4 Neuronal Representations of Bimanual Movements

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4.1 INTRODUCTION

Simultaneous movements of the two arms constitute a relatively simple example of complex movements and may serve to test whether and how the brain generates unique representations of complex movements from their constituent elements, as suggested by Leyton and Sherrington: “[T]he motor cortex may be regarded as a synthetic organ for compounding … movements … from fractional movements.”

This chapter describes studies in which we attempted to investigate how the brain assembles coordinated complex movements from their constituents, using the relatively simple example of bimanual coordination.*

To do so, we have taken a neurophysiological approach, investigating neuronal activity in behaving monkeys. The first question we ask is how the neuronal representations of unimanual movements are combined to form bimanual movements. To answer it, we compare neuronal activity during bimanual movements to the activity observed during performance of their unimanual constituents. This approach may provide preliminary evidence as to whether complex movements are coded differently from simple movements. Second, we need to define an approach to deciphering the neuronal code for complex movements; namely, how we can pinpoint which parameters of neuronal activity contain relevant information about the movement to be executed. Previous work has suggested that in the motor system, rates of neuronal populations are especially informative about the directions of upcoming movements. However, a number of studies, mainly on the visual system, have suggested that temporal correlations between neuronal activities may contain information that is particularly related to the compositionality of the coded items (e.g., the coherence of moving bars). Given that each arm is mainly controlled by the contralateral hemisphere, it is also likely that the temporal relationships between the hemispheres are relevant to bimanual movements.

This chapter summarizes results we have accumulated to answer the above questions, at least partially. We present evidence that bimanual representations indeed exist, both at the level of single neurons and at the level of neuronal populations (in local field potentials). We further show that population rates and dynamic interactions between the hemispheres contain information about the kind of bimanual movement to be executed.

4.2 BIMANUAL-RELATED ACTIVITY OF SINGLE NEURONS IN MOTOR CORTICAL FIELDS

One of the first efforts to resolve the first question electrophysiologically was made by Tanji et al., who trained a monkey to press buttons with the fingers of either hand separately or with both hands together. They recorded cortical neurons in the medial aspect of the frontal cortex, which was called at the time the supplementary

* The term “bimanual coordination” literally means “coordination of the two hands,” yet this term has been used in the literature in studies that relate not only to the coordination of the left and right hands, but also of the left and right fingers, or of the left and right arms. This is also how we use the term in this article.
motor area (SMA*). Tanji et al. found that a substantial fraction of neurons in this area were active during bimanual finger tapping and not during movements of the finger of the right or left hand separately. This finding suggests that there are some neurons that seem to be specific to bimanual movements. Their work appeared after a behavioral study by Brinkman who reported bimanual deficits consecutive to SMA lesion. These and other studies (including clinical reports; for review, see Brust) inspired further studies focusing on the SMA as a major candidate area for the control of bimanual coordination. Neuronal activity in SMA that is specific to bimanual movements has now been described by a number of groups using different tasks, although this specificity has been defined differently by different groups. Neuronal activity during performance of a “drawer pulling task” was tested by Wiesendanger et al., where monkeys performed naturally coordinated movements without specific training. This task involved whole arm movements, where the monkey was required to open a drawer with one hand and retrieve a raisin from it with the other. Bimanual specific SMA activity has also been described by Kermadi et al., although a different study on the same task reported that only a small percentage of neurons was exclusively activated during bimanual movements.

Our group (including the authors of this chapter and Opher Donchin, Orna Steinberg, and Anna Gribova) took another approach in an attempt to capitalize on knowledge from the extensive studies of neuronal activity during arm reaching in a center-out task. In what follows, we summarize a number of studies in which we used a bimanual center-out reaching task to explore neuronal representations of bimanual movements in the cortex.

4.2.1 The Bimanual Task

Macaque monkeys were trained to operate two separate manipulanda, one with each arm. The manipulanda were low weight, low friction, two-joint mechanical arms, oriented in the horizontal plane. Movement of each manipulandum produced movement of a corresponding cursor on a vertical 21” video screen. The movement of each cursor was mapped to its corresponding manipulandum movement such that each millimeter of manipulandum movement yielded one millimeter of movement of the cursor on the video display. The angular origin, 0°, was to the monkey’s right, and 90° was away from the monkey for the manipulandum movement and toward the top of the screen for the display.

