doi: 10.1093/cercor/bhx052 Advance Access Publication Date: 24 March 2017 Original Article

# ORIGINAL ARTICLE

OXFORD

# Single Units in the Posterior Parietal Cortex Encode Patterns of Bimanual Coordination

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# Abstract

Bimanual coordination is critical for a broad array of behaviors. Drummers, for example, must carefully coordinate movements of their 2 arms, sometimes beating on the same drum and sometimes on different ones. While coordinated behavior is well-studied, the early stages of planning are not well understood. In the parietal reach region (PRR) of the posterior parietal cortex (PPC), the presence of neurons that modulate when either arm moves by itself has been taken as evidence for a role in bimanual coordination. To test this notion, we recorded neurons during both unilateral and bimanual movements. We find that the activity that precedes an ipsilateral arm movement is primarily a sensory response to a target in the neuron's visual receptive field and not a plan to move the ipsilateral arm. In contrast, the activity that precedes a contralateral arm movement is the sum of a movement plan plus a sensory response. Despite not coding ipsilateral arm movements, about half of neurons discriminate between different patterns of bimanual movements. These results provide direct evidence that PRR neurons represent bimanual reach plans, and suggest that bimanual coordination originates in the sensory-to-motor processing stream prior to the motor cortex, within the PPC.

Key words: monkey, motor planning, reach, visually guided, visuomotor

## Introduction

Understanding how the brain coordinates the movement of multiple body parts is of fundamental importance to systems neuroscience. Yet the cortical representation of coordinated movements is not well understood. Single-unit recording studies in nonhuman primates have focused primarily on the frontal cortex during coordinated movement execution and have shown that neurons in the supplementary motor area (SMA), dorsal premotor (PMd), cingulate motor area, and primary motor cortex show activity related specifically to bimanual movements (Tanji et al. 1988; Donchin et al. 1998, 2002; Kermadi 1998). Human patients with damage to the posterior parietal cortex (PPC) exhibit impaired bimanual coordination (Halsband et al. 2001; Serrien et al. 2001). However, with one exception (Kermadi et al. 2000), neurophysiological studies of bimanual movements have not investigated cortical areas outside of frontal cortex.

The PPC is critical for the visual guidance of action. Lesions to the PPC result in deficits in visually guided reaching in both monkeys (Hwang et al. 2012; Battaglia-Mayer et al. 2013; Yttri et al. 2014) and humans (Perenin and Vighetto 1988), mainly affecting the contralateral arm (Hartje and Ettlinger 1973). The parietal reach region (PRR), located in the posterior portion of the macaque intraparietal sulcus (IPS), primarily but not entirely on the medial bank, is a functionally defined region containing neurons that respond preferentially to reaches compared with saccades (Snyder et al. 1997; Calton et al. 2002). Most PRR neurons show sustained activity prior to upcoming reaches in a particular "preferred" direction (Galletti et al. 1997; Battaglia-Mayer et al. 2000, 2001). Directionally tuned responses tend to be stronger for reaches that will be made with the contralateral arm, but approximately half of neurons show tuned responses prior to reaches made with either arm (Chang et al. 2008;

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Chang and Snyder 2012). These properties, along with direct projections forward to PMd in the same hemisphere (Kurata 1991; Tanné et al. 1995; Johnson et al. 1996; Wise et al. 1997), point to a possible role for PRR in bimanual reaching.

Here, we compare single-unit activity prior to reaches made with one or both arms (Fig. 1A,B). We consider several hypotheses. PRR might represent only movement goals (Gail and Andersen 2006), in which case unimanual and bimanual reaches directed toward the same target would evoke similar activity. Alternatively, PRR neurons might show an entirely unique representation when there is a plan to move both limbs, in which case bimanual planning activity might be a linear or nonlinear combination of the activity observed for independent contralateral and ipsilateral reaches. Testing whether the activity observed for each limb combines linearly or nonlinearly can inform whether PRR is directly involved in bimanual coordination (Kermadi et al. 2000; Donchin et al. 2002). The simplest way to combine the activity for the 2 limbs is to add them together. In that case, we would expect more activity on bimanual compared with single limb trials. This outcome, however, would not implicate PRR in bimanual coordination since merely adding signals together is a reversible operation that rearranges the signals but produces no fundamental change in information. Alternatively, limb activity might combine in a nonlinear fashion, consistent with a role for PRR in bimanual coordination.

# **Materials and Methods**

All procedures conformed to the *Guide* for the *Care* and *Use* of *Laboratory Animals* and were approved by the Washington University Institutional Animal Care and Use Committee. Two male rhesus macaques (*Macaca mulatta*) (M1 and M2) participated in the study.

### Apparatus

Head-fixed animals sat in a custom-designed monkey chair (Crist Instrument) with a fully open front to allow unimpaired reaching movements with both arms. Visual stimuli were back-projected by an LCD projector onto a translucent plexiglass screen mounted vertically, approximately 40 cm in front of the animal.

Eye position was monitored using the 120 Hz ISCAN eyetracking laboratory (ETL-400). Touches were monitored every 2 ms using multiple capacitive sensors, mounted at the home pads (to sense reach starting positions) and behind the plexiglass projection screen (to sense reach endpoints) (Fig. 1A, inset). Touch positions on the screen were organized in a virtual  $3 \times 3$ grid centered on the fixation point. Eight 3" vertical plexiglass dividers were mounted on the front of the screen at the middle of each peripheral target location. For convenience, we will refer to each component of the  $3 \times 3$  grid as a single target. For any given target, the animals were trained to reach with the left hand to the left side of the divider and with the right hand to the right side of the divider. Capacitive sensors were mounted behind the projection screen, ~1 inch to the right and left of each plexiglass divider. As a result, the left and right hands activated unique sensors even when both hands reached toward the same target. Animals were monitored in the testing room at all times using an infrared camera equipped with an infrared illuminator.

## Visually Guided Delayed Movement Tasks

The task design and the movement conditions are shown in Fig. 1. The animals performed delayed saccades or reaches with



Figure 1. Delayed movement tasks. (A) A peripheral target (blue in this example; see below) instructs the spatial location and effector to be used (eyes or arm) for each trial. The stimulus remains visible during the delay period. With the disappearance of the central fixation point (go signal), animals either reach or make saccadic eye movements to the visuospatial location of the target. The inset shows the arrangement of the plexiglass divider (vertical black line) that was mounted on the front of the projection screen and capacitive sensors (dashed circles) that were mounted behind the projection screen at each target location. See text for details. (B) On reach trials, movements were made with the contralateral arm only, ipsilateral arm only, both arms together, or each arm to a different target. On saccade trials, only the eyes moved. Movements were either in the preferred direction or the null direction, defined as the location  $180^\circ$  from the preferred direction relative to the central fixation. Movement directions and movement types were randomly interleaved. A green peripheral target instructed a reach with the left arm, red instructed a reach with the right arm, blue instructed a reach with both arms, and white instructed a saccade.

the left, right, or both arms (Mooshagian et al. 2014). Animals first fixated on a circular white stimulus  $(1.5^{\circ} \times 1.5^{\circ})$  centered on the screen in front of them. Left and right hands touched

"home" pads situated at waist height and 20 cm in front of each shoulder. After 500 ms of holding the initial eye  $(\pm 3^{\circ})$  and arm positions, either one or two peripheral target(s) ( $5^{\circ} \times 5^{\circ}$ ) appeared on the screen. When 2 targets appeared, they were at diametrically opposed locations relative to the fixation point, that is, on the left and right, top and bottom, or at opposed diagonal locations. After 1200-1600 ms, the central eye fixation target disappeared, cueing the animal to move to the peripheral target(s) in accordance with a specifically trained code conveyed by target color. A green target instructed a left arm reach, a red target instructed a right arm reach, a blue target instructed a combined reach with both arms, and a white target instructed a saccade (no reach). Trials could be unimanual or bimanual. Bimanual trials could have a single blue target ("bimanual-together") or 2 targets (red and green) separated by 180° relative to the central fixation point ("bimanual-apart"). All trial types were randomly interleaved, within sets of 10 or 40 trials (one each per condition and direction; see below). Throughout saccade and unimanual reach trials, hand(s) not instructed to move were required to remain on the home button(s). On unimanual reach trials, eye movements were constrained to move to the target. On bimanual reach trials, eye movements were unconstrained after the go cue, and the left and right hands were required to hit their target(s) within 500 ms of one another. In fact, temporal coordination was much tighter than this. In 80% of trials, the 2 hands hit their targets within 124 ms of one another. Neither animal showed a strong preference to arrive first with one or the other hand: The average left minus right hand arrival time for bimanual reaches was 11.4 and 23.3 ms for the 2 animals, respectively. For single-target trials, the animals were required to maintain their gaze on the final target for 300 ms. They also needed to maintain their hand(s) on the final target(s) for the same 300 ms interval. Spatial tolerances were  $\pm 3^\circ$  for reaches and  $\pm 2^\circ$  for saccades. When an error occurred (a failure to achieve or maintain the required eye or hand positions), the trial was aborted and a short (1500 ms) time-out ensued. Aborted trials were excluded from further analyses. Successful trials were rewarded with a drop of water or juice.

