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Viewpoint

Cortical Preparatory Activity: Representation of Movement or First Cog in a Dynamical Machine?

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SUMMARY

The motor cortices are active during both movement and movement preparation. A common assumption is that preparatory activity constitutes a subthreshold form of movement activity: a neuron active during rightward movements becomes modestly active during preparation of a rightward movement. We asked whether this pattern of activity is, in fact, observed. We found that it was not: at the level of a single neuron, preparatory tuning was weakly correlated with movement-period tuning. Yet, somewhat paradoxically, preparatory tuning could be captured by a preferred direction in an abstract "space" that described the population-level pattern of movement activity. In fact, this relationship accounted for preparatory responses better than did traditional tuning models. These results are expected if preparatory activity provides the initial state of a dynamical system whose evolution produces movement activity. Our results thus suggest that preparatory activity may not represent specific factors, and may instead play a more mechanistic role.

INTRODUCTION

Voluntary movements are prepared before they are generated (Ghez et al., 1991; Rosenbaum, 1980). Similarly, changes in neural activity occur well before movement onset in both motor and premotor cortex (Tanji and Evarts, 1976; Weinrich et al., 1984). Such "preparatory" activity likely plays a key role in movement generation: preparatory activity is predictive of reaction time and movement variability (Bastian et al., 2003; Churchland et al., 2006a; Churchland and Shenoy, 2007a; Churchland et al., 2006c; Riehle and Requin, 1993), and its disruption delays movement onset (Churchland and Shenoy, 2007a). An understanding of preparatory activity is also central to the study of the cognitive processes preceding movement. For example, an understanding of the preparatory activity preceding saccades has made approachable the cognitive processes that determine where and when to move the eyes (Schall and Thompson, 1999; Shadlen and Newsome, 2001). Yet it is still unclear how preparatory activity in motor and premotor cortex contributes to movement generation.

A common assumption is that preparatory activity constitutes a subthreshold version of movement activity. If a neuron will become active during rightward movement, it may be beneficial for that neuron to be weakly active during preparation of rightward movement. Assuming a threshold for producing movement, preparatory activity could advance the system closer to that threshold. This subthreshold view of preparatory activity dates to early studies (Tanji and Evarts, 1976), accords with our understanding of the saccadic system (e.g., Hanes and Schall, 1996), and is assumed by most models of reach generation (Bastian et al., 1998; Cisek, 2006a; Erlhagen and Schöner, 2002). A related hypothesis holds that preparatory and movement activities are tuned for different but concordant factors (e.g., rightward target locations and rightward hand velocity). An alternative proposal is that preparatory activity functions as the initial state of a dynamical system and may not explicitly represent movement parameters (Churchland et al., 2006b; Churchland et al., 2006c; Cisek, 2006b; Fetz, 1992). Under this hypothesis, preparatory and movement activity are closely related (via those dynamics), but that relationship need not be transparent at the level of the individual cell.

Neural responses consistent with the subthreshold view are often observed, especially in population averages (Bastian et al., 1998; Bastian et al., 2003; Cisek, 2006a; Erlhagen et al., 1999; Georgopoulos et al., 1989; Requin et al., 1988; Riehle and Requin, 1989). Yet other reports argue that, for individual neurons, tuning can differ during the two epochs (Crammond and Kalaska, 2000; Kaufman et al., 2010; Turner, 1991; Wise et al., 1986) and is in general inconstant with time (Churchland and Shenoy, 2007b; Fu et al., 1995; Hatsopoulos et al., 2007; Rickert et al., 2009).

If preparatory activity constitutes a subthreshold precursor of movement activity, the two should share similar tuning. Yet under the dynamical systems view there is little reason why "tuning" should be similar for the initial and subsequent states of the system. Muddying the waters further, preparatory activity appears tuned for a dizzying variety of factors, including reach direction and distance (Messier and Kalaska, 2000; Riehle and Requin, 1989), reach speed (Churchland et al., 2006b), visual location of the target (Shen and Alexander, 1997), target location

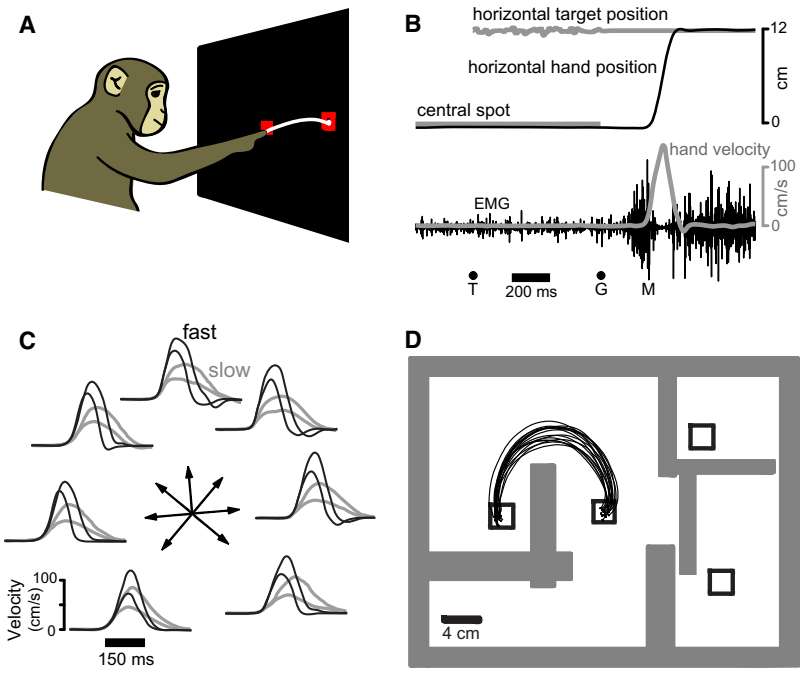

Figure 1. Illustration of Behavior

(A) Reaches were from a central spot to a target. An example trajectory is shown.

(B) Task timeline. Upon appearing (T), the target jittered slightly. Cessation of jitter provided the go cue (G). M indicates movement onset.

(C) Behavior: speed task. Velocity in the target direction for the seven directions, two distances and two instructed speeds is shown.

(D) Behavior: maze task. For this example condition, the reach had to curve over a virtual barrier. In other conditions, reaches avoided different arrangements of barriers or were straight with no barriers. Reaches lasted ~200 to ~600 ms (depending on distance/curvature).

relative to the eye and hand (Batista et al., 2007; Pesaran et al., 2006), and reach curvature (Hocherman and Wise, 1991). It is unclear which—if any—of those factors is primary. We are thus left with two open and fundamental questions: what is preparatory activity tuned for, and how does it relate to movement activity?

We addressed these questions using four data sets employing delayed-reach tasks. We found that the tuning of individual neurons was typically dissimilar during the preparatory and movement epochs. This finding is inconsistent with a subthreshold role for preparatory activity. Nevertheless, preparatory tuning could be captured by a preferred direction in a "space" describing the population-level movement-period responses. Remarkably, preferred directions in this unconventional space accounted for preparatory tuning better than did preferred directions in more traditional spaces (e.g., reach endpoint or velocity). This result has a simple mechanistic interpretation: it is expected under the hypothesis that preparatory activity acts as the initial state of a dynamical system.

RESULTS

Behavior and Recordings

Three monkeys performed variants of a delayed-reach task. In the "speed task" (monkeys A and B), target color instructed reach speed (28 conditions, Figure 1C). In the "maze task" (monkey J), reaches were either straight or curved to avoid virtual barriers (Figure 1D). In the present study, this complex cognitive-motor task simply provides a way to evoke many different reaching movements (27 and 108 conditions for "monkey J" and "monkey J-array" data sets).

Neural recordings employed single electrodes (monkeys A, B, and J data sets, 310 total single-unit isolations) and a pair of implanted 96-electrode arrays (J-array data set, 146 single- and multiunit isolations). Recordings were made from the caudal portion of dorsal premotor cortex (PMd) and from surface and sulcal primary motor cortex (M1). High trial counts (mean trials/neuron = 311, 492, 388, and 2166 for monkeys A, B, J, and J-array) allowed us to resolve perimovement responses that were often complex and multiphasic (Churchland and Shenoy, 2007b; see also example PSTHs below).

Neural Responses during Preparation and Movement

Figure 2A illustrates an idealized response pattern consistent with preparatory activity serving as a subthreshold form of movement activity. Preparatory activity shows a preference for one condition (red, perhaps the preferred direction) over another (green, perhaps the opposite direction). This preference is maintained as the plateau of preparatory activity gives rise to a burst of perimovement activity (defined as activity immediately before, during, and just after the movement).