A trial began when the monkey aligned both cursors on 0.8 cm diameter origins, as shown in Figure 4.1 (where both cursors, left and right, are at their respective origins) and held them still for 500 msec. For each arm, one of eight peripheral target circles (0.8 cm diameter) could appear at a distance of 3 cm from the origin. This small movement amplitude was chosen to minimize postural adjustments while performing the movements. Movements taking the cursor from the origin to the target were primarily small elbow and shoulder movements. Figure 4.2 presents a few examples of trial types. In unimanual trials, only one target appeared (the upper

* SMA was later divided into SMA-proper and pre-SMA. See Reference 7.
FIGURE 4.1 The monkey sits in a primate chair holding two manipulanda and facing a video screen. Two cursors indicating the location of the manipulanda are shown on the screen (+). Each cursor appears in the corresponding origin. Possible target locations are shown as circles surrounding each origin. (Modified with permission from Reference 15.)

FIGURE 4.2 The behavioral task illustrated by examples of types of trials that were used in the various experiments. The empty circles are not visible to the monkey. The figure displays examples of unimanual movements (upper two rows) to 90° (up) and 270° (down) and bimanual movements (lower row).
two rows in Figure 4.2) and the monkey moved the appropriate arm to bring the corresponding cursor into the target, but did not move the other arm. If two targets appeared — signaling a bimanual trial — the monkey had to move both arms, such that the two cursors were moved into the target circles on the screen.

These structured movements made it possible to study well-controlled bimanual movements of various types. For example, parallel movements and opposite movements (lower row, Figure 4.2) were composed of unimanual movements shown in the upper rows of Figure 4.2. (Figure 4.2 shows only one direction per arm; in all cases additional directions were studied.) Other combinations, where each arm was required to move in a different direction or to cover a different distance, were also tested, as for example the movements shown in Figure 4.2 (bottom-right plot) where the arms move at 90° to each other.

### 4.2.2 Monkey Behavior

Neuronal activity was sampled after the monkeys were over-trained to perform bimanual trials with the two arms starting to move together and reaching the targets together quite accurately. For example, the two monkeys used for the data presented in this section initiated the bimanual movements with average interarm intervals (IAIs) of 16 to 21 msec (SD = 56 to 74 msec) and reached the targets with an average IAI of 5 to 15 msec (SD = 106 to 125 msec). These IAIs are quite short, much shorter than would be required for successful performance of the task, meaning that the monkeys tended, like humans, to synchronize their movements rather than attempting to perform two separate movements. The movements used in the tasks were small (a length of 3 cm for all movement types presented in this section and up to 6 cm in some types of movements for the experiments described in Section 4.5). The hand trajectories made to a given direction were quite similar for different movement types (but not identical; see Figure 4.6). Further, video camera observations and electromyographic (EMG) recordings failed to detect consistent variations in postural adjustments during the arm movements. EMGs of muscles on the forearm, the upper arm, the shoulders, and the back were also recorded simultaneously with neuronal activity (selected sessions). Various analyses were carried out in order to detect changes in neuronal activity that could emerge from different patterns of muscle activation. (For details about specific control measures comparing EMG during unimanual and bimanual movements see Donchin et al.14)

### 4.2.3 Neuronal Recordings in M1 and SMA

Single-unit activity and local field potentials were recorded from homologous sites in the two hemispheres, from the primary motor cortex (M1) and from SMA proper. (For details on recording sites see Donchin et al.14) The activity of 8 to 30 isolated neurons and up to eight local field potential (LFP) channels was recorded each session. The data discussed in this article were recorded from 3 monkeys and included the activity of more than 438 neurons (232 in M1 and 206 in SMA). To detect evoked activity, we tested the firing rate in a 500-msec period from 100 msec
before movement initiation (the average activation onset across responsive units) to 400 msec after movement initiation.

The number of units whose activity varied significantly during performance of the task was high. Eighty-one percent (187/232) of the neurons recorded in M1 and 76% (157/206) of the neurons recorded in SMA were significantly modulated during performance of the task, despite the fact that no selection was made on this basis during the recording sessions.