### **Electrophysiological Recordings**

### **Recording Sites**

Recordings were made from the left hemispheres of 2 adult male rhesus monkeys. Recording chambers were centered at approximately 11 mm posterior to the ear canals and 8 mm lateral of the midline and placed flush to the skull. Extracellular recordings were made using glass-coated tungsten electrodes (Alpha Omega; electrode impedance 0.5-3.0 M ohms). Anatomical magnetic resonance images (MRI) along with information about gray/white boundaries from the recordings were used to localize recording sites (Fig. 2). We imaged a "MRI phantom" within each recording chamber. The phantom consisted of a calibrated plexiglass cylinder with 4 square rods (50 mm  $\times$  2 mm  $\times$  2 mm) filled with the MR-lucent contrast agent manganese (0.003 mM solution). The image of the animal's brain together with the calibrated phantom allowed us to reconstruct recording sites based on chamber X, Y coordinates and microdrive depths, with an error of no more than 2 mm. Neurons were recorded along the caudal portion of the IPS. In this study, we define PRR as that region of cortex containing a large proportion of neurons with visual transients and with sustained delay activity that is substantially greater for combined reaches plus saccades compared with saccades alone in a majority of cases. This functional definition covers much of anatomical areas PO and V6a, on the medial bank of the IPS and rostral bank of the parieto-occipital sulcus, the posterior half of the medial intraparietal area (MIP) on the medial bank, and a portion of lateral occipital-parietal area (LOP) on the lateral bank. This definition distinguishes PRR from nearby lateral intraparietal area (LIP), which lies on the lateral bank immediately rostral to LOP and where most neurons show similar responses to combined reaches plus saccades compared with saccades alone (data not shown). These boundaries, and in particular the finding that PRR extends onto the posterior portion of the lateral bank of the IPS, match the boundaries obtained previously for PRR by contrasting pure reaches (reaches without accompanying saccades) with pure saccades (Snyder et al. 1997; Calton et al. 2002; Chang et al. 2008).

### **Determination of Preferred Direction**

While searching for neurons, animals performed saccade and right arm only (contralateral) trials as described above. Previous work established that few neurons are active for ipsilateral but not contralateral reaches, and even those neurons are somewhat active during saccades (Chang et al. 2008). Online, the preferred direction was defined as the target location that resulted in the largest sustained firing during the delay period for the single target reach conditions (contralateral arm, ipsilateral arm, both arms together). The null direction was defined as the target location 180° from the preferred direction relative to the central fixation point. The preferred direction of the neurons with data for all directions was confirmed by offline analysis. We computed the modulation for each condition for each neuron as the activity for a movement in the preferred direction minus activity for a movement in the null direction. A single preferred direction was determined for each neuron and applied to all tasks (except in Fig. 2B).

### Data Analysis

Data were then collected for all trial types (Fig. 1B). We recorded from 60 isolated neurons in PRR from M1 and 63 from M2. Nine neurons were excluded due to low firing rates (less than 5 spikes during the entire delay interval for all 10 trial types), which made preferred and null directions difficult to unequivocally determine. Of the remaining 114 neurons, we obtained data either for targets in all 8 directions (96 neurons, 49 in M1 and 47 in M2) or for the preferred and null directions only (18 neurons, 10 in M1 and 8 in M2). We obtained an average of 12 repetitions for each of the 10 trial types, with 4 or more repetitions for 112 of the 114 neurons and 8 or more repetitions for 87 of 114 neurons.

### Measurement of Neuronal Activity

The analyses focused on the preparatory delay period between the appearance of the visual target and the cue to move. The delay period was typically 1200–1600 ms long, and the mean spike rate was computed over an interval from 500 to 1200 ms after stimulus onset. For some neurons collected early in the experiment, a shorter minimum delay was used. The mean spike rate interval was adjusted accordingly for these neurons.

### Model Fits

We aimed to find out what factors determine the firing rate of PRR neurons during the planning of an impending bimanual reach. In particular, we asked whether activity preceding bimanual movements is a linear sum of the activities preceding the



Figure 2. Localization and preferred directions of recorded neurons. (A) Anatomical localization of recording sites in each monkey. Coordinates of recorded neurons are projected to a single MRI section perpendicular to the path of the recording electrode (left; see Methods). The right side shows the same selection in expanded view. Major landmarks are shown. IPS, intraparietal sulcus; Midline, longitudinal fissure; POS, parieto-occipital sulcus; STS, superior temporal sulcus. The colored regions are from Lewis and Van Essen (2000); LIP, lateral intraparietal area; LOP, lateral occipital-parietal area; MIP, medial intraparietal area; PO, parietal-occipital area. The left, right, anterior, and posterior directions are labeled as L, R, A, and P, respectively. The size of each circle indicates the number of neurons recorded along that track. (B) Density function of the cosine fit for the contralateral (red), ipsilateral (green), and saccade (black) conditions with respect to bimanual together (vertical blue line). Data are from 96 neurons for which data in all 8 stimulus locations were collected. (C) Preferred directions for all 114 neurons in the data set. The 8 bars arranged in a circle represent the preferred directions for the population of neurons. The dark and light shadings indicate neurons from M1 and M2, respectively. The dark and light arrows indicate the vector sum of the preferred directions for each animal.

corresponding unimanual component movements. For each neuron, the data were fit to a component model,

Firing rate = intercept +  $C_p$  +  $C_n$  +  $I_p$  +  $I_n$  + error,

where *C* and *I* are contralateral and ipsilateral arm movements, respectively, and the subscripts p and n are movements in the preferred and null directions, respectively. The factors  $C_p$ ,  $C_n$ ,  $I_p$ , and  $I_n$ , therefore indicate the presence or absence of an arm movement in a particular direction on a particular trial. Factor weights are not shown. Null direction saccade trials determine the baseline firing, reflected in the intercept value.

Next, we modeled each neuron's activity based on just 2 factors, derived from inspection of responses averaged across all PRR neurons. This model,

Firing rate = intercept + RF + 
$$C_{p}$$
 + error,

included an intercept, one factor for whether or not a target appeared in the preferred direction (RF), and one factor for whether or not the contralateral arm moved in the preferred direction ( $C_p$ ). As in the component model, the baseline is set by the response to a saccade in the null direction.

We also took a more data-driven approach, testing each neuron using up to 9 factors. Five terms were movement components—the 4 from the component model, plus one for saccades in the preferred direction ( $S_p$ ). A sixth factor was RF—whether or not a target appeared in the receptive field. Most importantly, the final 3 factors encoded patterns of bimanual coordination.  $T_p$  indicates that both arms moved together (bimanual-together) in the preferred direction.  $A_p$  and  $A_n$  indicate that the arms moved in different directions (bimanual-apart) with the contralateral arm moving in either the preferred or null direction, respectively.

To determine which of the 9 factors were most important, we used a forward selection stepwise regression procedure. We began by asking which single variable provided the best fit to the data. Fit was determined using the Akaike information criterion (AIC) with a correction for small sample sizes (Cavanaugh 1997; Burnham and Anderson 2013). AIC assesses goodness of fit, and includes a penalty for each explanatory factor in the model. The model with the lowest AIC value is the most likely model. Having determined the most likely single factor model, we next asked which one of the remaining 8 factors, when added to the 1-factor model, would provide the best fit to the data. Once again, we used AIC to determine this, choosing the factor that produced a model with the lowest AIC value. We repeated this procedure serially until either all 9 factors were included in the model, or until adding the factor associated with the lowest AIC value caused the AIC value to increase rather than decrease. This indicates that the new model, with "n + 1" factors, is less likely than the previous n-factor model. Only main effects of each factor were considered.

To minimize overfitting, we built a single model for the entire population rather than building a separate model for each neuron, using the median AIC value across the population to select each factor. (Using variance explained rather than AIC produced similar results.) As a result, the model we arrive at is in some sense the best fit across the population of neurons. Individual neurons may be better fit by a different set of factors, or by the same factors but in a different order.

Given the known difficulties with stepwise regression (Burnham and Anderson 2013) we do not make strong claims about which factors contribute significantly to the model, although we are able to identify factors that do not contribute significantly (see Results). We used only the 112 neurons with at least 4 trials in each of the 10 conditions, although similar results were obtained using either less restrictive criteria (e.g., all 114 neurons) or more restrictive criteria (e.g., at least 6 trials in each condition).

#### Regression

Regression lines in Fig. 6, 7, and 9 are based on a type-II regression model, computed using principal component analysis (Legendre 2014; R Core Team 2015). A type I regression assumes that there is measurement error in the variable plotted on the Y-axis but not in the variable plotted on the X-axis. A type-II regression assumes that there is error in both variables.

#### Classification of Movement Type using Support Vector Machines

We used a support vector machine (SVM) algorithm to test how well the firing rates of individual trials from individual neurons could be used to classify movement type. Broadly, an SVM takes a training set of data points and builds a model to optimally classify those points. In our case, each data point consists of one firing rate obtained from each recorded neuron during performance of a particular trial type, and the model is trained to discriminate the trial type based on the data points. This resulting model is then used to predict the trial type of a single reserved "test" data point that was not included in the training set. This process is repeated many times, each time reserving a different data point, to determine how reliably the SVM can correctly identify the trial type of a reserved data point.

We combined movements in the null direction together into a single condition, leaving a total of 7 trial types: Preferred direction movements of the eyes, preferred direction movements with the ipsilateral arm, preferred direction movements with the contralateral arm, bimanual-together reaches (with both arms reaching in the preferred direction), bimanual-apart

reaches in which the contralateral arm reaches in the preferred direction and ipsilateral arm reaches in the null direction, bimanual-apart reaches in which the contralateral arm reaches in the null direction and ipsilateral arm reaches in the preferred direction, and null direction movements of the eyes and arms. SVM makes binary classifications, but we had 7 different trial types. The conventional approach to producing a multiway classification is to convert the single multiclass problem into multiple binary classification problems (Duan and Keerthi 2005). Therefore, to select a single trial type from among the 7 choices, we constructed and ran a separate SVM model for each pair of trial types or classes (21 total) using a one-versusone approach. Each SVM model was built using only the training data belonging to its pair of classes. The test point was then classified as belonging to one of those 2 classes. We then identified the trial type that appeared most often as the winner in each of these 21 binary contests. (The intuition for this method is that if a single binary contest contains the true trial type for the test point, then that trial type should "win." If the contest does not contain the true trial type, then the outcome should be a random choice. As a result, the true trial type should appear more often as a winner than any of the false trial types.)

