex (Lawrence and Snyder, 2006).

Internal Models: PPC Predicts the Current State of Effectors

Reach Dynamics

Clinical and transcranial magnetic stimulation studies provide evidence that the PPC in humans is involved in online corrections of reach movements (Desmurget et al., 1999; Della-Maggiore et al., 2004; Pisella et al., 2000). For reach movements, both somatosensory stimulation from the limb movement and visual stimulation from watching the movement are important. Somatosensory and visual signals converge in the PPC, particularly in PRR and adjoining Brodmann's area 5, and can provide feedback signals for making corrections during reaching. However, there is a considerable delay for these signals to reach PPC: ~30 ms for somatosensory and 90 ms for visual signals (Figure 5A). Such long delays in feedback systems can lead to instability. To obtain an accurate estimate of the current state, i.e., position, direction, and speed of a limb, requires more than sensory signals. It has been proposed that efference copy signals, replicas of movement commands from motor areas, are fed back to PPC to eliminate any delay (Jordan and Rumelhart, 1992; Wolpert et al., 1995; Shadmehr and Wise, 2005). Considerable evidence points to a "forward model" that uses

efference copy signals to predict the current state of the limb and integrates this information with delayed sensory observations to subsequently learn to improve this estimate (Figure 5A).

In addition to being used for online correction, a forward model can also be used to estimate the sensory consequences of a movement (Haarmeier et al., 1997). Such estimates can be used to distinguish movement of an effector from movement in the world. For instance, it is believed that the apparent stability of the world during eye movements, which sweep the visual scene across the

retinas, is achieved by a forward model that makes use of feedback of eye movement commands (VonHolst and Mittelstaedt, 1950; von Helmholtz, 1866; Haarmeier et al., 2001).

In a recent study of PPC, monkeys learned to use a hand-operated manipulandum ("joystick") to move a cursor on a computer screen. It was found that when the monkeys moved the cursor toward a target that not only the eventual goal of the movement but also the instantaneous direction of the cursor was represented (Mulliken et al., 2008a). Figure 5B shows the static goal angle—the vector from the fixation point to the target. The row of dots represents 15 ms samples of the cursor along the trajectory, and the instantaneous direction of movement at one point in the trajectory is shown and labeled the movement angle. Figure 5C shows four center-out movements, and Figure 5D shows two movements around obstacles. The obstacles were used to increase the range of movement angles. The task used 8 or 12 targets. All trials across all movement angles were used to construct space-time tuning functions for each cell. This tuning function measures the instantaneous firing rate as a function of angle and lag times. The lag time is the relative time difference between the instantaneous firing rate and the time that a particular movement angle occurred. A similar tuning curve can also be obtained for mutual information. Both types of measure produced single peaked tuning curves. Figure 5E plots the optimal lag time for the most information about movement angle for the population of neurons for the center-out and obstacle tasks. The optimal lag for the center-out task was peaked at 0 ms and for the obstacle task it led by 30 ms. Motor command signals would normally lead by 90 ms, and sensory feedback would lag by 30 (somatosensory) or 90 ms (visual). Although there are some cells that show these large lead and lag times, the population response is centered within the dynamic range in between. This is the dynamic range consistent with an efference copy that is used for forward state estimation (Figure 5E). Since the hand movement and cursor movement

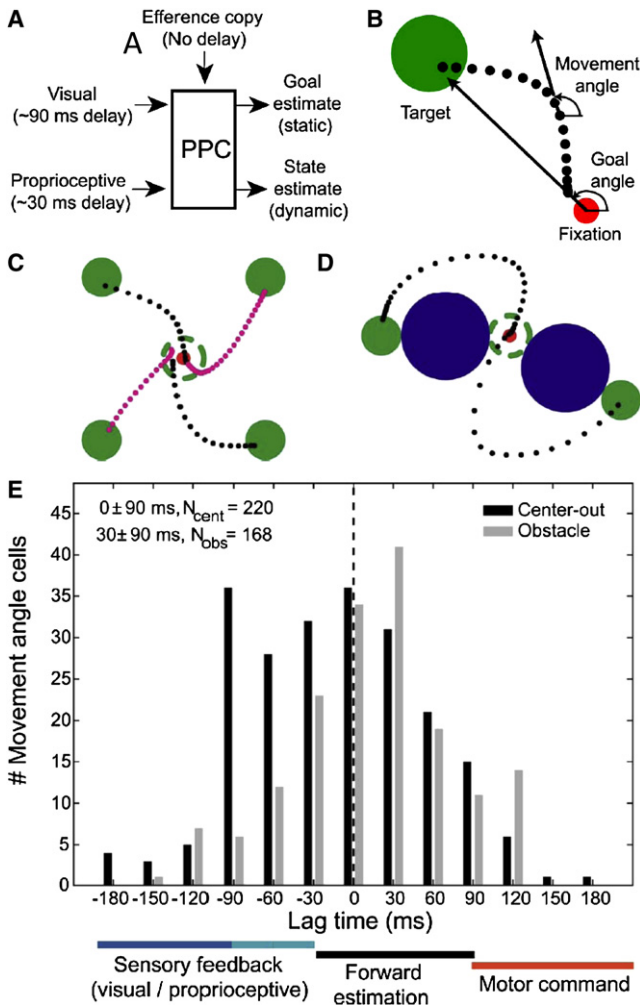


Figure 5. PPC Neurons Predict the Current State of Effector in the Joystick Control Task
 (A) Diagram of sensorimotor integration for online control in PPC. Inputs to PPC consist of visual and proprioceptive sensory signals and, potentially, an efference copy signal. Plausible PPC outputs are the static target direction (goal angle) and the dynamic cursor state (movement angle).
 (B) Diagram of actual trajectory showing the goal angle and movement angle and their respective origins of reference. The filled green and red circles represent the target and fixation point, respectively.
 (C) Example trajectories for center-out task. The dashed green circle is the starting location of the target and is not visible once the target has been jumped to the periphery. Dots represent cursor position sampled at 15 ms intervals along the trajectory (black, monkey 1; magenta, monkey 2).
 (D) Example trajectories for the obstacle task. Targets, fixation points, and cursor representations are identical to the center-out task. Blue filled circles represent the obstacles.
 (E) Histogram summarizing the optimal lag times (OLTs, the lag time that contained the maximal mutual information) for movement-angle neurons for both center-out and obstacle tasks. Many of these neurons' OLTs were consistent with a forward estimate of the state of the movement angle, which did not directly reflect delayed sensory feedback to PPC nor were they compatible with outgoing motor commands from PPC. Color-coded horizontal bars beneath the abscissa denote the approximate lag time ranges for sensory (blue), forward estimate (black), and motor (red) representations of the state of the movement angle. Reproduced with permission from Mulliken et al. (2008a).

were correlated, the results are consistent with both a forward model predicting the hand movement and the cursor movement.

Eye Movements

Eye movement activity may also be consistent with forward state estimation in the PPC. The eye-centered location of a target for a saccade in the superior colliculus and LIP (Mays and Sparks, 1980; Gnadt and Andersen, 1988) or a reach movement in PRR (Batista et al., 1999) compensates for intervening saccades. This compensation can occur as well for stimuli that are not the targets for a subsequent saccade (Duhamel et al., 1992). Although it has been proposed that the response fields shift to take into account the eye movement, it is more parsimonious to consider the activity shifting within the eye-centered map (Xing and Andersen, 2000a). The shift of activity in LIP often begins prior to the eye movement (Duhamel et al., 1992). Since the location can be identified after the eye movement by sensory input, it has been proposed that this predictive shifting is a signature of a forward model predicting the location of a stimulus after the eye movement (Vaziri et al., 2006).

Eye-movement-related signals for pursuit, fixation, and saccades have been reported in PPC (Lynch et al., 1977; Mountcastle et al., 1975). It would be interesting to examine whether the pursuit signals indicate the instantaneous direction of the eye movement with zero lag time, similar to the reach-related signals in PRR. MST neurons are tuned for the focus of expansion in simulated optic flow stimuli, and these signals compensate for eye movements using an efference copy of pursuit eye movements and head movements (Bradley et al., 1996; Shenoy et al., 1999; Lee et al., 2007). Such compensation is again indicative of forward models for the purpose of perceptual stability.

As has been shown for saccades, it may be possible that the fixation-related activity is also predictive in PPC; in this case, the predictive component would provide the current fixation location of the eyes beginning at zero lag after an eye movement has brought the eye to the fixation location. Such a finding would point toward a generalization that many movement-related responses in PPC are efference copies for forward state estimations.