Figure 2B plots the response of a neuron that approximates the schematic in Figure 2A. Data are for one distance/instructed speed. Traces (one per condition) are colored based on the level of preparatory activity in order to allow visual comparison with the subsequent pattern of perimovement activity. This neuron "prefers" reaches ending up and leftward. This preference is shared between preparatory and perimovement epochs. This agreement is not perfect (two green traces surpass the black trace), but the overall correlation is quite high (r = 0.72; see section on correlations below for details).

Figures 2C–2E plot responses of three additional neurons recorded using the speed task. Despite clear preparatory tuning, preferences are not maintained between the preparatory and perimovement epochs (color ordering differs between epochs). Furthermore, perimovement activity was often complex and multiphasic (Churchland and Shenoy, 2007b; Sergio et al., 2005). These neurons show negative correlations between preparatory and perimovement tuning.

Figure 3 plots responses of six neurons recorded using the maze task. Panels (A)–(D) plot single-electrode recordings (27 conditions). Panels (E) and (F) plot array-based recordings

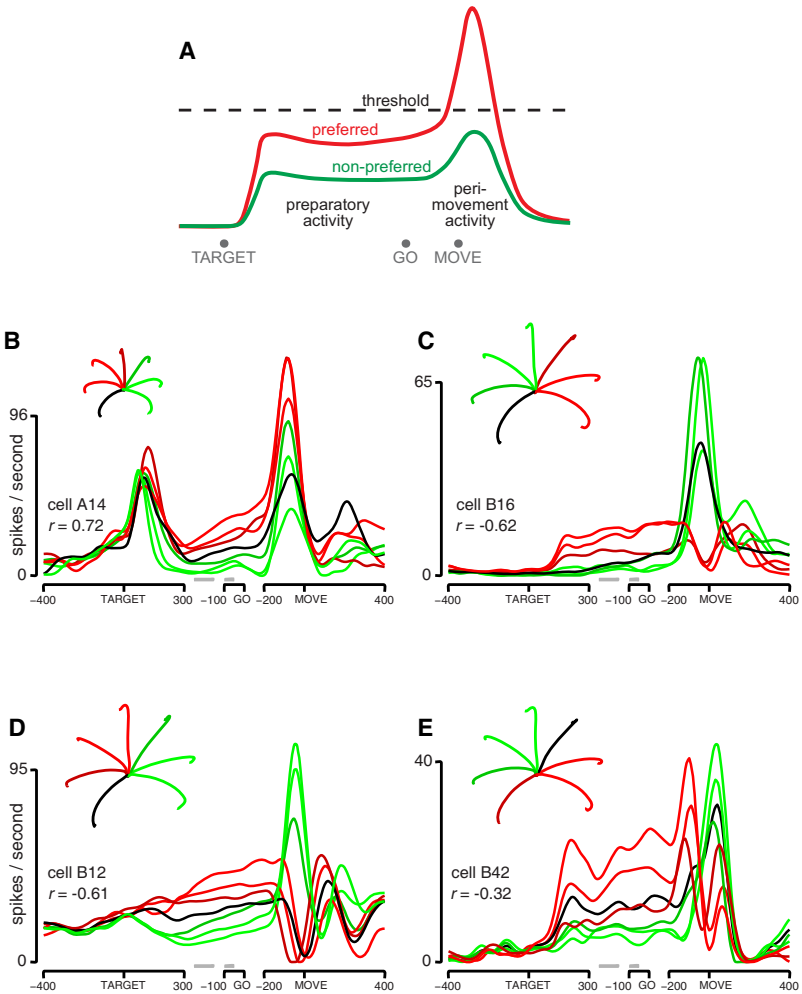

Figure 2. An Idealized Schematic of Neural Activity and Responses of Example Neurons

(A) Traces are colored red (preferred) and green (nonpreferred). In this conception, preparatory activity is present during the delay period, rises to a threshold following the go cue, and produces a burst of perimovement activity.

(B) Firing rate versus time for an example neuron whose responses resemble the schematic in (A). Responses are shown for all seven reach directions for the fast instructed speed and shorter distance. Traces are shaded from red to green based on the firing rate 50 ms before the go cue. Data were averaged separately, locked to target onset, the go cue, and movement onset. To aid viewing, we have interpolated data across the gaps between these three epochs. See Figure S4 for a description of the smoothing used to produce these PSTHs. Inset plots mean hand trajectory using the same color coding.

(C–E) Similar plots for three more example neurons. Data have been down selected to a single distance and instructed speed (far/fast for these panels). These three neurons were selected to illustrate the fact that preparatory and perimovement tunings were typically different, even in the simplest paradigm: straight reaches at one distance/instructed speed.

(108 conditions). Some neurons maintained similar tuning between preparatory and perimovement epochs (panel A), but most did not. Also, although most neurons showed a rough directional preference during the preparatory period (insets), it was not uncommon for a few (panel B) or even many (panels E and F) conditions to evoke activity not easily explained by a pure directional preference.

Perimovement response complexity is not due to noise, but is instead a real feature of most neural responses (Churchland and Shenoy, 2007b). Still, in Figure 3, response complexity is partly a result of the variety of reach paths. Given this, it is worth stressing two things. First, any model regarding how preparatory activity leads to perimovement activity should work for curved as well as straight reaches. Second, both perimovement response complexity and the failure of preparatory tuning to predict perimovement tuning are quite apparent even for simple center-out reaches (Figure 2).

Correlations between Preparatory and Perimovement Tuning

Similar levels of preparatory activity can lead to opposing patterns of perimovement activity (e.g., middlemost traces in Figure 2D and traces near the top of Figure 3C). Thus, it is not simply that tuning preferences can reverse; tuning is often weakly correlated between the two epochs (population analysis in Figures 4A–4D). To compute correlations, we took the average firing rate during the preparatory and perimovement epochs for each condition (Experimental Procedures). A neuron's tuning in one epoch is then described by a vector of firing rates, with one entry per condition. We intentionally chose to not fit a specific tuning model and instead simply computed the correlation between epochs. This correlation will be high if a neuron's preference remains similar. Across the four data sets, the mean correlation was positive ($p = 0.01$, $p = 0.01$, $p = 0.12$, $p = 0.03$), but only very modestly so (mean $r = 0.21$, 0.19, 0.06, and 0.13). Nonparametric correlations were similarly modest (mean Spearman's $r = 0.20$, 0.20, 0.06, and 0.11). Thus, preparatory and perimovement tuning agree weakly on average, and individual neurons span a wide spectrum.

The example neurons with correlations closest to the population mean are shown in Figures 3A, 3C, and 3E. These neurons illustrate a further point: preparatory and perimovement tuning often agreed when the latter was assessed ~150 ms before movement onset, but not when assessed close to movement onset. To examine this time course, we measured perimovement activity at individual time points. The correlation with preparatory activity began to decline ~200 ms prior to movement onset and reached values near zero by movement onset (Figure 4E).

The above results agree with some prior observations at the single-neuron level (Churchland and Shenoy, 2007b; Crammond and Kalaska, 2000; Kaufman et al., 2010; Wise et al., 1986) but appear to disagree with findings made at the population level