We treated our sequentially recorded neurons as if they were recorded simultaneously. We started by generating many synthetic data points by bootstrapping from our recorded data. Each data point had 114 dimensions, corresponding to the number of recorded neurons. For each data point that we synthesized, we first specified a trial type. For each dimension k of that data point, we randomly selected one trial from among all the trials of the specified type recorded from the kth neuron and measured its mean firing rate. In this way, all 114 dimensions were specified. The very first data point to be constructed in this manner was set aside for later use as the test point. The trials from which this data point was selected were also set aside. A training set of 700 data points (100 for each of the 7 trial types) was constructed by sampling randomly, with replacement, from each of the remaining trials. Training of the classifiers and cross-validation were achieved according to the multiclass approach described above: A separate linear classifier was trained for each binary classification using only the relevant data. After training, cross-validation was achieved by classifying the test point as one of the 7 trial types and determining whether the classification was correct or not. We performed 5000 classifications, each time repeating our entire procedure to generate a unique test point and training set. All classifier computations were implemented using the LIBSVM library (http://www.csie.ntu.edu.tw/~cjlin/libsvm/) in Matlab (Mathworks) (Chang and Lin 2011).

Several other SVM analyses were also performed. First, analyses performed on only a subset of neurons were used to determine the minimum number of neurons required for successful classification. These analyses were carried out in an identical fashion as above, except that for each iteration, the number of neurons (and hence the number of dimensions in each data point) was reduced by randomly selecting neurons from the complete set. Analyses with 10-100 neurons were performed. Second, a shuffle analysis was used to compare the SVM classifier performance to a classifier based on random data. This analysis was carried out in identical fashion as above, except that before the test point and training set were constructed, the trial type labels were randomly shuffled. Third, additional SVM analyses were also performed after removing subsets of neurons that had 1) differences in activity for saccades versus ipsilateral reaches, 2) differences in activity

for bimanual-together or bimanual-apart versus contralateral only, or 3) no difference in activity for bimanual-together or bimanual-apart versus contralateral only.

## Results

### Behavior

Cumulative distributions for saccade and reach reaction times (RT) across all target directions, reach conditions and animals are shown in Supplementary Fig. S1. Means, standard deviations and comparisons among reach conditions are reported for each animal separately in Supplementary Table S1. Saccades led reaches in all conditions, and in most cases, the saccade was completed before the reach was initiated. For M1, saccades on unimanual reach trials had the shortest RTs. Saccade RTs on bimanual together trials were longer, and saccade RTs on bimanual-apart trials were longest (one-way ANOVA, M1: F(2, 10245) = 167, P < 0.001, whereas for M2, the saccade RTs were similar for unimanual and bimanual-together, but longer for bimanual-apart trials (M2: F(2, 5506) = 60, P < 0.001) (Supplementary Fig. S1, left traces; Supplementary Table S1). For M1, reaches on unimanual reach trials had the shortest RTs. Reach RTs for bimanual together were longer, and reach RTs for bimanual-apart reach trials were longest (one-way ANOVA, M1: F(2, 10247) = 335, P < 0.001), whereas for M2, the reach RTs for unimanual and bimanual-apart reach trials were similar, but in both cases were shorter than for bimanual together (M2: F(2, 5520) = 103, P < 0.001) (Supplementary Fig. S1, right; Supplementary Table S1). A critical point, not shown in the table, is that bimanual-together reaches were coordinated not only in space, being directed to the same target, but also in time. In 80% of bimanual-together trials, the 2 arms landed on target within 83 ms of one another. Bimanual-apart trials also showed temporal synchrony: In 80% of trials, the 2 arms landing within 196 ms of one another on 80% of trials. Additional details about where the animals looked on bimanual-apart trials are provided in the final section of the results. For a detailed behavioral report based on a similar paradigm (but different data), see Mooshagian et al. (2014).

### Electrophysiology

Data were collected from 114 neurons in 2 animals. For 96 of those neurons, targets in all 8 directions were used. For each of the neurons with data for all 8 directions, we computed the angle of the vector sum. We did this computation separately for each movement condition. The resulting angle is mathematically the same as the direction of maximum amplitude for a cosine fit, that is, the preferred direction. We represent the preferred directions for unimanual (ipsilateral and contralateral arm) reaches and for saccades as density functions smoothed with a bandwidth of 25° and plotted relative to the preferred direction for a bimanual-together reach (Fig. 2B). Preferred directions were similar for each movement condition. If the preferred directions were all independent and equally distributed, then a flat line would result. Instead, the average fits all show a peak within 4° of zero. This result was not unexpected, given that contralateral and ipsilateral reaches show essentially identical tuning (Chang et al. 2008) and that during a contralateral reach, tuning remains similar across different time epochs ("global tuning fields"; Battaglia-Mayer et al. 2000, 2001). For each of the remaining 18 neurons, a full data set (all 5 trial types, see below) was collected for only 2 (diametrically opposed) directions. The preferred direction was chosen online as the target location that,

when considered over all 3 single target reach conditions (contralateral arm, ipsilateral arm, both arms together), resulted in the largest sustained firing during the delay period. Across all 114 neurons, preferred directions were found in both visual hemifields, with a strong bias for the lower visual field and a weak bias for the contralateral visual hemifield (Fig 2C; Rayleigh test, P <0.001; P < 0.0001 and P < 0.005 for monkeys M1 and M2, respectively).

Approximately 30% of all of the PRR neurons encountered during the recording session showed clear spatial tuning for one of the 8 directions while planning either an ipsilateral or contralateral arm reach. Of these, almost all showed tuning for reaches with just the contralateral arm, while tuning strength for reaches with the ipsilateral arm varied over a wide range (Fig. 3, left column). For example, the neuron in Fig. 3A was most active for reaches with the contralateral arm down and to the left (solid red: 71.85  $\pm$  4.27 sp/s, mean  $\pm$  SEM). Reaches with the contralateral arm in the null direction (up and to the right) evoked much less activity (dashed red: 23.33  $\pm$  1.96 sp/s, P < 0.01, t-test). Reaches with the ipsilateral arm (solid and dashed green) did not pass our criterion for significance for spatial tuning (22.04  $\pm$ 2.89 vs. 14.63  $\pm$  2.21 sp/s, P = 0.05) and reaches with the ipsilateral arm in the preferred direction were indistinguishable from a reach with the contralateral arm in the null direction (P = 0.71). In contrast, the neuron in Fig. 3B exhibited sustained firing during the delay period when the animal planned to move either the contralateral or ipsilateral arm toward a target in the preferred direction (straight up relative to the fixation point) with about twice as much activity for reaches with the contralateral arm (59.33  $\pm$  4.28 vs. 32.67  $\pm$  3.07 sp/s, P < 0.001). Finally, the neuron in Fig. 3C was spatially tuned but not selective for either arm  $(48.75 \pm 2.42 \text{ vs. } 49.38 \pm 1.92 \text{ sp/s}; P > 0.05)$ . Tuned responses prior to ipsilateral reaches, like those depicted in Fig. 3B,C, have been taken to indicate that some neurons in PRR represent movement plans for both the ipsilateral and the contralateral arm (Chang et al. 2008) and therefore that PRR is involved in bimanual control of reaching. In general, across the population of tuned neurons, most neurons increased their firing rates prior to reaches with either arm (Fig. 3D).

Next, we show how these same 3 example neurons responded when the animal planned a bimanual reach (right column of Fig. 3; data from left column are replotted for comparison). In panel E, the activity when both arms were cued to move together in the preferred direction (bimanual-together: solid blue) was similar to the activity when the contralateral arm alone was cued (solid red) (76.67  $\pm$  4.59 vs. 71.85  $\pm$  4.27 sp/s, P = 0.45). There was slightly more activity initially but similar sustained levels. The activity when the contralateral arm was cued to move in the preferred direction and the ipsilateral arm was cued to move in the null direction (bimanual-apart: solid purple) was also similar to that obtained when the contralateral arm alone was cued (75.00  $\pm$  3.47 vs. 71.85  $\pm$  4.27 sp/s, P = 0.57). The onset of activity in the bimanual-apart (contralateral arm in preferred direction) condition lags the onsets in the contralateral and bimanual-together conditions by ~50 ms, but the traces are otherwise similar. All other conditions shown result in uniformly low activity. In summary, for this neuron, the sustained firing for both bimanual-together and bimanual-apart (contralateral arm in preferred direction) trials was similar to that of the corresponding unimanual contralateral arm trial. Across conditions, the firing level was either high or low depending only on whether the contralateral arm moved in the preferred or null direction. However, since there was almost no modulation with unimanual ipsilateral reaches, this neuron



Figure 3. Responses of 3 example PRR neurons in the delayed reach tasks. Each row is a different neuron. (A–C) Each panel shows the responses to contralateral (red) and ipsilateral (green) arm movements, in the preferred (solid) or null (dashed) directions, with raster plots in the upper part and the mean firing rates in the lower part of each panel. Rasters are shown for the preferred direction trials. Each tic represents a spike and each row represents a single trial. Vertical lines indicate the target onset and earliest go cue. Shaded region indicates area used to measure delay period activity. (A) A neuron modulated by planned movements of the contralateral arm only. (B) A neuron modulated by planned movements of either arm, but with a larger effect for the contralateral arm. (C) A neuron modulated equally by planned movements of either arm. (D) Histogram of modulation (delay period firing rate in preferred direction trials) for reaches with the contralateral (red) and ipsilateral (green) arms. Two separate histograms are

cannot be used to distinguish between our 3 alternative hypotheses: Additive activity from the 2 arms, similar activity on unimanual and bimanual reaches to the same single target (a simple nonadditive interaction), or some other nonadditive interaction.