### 4.2.4 Unimanual Activity of Single Cells

Figure 4.3 shows the activity of two neurons recorded from the left M1 during unimanual movements of the right and the left arm. The neuron in part A of the figure was strongly modulated during right-handed (contralateral) movements, whereas the neuron in part B was strongly modulated during left-handed (ipsilateral) movements. A simple measure for the arm preference of a single cell is the laterality index:

\[
\text{Laterality Index} = \frac{EA_{contra} - EA_{ipsi}}{EA_{contra} + EA_{ipsi}}
\]

(4.1)

The unit shown in Figure 4.3A had a laterality index of 0.59 (indicating contralateral preference); the neuron shown in Figure 4.3B had a laterality index of –0.77 (ipsilateral preference). In both recording areas, about one third of the neurons was activated solely during contralateral movements, whereas approximately one fifth of the neurons was only activated ipsilaterally. Analysis of the distribution of laterality indices in the two areas showed only a slight contralateral preference and a tendency for neurons in M1 to be more contralaterally activated than neurons in SMA. However, a detailed \(\chi^2\) analysis of the results (not shown) revealed no significant differences between M1 and SMA for laterality preferences.

### 4.2.5 Bimanual-Related Activity

Comparisons of the cells’ evoked activity in unimanual and bimanual trials revealed bimanual-related components of activity, which are shown in Figures 4.4 and 4.5. Figure 4.4 shows the activity of one neuron recorded in the right hemisphere. It was inactive when the monkey made unimanual movements toward either 45° or 225° (middle and rightmost columns). However, the same neuron was strongly activated when the two arms moved in parallel toward 225° (row b). It was also active, but less so, in another type of bimanual trial where the two arms moved in opposite directions (row c), but did not respond at all during the other bimanual movements (rows a and d). Figure 4.5 shows another example. Here, the neuron exhibited the opposite effect: the strong responses during unimanual movements of the contralateral arm to 45° disappeared when the same arm moved in a bimanual context with the ipsilateral arm (left column, rows a and c).
Many neurons showed bimanual-related activity that was less dramatic than the two examples above. To quantitatively compare evoked activity during bimanual movements to evoked activity during unimanual movements, it is necessary to correctly compare the evoked activity during performance of a given bimanual movement to the unimanually evoked activities. In the task used here, there were four different bimanual movements performed by the monkey — two bimanual parallel movements and two bimanual opposite movements (the four left-hand plots of Figure 4.4). We chose two types of comparisons.

**FIGURE 4.3** Activity of two neurons recorded in M1 (left hemisphere) during unimanual movements. (A) Neuron with strong contralateral preference (laterality index = 0.59; see Equation 4.1). (B) Neuron with strong ipsilateral preference (laterality index = –0.77). Each horizontal line of dots represents a trial; each action potential is represented by a dot. Trials are aligned on the beginning of movement and sorted by reaction time; the line below each plot indicates the range of target appearance times. The peri-event time histograms (PETHs) (filled black histograms above raster display) have a bin width of 2.5 msec and were smoothed using a filter with a cutoff frequency of 100 msec.
FIGURE 4.4 Bimanual-related activity of a single unit recorded in SMA (from Reference 15). Each row contains PETHs and raster displays depicting the cell activity in one type of trial. The cell only had strong activation during bimanual movements (b, left column) and no activity in unimanual trials (right column is unimanual right; middle column is unimanual left). The direction of movement of each arm is indicated by arrows or a dot if the arm does not move. Trials are aligned on the beginning of the movement (of the first arm) and sorted by reaction time. The target onset is indicated by black squares. The PETH scales are identical in all plots. The movement directions were 45° and 225°.
4.2.5.1 Comparing Bimanual-Evoked Activity to One of the Unimanual Components

Here, the evoked activity for each of the four types of bimanual movements was compared to the activity during one of the unimanual movements that composed it. The question is which of the two unimanual movements forms the appropriate comparison. One possibility is always to compare activity during bimanual movements to activity during a unimanual contralateral movement. However, this choice disregards neurons with an ipsilateral preference in unimanual movements. If the focus is whether there is a difference between maximal activation in bimanual movements and maximal activation in unimanual movements, it is appropriate to compare neural activity during bimanual movements to the neural activity in the

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**FIGURE 4.5** This cell from right SMA demonstrates bimanual related activity opposite to the activity shown in Figure 4.4. The activity evoked during unimanual contralateral movements disappears and is even suppressed (row C) during bimanual movements. The strength of the bimanual-related effect is \(-0.84\). Format is the same as in Figure 4.4. (Reproduced with permission from Reference 14.)