Coordinate Transformations: Relative Encoding for Hand-Eye Coordination

Areas involved in eye movements such as LIP and FEF encode targets in predominantly eye-centered coordinates, although the responses of LIP neurons can be modulated by eye and head position signals and FEF by eye position (Andersen et al., 1990b; Brochie et al., 1995; Cassanello and Ferrera, 2007). These modulations, referred to as gain fields, can be either multiplicative or nonlinear additive effects and are believed to be a first step in the transformation from eye coordinates to head and body coordinates (Andersen et al., 1985b; Zipser and Andersen, 1988; Brozovic et al., 2008). Electrical stimulation of LIP produces fixed-vector saccades in eye coordinates, consistent with an eye-centered representation (Thier and Andersen, 1996, 1998; Constantin et al., 2007).

Visually guided reaching requires transformation from eye- to limb-centered coordinates. The ventral premotor cortex in the frontal lobe codes visual targets for reaching in body-centered coordinates (Graziano et al., 1994). Interestingly, although PRR

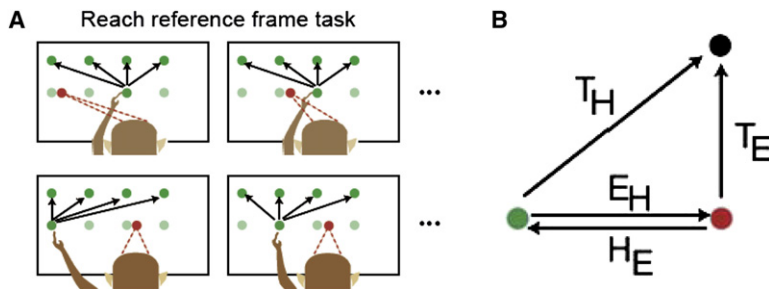


Figure 6. The Reference Frame Dissociation Task Used to Examine the Relative Coding of Hand and Eye Positions

(A) The reference frame dissociation task. In the upper panels a reach from the same initial hand position is made to one of four target positions while fixation is maintained at one of four eye positions. In the lower panels, four reaches are made from four different initial hand positions and a single eye position. The overall matrix contains four initial hand positions by four reach targets for 64 trial types.

(B) Geometry of relative coding. PMd neurons represent the relative positions of the hand, eye, and reach target. Reproduced with permission Pesaran et al. (2006).

is involved in reaching, it represents visual reach targets more consistently in eye coordinates. This result was found in three different studies using two very different analysis techniques (Batista et al., 1999; Buneo et al., 2002; Pesaran et al., 2006) and with stimulus configurations that cannot bias for eye-centered coordinates (Pesaran et al., 2006). Area 5 on the other hand has been shown to code reaches simultaneously in eye and limb coordinates (Buneo et al., 2002). Its cells show partial shifts in their response fields with either eye position or limb position.

Experiments examining the representation of auditory targets for saccades in LIP showed cells with response fields in eye coordinates, head coordinates, and “intermediate cells,” which showed only partial shifting in eye coordinates (Stricanne et al., 1996). The cells with eye-centered coordinates are interesting since sound localization begins as interaural differences in intensity, timing, and spectra (i.e., head-referenced) but needs to be converted to eye coordinates to saccade to auditory stimuli. A similar distribution between head, eye, and intermediate representations was found for reaching to auditory targets (Cohen and Andersen, 2000). Intermediate representations, i.e., partially shifted response fields, have been examined in three-layer neural network models that transform coordinates between the input and output layers. Intermediate representations occur in the middle layer if there is strong recurrent feedback from the output layer or if the network has separate output layers that code in different coordinate frames (Deneve et al., 2001; Xing and Andersen, 2000b). Both of these conditions are biologically plausible for PPC areas.

Recent studies by Mullette-Gillman et al. (2005, 2009) investigated auditory and visual saccades from different eye positions and reported that almost all LIP and PRR neurons in their study code in intermediate coordinates for both auditory and visual targets. Likely reasons for such results are noisy data, the probable analysis of many untuned cells given their selection criteria and use of only saccades, and the widespread sampling and lumping together of data with poor histological verification. Unfortunately, all of these factors would sum and strongly bias the results toward a single overarching category.

Hand-eye coordination requires an interaction between body parts, and it is of interest to determine in what coordinate frame these interactions are accomplished. Recently a unique, relative representation of coordinates has been found in PMd (Pesaran et al., 2006). The coordinate frame of reach targets was determined by independently changing the relative positions of the reach target, initial hand position, and eye position (Figure 6A). Within PMd, cells are found that code the target of a reach rela-

tive to the eye (eye-centered, T_e), the target relative to the hand (limb-centered, T_h), the eye relative to the hand (eye-in-hand, E_h or equivalently hand-in-eye, H_e), as well as combinations of two or even all three (Figure 6B). These results predict that, in some neurons, a unique relative spatial relation of all three variables will produce the same activity for different absolute positions in space. Likewise, the relative position of these parameters is encoded within the population activity of PMd. This form of encoding has an advantage for hand-eye coordination in defining a coordinate frame based on the “work space” of the hand, eyes, and reach target.

In the same study outlined above, it was found that PRR codes only in eye coordinates (T_e), consistent with previous studies (Batista et al., 1999; Buneo et al., 2002). An earlier study of the coordinates of reach planning in parietal area 5 found neurons coding simultaneously in eye (T_e) and hand (T_h) coordinates (Buneo et al., 2002). It remains to be determined if cells in area 5 also code hand-in-eye coordinates (H_e) and thus have a similar relative coordinate code as PMd.

If PMd is involved in hand-eye coordination, then the cells in this area should also code the plan to make saccades and would be distinct from PRR, which has primarily postsaccadic responses (Snyder et al., 2000). If PMd cells code both reaches and saccades, then an additional prediction can be made that the saccade targets should be encoded in the same relative coordinate frame as reaches, that is relative to the hand, eye, and saccade target.

Attention

The current review has emphasized planning, decision making, forward state estimation, and coordinate transformation roles for the PPC and areas of the frontal lobe to which it connects. Of course, another role of PPC is in attention. Classically, attention has been considered a sensory phenomenon in which stimuli are selected from the environment for further neuronal processing. However, the definition and scope of attention have been expanding in the literature to embrace such concepts as “motor attention” that is specific to the responding effector (Rushworth et al., 2001) or that includes decision making by attentional selection among motor plans (Goldberg and Segraves, 1987). A distinction has been made between overt and covert orienting for attention with overt changes observed by shifts of gaze and covert changes observed by other means (Posner, 1980). While voluntary eye movements are a behavioral measure of shifts of attention, it would be erroneous to argue that all neural correlates of voluntary eye movements should be considered attention. For example, asserting that the oculomotor

neurons in the brainstem control attention rather than move the eyes would not be a useful construct. In this review, we have adhered to the more classical definition of attention as sensory selection for further processing. Of course, attention interacts with movement planning since attention is directed to locations of planned movements (Rizzolatti et al., 1987; Deubel and Schneider, 1996; Kowler et al., 1996). Attention may influence the inputs to decision processes and make use of forward state estimations for prediction of where to reallocate attention to compensate for eye and hand movements. The study of how attention interacts with other neural processing systems is a most important endeavor. However, we think that over-generalizing attention to encompass a large variety of different neural processes weakens the concept and undercuts the ability to develop a robust understanding of other cognitive functions.

Some studies have proposed that LIP in particular has the sole purpose of controlling attention (Goldberg et al., 2002, 2006; Bissley and Goldberg, 2003). However, LIP has been reported to have activity related to a variety of functions, including the representation of value, planning of eye movements, prediction, categorization, cognitive set, shape recognition, decision making, and timing (Platt and Glimcher, 1999; Snyder et al., 1997; Freedman and Assad, 2006; Shadlen and Newsome, 2001; Maimon and Assad, 2006; Eskandar and Assad, 1999; Janssen and Shadlen, 2005; Sereno and Maunsell, 1998; Stoet and Snyder, 2004). More recently, proponents of a primarily attentional role for LIP have proposed that LIP still controls attention but that it uses these various other functions to train the attentional controller (Gottlieb et al., 2009). Another recent proposal is that of a priority map, which does not control attention or eye movements but highlights areas of interest that can be used by the oculomotor or attention systems (Ipata et al., 2009). This latter idea fits more closely with our proposal that the region is generally important as an interface between sensory and motor areas for sensorimotor transformations, and its functions are neither strictly sensory nor motor (Andersen et al., 1987; Buneo and Andersen, 2006; Ipata et al., 2009). The priority map concept does account for some aspects of attention and movement planning, although there are cases where LIP and PRR do not indicate the locus of attention (Snyder et al., 1997; Cui and Andersen, 2007; Gail and Andersen, 2006; Baldauf et al., 2008). Also this idea of a priority map does not capture the intricacies and essence of forward state estimation, decision making, or coordinate transformations that are central elements of this review.