The neurons in panels F and G responded to unimanual ipsilateral arm reaches, and so provide a better test of our hypotheses than the neuron in panel E. For the neuron in panel F, activity was not significantly different when the 2 arms were cued to move together (blue trace:  $57.11 \pm 3.69 \text{ sp/s}$ , P = 0.70) or apart (contralateral arm in preferred direction: solid purple:  $58.22 \pm 3.56$  sp/s, P = 0.84), compared with the contralateral arm alone (red trace: 59.33  $\pm$  4.28 sp/s). For the neuron in panel G, activity was slightly higher when the 2 arms were cued to move together (blue trace:  $57.67 \pm 2.05 \text{ sp/s}$ , P = 0.008) and slightly lower when the 2 arms were cued to move apart (contralateral arm in preferred direction: solid purple: 40.25  $\pm$ 2.06 sp/s, P = 0.01), compared with the contralateral arm alone  $(48.75 \pm 2.05 \text{ sp/s})$ . For these 2 neurons, we can clearly rule out the additive hypothesis. Instead, the activity during bimanual movements was broadly similar to the activity seen when the contralateral arm moved by itself, though the patterns are also consistent with additional subtle nonadditive interactions on bimanual trials (see below). In general, across the population, most neurons increased their firing rates on bimanual reaches when the contralateral arm moved in the preferred direction (bimanual-together, 99%; bimanual-apart, 77%, Fig. 3H).

### A 4-Factor Component Model

In a strictly additive (linear) model, firing rate for bimanual movements is the linear sum of firing rates evoked by the 2 component movements, that is, the movements of the left and right arm (Kermadi et al. 2000; Donchin et al. 2002). To test this model, each neuron was fit with a linear regression that included an intercept plus 4 binary factors: One each for contralateral arm in the preferred direction ( $C_p$ ), ipsilateral arm in the preferred direction ( $C_n$ ), and ipsilateral arm in the null direction ( $I_n$ ). The median variance explained ( $r^2$ ) across all neurons by the component model was 42% (Fig. 4). Next, we consider the average activity over the entire population of neurons, and use that to develop a more parsimonious model.

### The Population Response Suggests a 2-Factor Model

Figure 5 shows average firing rate as a function of time across all neurons in each of the 8 reaching conditions and 2 saccade conditions. For all conditions involving a preferred direction movement (solid lines and dashed purple), there was a steep increase in activity starting ~100 ms following the onset of the visual target. The peak response depended on the type of

plotted, one on top of the other, with the overlap indicated by yellow. A single preferred direction is determined for each neuron, based on all 3 single target reach conditions (contralateral, ipsilateral, bimanual together; see Methods). As a result, it is possible for a single preferred direction movement type to evoke a negative firing rate. This occurs more often for conditions that evoke weak responses, like ipsilateral reaches. In almost every case, the negative modulation for ipsilateral reaches is not statistically significant (14 of 15 cases, P > 0.05). Arrows indicate means. Bin width is 10 sp/s. (*E–G*) Same format and neurons as (A–C), with additional traces for bimanual-together (blue) or bimanual-apart reaches (contralateral arm in preferred direction; purple). For all 3 neurons, bimanual responses were similar to the unimanual contralateral arm response. (H) Histogram of modulation for bimanual-together and bimanual-apart reaches (contralateral arm in preferred mirection). The light blue region indicates overlap of values for bimanual-together and bimanual-apart reaches. Bin width is 10 sp/s.



Figure 4. Contribution of each factor to the component regression model. The height of each bar indicates the total variance explained by including that factor along with any factors to its left. (This value is also printed at the base of each bar.) The factors are ordered by their cumulative contribution to the model fit, as determined by AIC. The dark shading indicates the change in variance explained by inclusion of the factor.  $C_p$ , contralateral reach in the preferred direction;  $I_p$ , ipsilateral reach in the null direction.

movement being cued (ANOVA, P < 0.01). The response was highest when both arms were cued to move in the preferred direction (41.70 ± 2.69 sp/s), least when the ipsilateral arm was cued to the preferred direction and the contralateral arm to the null direction (30.73 ± 2.50 sp/s), and intermediate in all other conditions. Given a cue to reach in the preferred direction by either the contralateral or ipsilateral arm, cueing the other arm to move in the null direction reduced peak firing by 3.76 and 3.99 sp/s, respectively, though the changes were not significant (t-tests, P > 0.05). There was no increase in activity when movements were cued only in the null direction (dashed lines except for dashed purple). This pattern of transient responses is consistent with a visual response to targets in the preferred direction, with some modulation that depends on the movement being instructed.

After the initial transient, the firing rate settled into one of 3 sustained levels. Activity was highest prior to contralateral arm movements in the preferred direction, regardless of whether the ipsilateral arm moved in the same direction (bimanual-together:  $31.01 \pm 1.87$  sp/s), moved in the null direction (bimanual-apart, contralateral arm in preferred direction:  $32.40 \pm 2.09 \text{ sp/s}$ ), or did not move at all (contralateral only:  $31.01 \pm 1.93$  sp/s). These differences in firing were small but significant (one-way ANOVA, F(2, 226) = 304.5, P = 0.009). We address these small but important differences in later sections. Activity was intermediate when either the ipsilateral arm or the eyes moved in the preferred direction (ipsilateral [solid green]: 21.94 ± 1.33 sp/s; saccades [solid black]: 22.44 ± 1.54 sp/s; bimanual-apart [dashed purple; ipsilateral arm in preferred direction, contralateral arm in null direction]: 19.86 ± 1.63 sp/s). The small differences in firing across these 3 conditions did not reach significance (one-way ANOVA, F(2, 226) = 2.69, P = 0.07). Finally, activity was lowest when one or more effectors moved in the null direction (contralateral arm:  $10.56 \pm 1.01$  sp/s; ipsilateral arm:  $10.72 \pm 0.88$  sp/s; bimanual-together:  $11.23 \pm 1.08$  sp/s; saccades: 9.68  $\pm$  0.77 sp/s), with no significant differences across types (one-way ANOVA, F(3, 339) = 1.63, P = 0.18). Similar patterns of activity were observed in each individual animal's data (Supplementary Fig. S2).



Figure 5. PRR population activity for all 10 conditions. Across the population, PRR neurons respond when the animal prepares a movement of the eyes, eyes plus one arm or eyes plus both arms. Three levels of activity are apparent. Firing is high when the contralateral arm will move in the preferred direction, regardless of what the ipsilateral arm does (red, contralateral arm moves by itself; blue, contralateral and ipsilateral arms move together to a single target; purple, contralateral and ipsilateral arms move in the preferred and null directions, respectively). An intermediate level of activation occurs when only the eyes move in the preferred direction (black), when only the ipsilateral arm moves in the preferred direction (green), or when the ipsilateral arm moves in the preferred direction and the contralateral arm moves in the null direction (dashed purple). Activity is suppressed below baseline for any movements in the non-preferred direction (dashed blue, red, green, and black). Vertical lines indicate target onset and earliest go cue. The broad pink surrounding the preferred and non-preferred red lines indicate  $\pm 1$  SEM for that condition, computed over 114 neurons. Standard errors for the other conditions are comparable. Gray shading indicates the interval used to measure delay activity.

This pattern suggests a simpler model containing just a baseline firing level and 2 binary factors. When a task-relevant target appears in the preferred direction, sustained activity is elevated to an intermediate level. If there is also a plan for the contralateral arm to move in the preferred direction, then sustained activity is elevated still further to a high level. We will first present data supporting the inclusion of these 2 factors and then consider evidence supporting the addition of factors related specifically to patterns of bimanual coordination.

### On Ipsilateral Reach Trials Responses Primarily Reflect a Target in the Response Field, Not the Movement Per Se

The fact that neurons are activated when the ipsilateral arm moves in the preferred direction has been interpreted as evidence that some PRR neurons encode the intention to move the ipsilateral arm (Chang et al. 2008). This interpretation inspired the 4-factor component model. In the 2-factor model, however, responses on ipsilateral arm trials are driven by a task-relevant visual stimulus in the preferred direction, and not by a movement plan. To gain insight into this issue, we compared 2 types of response plans: A reach with the ipsilateral arm versus a saccade without an accompanying arm movement. If the response on ipsilateral reach trials reflects a plan to move the arm, then this response should be different from the response on saccade-only trials. On the other hand, if the response reflects the presence of a behaviorally relevant visual stimulus in the preferred direction, then the responses on ipsilateral reach and saccade-only trials should be identical.



**Figure 6.** Scatterplot of the individual neuron firing rates for preferred direction saccades versus preferred direction reaches with the ipsilateral arm. Each point represents a single neuron (M1, n = 59, filled circles; M2, n = 55, open circles). The unity line is in gray. The black line is a type-II regression line.

At the population level, the responses are very similar (Fig. 5, solid green and solid black traces; t-test, P = 0.81). This was also true for individual neurons. Figure 6 shows a scatterplot of the sustained activity of individual neurons for reaches with the ipsilateral arm (abscissa) versus saccades (ordinate). In 74% of neurons, the firing rate for ipsilateral arm reaches was not significantly different from the firing rate for saccade-only movements (84 of 114 neurons, 2-tailed t-test, P > 0.05), with an overall  $r^2$  of 0.70. Thus, a single factor can explain the responses to both ipsilateral arm reaches and saccades in the preferred direction in a majority of neurons. We address the remaining 30 neurons in which the firing rate was different for ipsilateral arm reaches and saccade-only movements and saccade-only movements in a later section.