4.2.5.1 Comparing Bimanual-Evoked Activity to One of the Unimanual Components

Here, the evoked activity for each of the four types of bimanual movements was compared to the activity during one of the unimanual movements that composed it. The question is which of the two unimanual movements forms the appropriate comparison. One possibility is always to compare activity during bimanual movements to activity during a unimanual contralateral movement. However, this choice disregards neurons with an ipsilateral preference in unimanual movements. If the focus is whether there is a difference between maximal activation in bimanual movements and maximal activation in unimanual movements, it is appropriate to compare neural activity during bimanual movements to the neural activity in the
unimanual component that evoked the strongest response. This *bimanual-related effect* is quantified by Equation 4.2.

\[
\text{Bimanual-Related Effect} = \frac{\text{E}_a^{\text{bimanual}} - \text{E}_a^{\text{unimanual}}}{\text{E}_a^{\text{bimanual}} + \text{E}_a^{\text{unimanual}}}
\]  

(4.2)

where \(\text{E}_a^{\text{bimanual}}\) is the evoked activity during a bimanual movement, and \(\text{E}_a^{\text{unimanual}}\) is the evoked activity during one of the unimanual movements that composed it (the one that evoked the stronger activity). To test the statistical significance of this effect, we performed four Mann-Whitney tests. Note that the bimanual-related effect is not influenced by the baseline firing rate; it represents a direct comparison of the firing rates in the activation epochs of unimanual and bimanual movements.

The percentage of cells that exhibited significant bimanual-related effects was high in both M1 and SMA: 55% (129/232) in M1, and 52% (107/206) in SMA. The effect could be negative, meaning that evoked activity is stronger in unimanual than in bimanual movements (as in Figure 4.5), or positive, meaning that the bimanual activity was stronger than the unimanual one (as in Figure 4.4). The distribution of strengths of the effect was also similar in M1 and in SMA (verified by a Kolmogorov-Smirnov statistic that showed no significant difference between the distributions of bimanual-related effects in the two areas, \(p > 0.1\)).

### 4.2.5.2 Linear Summation

The second type of comparison posits that the activity in a given bimanual movement should be compared to a combination of the activities during the two unimanual movements that compose it. To conduct this comparison, we tested whether the *normalized evoked activity (NEA)* (the change from the baseline firing) during bimanual movements could be explained by a simple linear summation of the unimanual movements that compose it, which requires that the linear summation hold true for all four bimanual movements. For this purpose, the deviations from linearity in each type of bimanual movement were combined to produce a statistic that was expected to distribute like an \(\chi^2\) with 3 degrees of freedom (specifically, we calculated the sum of the squared differences between bimanual NEA and the sum of the unimanual NEAs divided by the combined variance of the bimanual and unimanual NEAs). We also tested for the possibility that NEA in bimanual movements is equal to NEA during contralateral movements, and for the third possibility that it is equal to NEA during ipsilateral movements. If all three of these null hypotheses could be rejected at \(p < 0.05\), the bimanual activity of this neuron could not be accounted for by the hypothesis of linear summation. Note that our failure to correct for the multiple statistical tests effectively increases the significance level since all three null hypotheses and not just one must be rejected.

The results clearly indicate that for most of the bimanual-related neurons (~80%), the bimanual-evoked activity could not be explained by the linear summation hypothesis. In contrast, for neurons that were not bimanual-related, 60% of the neurons in M1 and 72% of the neurons in SMA failed to reject one or more of the
hypotheses at this level. Their responses might be explained by a linear combination of the unimanual responses.

In an additional analysis, we fit the neuronal activity with a model that attempts to explain bimanual NEA using a more general linear combination of unimanual NEAs (see Donchin et al. for details). This model again fit only a minority of the bimanual-related neurons (19 to 26% in SMA and M1, respectively). In addition, the parameters of the fit for different neurons were not clustered in any way, suggesting that there was no general rule for the combination of unimanual activities. To conclude, both analyses indicated that the majority of the bimanual-related neurons failed to be accounted for by any linear explanation of their bimanual activity.

4.2.6 Comparing Movement Kinematics and Single-Unit Activity

In all the experiments described in this section, the monkey performed short movements (3 cm) that did not require noticeable postural adjustment. Actual observation of the monkey during task performance (aided by video recordings) revealed no postural adjustments or other differences that differentiated movements during bimanual as compared to unimanual trials. Moreover, detailed analyses further demonstrated that for many of the recorded cells, the bimanual related effect was unlikely to be related to differences in kinematics or muscular activity during movements of each arm in unimanual and bimanual contexts. An example is shown in Color Figure 4.6.* The figure depicts the activity of one bimanual related cell, recorded in M1 during performance of unimanual and bimanual trials. Trials in which unimanual and bimanual movements were more similar are shown in the top displays, while trials in which the movements were less similar are shown in the lower displays. The figure demonstrates that selection of trials with similar trajectories in unimanual and bimanual conditions did not lessen the bimanual-related effect, and selection of trials with different trajectories did not increase it. Moreover, the temporal pattern of the neuron’s activity was unaffected by the selection of trials.