A Medical Application: Decoding Intention Signals Cognitive Neural Prosthetics

A relatively new and accelerating field of research is neural prosthetics. The goal of this research is to decode intention signals in patients with movement disorders such as paralysis and use these signals to control external assistive devices. Most efforts have concentrated on the motor cortex for obtaining movement intention signals (Donoghue, 2002; Schwartz, 2004; Nicolelis, 2003; Kennedy and Bakay, 2000; Moritz et al., 2008). However, some recent studies have focused on intention signals in pre-motor and parietal cortex for neuroprosthetic applications (Musallam et al., 2004; Mulliken et al., 2008b; Santhanam et al., 2006). The fact that these areas, particularly PPC, provide

such robust performance can be considered strong support that intention signals exist in these areas and can be harnessed by the individual for controlling devices. Besides this proof-of-concept, there are advantages to using these more high-level and abstract intention signals, discussed below. The field of neural prosthetics is rapidly evolving, and it is not clear at this point which cortical and subcortical areas, or combination of areas, will be the most optimal for particular types of neural injury and paralysis.

Goal Decoding

The motor cortex provides control signals for the movement trajectory of the limbs. As such, motor-prosthetics have used this activity to guide the trajectory of a cursor or a robot limb (Schwartz, 2004; Velliste et al., 2008; Nicolelis, 2003; Donoghue, 2002; Hochberg et al., 2006). However, to achieve a goal using this methodology typically takes a second or more. This length of time is required because the cursor (or robot limb) must be guided incrementally to the goal. Although intermediate steps along the trajectory can be decoded quickly (Velliste et al., 2008), the attainment of the final goal requires considerable time. On the other hand, the PPC and PMd provide signals related to the final goal of the movement rather than the steps to get there. This goal-related activity has been used in “brain control” experiments to position a cursor directly at the intended location. Moreover, it has been shown that these goals can be decoded in 100 ms (Musallam et al., 2004). Thus, in principle many goals can be decoded in sequence, not unlike typing, and would have obvious advantages for communication and other applications that require a high throughput of control signals. To this point, sequential goals have been decoded in brain control tasks using PMd activity (Santhanam et al., 2006).

Decision Variable Decoding

As reviewed above, the areas that code movement intentions could be within the decision-making network since they show activity for potential plans and outcomes of the decision. One hallmark of this involvement in decision making for the PPC is the coding of expected value in LIP (Platt and Glimcher, 1999).

To test whether PRR also encodes the expected value for an action, the effect of expected reward on its activity was measured (Musallam et al., 2004). It was found that type of reward (juice versus water), amount of reward, and probability of reward all strongly modulated PRR cell activity with increased responsiveness for the expectation of the preferred reward (Figures 7A–7C). To test whether this expected value signal could be used for practical neuroprosthetics applications, decodings were performed for both “brain control” and reach tasks. It was found that the expectation of the animal could be decoded for both types of task (Figures 7D and 7E). Moreover, expected value (preferred versus nonpreferred for type, magnitude, or probability) and reach goals could be simultaneously decoded with a mean accuracy of 51.2% ± 8.0% (mean, SD; chance 12.5%).

This finding, that such a high-level signal as expected value can be decoded in brain control trials, is very important for the concept of cognitive prosthetics. There are some potential practical advantages of decoding the expected value, since it provides information about the preferences and mood of the patient. After all, the first thing a doctor asks is “how are

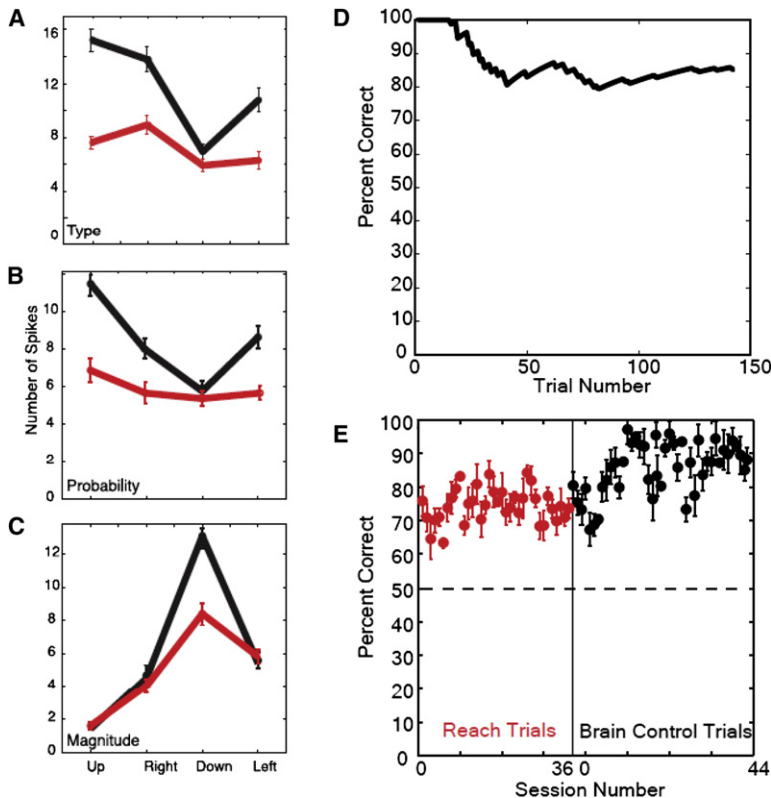


Figure 7. Decoding Expected Value

(A) Tuning curve of a neuron during brain control trials for decoding goals up, right, down, and left in which reward type was varied; orange juice (black) versus water (red) and (B) its tuning curve. Rasters are aligned to the onset of the memory period.

(B and C) Tuning curves calculated from the firing rates of two additional cells while the probability (B; high probability 80%, low probability 40%) and magnitude (C; high volume 0.12 ml, low volume 0.05 ml) of reward was varied.

(D) Decoding result of expected value from a single brain control session and (E) all the sessions where expected value of reward was manipulated. Error bars are standard deviation obtained by crossvalidation (leaving 30 trials out per 11 [iteration]). Sessions are not in consecutive order. The first 36 sessions are reach sessions (red), and the last 44 sessions are brain control sessions (black). Dashed line is chance. Reproduced with permission Musallam et al. (2004).

you feeling”? However, more importantly this demonstration indicates that a large number of high-level cognitive signals are likely to be amenable to decoding and neural prosthetics applications. For instance, speech may be decoded for mute patients by recording activity from speech centers, executive functions from prefrontal areas, and emotions and social context from areas such as the amygdala.

Trajectory Decoding

One possible criticism for using PPC for neural prosthetics is that trajectories cannot be decoded and used. Such signals would be of benefit for “mouse-like” drags for computer control or for controlling the dynamics of robot limbs. However, there is an efference copy signal used for forward state estimation in PPC as indicated above. Recently, it has been demonstrated that monkeys can generate trajectories, without actually moving the limb, using PPC in brain-control experiments (Mulliken et al., 2008b). A possible advantage of using the PPC recordings is that both the trajectory and goal are encoded and can be used to increase decoding performance (Srinivasan et al., 2006; Mulliken et al., 2008b).

Hand-Eye Coordination and Relative Coordinates

Recordings from eye movement areas may be used for improving the decoding of reaches, since eye and hand movements are coordinated, and we look to where we reach. Using eye-position information recorded from an external eye tracker or estimated from neural activity, the success for decoding reach targets can be improved (Batista et al., 2008).

Cells in LIP and PRR encode visual targets predominantly in eye coordinates (Andersen et al., 1990b; Batista et al.,

1999). Common coordinate frames between these areas may facilitate decoding during hand-eye coordination.