# On Bimanual Reach Trials, Responses Primarily Reflect What the Contralateral Arm Does

In the 2-factor model, there is no information about bimanual movement patterns; only movement of the contralateral arm drives activity. If this model is correct, then activity on bimanual reach trials should depend only on the direction in which the contralateral arm moves. Alternatively, the original 4 factor model assumed that activity on bimanual reach trials would be a linear combination (sum) of the activity seen when each arm was moved independently. In Fig. 7, we compare these models for bimanual-together (upper row) and bimanualapart (lower row) trials. Consider first the left and middle panels on the top, which address bimanual-together preferred direction trials. The observed responses are plotted on the abscissa. We test hypothesis (1) on the left: The response to the bimanual-together preferred direction reach will be equal to the response to a contralateral arm preferred direction reach, so that the unimanual and bimanual responses will be identical. The predicted response is plotted on the ordinate. The red data points and regression line fall close to the line of identity (Fig. 7, top left, model II regression of the red data points:  $r^2 =$ 0.81, slope = 1.03, not significantly different from the gray line with a slope of 1). Seventy-three percent of the individual neurons (83 of 114) show no difference between the predicted and observed responses (2-tailed t-test, P > 0.05). This supports hypothesis (1). In the middle column, we test hypothesis (2): The response to the bimanual-together preferred direction reach will be equal to the sum of the responses of the 2 component reaches. The predicted response is again plotted on the ordinate. Gold data points and the gold regression line fall far from the gray line of identity (top middle,  $r^2 = 0.67$ , slope = 1.41, significantly different from 1 [P < 0.05]). Predicted and observed responses differ significantly in nearly half of the individual neurons (48 of 114). Thus, we can reject hypothesis (2).

A similar result was obtained when comparing bimanualapart trials to the component unimanual trials (lower panels). Sustained activity when the contralateral arm moves to the preferred target and the ipsilateral arm moves to the null target (bimanual-apart trials, abscissa) is compared, first, against sustained activity from unimanual trials in which the contralateral arm moves in the preferred direction (lower left, red data points) and second, against the sum of the sustained activity in unimanual trials involving the 2 individual components of the bimanual movement (contralateral arm in the preferred direction plus ipsilateral arm in the null direction) (lower row, middle column, gold data points). In both cases, the regression lines lay close to the line of identity (bottom left,  $r^2 = 0.73$ , slope = 0.96; bottom middle,  $r^2 = 0.60$ , slope = 0.84). The regression slopes do not significantly differ from the identity line in either case, but the single neuron activity is better predicted by model 1 than by model 2 (bottom left vs. bottom middle, similar activities for 85 vs. 65 [out of 114] individual neurons, respectively, which represents a significantly larger proportion [proportion test with Yates' continuity correction, P = 0.008]). Thus, for both types of bimanual movements, the firing rates of most neurons are better predicted by movement of the contralateral arm alone compared with the sum of the contralateral and ipsilateral movements.

Another possibility is that individual neurons only encode movements of either the contralateral or ipsilateral arm and that encoding of bimanual movements thereby emerges at the population level by taking into account the responses of both types of neurons. In such a case, for some neurons, activity on bimanual reach trials should depend only on the direction in which the ipsilateral arm moves. We test this hypothesis in the third column. Only a few neurons code ipsilateral reach plans. Green data points and the green regression line fall far from the gray line of identity for both types of bimanual reaches (top right, bimanual-together,  $r^2 = 0.45$ , slope = 0.61, significantly different from 1 [P < 0.05]; bottom right, bimanual-apart,  $r^2 = 0.04$ [P < 0.05], slope = 0.15, significantly different from 1 [P < 0.05]). Thus, we can rule out the possibility that bimanual movements are coded within a single hemisphere by individual neurons that represent only one or the other arm.

To summarize, the 3 levels of firing observed in the population mean indicate that the firing of PRR neurons is largely (but not completely; see below) determined by just 2 factors: Whether a target appears in the preferred direction, and whether there is a plan for the contralateral arm to move in that direction. The correlation of the responses on saccadeonly and ipsilateral arm trials, and the fact that the response when the animal reaches with both arms is similar to when it reaches with the contralateral arm alone, provide evidence against a true ipsilateral reach representation.

# SVMs Reliably Classify Movement Type Based on Single Trial Firing Rates

The analyses presented so far do not show clear coding of particular bimanual arm movement patterns in PRR. At the



Figure 7. Comparison of 3 models of bimanual activity. The left, middle, and right columns are each based on a different hypothesis. Left column: The bimanual reach response equals the contralateral arm reach response. Middle column: The bimanual reach response equals the sum of the contralateral and ipsilateral arm responses. Right column: The bimanual reach response equals the ipsilateral arm reach response. The upper row is for bimanual together movements. The lower row is for bimanual-apart movements (contralateral arm in preferred direction). Scatterplots contrast predicted and observed firing rates under each hypothesis, with each point representing one neuron. The unity line is indicated in gray. The broad lines through the data points are type-II regression lines. In each row, the first model provides a better fit to the data. See text for details.

population level, mean activity is well-described using just 2 factors: A plan to move the contralateral arm in the preferred direction and the presence of a target in the receptive field. However, single neuron analyses suggest that individual neurons may show neuron-specific (idiosyncratic) differences in their responses to the different trial types. To test whether these idiosyncrasies are reliable when many neurons are considered at once, we trained an SVM to classify movement types based on the responses of individual neurons on individual trials. We pooled 4 null direction movements together, leaving 7 movement types (see Materials and Methods). The accuracy of the trained model on each of the 7 types is presented as a confusion matrix (Table 1). Overall, the model did well. The blue, green, and red regions reflect the 3 levels of activity seen in the population data. As expected, the SVM distinguished trial types between these levels perfectly. Surprisingly, however, the SVM also distinguished trial types within these levels. Accuracy was 95% or better in all conditions. These results were obtained using all 114 recorded neurons; similar results were obtained using as few as 15 neurons (Supplementary Table S2). Models trained on shuffled data had no predictive value (Supplementary Table S3). Thus, despite limited information being available in the mean population response, individual neurons contained information about different patterns of unimanual and bimanual reaching.

# Some Neurons Distinguish Between Saccades and Ipsilateral Reaches

We showed above that saccades and reaches are indistinguishable at the population level and for most individual neurons. Across the population, the comparison between saccade and ipsilateral arm movements was significant for 30 (26%) of the 114 neurons (5% is expected by chance). Figure 8A shows an example neuron that is more sensitive to saccades than to reaches with the ipsilateral arm (black vs. green traces). For this neuron, a t-test between saccade and ipsilateral arm movements was significant (P < 0.05). Figure 8B shows a histogram of the differences between saccade and ipsilateral conditions for all neurons, plotted as effect sizes, that is, normalized to the standard deviation of the difference (Cohen's D). The dark gray shaded bars indicate significant effects (planned t-tests). Although significant effects occur at the edges of the distributions, they cannot be dismissed as outliers (false

	Predicted values						
	Null	Bimanual- apart (Null)	Saccades	Ipsilateral	Contralateral	Bimanual- together	Bimanual- apart
True values							
Null	100	0	0	0	0	0	0
Bimanual-apart (Null)	0	100	0	0	0	0	0
Saccades	0	0	98	2	0	0	0
Ipsilateral	0	0	2	98	0	0	0
Contralateral	0	0	0	0	95	4	1
Bimanual- together	0	0	0	0	5	95	0
Bimanual-apart	0	0	0	0	0	0	100

#### Table 1. SVM confusion matrix

Values represent the percentage of correct predictions. The blue, green, and red regions reflect the 3 levels of activity seen in the population data. Ipsilateral and Contralateral = the respective limb in the preferred direction. Bimanual-Apart = contralateral arm to the preferred direction, ipsilateral arm to the null direction; Bimanual-Apart (Null) = contralateral arm to the null direction, ipsilateral arm to the preferred direction. Saccades = saccade in the preferred direction.

positives) since their numbers far exceed the numbers expected by chance alone (proportion test, P < 0.001). Of the 30 neurons with a significant effect of saccade versus ipsilateral reach, the difference was positive in 17 (n = 7 in M1; n = 6 in M2) and negative in 13 (n = 14 in M1; n = 3 in M2). SVM models trained on data excluding neurons that showed a significant difference between saccade and ipsilateral conditions distinguished among the 3 broad levels of activity observed in the population; however, these models were unable to distinguish saccades from ipsilateral reaches above chance levels (Supplementary Table S4).

# Some Neurons Distinguish Between Unimanual and Bimanual Reaches

Figure 8C shows an example neuron that is sensitive to different patterns of reaching movements. Like the example neuron of Fig. 3B, it was more active for reaches with the contralateral compared with the ipsilateral arm (red vs. green traces). Unlike that example neuron, there were significant effects of bimanual conditions:  $43.4 \pm 2.11$  sp/s for contralateral arm alone versus  $35.6 \pm 1.32$  sp/s for bimanual together (blue) and  $53.8 \pm 1.01$  sp/s for bimanual-apart (purple; contralateral arm in preferred direction). For this neuron, a 3-level ANOVA was significant (F(2, 21) = 3.8, P < 0.05) as were planned t-tests (P = 0.007 and P)0.0007 for bimanual together and apart, respectively, vs. contralateral alone). Across the population, the ANOVA was significant for 47 (41%) of the 114 neurons. Figure 8D,E shows histograms of the differences between bimanual and unimanual conditions. (Note that this analysis applies almost exactly the same heuristic as used by Steinberg et al. (2002) and many fMRI studies to identify bimanual activity, namely, whether a bimanual task evokes activity which differs substantially from the maximal activity observed for moving either arm.)

The difference between the bimanual and contralateral alone conditions is not evident in the population response (Fig. 5) because the effects of bimanual coordination were idio-syncratic for each neuron, with different neurons showing different patterns. Of 31 neurons with a significant effect of bimanual-together versus contralateral-only trials, the difference was positive in 24 (n = 17 in M1; n = 7 in M2) and negative in 7 (n = 4 in M1; n = 3 in M2). Similarly, of 29 neurons with a significant effect of bimanual-apart (contralateral arm in preferred direction) versus contralateral-only trials, the difference was positive in 19 (n = 14 in M1; n = 5 in M2) and negative in 10

(n = 6 in M1; n = 4 in M2). Thus, the neurons that modulate with bimanual coordination do not show a common coding pattern. Instead, the tuning varies from neuron to neuron.