4.3 Bimanual-Related Activity in Evoked LFP Activation

Besides the activity of single cells, our physiological recordings also served to measure local field potentials. The LFP is thought mainly to reflect synaptic activity in the area of the recording electrode and thus may be an important tool for investigating population activity. Animal research on field potentials in the motor cortex has focused on the relationship of synchronous LFP oscillations to movements and to single-unit activity.

More recent studies, however, have provided evidence that LFP recorded in the parietal cortex and in the motor cortex contains much more concrete information about behavior than was previously thought. In the study by Donchin et al., we

* See color insert following page 170.
specifically addressed the question of whether the LFP also contains information about bimanual movements.

To observe movement-evoked LFP activity, the LFP signal in repeated trials was averaged by aligning trials on the beginning of movement, producing the movement-evoked potential (mEP). Figure 4.7 shows examples of individual LFP traces, and the average of 100 traces from which the examples were taken. The resulting mEPs seen in the motor cortex have a characteristic shape of positive and negative deflections exemplified in the figure. The strength of an mEP may be calculated in several

FIGURE 4.6 (see color figure) Raster displays and PETHs illustrating the activity from a right M1 cell in four conditions. The activity of the cell during bimanual parallel movements is on the left (red). The activity of the cell during unimanual left movements is on the right (blue). The middle plots show the movement paths of the left hand for bimanual parallel (red) and unimanual left (blue) movements. Row A only contains trials in which the movement path passed through a narrow band (thick green line) located between the origin and the target. Row B only contains trials that did not pass through the band. The green band was placed to maximize the difference between the trajectories in the lower display. PETHs are centered on the beginning of movement, and the scale for all PETHs is the same. The trajectories begin in the upper right and end in the lower left of the frame. Note that the cell activity in bimanual trials (in red) remains similar regardless of the precise trajectories. (Used with permission from Reference 15.)
ways. For the purpose of this chapter we used the total root mean square (RMS) measure of the response (the square root of the integral of the squared mEP).

4.3.1 Movement-Evoked Potentials during Unimanual Movements

Figure 4.8 shows mEPs recorded by one microelectrode in M1, during performance of unimanual movements of the left (contralateral) and the right arm. Interestingly, mEPs, like single cells in the motor cortex, are directionally tuned. (See the example in Figure 4.8, which was particularly tuned for the contralateral arm.) This feature has further implications for the functional anatomy of M1 and the possible existence of clusters with correlated directional preference. Another main feature of the
FIGURE 4.8 Movement-evoked potentials (mEPs) recorded by one microelectrode in M1 during performance of unimanual movements of the left (contralateral) and the right arm. The position of each subdisplay corresponds to the target direction for each kind of trial. The numbers in each rectangle indicate the number of trials used to generate the averaged mEP. Note the directional tuning, in particular to the contralateral arm.
mEPs differed markedly from the evoked single-unit activity. The figure shows a clear contralateral preference in the mEPs. A detailed analysis of all the recording sites in M1 indicated that for most sites, the mEP showed strong contralateral preference. As described above, this was not the case for single-unit spike activity in M1. Interestingly, recording sites in SMA did not share this property. Rather, mEPs in SMA were of similar strength for the two arms with even a slight ipsilateral preference.

4.3.2 Comparing mEPs in Different Movements

To evaluate the mEPs and compare different movement types, Donchin et al. quantified the contralateral preference and the strength of the bimanual-related effect.

\[
\text{Contralateral preference} = \frac{\text{mEP}_{\text{contra}} - \text{mEP}_{\text{ipsi}}}{\sigma_{\text{mEP}}} \quad (4.3)
\]

where \( \sigma_{\text{mEP}} \) represents the standard deviation combined from the mEP in the two movements, the square root of a weighted average of the two variances.

The strength of the bimanual-related effect was generated using a very similar formula:

\[
\text{Bimanual-Related Effect} = \frac{\text{mEP}_{\text{Bimanual}} - \text{mEP}_{\text{Unimanual}}}{\sigma_{\text{mEP}}} \quad (4.4)
\]

where \( \sigma_{\text{mEP}} \) is now calculated using the variances from the evoked response during the unimanual and bimanual movements.