PMd encodes simultaneously the target with respect to the eye (eye-centered), the target with respect to the hand (hand-centered), the hand with respect to the eye (hand-in-eye), and combinations of two or three of the above (Pesaran et al., 2006). This relative coordinate frame encoding has potential advantages for neuroprosthetic applications. It defines a “work space” that can be used to coordinate movements involving multi-

ple effectors. Relative codes can reduce the accumulation of errors that may result from maintaining absolute encodings of spatial locations (Csorba and Durrant-Whyte, 1997; Newman, 1999; Olfati and Murray, 2002).

Learning

Over the course of training for goal decoding in PRR, animals learn to perform better over a period of weeks (Musallam et al., 2004). This learning is in the form of greater mutual information for each neuron, essentially a sharpening in the tuning of the PRR neurons. In decoding of trajectories for PPC, rapid learning was also seen (Mulliken et al., 2008b). As shown in Figure 8, the performance greatly improved in the matter of a few days. This was again a result of better tuning and also a dispersion of the response fields to better tile the work space.

During the learning of new trajectories around obstacles, monkeys show immediate spatial adjustment of the path but require a period of learning to master the dynamics (Torres and Andersen, 2006). Initially the speed profiles are multi-peaked and highly variable but adjust to more constant and smooth single-peaked profiles during the day, and over days, of training. It would be interesting to know if PPC is involved in such learning effects and if this robust plasticity can be utilized in neural prosthetic applications.

LFPs are also a potential source of learning for the control of neural prosthetics. These signals can be used to augment spike decoding by providing additional information or can be used on their own for decoding (Pesaran et al., 2002; Scherberger et al., 2005). One possible concern with PPC as a source of control signals for prosthetics is that the spiking activity does

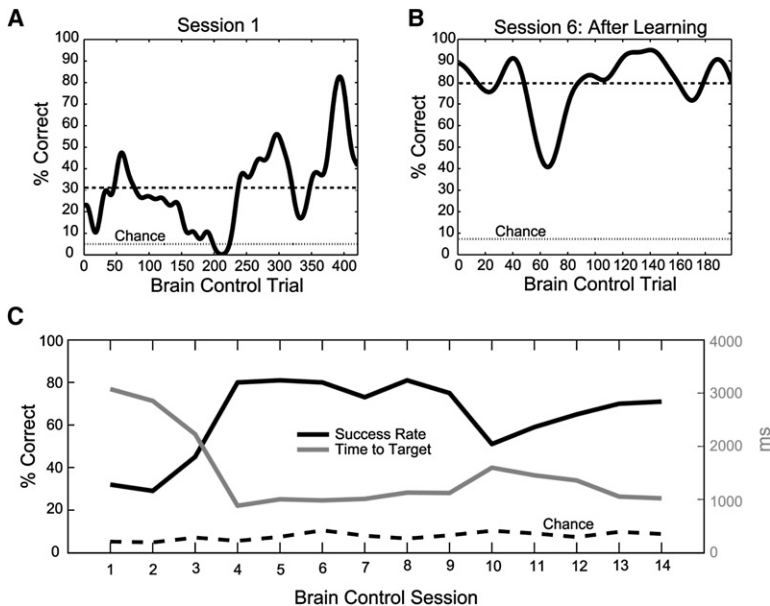


Figure 8. Performance Improvement over Multiple Sessions in the Brain Control Joystick Trials

(A) Thirty-trial averaged success rate during the first closed-loop, brain control session. Dashed line denotes average success rate for the session, and lighter dashed line denotes the chance level calculated for that session. (B) Improved brain control success rate measured during session 6, after learning had occurred. (C) After several days, behavioral performance improved significantly. Session-average success rate increased more than 2-fold, and the time needed for the cursor to reach the target decreased by more than 2-fold. Reproduced with permission Mulliken et al. (2008b).

not generate an execution or GO signal. As indicated above, the movement related signals in PPC have dynamics consistent with an efference copy signal rather than an execution signal. These efference copy signals can in principle be used as GO signals similar to the trajectory signal's use in brain control experiments. There is also a very robust GO-related decrease in gamma band signals and increase in beta band signals at the time of eye movements in LIP and reaching in PRR (Pesaran et al., 2002; Scherberger et al., 2005). The lower band signals may reflect efference copies derived from frontal lobe areas that are seen, for LFPs, largely as an increase in synaptic potentials as a result of feedback projections to PPC. It will be of interest to determine if these LFP GO signals can be trained for prosthetic control without the subject actually making a movement.

Conclusions

Parietal-frontal circuits appear to be involved in deciding and planning actions. Neurons in both frontal and parietal cortex show activity related to intended movements. These high-level planning signals can be used for neural prosthetic applications.

Future experiments will no doubt continue to dissect the circuitry for selecting and planning actions. In particular it will be important to know what different roles the frontal and parietal regions play in decision making and planning and how they interact. Subcortical structures, such as the pulvinar, may coordinate activity between these cortical areas. Another important question is how these circuits in frontal-parietal cortex that are involved in deciding between action plans are interfaced with areas such as orbitofrontal cortex that are concerned with choosing goods (Padoa-Schioppa and Assad 2006, 2008), but not necessarily the actions to obtain them. Brain-machine interface applications for neuroprosthetics may be extended to the orbitofrontal cortex to bring reward signals under conscious control with biofeedback. Such control may have applications

for brain disorders that may be related to reward processes such as obsessive compulsive disorders and addictions. Finally, it will be interesting to determine if other movement-related signals in the PPC, such as saccade, pursuit, and fixation activity, have dynamics similar to the reach-related responses and consistent with their being efference copy signals. If so, this would provide additional evidence for the hypothesis that the PPC is involved in forward state estimation for movement correction and spatial stability.

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REFERENCES

- Andersen, R.A. (1987). The role of the inferior parietal lobule in spatial perception and visual-motor integration. In *The Handbook of Physiology. Section I: The Nervous System, Volume V. Higher Functions of the Brain Part 2*, F. Plum, V.B. Mountcastle, and S.R. Geiger, eds. (Bethesda, MD: American Physiological Society), pp. 483–518.
- Andersen, R.A., and Buneo, C.A. (2002). Intentional maps in posterior parietal cortex. *Annu. Rev. Neurosci.* 25, 189–220.
- Andersen, R.A., Asanuma, C., and Cowan, W.M. (1985a). Callosal and prefrontal associational projecting cell populations in area 7a of the macaque monkey: A study using retrogradely transported fluorescent dyes. *J. Comp. Neurol.* 232, 443–455.
- Andersen, R.A., Essick, G.K., and Siegel, R.M. (1985b). The encoding of spatial location by posterior parietal neurons. *Science* 230, 456–458.
- Andersen, R.A., Essick, G.K., and Siegel, R.M. (1987). Neurons of area 7 activated by both visual stimuli and oculomotor behavior. *Exp. Brain Res.* 67, 316–322.
- Andersen, R.A., Asanuma, C., Essick, G., and Siegel, R.M. (1990a). Cortico-cortical connections of anatomically and physiologically defined subdivisions within the inferior parietal lobule. *J. Comp. Neurol.* 296, 65–113.
- Andersen, R.A., Bracewell, R.M., Barash, S., Gnadt, J.W., and Forgassi, L. (1990b). Eye position effects on visual, memory and saccade-related activity in areas LIP and 7A of macaque. *J. Neurosci.* 10, 1176–1196.
- Andersen, R.A., Snyder, L.H., Bradley, D.C., and Xing, J. (1997). Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annu. Rev. Neurosci.* 20, 303–330.