The SVM analysis shows that unimanual and bimanual movements are distinguishable. However, it might be the case that the SVM succeeds because bimanual movements are encoded at the population level, not by individual neurons. If we have correctly identified the neurons carrying information about bimanual versus unimanual movements, as we claim, then the SVM should fail when the neurons carrying bimanual information are excluded, and should succeed when these bimanual information neurons are included. Overall, both of the models distinguished nearly perfectly between the 3 broad levels of activity seen in the population. As expected, the SVM on the 41% (n = 47) of neurons that showed differences among contralateral and bimanual conditions distinguished among all 7 conditions nearly perfectly (Supplementary Table S5). However, the SVM on the 59% (n = 67) of neurons that did not show differences among contralateral and bimanual conditions could not distinguish among contralateral, bimanual-together, and bimanual-apart conditions (Supplementary Table S6). This analysis does not provide new information, but it does confirm that we correctly identified the neurons carrying information about bimanual versus unimanual movements.

We also considered the possibility that differences in activity across different reaching conditions might be driven by differences in behavioral performance on those conditions. We asked if there was a correlation between the spike rate and the RT or movement duration. We would expect the spike rates of neurons with significant differences between unimanual and bimanual conditions to vary systematically with either RT or movement duration. Individual neurons showed negative or positive correlations between their spike rate and the animals' behavior. Overall, there was no systematic relationship between the neurons with significant effects of either bimanual-together or bimanual-apart versus contralateral only and either reach RT or reach duration (Supplementary Fig. S3).

The above analyses do not suggest an explicit coding of ipsilateral arm movements, either on its own or in combination with the contralateral arm. First, if it were the case that bimanual coordination effects occur when a neuron receives information about the ipsilateral arm movement per se, then we might expect overlap between the neurons that showed a significant difference between bimanual-together versus contralateral-only and bimanual-apart versus contralateral-only.



Figure 8. Additional effects not fully accounted for by the 2-factor model. (A) Time course of delay period activity for reaches with the ipsilateral arm alone (green) and saccades alone (black) for one example neuron. Activity is increased for saccades compared with ipsilateral arm reaches. Format as in Figs 3 and 5. (B) Histogram of effect size of saccade minus unimanual ipsilateral reaches for all neurons. The example neuron from A is indicated in red. (C) Time course of delay period activity for reaches with the contralateral arm alone (red), the contralateral and ipsilateral arms moving to the same target (blue; bimanual-together), and the contralateral and ipsilateral arms moving to different targets (purple; bimanual-apart), for one example neuron. Activity is increased for bimanual-apart (contralateral arm in pre-ferred direction) reaches and decreased for bimanual-together reaches, compared with the contralateral arm lone. Format as in Figs 3 and 5. (D) Histogram of firing rate differences, normalized by standard deviation (effect size of bimanual-together minus unimanual contralateral arm in preferred direction) minus unimanual contralateral reaches for all neurons. The example neuron C is indicated in red. (E) Histogram of effect size of bimanual-apart (contralateral arm in preferred direction) minus unimanual contralateral reaches for all neurons. The example neuron from C is indicated in red. (E) Histogram of effect size of bimanual-apart (contralateral arm in preferred direction) minus unimanual contralateral reaches for all neurons. The example neuron from C is indicated in red. Solid shading indicates significant differences (t-tests; P < 0.05). See also Supplementary Fig. S3.

Instead, different neurons showed different combinations of significance. Of the 48 neurons that showed significant differences in either bimanual-together or bimanual-apart (contralateral arm in preferred direction) conditions, only 12 showed effects in both. Of those 12, 6 showed increases for both comparisons, 2 showed increases for bimanual-apart (contralateral arm in preferred direction) and decreases for bimanual-together, and 4 showed increases for bimanual-together and decreases for bimanual-apart (contralateral arm in preferred direction). Second, we might expect overlap between those neurons that encode bimanual versus contralateral differences and those neurons that encode saccade versus ipsilateral arm movement differences. This was not observed; the overlap was no more than expected by chance (bimanual together vs. contralateral and saccade vs. ipsilateral, 11 neurons; bimanual-apart vs. contralateral and saccade vs. ipsilateral, 7 neurons; proportion test, P > 0.05). Finally, the outcomes of the SVM models also support our claim that the neurons that show differences between bimanual and contralateral-only conditions are responsible for coding bimanual coordination. Removing the neurons that encode bimanual-apart or bimanual-together versus contralateral arm movement differences affected the classification of bimanual movements but had no effect on the classification of the saccade versus ipsilateral movements (Supplementary Table S5), whereas removing the neurons that encode saccade versus ipsilateral arm movement differences affected the classification of saccade versus ipsilateral movements but had little effect on the classification of bimanual reaches (Supplementary Table S4). Thus, the differences in activity observed in these neurons can be best described as an effect of the pattern of

bimanual coordination, and not a coding of the ipsilateral arm movement per se.

### A Combination Regression Model

Given the results of the population analysis (Fig. 5), we asked if a model that includes factors for the 2 broad levels of population activity might outperform the component model described above. A simple alternative model includes an intercept plus 2 binary factors: One for targets appearing in the preferred direction (RF) and one for a plan to move the contralateral arm in the preferred direction (Cp). This model explained more variance than the component model in 48% of neurons, despite having only 2 rather than 4 factors (median  $r^2$  across all neurons: 0.41). For full generality, we considered 9 factors and asked which were the most important. The 9 factors included the 5 from the component model and the simple alternative model (C<sub>p</sub>, C<sub>n</sub>, I<sub>p</sub>, I<sub>n</sub>, RF). Given the results shown in Fig. 8D,E, we included 3 factors for particular patterns of bimanual coordination: bimanual-together in the preferred direction  $(T_p)$ ; bimanual-apart with the contralateral arm in the preferred direction  $(A_p)$ ; and bimanual-apart with the contralateral arm in the null direction (An). Finally, given the results shown in Fig. 8B, we included a factor to distinguish a saccade in the preferred direction from an ipsilateral reach in the preferred direction  $(S_p)$  (Fig. 8B). We ordered the factors by cumulative importance based on the median AIC value across all neurons: RF, C<sub>p</sub>, A<sub>n</sub>, T<sub>p</sub>, A<sub>p</sub>, I<sub>p</sub>, S<sub>p</sub>, I<sub>n</sub>, C<sub>n</sub>. The AIC value decreases or remains constant as the first 6 factors are added. When a seventh factor is added, the AIC value increases. This indicates

that, for the majority of neurons, including the factors  $S_p$ ,  $I_n$ , or  $C_n$  results in an overfitting of the data. Figure 9A shows the variance explained by the first 6 factors. A model consisting of just the first 4 factors, thereby matching the number of factors in the component model, explains more variance than the component model for 73% of neurons (median  $r^2$ : 0.47; Fig. 9B). (Ordering the factors by cumulative variance explained yields similar results, although  $A_p$  replaces  $T_p$  as the fourth factor.) We call this new model a "combination" model, to highlight the fact that, unlike the "component" model, 2 of the 4 factors of this model represent particular combinations of arm movements.

### **Responses During the Movement Period**

PRR activity during a bimanual reach closely resembles the activity during a contralateral reach, similar to the effect seen in the delay period (Supplementary Fig. S4; compare with Fig. 7). As in the delay period, however, some neurons show a small but significant component of activity specifically related to the pattern of bimanual coordination (Supplementary Fig. S5; compare with Fig. 8). Interestingly, the multiple regression analysis reveals quantitative differences in the movement period compared with the delay period (Supplementary Fig. S6; compare with Fig. 9). Movement period activity is more strongly driven by movement of the contralateral arm. Moving the contralateral arm in the null direction had essentially no effect in the delay period, but a substantial effect during the movement period (second most prominent regression factor). While adding a congruent ipsilateral limb movement to a contralateral reach has an equally strong effect in both the delay and movement periods, adding an opposed ipsilateral limb movement has a substantial effect only in the delay period (third and fifth most prominent factors vs. sixth most prominent factor). One interpretation of the multiple regression analysis is that the delay period activity is misleading, and that in fact PRR neurons drive movements of the contralateral arm with relatively little effect of the pattern of bimanual coordination. Another possibility is that the increased prominence of contralateral arm movements on PRR activity during movement,

compared with the preparatory period, may reflect proprioceptive feedback that comes exclusively from the contralateral arm (Kalaska et al. 1983; Lacquaniti et al. 1995; Galletti et al. 1997; Breveglieri et al. 2002).

### Neuron Selection

While searching for neurons, the animals performed only saccade and contralateral reach tasks. A previous study showed that searching using either contralateral reaches or ipsilateral reaches produces very similar results (Chang et al. 2008). However, it is possible that we missed neurons that are active only for bimanual reaches. We therefore searched for a new set of neurons from one animal using only the bimanual-together and bimanual-apart reach tasks. We collected 14 neurons with clear modulation (greater than 5 sp/s) in at least one of the 2 bimanual tasks. When subsequently tested in a unimanual reach task, all but one showed clear modulation (greater than 5 sp/s). We conclude that neurons that are active in bimanual tasks but not in unimanual tasks are uncommon and that our results were not unduly influenced by our selection procedure.