4.3.3 Bimanual-Related Effect in mEPs

Figure 4.9 compares mEPs recorded by one microelectrode during performance of bimanual movements and the corresponding unimanual movements that compose them. (The format is the same as for Figure 4.4.) The difference between the mEP during bimanual movements and unimanual movements was particularly evident in bimanual parallel movements to 315° where the bimanual-related effect value was 2.60 (significant at \( p < 0.001 \)).

Figure 4.10 demonstrates that positive bimanual-related effects characterize the population. The figure shows the bimanual-related effect for all recording sites in both M1 and SMA for the full mEP. In both areas, the RMS of mEP was greater during bimanual movements than during unimanual movements for a vast majority of the recording sites.

To conclude the results of the mEP analysis, we showed that mEPs differ from single-cell activity in two major ways. First, we found a difference in the contralateral preference of M1 and SMA. Second, for nearly all recording sites, bimanual mEPs were greater than unimanual mEPs. This increase was caused mainly by an increase in the positive components of the mEP, particularly the P2 component (see Figure 4.7). This result was different from the single-unit result where the bimanual-related effect manifested as either an increase or a decrease in activity during bimanual movements.
The unidirectional nature of the bimanual-related effect in mEPs that were recorded in each of the two hemispheres supports the hypothesis that the motor cortices represent bimanual movements specifically, requiring neuronal control beyond the simultaneous production of activation represented by the two unimanual control signals. However, while lending weight to the hypothesis above, the result raises its own questions. Is there any physiological explanation for the increased LFP activation during bimanual movements? Is there any functional significance in the result?

**FIGURE 4.9** Example of a recording site in M1 with a bimanual-related effect. Each row shows the mEP in one bimanual movement and the two unimanual movements that comprise it. All plots are at the same scale. (Reproduced with permission from Reference 23.)

**FIGURE 4.10** Distribution of the strength of bimanual-related effects in the mEPs. The histograms show the strength of the effect in the overall RMS of the mEP in M1 and SMA. Note that for almost all sites the deviation is positive.

The unidirectional nature of the bimanual-related effect in mEPs that were recorded in each of the two hemispheres supports the hypothesis that the motor cortices represent bimanual movements specifically, requiring neuronal control beyond the simultaneous production of activation represented by the two unimanual control signals. However, while lending weight to the hypothesis above, the result raises its own questions. Is there any physiological explanation for the increased LFP activation during bimanual movements? Is there any functional significance in the result?
There are three (not mutually exclusive) possibilities that provide an immediate explanation for the increased mEP during bimanual movements:

1. More neurons are active in the area of the electrode.
2. The number of neurons that send inputs (inhibitory or excitatory) to the electrode site increases during bimanual movements.
3. The synaptic activity in the area of the electrode is more synchronized.

The first possibility can be rejected because (as shown in Donchin et al.\textsuperscript{14}) the total spike activity in both M1 and SMA does not increase during bimanual movements. The second possibility is not implausible. While for any particular neuron, maximal bimanual activation may be less than maximal unimanual activation, the sum of bimanual activation across both hemispheres could still be greater than the sum of unimanual activation. For instance, neurons in the left cortex may be more active during movements of the right hand, whereas neurons in right cortex are more active during movements of the left hand, but during bimanual movements both sets of neurons are active. Because M1 and SMA receive inputs from both the contralateral and the ipsilateral cortex, the amount of input that each cortical area receives may be greater during bimanual movements than during unimanual movements. A group investigating the neuronal response as a function of stimulus size in visual cortex found a similar result: induced oscillations in LFP increase with increased stimulus size, whereas single-unit discharge rates may increase or decrease.\textsuperscript{26}

Whether the third possibility can also account for increased mEP size is still unclear. Work on synchronization of LFP oscillations has shown a relationship between synchronized oscillations in the LFP and synchrony in single-unit activity,\textsuperscript{27} but this study did not find increased LFP synchrony during bimanual movements.\textsuperscript{18} Our own study on LFP synchronization\textsuperscript{28} revealed, in only one of the two monkeys tested, a slight transient increase of synchronization around movement onset. The major and consistent effect was a net decrease of synchronization during movements. On the other hand, it cannot be excluded that only a specific subset of neurons increased their synchronization during bimanual movements, which could account for the increased LFP size. In order to clarify this question, the circuitry of the recorded neurons should be known to the experimenter, which was not the case in the previous experiments.