- Astafiev, S.V., Shulman, G.L., Stanley, C.M., Snyder, A.Z., Van Essen, D.C., and Corbetta, M. (2003). Functional organization of human intraparietal and frontal cortex for attending, looking, and pointing. *J. Neurosci.* *23*, 4689–4699.
- Averbeck, B.B., Sohn, J.W., and Lee, D. (2006). Activity in prefrontal cortex during dynamic selection of action sequences. *Nat. Neurosci.* *9*, 276–282.
- Baldauf, D., Wolf, M., and Deubel, H. (2006). Deployment of visual attention before sequences of goal-directed hand movements. *Vision Res.* *46*, 4355–4374.
- Baldauf, D., Cui, H., and Andersen, R.A. (2008). The posterior parietal cortex encodes in parallel both goals for double-reach sequences. *J. Neurosci.* *28*, 10081–10089.
- Barracough, D.J., Conroy, M.L., and Lee, D. (2004). Prefrontal cortex and decision making in a mixed-strategy game. *Nat. Neurosci.* *7*, 404–410.
- Basso, M.A., and Wurtz, R.H. (1998). Modulation of neuronal activity in superior colliculus by changes in target probability. *J. Neurosci.* *18*, 7519–7534.
- Bastian, A., Schoner, G., and Riehle, A. (2003). Preshaping and continuous evolution of motor cortical representations during movement preparation. *Eur. J. Neurosci.* *18*, 2047–2058.
- Batista, A.P., and Andersen, R.A. (2001). The parietal reach region codes the next planned movement in a sequential reach task. *J. Neurophysiol.* *85*, 539–544.
- Batista, A.P., Buneo, C.A., Snyder, L.H., and Andersen, R.A. (1999). Reach plans in eye-centered coordinates. *Science* *285*, 257–260.
- Batista, A.P., Yu, B.M., Santhanam, G., Ryu, S.I., Afshar, A., and Shenoy, K.V. (2008). Cortical neural prosthesis performance improves when eye position is monitored. *IEEE Trans. Neural. Syst. Rehabil. Eng.* *16*, 24–31.
- Baumann, M.A., Fluet, M.-C., and Scherberger, H. (2009). Context-specific grasp movement representation in the anterior intraparietal area. *J. Neurosci.* *29*, 6436–6448.
- Beck, J., Ma, W.J., Kiani, R., Hanks, T., Churchland, A.K., Roitman, J., Shadlen, M.N., Latham, P.E., and Pouget, A. (2008). Probabilistic population codes for Bayesian decision making. *Neuron* *60*, 1142–1152.
- Bhattacharyya, R., Musallam, S., and Andersen, R.A. (2009). Parietal reach region encodes reach depth using retinal disparity and vergence angle signals. *J. Neurophysiol.* *102*, 805–816.
- Bisley, J.W., and Goldberg, M.E. (2003). Neuronal activity in the lateral intraparietal area and spatial attention. *Science* *299*, 81–86.
- Blatt, G., Andersen, R.A., and Stoner, G. (1990). Visual receptive field organization and cortico-cortical connections of area LIP in the macaque. *J. Comp. Neurol.* *299*, 421–445.
- Bradley, D.C., Maxwell, M., Andersen, R.A., Banks, M.S., and Shenoy, K.V. (1996). Mechanisms of heading perception in primate visual cortex. *Science* *273*, 1544–1547.
- Bradley, D.C., Chang, G.C., and Andersen, R.A. (1998). Encoding of three-dimensional structure-from-motion by primate area MT neurons. *Nature* *392*, 714–717.
- Britten, K.H., Newsome, W.T., Shadlen, M.N., Celebrini, S., and Movshon, J.A. (1996). A relationship between behavioral choice and the visual responses of neurons in macaque MT. *Vis. Neurosci.* *13*, 87–100.
- Brodmann, K. (1909). Vergleichende lokalisationslehre der grosshirnrinde in ihren prinzipien dargestellt auf grund des zellenhaues (Leipzig: Barth).
- Brotchie, P.R., Andersen, R.A., Snyder, L.H., and Goodman, S.J. (1995). Head position signals used by parietal neurons to encode locations of visual stimuli. *Nature* *375*, 232–235.
- Brozovic, M., Gail, A., and Andersen, R.A. (2007). Gain mechanisms for contextually guided visuomotor transformations. *J. Neurosci.* *27*, 10588–10596.
- Brozovic, M., Abbott, L.F., and Andersen, R.A. (2008). Mechanism of gain modulation at single neuron and network levels. *J. Comput. Neurosci.* *25*, 158–168.
- Buneo, C.A., and Andersen, R.A. (2006). The posterior parietal cortex: Sensorimotor interface for the planning and online control of visually guided movements. *Neuropsychologia* *44*, 2594–2606.
- Buneo, C.A., Jarvis, M.R., Batista, A.P., and Andersen, R.A. (2002). Direct visuomotor transformations for reaching. *Nature* *416*, 632–636.
- Burnod, Y., Baraduc, P., Battaglia-Mayer, A., Guigon, E., Koechlin, E., Ferraina, S., Lacquaniti, F., and Caminiti, R. (1999). Parieto-frontal coding of reaching: an integrated framework. *Exp. Brain Res.* *129*, 325–346.
- Buschman, T.J., and Miller, E.K. (2007). Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science* *315*, 1860–1862.
- Campos, M., Breznen, B., and Andersen, R.A. (2009). Separate representations of target and timing cue locations in SEF. *J. Neurophysiol.* *101*, 448–459.
- Cassanello, C.R., and Ferrera, V.P. (2007). Computing vector differences using a gain field-like mechanism in monkey frontal eye field. *J. Physiol.* *582*, 647–664.
- Cisek, P. (2006). Integrated neural processes for defining potential actions and deciding between them: a computational model. *J. Neurosci.* *26*, 9761–9770.
- Cisek, P. (2007). Cortical mechanisms of action selection: The affordance competition hypothesis. *Philos. Trans. R Soc. Lond. B. Biol. Sci.* *362*, 1585–1599.
- Cisek, P., and Kalaska, J.F. (2005). Neural correlates of reaching decisions in dorsal premotor cortex: Specification of multiple direction choices and final selection of action. *Neuron* *45*, 801–814.
- Coe, B., Tomihara, K., Matsuzawa, M., and Hikosaka, O. (2002). Visual and anticipatory bias in three cortical eye fields of the monkey during an adaptive decision-making task. *J. Neurosci.* *22*, 5081–5090.
- Cohen, Y.E., and Andersen, R.A. (2000). Eye position modulates reach activity to sounds. *Neuron* *27*, 647–652.
- Colby, C.L., and Goldberg, M.E. (1999). Space and attention in parietal cortex. *Annu. Rev. Neurosci.* *22*, 319–349.
- Connolly, J.D., Andersen, R.A., and Goodale, M.A. (2003). fMRI evidence for a 'parietal reach region' in the human brain. *Exp. Brain Res.* *153*, 140–145.
- Constantin, A.G., Wang, H., Martinez-Trujillo, J.C., and Crawford, J.D. (2007). Frames of reference for gaze saccades evoked during stimulation of lateral intraparietal cortex. *J. Neurophysiol.* *98*, 696–709.
- Critchley, M. (1953). *The Parietal Lobe* (London: Arnold).
- Csorba, M., and Durrant-Whyte, H.F. (1997). New approach to map building using relative position estimates. Paper presented at SPIE (Orlando, FL).
- Cui, H., and Andersen, R.A. (2007). Posterior parietal cortex encodes autonomously selected motor plans. *Neuron* *56*, 552–559.
- Della-Maggiore, V., Malfait, N., Ostry, D.J., and Paus, T. (2004). Stimulation of the posterior parietal cortex interferes with arm trajectory adjustments during the learning of new dynamics. *J. Neurosci.* *24*, 9971–9976.
- Deneve, S., Latham, P.E., and Pouget, A. (2001). Efficient computation and cue integration with noisy population codes. *Nat. Neurosci.* *4*, 826–831.
- Desimone, R., and Duncan, J. (1995). Neural mechanisms of selective visual attention. *Annu. Rev. Neurosci.* *18*, 193–222.
- Desmurget, M., Epstein, C.M., Turner, R.S., Prablanc, C., Alexander, G., and Grafton, S.T. (1999). Role of the posterior parietal cortex in updating reaching movements to a visual target. *Nat. Neurosci.* *2*, 563–567.
- Desmurget, M., Reilly, K.T., Richard, N., Szathmari, A., Mottolese, C., and Sirigu, A. (2009). Movement intention after parietal cortex stimulation in humans. *Science* *324*, 811–813.
- Deubel, H., and Schneider, W.X. (1996). Saccade target selection and object recognition: evidence for a common attention mechanism. *Vision Res.* *36*, 1827–1837.