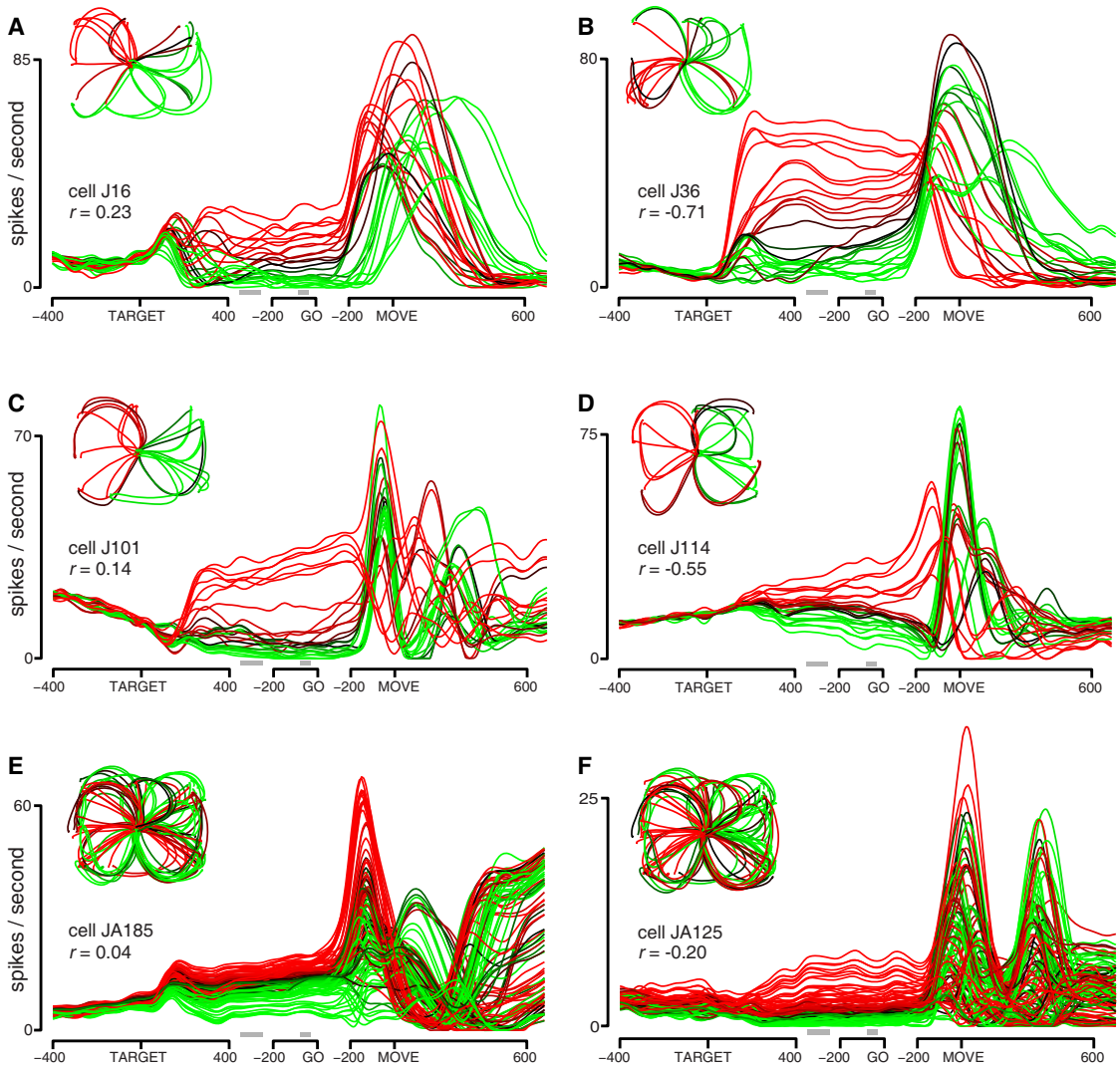

Figure 3. Responses of Six Example Neurons, Similar Format to Figure 2

(A–F) Responses are shown for all conditions, including straight and curved reaches. Different conditions, involving different maze configurations, sometimes evoked similar reach trajectories (although not necessarily with similar velocity profiles). The same 108 conditions were used for the J and J-array data sets. For the former, a given neuron was recorded using one of four 27-condition subsets. The insets in (A)–(D) thus show different reach patterns, corresponding to different subsets. In addition to temporal filtering, additional denoising was accomplished via the method in Figure S4. This method removes uncorrelated noise and thus cannot eliminate noise in the firing rate that is accidentally similar across conditions (e.g., during the delay period in F).

(Bastian et al., 1998; Bastian et al., 2003; Cisek, 2006a; Georgopoulos et al., 1989). This discrepancy can be resolved by noting that preparatory and perimovement tuning are weakly but positively correlated on average, especially early in the perimovement epoch (Figure 4). In population averages (see Figure S1 available online), the lack of correlation averages out and the means are dominated by the weak agreement between preparatory and perimovement tuning. However, such effects grow dramatically smaller with time. By movement onset, even population averages show little relationship with preparatory tuning (Figure S1).

Our results argue against a common assumption: that preparatory activity constitutes a subthreshold version of perimovement activity. The cartoon in Figure 2A bears little resemblance to the responses of most neurons. Even more disconcertingly, different neurons show markedly different relationships between preparatory and perimovement activity, with a broad range of correlations centered near zero. It has been suggested that neurons with concordant preparatory and perimovement tuning might prime the desired movement, whereas neurons with opposing tuning might suppress movement until execution (Wise et al., 1986). Yet there is little evidence in Figure 4 (except perhaps weakly in panel B) for one population of concordant tuning ($r \approx 1$) and another of opposing tuning ($r \approx -1$). Instead, most neurons have weakly correlated tuning.

There are at least four possible explanations for the above findings. First, perhaps preparatory activity is a largely idiosyncratic phenomenon with no lawful relationship with

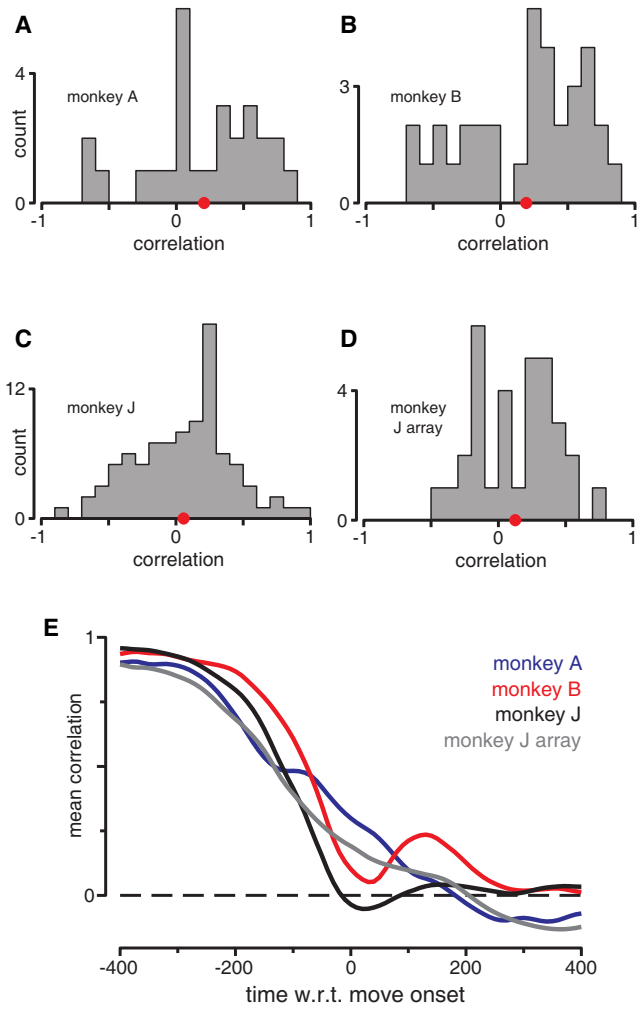

Figure 4. Correlation between Preparatory and Perimovement Tuning

(A–D) Distribution of correlations (measured once per neuron) for the four data sets. Analysis was restricted to neurons robustly tuned during both epochs (Experimental Procedures). Red dot indicates the distribution mean.

(E) Average correlation as a function of when perimovement activity was assessed. Perimovement activity was measured at a single time point, after smoothing with a 20 ms Gaussian kernel. Correlations are initially high, because preparatory tuning is being correlated with itself.

perimovement activity. Second, perhaps preparatory and perimovement activity code the same thing (e.g., reach direction) with unrelated preferences (e.g., different preferred directions). Third, preparatory and perimovement activity may code fundamentally different things and do so with unrelated preferences. The motor system might decode reach endpoint from preparatory activity and then produce perimovement activity representing the velocity trajectory necessary to reach that endpoint. Finally, under the dynamical systems view, preparatory activity may be directly and mechanistically linked with perimovement activity, but in a manner not obvious at the single-neuron level (Churchland et al., 2006b; Cisek, 2006b). These possibilities are addressed below.

Testing Preparatory Tuning in Different Spaces/Reference Frames

Of the above hypotheses, the first supposes that preparatory activity is tuned for nothing reliable. The next two suppose that preparatory activity is tuned for task or movement parameters (e.g., reach endpoint, trajectory, or speed). The last supposes that preparatory activity should somehow relate to the population-level pattern of perimovement activity. What is preparatory activity in fact tuned for?

It is worth expanding upon the usual caveat that most experimentally quantifiable variables (reach endpoint, reach velocity, muscle activity) correlate with one another (Mussa-Ivaldi, 1988; Sanger, 1994; Scott, 2000; Scott, 2008). This has important consequences. Suppose preparatory activity truly represents reach endpoint (i.e., is some straightforward function of reach endpoint and can be readily decoded to infer endpoint). Suppose perimovement activity represents reach velocity. Preparatory activity will then appear tuned not only for reach endpoint but also for reach velocity and perimovement activity (all these factors are correlated). Yet reach endpoint does not correlate perfectly with reach velocity, particularly for the tasks used here. Preparatory activity (which, in this example, is tuned for endpoint) would therefore have its strongest relationship with endpoint and would have somewhat weaker relationships with the other variables. The central question is thus: what is preparatory activity best tuned for?