In conclusion, although many questions remain regarding the interpretation of the mEP in LFPs, it seems clear that this signal does contain information about bimanual movements. The fact that the LFP shows a specific bimanual effect demonstrates that bimanual-specific signals also occur on the population level and are not confined to single neurons. In the next two sections, we will deal with the question of how the neuronal activity during bimanual movements may be read out by the system and used for the task of bimanual coordination.

### 4.4 REPRESENTATION OF BIMANUAL MOVEMENTS IN A POPULATION RATE CODE

It has been repeatedly suggested that single neurons in M1 are tuned to the direction of arm movements and that the activity of a population of tuned neurons faithfully
predicts the direction of upcoming movements. However, the existence of bimanual-related activity means that a single neuron may be activated differently when one arm makes the very same movements as part of a unimanual movement or a bimanual movement. This was the rationale for investigating whether the population vector approach could produce reliable movement predictions for bimanual movements as well, in spite of the related bimanual effects. In the study by Steinberg et al., we tested this question by comparing the predictive quality of population vectors for unimanual and bimanual arm movements. The behavioral task was essentially similar to the bimanual task described above. Again, monkeys performed the unimanual center-out task and two classes of bimanual movements (parallel and opposite). Here, however, neuronal activity was recorded during performance of movements in all 8 directions, in all sessions.

For most cells, the directional tuning curve can be approximated by a cosine function, although the method probably overestimates tuning width. In order to allow for comparison of our results with previous studies, we used the cosine approximation for directional tuning when applying the population vector approach. For the same reason, the cells were characterized in terms of preferred direction (PD), the direction of movement to which the cell has the strongest response, and the fit of its tuning to a cosine, estimated by the coefficient of determination ($R^2$). Cells with $R^2$ above 0.7 were defined as “directionally tuned” and the others as “non-tuned.” Again, this value was selected to facilitate comparison with previous PD studies. (See for instance References 13,31,32.)

4.4.1 **Directional Tuning in Unimanual and Bimanual Movements**

As was expected from repeated reports of the arm area in M1, most of the sampled cells (156/212) exhibited broad symmetrical directional tuning around a preferred direction for at least one movement type. (For details, see Steinberg et al.) Interestingly, about one-third of the tuned cells were directionally tuned to movements of the ipsilateral arm ($R^2 \geq 0.7$). Only a few cells (7%) were significantly tuned to all four types of movements. However, the majority of the tuned cells were tuned to more than one type (58%). An example of a cell that was tuned to all four movement types is shown in Figure 4.11.

4.4.2 **Comparisons of Preferred Directions in Different Movement Types**

For the population vector approach, the critical question is whether the PD of motor cortical cells changes during bimanual movements. Recently, evidence has been accumulating that directional tuning and PD may in fact change under certain conditions. Comparing PDs in unimanual and bimanual movements has yielded intriguing results which are summarized in Figure 4.12 (restricted to cosine tuned cells with $R^2 > 0.7$ for the two compared movement types). The figure shows that the PDs calculated from (a) bimanual parallel, (b) bimanual opposite, or (c) ipsilateral unimanual movements were all correlated to the PDs calculated for contralateral...
unimanual movements (the differences for all three comparisons are not uniformly distributed, Rao test, $p < 0.01$). However, the figure also illustrates that the PD of some cells can change substantially, as is most clearly seen in the comparison of the contralateral with the ipsilateral tuning (in unimanual trails).

### 4.4.3 Population Vectors Predict Bimanual Movements Well

In order to be able to calculate population vectors (PVs), Steinberg et al.\textsuperscript{29} first estimated the PD of each cell as a constant, using an estimated best-fit PD taken from all four movement types. To construct separate population vectors for the two
arms, the population of sampled cells was divided into two subpopulations, guided by the hypothesis that bimanual movements are generated by two separate (although possibly coordinated) neuronal networks. The division into two subpopulations was motivated by two different approaches. The first natural choice was to divide the cells according to the hemisphere in which they resided. Color Figure 4.13A show PVs, for movements in 315º, where each pair was generated by the two subpopulations, one from the left hemisphere (for the right arm, in blue) and one from the right hemisphere (for the left arm, in red). The figure shows PVs for four types of movements. The two plots on the left show the prediction for unimanual movements. Note that for unimanual movements, PVs were also obtained for the non-moving arm. Although very small, these PVs did not point in random directions, but were