- Deubel, H., Schneider, W.X., and Paprotta, I. (1998). Selective dorsal and ventral processing: Evidence for a common attentional mechanism in reaching and perception. *Vis. Cogn.* 5, 81–107.
- Dodd, J.V., Krug, K., Cumming, B.G., and Parker, A.J. (2001). Perceptually bistable three-dimensional figures evoke high choice probabilities in cortical area MT. *J. Neurosci.* 21, 4809–4821.
- Donoghue, J.P. (2002). Connecting cortex to machines: recent advances in brain interfaces. *Nat. Neurosci.* 5, 1085–1088.
- Duhamel, J.-R., Colby, C., and Goldberg, M.E. (1992). The updating of the representation of the visual space in parietal cortex by intended eye movement. *Science* 255, 90–92.
- Eskandar, E.N., and Assad, J.A. (1999). Dissociation of visual, motor and predictive signals in parietal cortex during visual guidance. *Nat. Neurosci.* 2, 88–93.
- Evarts, E.V., and Thach, W.T. (1969). Motor mechanisms of the CNS: cerebrocerebellar interrelations. *Annu. Rev. Physiol.* 31, 451–498.
- Fagg, A.H., and Arbib, M.A. (1998). Modeling parietal-premotor interactions in primate control of grasping. *Neural Netw.* 11, 1277–1303.
- Ferrier, D. (1876). *The Function of the Brain* (London: Smith Elder).
- Fogassi, L., Ferrari, P.F., Gesierich, B., Rozzi, S., Chersi, F., and Rizzolatti, G. (2005). Parietal lobe: from action organization to intention understanding. *Science* 308, 662–667.
- Freedman, D.J., and Assad, J.A. (2006). Experience-dependent representation of visual categories in parietal cortex. *Nature* 443, 85–88.
- Fries, P., Reynolds, J.H., Rorie, A.E., and Desimone, R. (2001). Modulation of oscillatory neuronal synchronization by selective visual attention. *Science* 291, 1560–1563.
- Fritsch, G.T., and Hitzig, E. (1870). On the electrical excitability of the cerebrum. In *Some Papers on the Cerebral Cortex*, von Bonin (1960), translation (Springfield, IL: Charles C. Thomas).
- Fujii, N., and Graybiel, A.M. (2003). Representation of action sequence boundaries by macaque prefrontal cortical neurons. *Science* 301, 1246–1249.
- Gail, A., and Andersen, R.A. (2006). Neural dynamics in monkey parietal reach region reflect context-specific sensorimotor transformations. *J. Neurosci.* 26, 9376–9384.
- Gail, A., Klaes, C., and Westendorff, S. (2009). Implementation of spatial transformation rules for goal-directed reaching via gain modulation in monkey parietal and premotor cortex. *J. Neurosci.* 29, 9490–9499.
- Gnadt, J.W., and Andersen, R.A. (1988). Memory related motor planning activity in posterior parietal cortex of macaque. *Exp. Brain Res.* 70, 216–220.
- Gold, J.I., and Shadlen, M.N. (2007). The neural basis of decision making. *Annu. Rev. Neurosci.* 30, 535–574.
- Goldberg, M.E., and Segraves, M.A. (1987). Visuospatial and motor attention in the monkey. *Neuropsychologia* 25, 107–118.
- Goldberg, M.E., Bisley, J., Powell, K.D., Gottlieb, J., and Kusunoki, M. (2002). The role of the lateral intraparietal area of the monkey in the generation of saccades and visuospatial attention. *Ann. N.Y. Acad. Sci.* 956, 205–215.
- Goldberg, M.E., Bisley, J.W., Powell, K.D., and Gottlieb, J. (2006). Saccades, salience, and attention: the role of the lateral intraparietal area in visual behavior. *Prog. Brain Res.* 155, 157–175.
- Goldman-Rakic, P.S. (1988). Parallel distributed networks in primate association cortex. *Annu. Rev. Neurosci.* 11, 137–156.
- Gottlieb, J., and Goldberg, M.E. (1999). Activity of neurons in the lateral intraparietal area of the monkey during an antisaccade task. *Nat. Neurosci.* 2, 906–912.
- Gottlieb, J., Balan, P.F., Oristaglio, J., and Schneider, D. (2009). Task specific computations in attentional maps. *Vision Res.* 49, 1216–1226.
- Graziano, M.S., and Gross, C.G. (1998). Spatial maps for the control of movement. *Curr. Opin. Neurobiol.* 8, 195–201.
- Graziano, M.S.A., Yap, G.S., and Gross, C.G. (1994). Coding of visual space by premotor neurons. *Science* 266, 1054–1057.
- Gregoriou, G.G., Gots, S.J., Zhou, H., and Desimone, R. (2009). High-frequency, long-range coupling between prefrontal and visual cortex during attention. *Science* 324, 1207–1210.
- Haarmeier, T., Thier, P., Repnow, M., and Petersen, D. (1997). False perception of motion in a patient who cannot compensate for eye movements. *Nature* 389, 849–852.
- Haarmeier, T., Bunjes, F., Lindner, A., Berret, E., and Thier, P. (2001). Optimizing visual motion perception during eye movements. *Neuron* 32, 527–535.
- Haggard, P. (2008). Human volition: towards a neuroscience of will. *Nature Rev. Neurosci.* 9, 934–946.
- Hagler, D.J., Jr., Riecke, L., and Sereno, M.I. (2007). Parietal and superior frontal visuospatial maps activated by pointing and saccades. *Neuroimage* 35, 1562–1577.
- Histed, M.H., and Miller, E.K. (2006). Microstimulation of frontal cortex can reorder a remembered spatial sequence. *PLoS Biol.* 4, e134.
- Hochberg, L.R., Serruya, M.D., Friebs, G.M., Mukand, J.A., Saleh, M., Caplan, A.H., Branner, A., Chen, D., Penn, R.D., and Donoghue, J.P. (2006). Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* 442, 164–171.
- Ipata, A.E., Gee, A.L., Gottlieb, J., Bisley, J.W., and Goldberg, M.E. (2006). LIP responses to a popout stimulus are reduced if it is overtly ignored. *Nat. Neurosci.* 9, 1071–1076.
- Ipata, A.E., Gee, A.L., Goldberg, M.E., and Bisley, J.W. (2009). Activity in the lateral intraparietal area predicts the goal and latency of saccades in a free-viewing visual search task. *J. Neurosci.* 26, 3656–3661.
- Janssen, P., and Shadlen, M.N. (2005). A representation of the hazard rate of elapsed time in macaque area LIP. *Nat. Neurosci.* 8, 234–241.
- Johnson, P.B., Ferraina, S., Bianchi, L., and Caminiti, R. (1996). Cortical networks for visual reaching: physiological and anatomical organization of frontal and parietal lobe arm regions. *Cereb. Cortex* 6, 102–119.
- Jordan, M.I., and Rumelhart, D.E. (1992). Forward models—supervised learning with a distal teacher. *Cogn. Sci.* 16, 307–354.
- Kalaska, J.F. (1996). Parietal cortex area 5 and visuomotor behavior. *Can. J. Physiol. Pharmacol.* 74, 483–498.
- Kalaska, J.F., Scott, S.H., Cisek, P., and Sergio, L.E. (1997). Cortical control of reaching movements. *Curr. Opin. Neurobiol.* 7, 849–859.
- Katzner, S., Nauhaus, I., Benucci, A., Bonin, V., Ringach, D.L., and Carandini, M. (2009). Local origin of field potentials in visual cortex. *Neuron* 61, 35–41.
- Kennedy, P.R., and Bakay, R.A.E. (2000). Restoration of neural output from a paralyzed patient by a direct brain connection. *Neuroreport* 9, 1707–1711.
- Kowler, E., Anderson, E., Doshier, B., and Blaser, E. (1996). The role of attention in the programming of saccades. *Vision Res.* 35, 1897–1916.
- Lacquaniti, F., Guigon, E., Bianchi, L., Ferraina, S., and Caminiti, R. (1995). Representing spatial information for limb movement: role of area 5 in the monkey. *Cereb. Cortex* 5, 391–409.
- Lau, B., and Glimcher, P.W. (2008). Value representations in the primate striatum during matching behavior. *Neuron* 58, 451–463.
- Lawrence, B.M., and Snyder, L.H. (2006). Comparison of effector-specific signals in frontal and parietal cortices. *J. Neurophysiol.* 96, 1393–1400.
- Lee, B., Pesaran, B., and Andersen, R.A. (2007). Translation speed compensation in the dorsal aspect of the medial superior temporal area. *J. Neurosci.* 27, 2582–2591.
- Levy, I., Schluppeck, D., Heeger, D.J., and Glimcher, P.W. (2007). Specificity of human cortical areas for reaches and saccades. *J. Neurosci.* 27, 4687–4696.