To investigate this question, we measured how well a preferred direction (PD) accounts for preparatory tuning. We asked in what space that PD best captures tuning. If preparatory activity is tuned for endpoint, then the PD will capture tuning most effectively when expressed in a "reach-endpoint space," where the axes capture horizontal and vertical endpoint. If preparatory activity is tuned for initial reach velocity, the PD will be most effective in an "initial-velocity space." A wide variety of such spaces is possible. Indeed, a central goal of this field has been to determine in which space, or reference frame, the PD best captures tuning.

Figure 5 illustrates, for one example neuron, how the PD can capture tuning in different spaces. Preparatory activity showed a clear preference for some conditions (shaded red) over others (shaded green). Figure 5B illustrates a traditional method for accounting for such preferences. The 28 conditions (each corresponding to a target location and instructed speed) are located in a space defined by the horizontal and vertical reach endpoints. Preparatory firing rate is indicated by symbol size/color. The PD points toward the most active responses and attempts to provide a fit according to:

$$x_n \approx b_o + g \times \mathrm{S} \times \mathrm{PD}, \qquad \text{Equation 1}$$

where x_n is a $c \times 1$ vector containing the neuron's preparatory response for the c conditions, b_o and g are the firing rate offset and gain, S is a $c \times k$ matrix containing the location of each condition in a k-dimensional space, and the PD is a $k \times 1$ direction in that space. The performance of the PD can be gauged by plotting the true responses (x_n) versus the fit provided by the PD (right-hand side of Equation 1). Doing so (Figure 5D) shows that the PD in endpoint space captures the pattern of preparatory activity reasonably well.

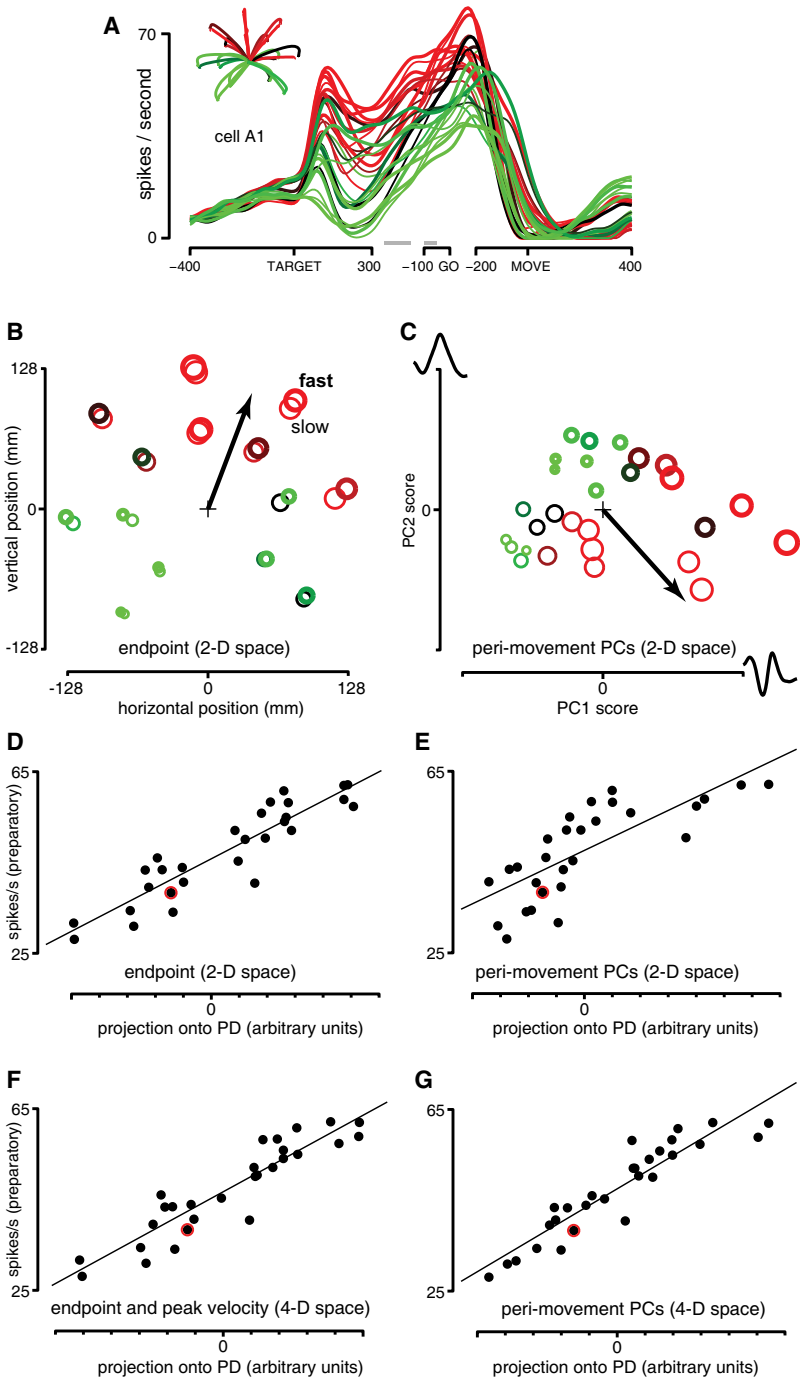

Figure 5. Example PDs in a Space Based on Movement Endpoints and the "Perimovement Space"

(A) Firing rate as a function of time for an example neuron. All 28 conditions are shown.

(B) Mean reach endpoint for each condition. Red-to-green shading and symbol size indicate preparatory firing rate for that condition. Symbol thickness indicates instructed speed. The PD (arrow) points toward conditions with the greatest preparatory activity.

(C) The same 28 conditions located in the perimovement space. Each axis corresponds to a population-level pattern of perimovement activity (a PC). The subsection of this pattern coming from a single neuron (A34, chosen arbitrarily) is plotted at the end of each axis. Thus, the rightmost red symbol corresponds to a condition in which the "PC1 pattern" was strongly present.

(D) Firing rate versus each condition's projection onto the PD, using the endpoint space from (B).

(E) Similar to (D), but for the perimovement space.

(F) Same as (D), but for a 4D space defined by reach endpoint and peak velocity.

(G) Same as (E), but for a 4D perimovement space.

Might the PD perform better still if expressed in a different space? Many spaces are possible. For example, to construct an "endpoint-and-peak-velocity" space, one needs simply to measure average endpoint and peak velocity for each condition. Each condition is then described by four numbers (horizontal and vertical endpoint and peak velocity) and lives in a four-dimensional space. We can then ask how well a PD in this four-dimensional space captures the pattern of preparatory activity (Figure 5F). We refer to spaces constructed in this manner as "task" spaces. Task spaces are constructed by the experimenter to capture salient aspects of the task (e.g., target location) or of performance (e.g., peak velocity). The use of such task spaces is common in systems neuroscience. The many studies that ask which reference frame best captures neural responses (e.g., Kakei et al., 1999) are asking which task space is preferable. More generally, whenever neural responses are posited to depend linearly on some set of *k* factors, that relationship can be formalized via a PD in *k*-dimensional space. How well the PD performs is a test of whether activity truly depends on those *k* factors. Traditional "cosine tuning" models fall into the above category: cosine tuning for velocity is equivalent to a linear dependence on horizontal and vertical velocity (Georgopoulos et al., 1982).

Testing Preparatory Tuning in PCA-Based Spaces

A presumed purpose of preparatory tuning is for changes in a given neuron's activity to contribute, in a small but specific way, to changes in some future aspect of movement. A neuron tuned for reach endpoint would, through its firing, contribute some small change to the eventual reach endpoint. Of course, preparatory activity might be tuned not for static factors (e.g., endpoint) but for time-varying parameters (e.g., velocity). A change in preparatory firing rate would then presumably impact the future temporal profile of that parameter (perhaps scaling velocity overall). This situation should still be experimentally tractable. Provided one can describe, using a small number of parameters, how velocity varies with condition, then preparatory activity should faithfully

covary with those parameters (if it is truly tuned for future velocity). Such parameterizations can be provided by dimensionality reduction techniques such as principal component analysis (PCA).

This approach can also address the hypothesis that preparatory activity constitutes an initial state that largely determines (via local and feedback dynamics) the population-level pattern of perimovement activity. In this view, changes in preparatory activity produce specific changes in the pattern of perimovement activity. For a large class of dynamical systems, this relationship is straightforward: the greater a given neuron's preparatory rate, the stronger some subsequent perimovement pattern becomes. PCA can be used to reduce perimovement activity to a simple set of component patterns. Under the dynamical systems view, preparatory activity should be tuned for these component patterns. If a particular pattern is prominent for a given condition, then the preparatory rate of a neuron contributing to that pattern should be high.