## Effect of Bimanual Congruency

In humans, unilateral finger movement increases blood-oxygen level-dependent signals (BOLD) in the contralateral hemisphere and decreases BOLD in the ipsilateral hemisphere (Verstynen et al. 2005; Diedrichsen et al. 2013). These results seem incongruent with our results—ipsilateral limb movement results in increased single-unit activity, not decreased activity. However, in BOLD imaging experiments, unlike single-unit recording experiments, one cannot easily separate out responses to reaches made in the preferred versus null directions. In addition, the cited experiments use only congruent effectorstimulus combinations. That is, responses are obtained when the left hand moves to a stimulus on the left, or the right hand moves to a stimulus on the right. We cannot simulate the BOLD response that we would predict in such an experiment, since BOLD signals are dominated by the consequences of



Figure 9. Combination regression models. (A) Variance explained by the 6 factors that contribute to the combination model; compared with Fig. 4. The height of each bar indicates the total variance explained by including that factor along with any factors to its left. (This value is also printed at the base of each bar.) The factors are ordered by their cumulative contribution to the model fit, as determined by AIC. The dark shading indicates the change in variance explained by inclusion of each factor. RF = target in the receptive field;  $C_p$  = contralateral reach in the preferred direction;  $A_n$  = bimanual-apart, contralateral arm in the null direction;  $T_p$  = bimanual-together in the preferred direction;  $A_p$  = bimanual-apart, contralateral arm in the preferred direction;  $I_p$  = ipsilateral reach in the preferred direction;  $I_p$  = ipsilateral reach in the null direction;  $C_n$  = contralateral reach in the null direction. (B) Scatterplot of the individual  $r^2$  values obtained in the 4 factor combination model ( $R_F$ ,  $C_p$ ,  $A_n$ ,  $T_p$ ) versus the 4 factor component model ( $C_p$ ,  $I_p$ ,  $C_n$ ,  $I_n$ ). Each point represents a single neuron, and most points fall above the identity line (gray).

presynaptic activity and related metabolic effects, and therefore have no direct connection with the activity of the putative pyramidal neurons from which we record. However, we can ask what the massed single-unit activity would look like under these conditions. The 2 sets of flanking bars in Fig. 10 show activity for congruent stimuli, split by preferred versus null direction. Their borders are colored to indicate the task conditions they correspond to. The dark center bars are the overall activity, a weighted average of the 2 respective flanking bars. The average reflects the fact that nearly two-thirds of neurons have contralateral response fields, so that, for congruent stimuli, preferred responses dominate for the contralateral arm while null responses dominate for the ipsilateral arm. The 3 bars on the left reflect planning activity in the hemisphere contralateral to the moving arm, and the 3 bars on the right reflect planning activity in the ipsilateral hemisphere. Compared with baseline (solid horizontal line), overall activity increased in the contralateral hemisphere (P < 0.05, paired t-test) and decreased in the ipsilateral hemisphere (n.s.).

### Effect of Eye-hand Congruency

It is not clear if PRR plays a role in eye-hand coordination (Hwang et al. 2014; Yttri et al. 2014). We asked whether the pattern of eye-hand coordination is reflected in PRR delay activity on bimanual-apart trials. Across all 2773 bimanual-apart trials in this study, the first saccade after the go cue moved to the target of the contralateral arm in 51.5% of trials, the target of the ipsilateral arm in 47.5% of trials, and to some other location on 1% of trials. There was no significant difference in delay period activity when the eyes moved to the contralateral arm's target compared with the ipsilateral arm's target (28.62  $\pm$  2.47 sp/s vs. 24.96  $\pm$  2.27 p/s; P > 0.05).



Figure 10. Mean delay period firing rates for movements of each arm to a target in its own hemifield. Responses are shown sorted by whether the movement is into or out of the response field (gray bars, "Preferred only" and "Null only") or combined ("Preferred and null"). The horizontal black line indicates the mean firing rate during the baseline period (500–300 ms prior to target presentation). N is the number of neurons contributing to each bar. The colored borders indicate the corresponding conditions in Fig. 5. The 2 dark bars simulate the conditions from typical human BOLD experiments, where targets are placed only on the same side of the body as the reaching arm, and preferred directions are not taken into account. "Significant difference from the condition-specific baseline at P < 0.05. (Each condition-specific baseline varies slightly but non-significantly from the mean baseline).

An alternative possibility is that PRR activity reflects not which arm the saccade will accompany, but rather, whether the saccade will be made in the preferred direction or not. Once again, however, at the population level, we found no effect: 27.41  $\pm$  2.85 sp/s for saccades in the preferred direction, and 26.25  $\pm$  2.07 sp/s for saccades in the non-preferred direction (P > 0.05). Next, we asked if individual neurons distinguished between saccades in the preferred and null directions. Supplementary Fig. S7A shows the mean activity for those neurons recorded when the animal chose to make at least 2 initial saccades in the preferred direction and at least 2 initial saccades in the null direction on bimanual-apart trials with identical arm instructions. Of our 114 neurons, 13 showed this behavior. Unlike our predictions for bimanual coordination for which activity on bimanual trials could be higher or lower than activity on contralateral only trials, here we have the strong expectation for activity to be higher for saccades into compared with out of the response field. If saccades into the response field on bimanual-apart trials increased firing compared with saccades out of the response field, we would expect most of the data points to lie above the diagonal line. This was not the case; the points are evenly distributed about the diagonal. The activity was not significantly different for saccade-in versus saccade-out in any of the 13 neurons (t-tests, P > 0.05). Finally, we split bimanual-apart trials by both reach and saccade direction to ask if there was an interaction of saccade direction and arm direction. Supplementary Fig. S7B shows there was no saccade effect; instead, there is only the effect of arm direction previously shown in Fig. 5: Modulation is roughly twice as large when the contralateral arm moves in the preferred direction (and the ipsilateral arm moves in the non-preferred direction; black) compared with when the contralateral arm moves in the non-preferred direction (and the ipsilateral arm moves in the preferred direction; gray), regardless of the direction of the saccade. Not only was there not a main effect of saccade direction, there was also not an interaction of saccade direction with arm direction (ANOVA, P > 0.05). Thus, even though the eyes were free to move to either target in the bimanual-apart reach condition, there were neither effects of saccade direction nor the pattern of eye-hand coordination on PRR delay activity during bimanual-apart trials.

## Discussion

We investigated whether PRR represents movement plans for bimanual reaches and if PRR is implicated in bimanual coordination. We found that the neuronal response to a bimanual arm movement depends primarily on the movement of the contralateral arm. However, secondary, nonadditive effects of bimanual movements were present in 41% of neurons. The particular movement of each arm could be decoded on individual trials using an SVM classifier. These results demonstrate that PRR neurons represent bimanual reach plans, and suggest at least some aspects of bimanual coordination are computed at the stage of visuomotor processing concomitant with target selection and at the time that effector specificity first arises.

An alternative hypothesis is that PRR encodes only reach endpoints and not the movement plans themselves. Our results clearly rule this out. A model in which PRR encodes only reach endpoints would give identical responses for reaching in the preferred direction with a single arm or with both arms, and would also give identical responses for reaching to 2 different targets with each arm, regardless of which arm went to which target. The data are clearly incompatible with this (Fig. 5). Another alternative hypothesis is that PRR is not functionally specialized for bimanual coordination, but instead linearly encodes the movements of each arm. In this scheme, contralateral and ipsilateral arm movements in the preferred or null directions are each associated with a particular response, and during movements of both arms, these responses simply add. This prediction can be easily ruled out by the population data, which show that moving both arms together produces much less activity than the sum of the activity evoked by moving each arm individually (Fig. 5).

Yet another possibility, supported by the population results, is that PRR neurons do not distinguish between a pure contralateral arm movement, a combined arm movement to a single target, or movements of each arm to different targets. At the level of PRR, all control could be for just the contralateral limb, with bimanual coordination arising only later in the motor stream, for example in premotor cortex or even subcortically. However, our classifier shows that bimanual information is indeed present in PRR. This finding is bolstered by the regression analyses. A model encoding only "target in the receptive field" and "contralateral movement in the preferred direction" performed better than a 4 factor component model (with terms for preferred and null movement directions for each arm) in just under half of neurons. A 4 factor "combination" model, coding (1) a target in the receptive field, (2) a contralateral movement in the preferred direction, and (3 and 4) 2 patterns of bimanual movement, fit the observed data better than the 4-factor component model in 74% of neurons. This, along with the classifier analysis, indicates that PRR does not simply represent movements of the contralateral arm, or even a linear sum of movements of the contralateral and ipsilateral arms. Instead, information about particular combinations of movements of the 2 arms is encoded in PRR, and PRR may play a role in bimanual coordination. An important caveat is that showing that information is present does not establish that the information is actually being used, or being used in the way that we expect; for this, interventional experiments are required. Likewise, showing that PRR has information sufficient to distinguish the particular patterns of reaches in our experiment does not establish that PRR encodes all of the information sufficient to distinguish intricate bimanual actions.

Finally, it is worth noting that our model—that neuron activity can be described as the sum of a factor related to whether there is a target in the RF, a factor related to whether the contralateral arm moves into the RF, and, in a subset of neurons, smaller factors related to particular patterns of bimanual movement—captures the specific bimanual-related activity with far more specificity than the models that have been used in the past, for example, that bimanual activity be substantially different from the maximum unimanual activity, or different from the sum of the unimanual activities. Furthermore, our model describes the activity seen with 10 types of movements (5 movement types, each in 2 directions), including ipsilateral reaches and saccades. Thus, the model provides a specific quantitative description of neuron activity over a wide range of tasks.

## Population Response in PRR Reflects the Visuospatial Cue and the Contralateral Arm Reach Goal

The classic view of limb control based on anatomical evidence has been that each hemisphere controls the movements of the limbs on the opposite side of the body (Brinkman and Kuypers 1973). This view has been challenged by functional evidence of ipsilateral limb activation in cortical motor areas using single-unit recording (Tanji et al. 1988; Kermadi 1998; Steinberg et al. 2002) as well as human imaging (Verstynen et al. 2005; Diedrichsen et al. 2013). Transcranial magnetic stimulation of motor cortex can lead to ipsilateral as well as contralateral muscle activation (Wassermann et al. 1991; Chen et al. 1997).