- Logothetis, N.K., and Wandell, B.A. (2004). Interpreting the BOLD signal. *Annu. Rev. Physiol.* 66, 735–769.
- Lu, X., and Ashe, J. (2005). Anticipatory activity in primary motor cortex codes memorized movement sequences. *Neuron* 45, 967–973.
- Lynch, J.C., Mountcastle, V.B., Talbot, W.H., and Yin, T.C.T. (1977). Parietal lobe mechanisms for directed visual-attention. *J. Neurophysiol.* 40, 362–389.
- Maimon, G., and Assad, J.A. (2006). A cognitive signal for the proactive timing of action in macaque LIP. *Nat. Neurosci.* 9, 948–955.
- Mays, L.E., and Sparks, D.L. (1980). Dissociation of visual and saccade-related responses in superior colliculus neurons. *J. Neurophysiol.* 43, 207–232.
- Mehring, C., Rickert, J., Vaadia, E., Cardoso de Oliveira, S., Aertsen, A., and Rotter, S. (2003). Inference of hand movements from local field potentials in monkey motor cortex. *Nat. Neurosci.* 6, 1253–1254.
- Miller, E.K., and Cohen, J.D. (2001). An integrative theory of prefrontal cortex function. *Annu. Rev. Neurosci.* 24, 167–202.
- Miller, E.K., and Wilson, M.A. (2008). All my circuits: using multiple electrodes to understand functioning neural networks. *Neuron* 60, 483–488.
- Mishra, J., Fellous, J.M., and Sejnowski, T.J. (2006). Selective attention through phase relationship of excitatory and inhibitory input synchrony in a model cortical neuron. *Neural Netw.* 19, 1329–1346.
- Mitzdorf, U. (1987). Properties of the evoked potential generators: current source-density analysis of visually evoked potentials in the cat cortex. *Int. J. Neurosci.* 33, 33–59.
- Monosov, I.E., Trageser, J.C., and Thompson, T.G. (2008). Measurements of simultaneously recorded spiking activity and local field potentials suggest that spatial selection emerges in the frontal eye field. *Neuron* 57, 614–625.
- Moore, T., and Armstrong, K.M. (2002). Selective gating of visual signals by microstimulation of frontal cortex. *Nature* 421, 370–373.
- Moritz, C.T., Perlmutter, S.I., and Fetz, E.E. (2008). Direct control of paralysed muscles by cortical neurons. *Nature* 456, 639–642.
- Mountcastle, V.B. (1957). Modality and topographic properties of single neurons of cat's somatic sensory cortex. *J. Neurophysiol.* 20, 408–434.
- Mountcastle, V.B. (1998). *Perceptual Neuroscience: The Cerebral Cortex* (Cambridge, MA: Harvard University Press).
- Mountcastle, V.B., Lynch, J.C., Georgopoulos, A., Sakata, H., and Acuna, C. (1975). Posterior parietal association cortex of monkey – command function for operations within extrapersonal space. *J. Neurophysiol.* 38, 871–908.
- Mullette-Gillman, O.A., Cohen, Y.E., and Groh, J.M. (2005). Eye-centered, head-centered, and complex coding of visual and auditory targets in the intraparietal sulcus. *J. Neurophysiol.* 94, 2331–2352.
- Mullette-Gillman, O.A., Cohen, Y.E., and Groh, J.M. (2009). Motor-related signals in the intraparietal cortex encode locations in a hybrid, rather than eye-centered reference frame. *Cereb. Cortex* 19, 1761–1775.
- Mulliken, G., Musallam, S., and Andersen, R.A. (2008a). Forward estimation of movement state in posterior parietal cortex. *Proc. Natl. Acad. Sci. USA* 105, 8170–8177.
- Mulliken, G., Musallam, S., and Andersen, R.A. (2008b). Decoding trajectories from posterior parietal cortex ensembles. *J. Neurosci.* 28, 12913–12926.
- Murthy, V.N., and Fetz, E.E. (1996). Synchronization of neurons during local field potential oscillations in sensorimotor cortex of awake monkeys. *J. Neurophysiol.* 76, 3968–3982.
- Musallam, S., Corneil, B.D., Greger, B., Scherberger, H., and Andersen, R.A. (2004). Cognitive control signals for neural prosthetics. *Science* 305, 258–262.
- Mushiaki, H., Saito, N., Sakamoto, K., Itoyama, Y., and Tanji, J. (2006). Activity in the lateral prefrontal cortex reflects multiple steps of future events in action plans. *Neuron* 50, 631–641.
- Newman, P.M. (1999). *On the Solution to the Simultaneous Localization and Map Building Problem* (Sydney, Australia: University of Sydney).
- Newsome, W.T., Britten, K.H., and Movshon, J.A. (1989). Neuronal correlates of a perceptual decision. *Nature* 341, 52–54.
- Nicolelis, M.A. (2003). Brain-machine interfaces to restore motor function and probe neural circuits. *Nat. Rev. Neurosci.* 3, 417–422.
- Ninokura, Y., Mushiaki, H., and Tanji, J. (2003). Representation of the temporal order of objects in the primate lateral prefrontal cortex. *J. Neurophysiol.* 89, 2869–2873.
- Ohbayashi, M., Ohki, K., and Miyashita, Y. (2003). Conversion of working memory to motor sequence in the monkey premotor cortex. *Science* 301, 233–236.
- Olfati, R., and Murray, R.M. 2002. Distributed cooperative control of multiple vehicle formations using structural potential functions. *Proc. 15th IFAC World Congress*.
- Padoa-Schioppa, C., and Assad, J.A. (2006). Neurons in the orbitofrontal cortex encode economic value. *Nature* 441, 223–226.
- Padoa-Schioppa, C., and Assad, J.A. (2008). The representation of economic value in the orbitofrontal cortex is invariant for changes of menu. *Nat. Neurosci.* 11, 95–102.
- Pesaran, B., Pezaris, J., Sahani, M., Mitra, P.M., and Andersen, R.A. (2002). Temporal structure in neuronal activity during working memory in Macaque parietal cortex. *Nat. Neurosci.* 5, 805–811.
- Pesaran, B., Nelson, M., and Andersen, R.A. (2006). Dorsal premotor neurons encode the relative position of the hand, eye, and goal during reach planning. *Neuron* 51, 125–134.
- Pesaran, B., Nelson, M.J., and Andersen, R.A. (2008). Free choice activates a decision circuit between frontal and parietal cortex. *Nature* 453, 406–409.
- Penfield, W., and Boldrey, E. (1937). Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain* 60, 389–443.
- Pisella, L., Grea, H., Tilikete, C., Vighetto, A., Desmurget, M., Rode, G., Biosson, D., and Rossetti, Y. (2000). An 'automatic pilot' for the hand in human posterior parietal cortex: toward reinterpreting optic ataxia. *Nat. Neurosci.* 3, 729–736.
- Platt, M.L., and Glimcher, P.W. (1997). Responses of intraparietal neurons to saccadic targets and visual distractors. *J. Neurophysiol.* 78, 1574–1589.
- Platt, M.L., and Glimcher, P.W. (1999). Neural correlates of decision variables in parietal cortex. *Nature* 400, 233–238.
- Posner, M.I. (1980). Orienting of attention. *Quarterly J. Exp. Psychology* 32, 3–25.
- Powell, K.D., and Goldberg, M.E. (2000). Response of neurons in the lateral intraparietal area to a distractor flashed during the delay period of a memory-guided saccade. *J. Neurophysiol.* 84, 301–310.
- Quiari Quiroga, R., Snyder, L.H., Batista, A.P., Cui, H., and Andersen, R.A. (2006). Movement intention is better predicted than attention in the posterior parietal cortex. *J. Neurosci.* 26, 3615–3620.
- Rangel, A. (2009). The computation and comparison of value in goal-directed choice. In *Neuroeconomics: Decision Making and the Brain*, P.W. Glimcher, C.F. Camerer, E. Fehr, and R.A. Poldrack, eds. (Amsterdam: Elsevier), pp. 425–441.
- Rizzolatti, G., Camarda, R., Fogassi, L., Gentilucci, M., Luppino, G., and Matelli, M. (1988). Functional organization of inferior area 6 in the macaque monkey. II. Area F5 and the control of distal movements. *Exp. Brain Res.* 71, 491–507.
- Rizzolatti, G., Riggio, L., Dascola, I., and Umiltà, C. (1987). Reorienting attention across the horizontal and vertical meridians—evidence in favour of a premotor theory of attention. *Neuropsychologia* 25, 31–40.
- Rizzolatti, G., Fogassi, L., and Gallese, V. (1997). Parietal cortex: from sight to action. *Curr. Opin. Neurobiol.* 7, 562–567.
- Rushworth, M.F.S., Ellison, A., and Walsh, V. (2001). Complementary localization and lateralization of orienting and motor attention. *Nat. Neurosci.* 4, 656–661.