The PCA-based approach (Figures 5C, 5E, and 5G; Figure S2) constructs a low-dimensional space that captures how time-varying factors (velocity, perimovement activity, etc.) differ across conditions. To illustrate the necessity of dimensionality reduction, consider the full-dimensional space describing the perimovement response. The relevant matrix (call this T) is large: $c \times nt$, where c is the number of conditions, n is the number of neurons, and t is the number of time points. The c conditions thus reside in a space with thousands of dimensions. PCA can reduce this dimensionality from $c \times nt$ to $c \times k$, with k in the range of 3–14. The resulting $c \times k$ matrix, T_{red}, then conveniently yields the location of each condition in a k-dimensional space (Figure S2).

To illustrate, Figure 5C plots the 28 conditions in a two-dimensional ($k = 2$) perimovement space. The location of each symbol indicates, for that condition, the strength of the two most prominent perimovement patterns (the first two PCs). The PD captures preparatory tuning reasonably well (Figures 5C and 5E). In fact, the PD generally performed adequately regardless of the space in which it was expressed. As discussed above, this is expected, given correlations between movement parameters. One thus wishes to ask in which space the PD best captures the pattern of preparatory responses. We tested a variety of spaces, falling into three categories. First, we tested task spaces, constructed by hand selecting likely important factors (as in Figure 5B). Second, we tested the perimovement space (Figure 5C). Finally, PCA was used to produce a kinematics-based space and an electromyogram (EMG)-based space (substituting time-varying kinematic variables or EMG records for perimovement activity).

Most tested spaces were greater than two-dimensional. Figures 5F and 5G plot PD performance in a four-dimensional task space and a four-dimensional perimovement space. The improvement in fit (relative to Figures 5D and 5E) is expected. The use of a PD is equivalent to linear regression; we are now regressing against four explanatory factors rather than two. To combat potential overfitting, we computed the PD based on all but one condition (red circled points in Figures 5D–5G) and assessed performance for the left-out condition. This cross-validation procedure was repeated, leaving out each condition in turn. We define performance as 1 minus the squared error, averaged across all left-out conditions and normalized appropriately (Experimental Procedures).

PD Performance in a Variety of Spaces

We quantified the ability of the PD, in each space, to account for preparatory tuning (Figure 6). Points above zero indicate performance considerably better than chance. Points below zero indicate that the PD provided a largely spurious fit (or suffered from overfitting), resulting in poor generalization. For task spaces (green), performance is plotted against the dimensionality of the space. Given the lack of agreement regarding the key task variables, we tried many candidate spaces. A number of task spaces performed reasonably well, including "targs + inst. spd.," a three-dimensional space based on the horizontal and vertical target location and the instructed speed (speed task only); "endpoints + max. spd.," a similar space based on the empirical reach endpoints and peak speeds; "segment dirs.," a six-dimensional space built by dividing the reach trajectory into three vectors; and "initial vel.," the average horizontal and vertical velocity during the first 150 ms of the reach. That the PD can perform well in different task spaces highlights the historical difficulty of determining which factors activity truly depends upon.

Performance of the PCA-based spaces is plotted for a range of dimensionalities (values of k). Performance typically improved with dimensionality. This increase is nontrivial, because generalization performance is being assessed. Still, because the dimensionality of preparatory activity itself is moderately high (at least 7–10 dimensions; Experimental Procedures), performance should increase with dimensionality, assuming the PD is in approximately the "right" space. Performance typically declined at dimensionalities > 10, an indication of overfitting.

The data in Figures 6A–6D lend themselves to many comparisons, but one central finding stands out: performance was nearly always best for the space derived from the population-level perimovement response. For every data set, the highest level of performance was achieved—usually for a middle range of dimensionalities—when PDs were expressed in the perimovement space. Even if we consider each dimensionality individually, performance was almost always higher for the perimovement space. An exception was that, among three-dimensional spaces, the "targs + instr. spd." and "endpoints + max. spd." performed very well for the data sets collected using the speed task. The former is undefined for the maze task, but the latter did not perform well.

We did not test all possible task spaces. Nor is it clear that the "right" space should stay constant across tasks. Still, if we restrict ourselves to the tested spaces and assume that the correct tuning model should account for both straight and curved reaches, then a clear rank order of spaces is present. Figure 6E summarizes performance across the data sets (excluding J-array, for which EMG was not recorded). For the first subpanel, performance was computed for spaces of three dimensions or less. The other subpanels allow spaces up to 6 and 12 dimensions. For PCA-based spaces, if the best dimensionality was less than the maximum dimensionality allowed, then the best was used. Performance (averaged across neurons) was highest when the PD employed the space based on perimovement neural activity. This performance differential

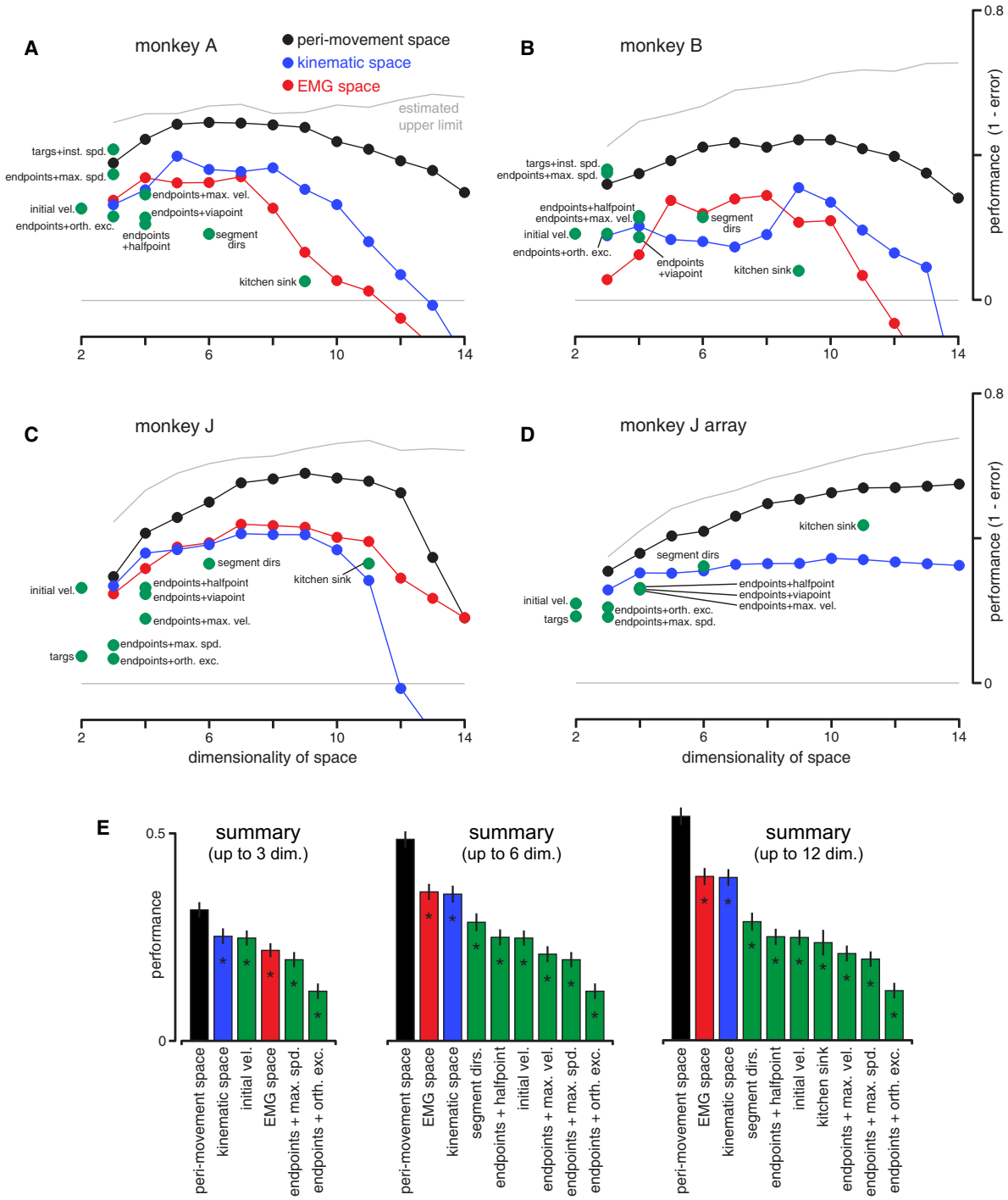

Figure 6. Ability of the PD to Account for Preparatory Tuning

(A–D) Performance of the PD for the four data sets. For PCA-based spaces (perimovement, kinematic, EMG), performance is plotted over a range of tested dimensionalities. Task spaces (green) are plotted versus their respective dimensionalities. Gray line is an estimate of the upper limit on performance, given measurement error (Experimental Procedures).