In the parietal cortex, the evidence for ipsilateral arm control has been mixed. Many individual neurons in PRR are modulated for reaches with either the contralateral or ipsilateral arm, albeit with a contralateral bias, suggesting that PRR controls movements of both arms (Chang et al. 2008; Chang and Snyder 2012). Yet firing rates correlate with the RT of only the contralateral arm (Snyder et al. 2006; Chang et al. 2008), and reversible inactivation with the GABAA agonist muscimol affects only the contralateral arm (Yttri et al. 2014). The current results provide an explanation for this apparent contradiction. Although activity was elevated prior to reaches with the ipsilateral arm, this elevation was similar to that seen with a saccade in the preferred direction. The similar modulation for saccades and ipsilateral arm movements, especially when taken in context with the findings just noted regarding RTs and reversible inactivation, suggests that activation prior to an ipsilateral arm movement does not reflect a plan to move the ipsilateral arm. Rather, it reflects a response to the presence of a task-relevant target in the neurons' receptive field.

In a standard unimanual visually guided delayed reach task, the spatial cue location and reach endpoint are conflated. One way to determine if the delay response reflects the presence of a target (a more sensory-like signal) or the coding of a reach (a more motor-like signal) is to require an anti-reach, that is, a reach away from rather than toward the target (Crammond and Kalaska 1994; Gail and Andersen 2006). Under these conditions, PRR and PMd neurons exhibit only a transient response when the target is in the response field and the anti-reach is out of the field, and a delayed but sustained response when the target is out and the anti-reach is in (Crammond and Kalaska 1994; Gail and Andersen 2006; Gail et al. 2009). This suggests that these areas code both task-relevant targets and reaches into the response field; for an anti-reach out of the field, the target is only transiently relevant, and thus evokes only a transient response. In the current report, by comparing responses to saccades, reaches with the ipsilateral arm and reaches with the contralateral arm, we can document separate target-related and reach-related responses without the use of an anti-reach.

PRR contains neurons with receptive fields in both ipsilateral and contralateral visual hemifields. We find a strong bias for the lower visual field and a weak bias for the contralateral field. These asymmetries are consistent with Chang et al. (2008) and Chang and Snyder (2012), but differ from Hwang et al. (2012) who found that the hemifield bias varies by animal, and from Battaglia-Mayer et al. (2000, 2001), who found preferred directions to be uniformly distributed.

## Relation to Other Recording Studies of Bimanual Coordination

Only one previous study has recorded from PPC neurons during a bimanual task. Kermadi et al. (2000) recorded from the anterior intraparietal area (AIP), a region well anterior of PRR that is selective for the shape, size, and orientation of objects to be grasped (Murata et al. 2000). Three-quarters of AIP neurons showed bimanual activity during a task that required the animal to pull a drawer with one hand and grasp a treat with the other. A small number of neurons were recorded and statistics were not reported, and so it is unclear whether these neurons exhibited an additive or nonadditive response for bimanual movements. Here, we focused on PRR, an area that is primarily involved in reaching, not grasping movements. Our conclusions are therefore limited to coordinated reaching movements. We speculate, however, that coordinated grasping or other manipulation by the 2 hands requires higher order representations that could draw on those in both PRR and AIP, among other areas.

While early recordings in primary motor cortex showed that responses were strongest for contralateral arm movements (Tanji et al. 1987, 1988), later work revealed neurons that were exclusively active for bimanual movements (Donchin et al. 1998; Kermadi 1998). Bilateral representations have also been found in SMA (Tanji and Kurata 1981; Tanji et al. 1988; Kermadi 1998) and premotor cortex (Gentilucci et al. 1988; Cisek et al. 2003). Here, when we specifically searched for neurons exclusively active for bimanual reaches, we found only 1 out of 14 PRR neurons was exclusively active for a bimanual reach. Thus, these types of neurons appear to be rare, though it is possible that a more complex bimanual task might yield different results.

### Relation to Human Studies of Bimanual Coordination

In humans, the role of the PPC in unimanual visuomotor function has been well-documented (Culham et al. 2006; Vesia and Crawford 2012). PPC has also been implicated in bimanual coordination. Damage to the parietal cortex impairs coordination of asymmetric bimanual movements (Halsband et al. 2001; Serrien et al. 2001). A patient who underwent serial resections of first the anterior and then the posterior portions of the corpus callosum exhibited marked deterioration in symmetric shape drawing and marked improvement in asymmetric shape drawing only after the posterior callosotomy (Eliassen et al. 1999). This is consistent with the notion that information about arm movements is shared via the posterior corpus callosum, which connects the parietal cortex of the 2 hemispheres (Seltzer and Pandya 1983), and is also consistent with the idea that bimanual coordination may first arise in PRR. Another source of indirect evidence for this view comes from the fact that, in a brain-machine interface designed to enable bimanual arm movements in monkeys, control was improved when signals from PPC were added to signals from primary motor cortex, SMA, and primary sensory cortex (Ifft et al. 2013).

Human imaging studies have reported PPC activations during bimanual tasks but they have been attributable to aspects of the task other than bimanual coordination per se, including task congruency (Wenderoth et al. 2005; Diedrichsen et al. 2006) and increased attentional demands (Nair et al. 2003). In some studies, activations observed during bimanual coordination were no different than those observed during a unimanual coordination condition (Koeneke et al. 2004; Szameitat et al. 2012). These studies have analyzed BOLD responses over periods that include the movement execution phase and so could not resolve whether the PPC activations were due to movement planning, movement execution or to visual and proprioceptive feedback during the movement (Filimon et al. 2009).

Unimanual reaching results in BOLD modulations in many areas and in both hemispheres (Kim et al. 1993; Verstynen et al. 2005). In parietal areas posterior to primary somatosensory cortex, Diedrichsen et al. (2013) found that ipsilateral movements were encoded nonlinearly, similar to what we find in PRR. In primary motor and sensory cortex, BOLD increased in both hemispheres in association with a single moving finger, but was suppressed in the ipsilateral hemisphere for non-moving fingers. We now show that mass activity recorded from monkey parietal cortex under similar conditions would likely show exactly this pattern of responses. However, it is important to note that BOLD responses should not be expected to be concordant with such mass activity. We oversample large pyramidal neurons; BOLD tracks metabolic events produced by all synapses and cell bodies in the cortex, including inhibitory interneurons and many small pyramidal neurons that we undersample or miss entirely. Thus, both our mass recording simulation and the fact that BOLD should not be expected to track large pyramidal cell activity indicate that there is no incongruency between previous BOLD results and our singleunit study.

## Responses During the Preparatory Versus Movement Periods

We have concentrated on the firing rate during the delay period, when the animal may be planning but is not executing a movement. The mechanisms underlying bimanual coordination may be different in the preparatory period leading up to a movement, compared with during the movement itself. Once movement begins, however, it is difficult to distinguish activity due to changing sensory feedback, including proprioceptive and visual afferents, from motor command signals. For example, synchronized activity in left and right PRR could reflect a synchronized motor command that is causal to the coordination. However, the synchronized activity could also reflect a common reafferent proprioceptive signal that is the result—not the cause—of the coordination. This problem is particularly acute when looking at signals from areas like the parietal cortex that are known to reflect movement plans as well as reafferent sensory signals. A second problem with interpreting neuronal activity once movement begins is that some of that activity may reflect the planning and execution of the next stage of movements, for example, the second of 2 saccades, or the return movement back to the start position.

Our solution to the problem of interpreting signals recorded during movement execution is to record instead just prior to the onset of movement. Reafference by definition occurs only after movement begins, and so cannot confound the preparatory period results. As for planning of the next movement, there is good evidence that, during the preparatory period, PRR reflects only the very next movement to be performed (Batista and Andersen 2001). Our solution is not perfect, since the mechanisms underlying bimanual coordination may differ in the preparatory period leading up to a movement, compared with during the movement itself. Another consideration is that delay period activity may not reflect a motor plan per se but rather set the state of a forward model that will be used for comparison with visual and proprioceptive feedback after movement onset (Miall and Wolpert 1996; Mulliken et al. 2008). We find, however, that results obtained during the movement period closely replicate the results obtained during the preparatory period.

An important general issue in sensory-motor processing is where and when sensory signals are converted into motor plans (Cisek 2007). In many systems, there is no single transition point. Instead, sensory and movement-related signals may both appear within the same cortical area or even within the same neuron (though at different times) (Bruce and Goldberg 1985; Ipata et al. 2009). Movement-related signals can range from endpoint coding to a detailed plan that includes trajectory and timing information. Here, we find that delay period activity in PRR represents a visuospatial goal (or goals) before all kinds of reaching

movements: Of the ipsilateral arm, of the contralateral arm, or of both arms simultaneously. In addition, PRR contributes to the computation of visuomotor transforms whenever a reaching movement involves the contralateral arm. About half of the neurons contain information about the context in which the contralateral arm will move. This information, which is not present in the population average, differentiates between contralateral movements alone, bilateral movements to the same target, and bilateral movements to 2 different targets. If the signals for unilateral movements of the 2 arms summed linearly, PRR could not encode this additional information. We do not know if other aspects of the bimanual motor plan are also encoded, for example, speed, trajectory, finger movements (Torres et al. 2013), but through nonlinear combinations of the relevant factors, multiple forms of bimanual coordination can be represented in parietofrontal sensorimotor networks.

# **Supplementary Material**

Supplementary material are available at Cerebral Cortex online.

# Author contributions

E.M. performed the experiment, analyzed the data, and wrote the manuscript; C.W. designed and performed the experiment; C.D.H. analyzed the data; L.H.S. designed the experiment, analyzed the data, and wrote the manuscript.

# Funding

The McDonnell Center for Systems Neuroscience at Washington University; the National Eye Institute at the National Institutes of Health (grant no. R01 EY-012135 to L.H.S.); the National Institute of Neurological Disorders and Stroke at the National Institutes of Health (grant no. F32 NS-076206 to E.M.).

# Notes

We thank Dr David M. Kaplan for helpful discussion and comments. *Conflict of Interest*: None declared.

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