- Sakata, H., Taira, M., Kusunok, M., Murata, A., and Tanaka, Y. (1997). The parietal association cortex in depth perception and visual control of hand action. *Trends Neurosci.* 20, 350–357.
- Salinas, E., and Sejnowski, T.J. (2000). Impact of correlated synaptic input on output firing rate and variability in simple neuronal models. *J. Neurosci.* 20, 6193–6209.
- Samejima, K., Yasumasa, U., Doya, D., and Kimura, M. (2005). Representation of action-specific reward values in the striatum. *Science* 310, 1337–1340.
- Sanes, J.N., and Donoghue, J.P. (1993). Oscillations in local field potentials of the primate motor cortex during voluntary movement. *Proc. Natl. Acad. Sci. USA* 90, 4470–4474.
- Santhanam, G., Ryu, S.I., Yu, B.M., Afshar, A., and Shenoy, K.V. (2006). A high-performance brain-computer interface. *Nature* 442, 195–198.
- Schall, J.D. (2002). The neural selection and control of saccades by the frontal eye field. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* 357, 1073–1082.
- Schall, J.D. (2004). On building a bridge between brain and behaviour. *Annu. Rev. Psychol.* 55, 23–50.
- Schall, J.D., Paré, M., and Woodman, G.F. (2007). Comment on “Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices”. *Science* 318, 44.
- Scherberger, H., and Andersen, R.A. (2007). Target selection signals for arm reaching in the posterior parietal cortex. *J. Neurosci.* 27, 2001–2012.
- Scherberger, H., Jarvis, M.R., and Andersen, R.A. (2005). Cortical local field potential encodes movement intentions in the posterior parietal cortex. *Neuron* 46, 347–354.
- Schwartz, A.B. (2004). Cortical neural prosthetics. *Annu. Rev. Neurosci.* 27, 487–507.
- Sejnowski, T.J., and Paulsen, O. (2006). Network oscillations: emerging computational principles. *J. Neurosci.* 26, 1673–1676.
- Sereno, A.B., and Maunsell, J.H.R. (1998). Shape selectivity in primate lateral intraparietal cortex. *Nature* 395, 500–503.
- Shadlen, M.N., and Newsome, W.T. (2001). Neural basis of a perceptual decision in the parietal cortex (area LIP) of the rhesus monkey. *J. Neurophysiol.* 86, 1916–1936.
- Shadlen, M.N., and Newsome, W.T. (1996). Motion perception: Seeing and deciding. *PNAS* 93, 628–633.
- Shadmehr, R., and Wise, S.P. (2005). *The Computational Neurobiology of Reaching and Pointing* (Cambridge, MA: MIT Press).
- Shenoy, K.V., Bradley, D.C., and Andersen, R.A. (1999). The influence of gaze rotation upon the visual response of primate MSTd neurons. *J. Neurophysiol.* 81, 2764–2786.
- Shima, K., and Tanji, J. (1998). Both supplementary and presupplementary motor areas are crucial for the temporal organization of multiple movements. *J. Neurophysiol.* 80, 3247–3260.
- Shima, K., Isoda, M., Mushiake, H., and Tanji, J. (2007). Categorization of behavioural sequences in the prefrontal cortex. *Nature* 445, 315–318.
- Snyder, L.H., Batista, A.P., and Andersen, R.A. (1997). Coding of intention in the posterior parietal cortex. *Nature* 386, 167–170.
- Snyder, L.H., Batista, A.P., and Andersen, R.A. (2000). Saccade-related activity in the parietal reach region. *J. Neurophysiol.* 83, 1099–1102.
- Srinivasan, L., Eden, U.T., Willsky, A.S., and Brown, E.N. (2006). A state-space analysis for reconstruction of goal-directed movements using neural signals. *Neural Comput.* 18, 2465–2494.
- Stoet, G., and Snyder, L.H. (2004). Single neurons in posterior parietal cortex of monkeys encode cognitive set. *Neuron* 42, 1003–1012.
- Striccanne, B., Andersen, R.A., and Mazzoni, P. (1996). Eye-centered, head-centered and intermediate coding of remembered sound locations in area LIP. *J. Neurophysiol.* 76, 2071–2076.
- Sugrue, L.P., Corrado, G.S., and Newsome, W.T. (2004). Matching behavior and the representation of value in the parietal cortex. *Science* 304, 1782–1787.
- Tanji, J., and Shima, K. (1994). Role for supplementary motor area cells in planning several movements ahead. *Nature* 371, 413–416.
- Tanne-Gariepy, J., Boussaoud, D., and Rouiller, E.M. (2002). Parietal inputs to dorsal versus ventral premotor areas in the macaque monkey: evidence for largely segregated visuomotor pathways. *Exp. Brain Res.* 145, 91–103.
- Thier, P., and Andersen, R.A. (1996). Electrical microstimulation suggests two different kinds of representation of head-centered space in the intraparietal sulcus of rhesus monkeys. *Proc. Natl. Acad. Sci.* 93, 4962–4967.
- Thier, P., and Andersen, R.A. (1998). Electrical microstimulation distinguishes distinct saccade-related areas in the posterior parietal cortex. *J. Neurophysiol.* 80, 1713–1735.
- Torres, E., and Andersen, R.A. (2006). Space-time separation during obstacle-avoidance learning in monkeys. *J. Neurophysiol.* 96, 2613–2632.
- Toth, L.J., and Assad, J.A. (2002). Dynamic coding of behaviourally relevant stimuli in parietal cortex. *Nature* 415, 165–168.
- Tversky, A., and Kahneman, D. (1981). The framing of decisions and the psychology of choice. *Science* 211, 453–458.
- Ungerleider, L.G., and Mishkin, M. (1982). Two cortical visual systems. In *Analysis of Visual Behavior*, D.J. Ingle, M.A. Goodale, and R.J.W. Mansfield, eds. (Cambridge: MIT), pp. 549.
- Vaziri, S., Diedrichsen, J., and Shadmehr, R. (2006). Why does the brain predict sensory consequences of oculomotor commands? Optimal integration of the predicted and the actual sensory feedback. *J. Neurosci.* 26, 4188–4197.
- Velliste, M., Perel, S., Spalding, M.C., Whitford, S., and Schwartz, A.B. (2008). Cortical control of a prosthetic arm for self-feeding. *Nature* 453, 1098–1101.
- Von Economo, C. (1929). *The Cytoarchitectonics of the Human Cerebral Cortex* (London: Oxford University Press).
- von Helmholtz, H. (1866). *Handbook of Physiological Optics*, Third Edition (New York: Dover Publications).
- VonHolst, E., and Mittelstaedt, H. (1950). Das reafferenzprinzip. *Naturwissenschaften* 37, 464–476.
- Wang, X.-J. (2008). Decision making in recurrent neuronal circuits. *Neuron* 60, 215–234.
- Wise, S.P. (1985). The primate premotor cortex: past, present, and preparatory. *Annu. Rev. Neurosci.* 8, 1–19.
- Wolpert, D.M., Ghahramani, Z., and Jordan, M.I. (1995). An internal model for sensorimotor integration. *Science* 269, 1880–1882.
- Xing, J., and Andersen, R.A. (2000a). The memory activity of LIP neurons in sequential eye movements simulated with neural networks. *J. Neurophysiol.* 84, 651–665.
- Xing, J., and Andersen, R.A. (2000b). Models of posterior parietal cortex which perform multimodal integration and represent space in several coordinate frames. *J. Cogn. Neurosci.* 12, 601–614.
- Yang, T., and Shadlen, M.N. (2007). Probabilistic reasoning by neurons. *Nature* 447, 1075–1083.
- Zhang, M., and Barash, S. (2000). Neuronal switching of sensorimotor transformations for antisaccades. *Nature* 408, 971–975.
- Zhang, M., and Barash, S. (2004). Persistent LIP activity in memory antisaccades: working memory for a sensorimotor transformation. *J. Neurophysiol.* 91, 1424–1441.
- Zipser, D., and Andersen, R.A. (1988). A back propagation programmed network that simulates response properties of a subset of posterior parietal neurons. *Nature* 331, 679–684.