(E) Summary of performance, spanning data sets from monkeys A, B, and J. We combined only across spaces defined for all data sets (e.g., "targs + inst. spd." was not included, but "endpoints + max. spd." was included). Subpanels plot performance for spaces of the indicated dimensionality or less.

Bars plot standard errors. Asterisks indicate performance significantly worse ($p < 0.001$) than the best space.

increased at higher dimensionalities, indicating that the perimovement space better captured higher-dimensional aspects of the data. Although a few task spaces performed well at lower dimensionalities, no single task space performed consistently well across data sets. As a result, the task spaces were largely outcompeted by the PCA-based kinematic and EMG spaces, which were in turn outperformed by the perimovement space. Notably, the perimovement space performed well despite the low correlation between preparatory and perimovement activity at the single-neuron level (Figure 4).

Controls

Might the perimovement space perform well because it is based in part on activity (the beginning of the perimovement epoch) that correlates with preparatory activity? This is unlikely for three reasons. First, when using a PD to capture a given neuron's preparatory activity, the perimovement space was based on the responses of all the other neurons (Experimental Procedures). Second, because perimovement activity is typically stronger than preparatory activity, the perimovement space is unlikely to be dominated by the trailing end of preparatory activity. To illustrate this, we employed a shuffled control in which each condition's perimovement response was randomly inverted on half the conditions (Figure 7, legend). The PCA-based "shuffled space" performed poorly (Figure 7A); any contribution from the trailing end of preparatory activity (preserved despite shuffling) is insufficient to allow good performance. Finally, the start of the perimovement window was 150 ms before movement onset but could be slid later in time with little decline in performance (Figure 7B). Even when the window began at movement onset (at which point the correlation between preparatory and perimovement tuning is almost zero; Figure 4E), performance was still at 97% (monkey J) and 94% (monkeys A and B) of its original value.

Might the perimovement space perform well simply because it is high dimensional? This is unlikely. Regressing against a high-dimensional space will improve fit, but not generalization performance (unless those higher dimensions really are relevant). For example, the shuffled space is high dimensional but performed poorly. Also, the high-dimensional task spaces (including the gratuitously high-dimensional "kitchen sink" space) always underperformed the perimovement space. Finally, the perimovement space performed well even at the lower dimensionalities.

A final possible concern is that the perimovement space is somehow at an advantage because it involves relating neural activity with other neural activity. This is unlikely for a number of reasons. First, the analysis in Figure 4 similarly related neural activity during the two epochs, yet found little consistent relationship. Second, the measurement of neural activity is noisier than the measurement of kinematic parameters or of EMG. Based on a finite number of neurons, the perimovement space will, if anything, be at a disadvantage. Third, a given neuron's preparatory activity was explained using a space derived from the perimovement activity of all the other neurons. Finally, one expects preparatory activity that is tuned for one thing (e.g., reach endpoint) to relate to perimovement activity tuned for another (e.g., reach velocity). Yet any such secondary relationship should be weaker than the direct relationship between preparatory activity and the factor it is truly tuned for. However, we found that preparatory activity was best explained in the perimovement space.

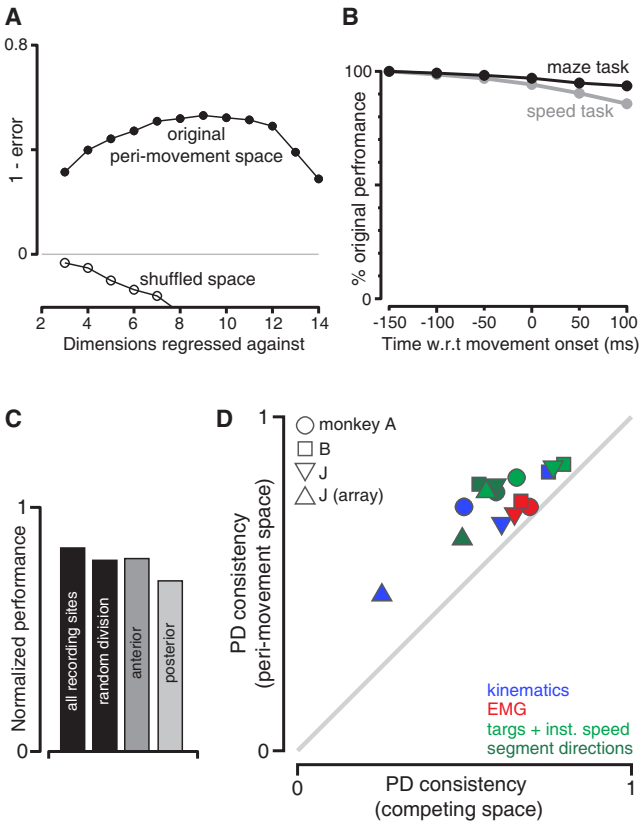

Figure 7. Further Controls and Analyses

(A) Performance of the "shuffled" perimovement spaces, averaged over all the data sets. During shuffling, either the firing rate for each neuron/condition was left intact (50% probability) or the perimovement pattern was inverted. This was done by preserving activity up to 150 ms before movement onset and reflecting (vertically) all subsequent activity around the firing rate at that time.

(B) Performance (averaged across neurons) versus the start of the perimovement interval. Performance was measured using the best dimensionality for that data set/start time.

(C) Performance of the perimovement space for subsets of the original data. Performance was computed for a six-dimensional space, normalized, and averaged across data sets. Leftmost bar: performance for all data. Gray bars: performance for sites with AP locations $\geq$ the median (anterior) or $\leq$ the median (posterior). Second black bar: performance when data were randomly subdivided.

(D) PD consistency for the perimovement space versus that for a variety of other spaces. Kinematic and EMG spaces were chosen because they had performed the best overall (after the perimovement space) in the analysis in Figure 6. "Targs. + inst. speed" and "segment directions" spaces were chosen because they performed well for the speed and maze tasks, respectively. "Targs. + inst. speed" was undefined for the maze task; the similar "endpoints + max. spd." space was analyzed instead.

Comparison of Anterior versus Posterior Sites

A number of response properties—including the prevalence of preparatory activity—vary with anterior/posterior location within

and between PMd/M1 (Kalaska et al., 1997; Kalaska et al., 1998; Weinrich et al., 1984). We similarly found preparatory activity to be more prevalent at anterior sites (data not shown). However, with respect to our central results, anterior and posterior sites were similar. The poor correlation between preparatory and perimovement tuning (at the single-cell level) was equally prevalent at anterior and posterior sites. Regressing tuning correlation (as in Figure 4) against AP location yielded little or no effect: $r = -0.05$, $p = 0.82$; $r = -0.03$, $p = 0.85$; $r = -0.07$, $p = 0.52$; and $r = 0.20$, $p = 0.27$ for the four data sets.

The ability of the perimovement space to capture tuning also held for both anterior and posterior sites (Figure 7C). Some caution is required: any division of the data will likely yield poorer performance, because the perimovement space is impacted more by sampling noise. To combat this complication, we normalized performance by its estimated upper limit (e.g., the gray line in Figures 6A–6D). Performance, after dividing based on anatomy, was only slightly different than if we down-selected the data randomly. Performance was slightly better at anterior sites, though this may occur simply because stronger tuning can be more accurately measured and thus more accurately captured by the PD.

Stability of the PD

A common experimental design involves measuring the PD before and after an imposed manipulation, such as a change in arm posture or the addition of a load (e.g., Caminiti et al., 1990; Kakei et al., 1999; Kalaska et al., 1989; Scott et al., 1997). Often, the manipulation is carefully chosen to be maximally revealing with respect to the candidate spaces being considered. However, the central logic holds more generally: if the PD is expressed in the "right" space, it ought not change when remeasured in another context. Our data sets employed many (27–108) conditions, affording the opportunity to perform a less creative, but not necessarily less effective, version of this class of experiment. For each neuron, we randomly chose 25 conditions (with replacement) and measured the PD, then randomly chose another 25 conditions and remeasured the PD. (This analysis is possible because the PD is computed via regression, which does not require a uniform arrangement of conditions.) "PD consistency" was the dot product of the two PDs.

Figure 7D plots average PD consistency in the perimovement space versus that in a variety of other spaces. The perimovement space always employed the same dimensionality as the space with which it was compared. We chose two task spaces that had performed well for at least one of the two tasks in the analysis in Figure 6. For PCA-based kinematic and EMG spaces, we employed the dimensionality that yielded the highest performance for that data set in Figure 6. Thus, the task, kinematic, and EMG spaces were given the best possible chance to compete favorably with the perimovement space. Yet for every comparison, and for all four data sets, the PD was most stable when measured in the perimovement space.

Tuning from a Dynamical Systems Perspective

The finding that the PD performs best in a perimovement space initially appears paradoxical, given the generally weak correlation between preparatory and perimovement tuning (Figure 4). More broadly, what kind of a representation does this finding imply? How might that representation be decoded? These issues can be addressed under the interpretation that preparatory activity serves as the initial state of a dynamical system whose subsequent evolution produces perimovement activity (Churchland et al., 2006b; Churchland et al., 2010; Cisek, 2006b; Fetz, 1992; Schaffer et al., 2006; Sussillo and Abbott, 2009; Yu et al., 2009). This suggestion is compatible with both of our basic findings. The critical observation is that the trajectory of a linear dynamical system is a weighted sum of component patterns. Changes in the initial state lead to linear changes in the magnitudes of those component patterns (Figure 8A). If one knows how strongly each pattern is present, one can infer the initial state. This will be approximately true for a nonlinear system, to the degree that it can be approximated by a time-varying linear system (see Supplemental Experimental Procedures for a derivation and further illustration).

To illustrate the above, Figure 8 shows simple simulated dynamics: circular trajectories through state space. We employed 25 initial states (25 "conditions"; Figure 8B). These determine the phase and amplitude of the subsequent activity. The system was held at its initial state (a rough analogy with preparatory activity) and then released. At the single-unit level (Figure 8C), preparatory activity seems to bear little relationship to perimovement activity. The correlation of preparatory activity with perimovement activity (averaged over the gray interval) was 0.08. Furthermore, a given preparatory firing rate could lead to opposing patterns of perimovement activity (asterisks, Figure 8C), much as was the case for the data (e.g., Figure 3C). This occurs because a given firing rate for unit 1 can correspond to different initial states (asterisks, Figure 8B).

Yet hidden in Figure 8C is a straightforward relationship. When the initial rate of unit 1 is high, the subsequent pattern contains a strong cosine-shaped modulation for unit 1 and a strong sine-shaped modulation for unit 2. The orthogonal activity pattern—a negative sine for unit 1 and a cosine for unit 2—is completely uncorrelated with the initial state of unit 1 (it relates to the initial state of unit 2). Thus, unit 1 can be said to have a "preferred direction" that points toward the first of these population-level patterns and is orthogonal to the second pattern.

Figure 8D illustrates such a PD (same format as for Figure 5C). PCA yields a space that captures all activity patterns that are possible for this system. Traces on each axis plot the pattern captured by that principal component (black and blue for units 1 and 2). Each symbol's location is given by the weights required so that those patterns sum to the actual perimovement pattern seen for that condition. Symbol size/color indicates the preparatory rate of unit 1 for that condition. The PD points toward the pattern recruited by the activity of unit 1 (Figure 8A) and perfectly captures preparatory tuning. This occurs because the space in Figure 8D is a linear transformation (in this case a nearly pure rotation) of the space in Figure 8B. Given that there was a direction in that original space (the horizontal axis) that captured the initial activity of unit 1, there will also be a direction (the PD) in the transformed space that captures the initial activity of unit 1.

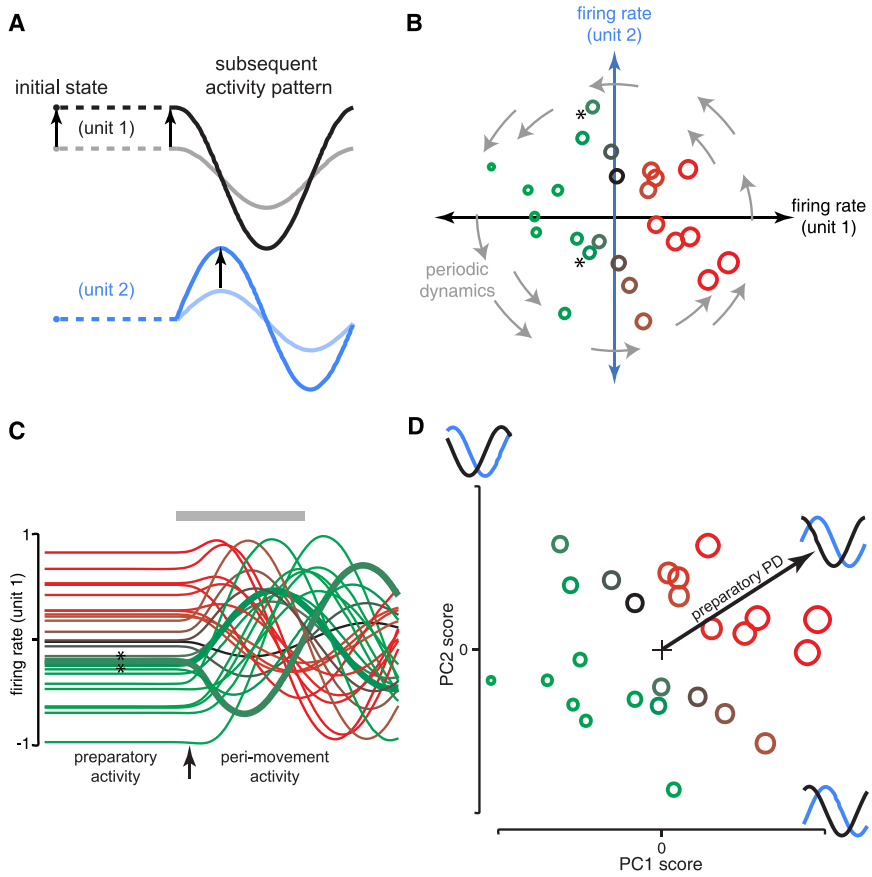

Figure 8. Illustration of the Behavior of a Simple Linear Dynamical System: A Harmonic Oscillator

(A) Changes in the initial state produce a linear scaling of the subsequent activity pattern. In this case, the larger the initial state of unit 1, the greater the amplitude of the oscillation.

(B) State space containing 25 randomly chosen initial states (25 "conditions"). Symbol size/color indicates the initial firing rate of unit 1. For the simulations below, activity evolved counterclockwise from the initial state: $x(t+1) = Wx(t)$, where x is the two-dimensional vector of unit activities, and the matrix $W = [1 - 2\pi/360;\ 2\pi/360 - 1]$. Thus, the state rotates 1° with each time step.

(C) Activity of unit 1 versus time for the initial states shown in (B). The initial state was at first held constant (as if W were the identity matrix) to emulate preparatory activity. The dynamics were then released to produce sinusoidal perimovement activity. Asterisks indicate the same two conditions as in (B).

(D) The pattern of initial states (the "preparatory tuning") from (C) is captured by a PD in perimovement space. Analysis and format are the same as for Figure 5C. Traces on each axis plot the time-evolving pattern corresponding to that PC (black and blue traces for units 1 and 2). The pattern at the end of the arrow is the weighted sum of the two PCs, with weights corresponding to the PD.

DISCUSSION

Preparatory activity—along with related forms of delay/memory-period activity—has ranked among the most heavily studied varieties of neural activity. This is not accidental: preparatory activity potentially provides a critical link between mechanisms related to cognition and those related to movement. Yet in motor and premotor cortex, the nature of the link between preparatory and movement activity has remained unclear.

We found that preparatory and perimovement tunings are typically dissimilar. This finding argues against models in which preparatory activity constitutes a subthreshold version of perimovement activity. This finding might initially appear to rule out any straightforward relationship between preparatory and perimovement activity. However, even simple mechanistic models (Figure 8) can reproduce two key features of the data. First, such models reproduce the poor correlation between preparatory and perimovement tuning at the single-neuron level. Second, such models reproduce a deeper relationship: preparatory tuning is captured by a PD in the space describing perimovement activity.

Thus, one interpretation of our data is that preparatory activity exists not to represent specific movement features but to initialize a dynamical system whose evolution will produce perimovement activity (Churchland et al., 2006b; Cisek, 2006b; Fetz, 1992; Schaffer et al., 2006; Sussillo and Abbott, 2009). Consistent with this interpretation, recent studies (Churchland and Shenoy, 2007a; Churchland et al., 2006c; Rickert et al., 2009; Yu et al., 2009) suggest that preparatory activity is optimized to a state appropriate to drive the movement. In this perspective, delay-period activity is truly preparatory in the causal sense of setting up the conditions that will permit the generation of appropriate perimovement activity. Preparatory activity is tuned for parameters such as direction and distance only in an indirect way via its relationship with perimovement activity. In this view, the two central questions—"What is preparatory activity tuned for?" and "How do preparatory and movement activity relate?"—are in fact the same question. This presents a possible escape (Cisek, 2006b) from the unresolved debate regarding what preparatory activity represents. It has been similarly suggested (Churchland and Shenoy, 2007b; Fetz, 1992; Scott et al., 2001; Todorov, 2000) that perimovement activity is best understood via its mechanistic role in producing movement.

Still, it remains possible that preparatory and perimovement activity represent unknown parameters and that they do so with tuning that is largely unrelated between preparation and movement. Preparatory activity may represent complex biomechanical features of the upcoming reach (features not currently measured or guessed at), and perimovement activity may represent similar features in a different way. If so, a space based on

perimovement activity would likely outperform all other tested spaces if none involved an accurate guess regarding the right features. In this view, the success of the perimovement space underscores our ignorance regarding the true factors being represented.

The "representational" and "dynamical systems" views are not necessarily at odds. Even if we accept the representational view, the dynamical systems perspective in some sense has to be true. Suppose preparatory activity represents reach endpoint and perimovement activity represents muscle activity. There must exist lawful and quantifiable dynamics that convert the former representation into the latter. However, such dynamics would need to be fairly complex and nonlinear. Preparatory activity would probably not be readily explained by a PD in perimovement space. Such a PD would certainly underperform the PD in the correct (endpoint) space. Under the representational perspective, if one can identify the correct factors, the PD should perform best in that space. Under the dynamical systems perspective, so long as the dynamics are even approximately linear, the perimovement space should outperform all traditional spaces.

A caveat under either interpretation is that, although the perimovement space performed better on average, there were individual neurons whose activity was better captured in one of the other spaces. It seems plausible that some neurons do truly "represent" known task parameters (e.g., visual target location) even if others play a different role. In particular, responses in rostral premotor cortex (from which we did not record) seem more closely tied to visual aspects of the task (Pesaran et al., 2006; Shen and Alexander, 1997).

In summary, we found that the preparatory tuning of an M1/PMd neuron was typically weakly related to its subsequent perimovement tuning. We then asked which set of variables (which "reference frame") best explained preparatory tuning. The most successful reference frame was a space built to capture the population-level patterns of movement-related activity. These findings are consistent with the view that preparatory tuning serves not to represent specific factors but to initialize a dynamical system whose future evolution will produce movement.

EXPERIMENTAL PROCEDURES

Task Design and Behavior

Animal protocols were approved by the Stanford University Institutional Animal Care and Use Committee. Our basic methods have been described previously (Churchland et al., 2006c). Briefly, monkeys performed delayed reaches on a frontoparallel screen. Delays ranged from 0 to 1000 ms (the exact range varied by monkey). To allow sufficient preparatory activity, we analyzed only trials with delays >400 ms. Fixation was enforced (at the central spot) during the delay for monkey J only.

For single-electrode recordings using the maze task, we employed four sets of 27 mazes each. Each neuron was recorded for one or more of these, but rarely for all. The monkey J data set thus consists of four smaller data sets of ~53 neurons each. Population-level analyses were performed at the level of these smaller data sets and then averaged. For the monkey J-array data set, all 108 conditions were interleaved in the standard way.

Neural Recordings and Data Sets

Penetrations were guided by stereotaxic criteria, the known response properties of M1 and PMd, and the effects of microstimulation. Recordings were medial to the arcuate spur and lateral to—or, in a few instances, within the lateral bank of—the precentral dimple. Few, if any, recordings were made within rostral PMd, near the arcuate sulcus. Analysis of preparatory responses was restricted to neurons with at least 10 spikes/s of preparatory tuning.

Electrode arrays were implanted in PMd and surface M1 (Figure S3). The resulting data set involved simultaneous recordings and much larger trial counts per neuron (2155). However, isolations were only occasionally of the same high isolation quality as for the single-electrode recordings. Many array recordings were of contaminated single-unit isolations or isolations of two or more neurons. Still, some array-based isolations were of high quality, including those in Figures 3E and 3F. Firing rate modulation was typically lower for the array recordings, presumably because of the lack of selection bias. We thus used a lower inclusion criterion: >5 spikes/s of preparatory tuning, which was acceptable given the higher signal-to-noise ratio provided by the higher trial count.

Correlations between Preparatory and Perimovement Tuning

For the preparatory epoch, firing rate was averaged from 200 ms before the go cue until 100 ms after. For the perimovement epoch, activity was averaged from 100 ms before movement onset until 350 ms after. The vector of preparatory rates (one per condition) was correlated with the vector of perimovement rates. Analysis was restricted to neurons with robust perimovement tuning (at least 1.5 times as strong as preparatory tuning). For all other analyses (e.g., those in Figure 5, Figure 6, and Figure 7), neurons were analyzed regardless of the strength of perimovement activity.

Using a PD to Capture Preparatory Tuning

Activity during the preparatory epoch was fit using the model $x_n \approx b_o + Sb$, where x_n is a $c \times 1$ vector of preparatory firing rates (one for each of the c conditions) for neuron n, S is a $c \times k$ matrix containing the location of every condition in a k-dimensional space, b_o is a scalar firing rate offset, and b is a $k \times 1$ vector of coefficients. b and b_o were found using linear regression (Matlab, Mathworks). E.g., if S describes the location of each condition in the space of horizontal and vertical target locations, b might be [1;0] for a neuron with a rightward preference. The matrix S is the same for every neuron, but all other variables differ. The vector b can be represented as $g \times$ PD: a gain times a preferred direction of unit length.

Task Spaces

The "targets + instructed speed" space was three-dimensional: horizontal and vertical target location plus instructed speed (1 for slow, 2 for fast). A similar space, "endpoints + maximum speed," was constructed based on the actual reach endpoints and peak speed. Other task spaces were "initial velocity" (2D), the average horizontal and vertical velocity during the first 150 ms of the reach; "endpoints + orthogonal excursion" (3D), the horizontal and vertical endpoints and the maximum excursion from a straight reach (positive for counterclockwise); "endpoints + viapoint" (4D), the horizontal and vertical endpoints and the horizontal and vertical coordinates of the maximum departure from a straight reach; "endpoints + maximum velocity" (4D), the horizontal and vertical endpoints and peak horizontal and vertical velocities; "endpoints + halfpoint" (4D), the horizontal and vertical endpoints and horizontal and vertical coordinates of the point halfway along the reach trajectory; "segment directions" (6D), the individual horizontal and vertical displacements after dividing the reach trajectory into three segments; and "kitchen sink" (9D and 11D for the speed and maze tasks). This last space was designed primarily as a control for whether high dimensionality alone is sufficient to yield good performance. It included the segment directions, the maximum counterclockwise excursion from a straight line, and the horizontal and vertical location of that maximum excursion. For monkey J, it also included whether any barriers were present (0 or 1) and whether distractor targets were present (0 or 1).

PCA-Based Spaces

To illustrate this approach, consider that reaches for different conditions differ in velocity at most times. To fully characterize such differences, we can create a $c \times 2t$ matrix T, in which each row corresponds to a condition and contains horizontal and vertical reach velocities for all t times. We can then use PCA to reduce dimensionality from $c \times 2t$ to $c \times k$. The resulting matrix, T_{red}, then

captures the differences between conditions in a *k*-dimensional space. Note that PCA is more commonly applied to a matrix in which each row corresponds to a time and each column to a neuron. Dimensionality reduction is then used to denoise and visualize responses (for review, see Churchland et al., 2007). Here PCA is used to parameterize key differences between conditions, rather as one could have done by hand picking *k* features such as peak velocity. See Figure S2 for further illustration.

The perimovement T matrix contained data from 150 ms before movement onset until 400 ms (speed task) or 800 ms (maze task) after onset. Each row contained data from all neurons except the neuron whose preparatory activity we were trying to capture. Responses were not normalized; neurons with weak perimovement activity were included but had little impact on T_{red}.

Each row of the kinematic T matrix included horizontal and vertical position, velocity, and acceleration (150 ms before movement onset until after the reach), normalized to have unity range across times/conditions. Each neuron contributed one kinematic variable (so that the T matrix was of similar size to that for perimovement activity).

Each row of the EMG T matrix contained activity for multiple muscles (same time window as for the neural data). Each muscle's activity was normalized to have a unity range across times/conditions (a necessity, given the arbitrary units of EMG).

PD Performance

Performance was assessed using leave-one-out cross validation. One condition was left out, and we found the PD that best captured tuning for the remaining conditions. We then computed the error between the left-out preparatory firing rate and that predicted by the PD. Performance was quantified as 1 minus the mean squared error (averaged across all conditions, each left out in turn) normalized by the variance of the data. Thus, performance equal to 1 indicates that the PD generalized perfectly. Performance equal to 0 indicates that one could have done similarly well by ignoring the PD and predicting every condition's firing rate to be the mean firing rate. Performance below 0 typically indicates overfitting.

SUPPLEMENTAL INFORMATION

Supplemental Information includes five figures and Supplemental Experimental Procedures and can be found with this article online at doi:10.1016/j.neuron.2010.09.015.

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