**FIGURE 4.12** Comparison of PDs in different movement types. The figure shows the distributions of differences in PDs, comparing the PD during unimanual movements of the contralateral arm to (from top to bottom) bimanual parallel, bimanual opposite, and ipsilateral movements. Only cells with $R^2 \geq 0.7$ in both movement types were included in this analysis. $N$ represents the number of cells included in each plot. (Reproduced with permission from Reference 29.)
generally aligned with the direction of the moving arm. PVs for bimanual movements are shown on the right side of the figure. Color Figure 4.13B shows predictions guided by the second approach. Here, cells were selected for each arm on the basis of their activation, under the assumption that each cell can be characterized by its “preferred arm” (PA) — i.e., the arm for which unimanual movements evoked the strongest activity — regardless of the hemisphere in which it resides.

PVs for movements in the direction of 315º generated by “PA selection” of sub-populations are shown in Color Figure 4.13B. For this specific direction, the PA-based sub-populations seem to represent the direction of simultaneous movements of the two arms somewhat better than selection by the hemispheric locations of the cells. Also, the PVs for the nonmoving arm are a little smaller in Color Figure 4.13B as compared to Color Figure 4.13A. For unimanual movements, this is an inevitable result of the reselection, but the improvement in the bimanual movements is not a trivial result. Nevertheless, when examining the PVs for all movement directions, it was impossible to demonstrate that the accuracy of PA-based PVs is higher than that of hemisphere-based PVs.

To conclude, these results show that large enough populations of neurons contain enough information to simultaneously encode for the direction of movements of the two arms in bimanual movements, despite the bimanual specific activity changes. Cells were divided into two subpopulations, either by hemisphere or by their arm preference. Even though the latter division “replaces” approximately a quarter of the cells in the
contralateral hemisphere with cells from the ipsilateral one, the PVs calculated in bimanual movements from this division are not less accurate than PVs calculated when dividing by hemisphere. This result further supports the notion that both hemispheres are active and contribute to execution of both unimanual and bimanual movements.

Exactly how the two hemispheres interact and collaborate with each other was the subject of two additional studies, described below.28,34

4.5 NEURONAL INTERACTIONS AS A POSSIBLE MECHANISM FOR MODULATION OF BIMANUAL COORDINATION

Cortico-cortical connections through the corpus callosum are a major candidate for mediating bimanual coordination. The effect of callosotomy on the nature of bimanual performance has been repeatedly demonstrated.35–37 However, little is known about the physiological basis of the processes mediated by the callosum. A recent modeling work by Rokni et al.34 studied the related nonlinear bimanual effects described above and proposed a mechanism of callosal inhibition to explain this effect. Cardoso de Oliveira et al.28 addressed this question experimentally by simultaneous recordings from multiple sites within the arm area of the motor cortex in both hemispheres. For technical and statistical reasons, studying temporal correlations between single units is problematic when firing rates are relatively low and the number of similar trials is limited (as is the case in the experiments we describe here). However, LFP correlations turned out to be quite useful, as described below.

4.5.1 Time-Averaged Correlations

The time-averaged correlation method has been used to study neuronal interactions for many years.38,39 This measure was calculated here for LFP signals using Equation 4.5, which defines the correlation coefficient (CC) for different temporal delays (τ) in a single trial of duration T (also called the correlogram):

\[
CC(\tau) = \frac{\sum_{t=1}^{T} \left( LFP1(t) - \overline{LFP1} \right) \left( LFP2(t+\tau) - \overline{LFP2} \right)}{\sqrt{\sum_{t=1}^{T} \left( LFP1(t) - \overline{LFP1} \right)^2 \sum_{t=1}^{T} \left( LFP2(t+\tau) - \overline{LFP2} \right)^2}}
\] (4.5)

where \( LFP1(t) \) and \( LFP2(t+\tau) \) are values of LFPs from two electrodes, at times \( t \) and \( t+\tau \). \( LFP1 \) and \( \overline{LFP1} \) are the corresponding average values of the two channels across the measurement time T (trial duration).

The analysis was performed separately for two epochs in each trial.

1. Hold period. An interval of 500 msec before movement onset during which the monkey held its hands stationary at the origins and waited for the target (or targets) to appear. During this period the monkey could not predict the type of movement (bimanual or unimanual) or its direction.
2. **Movement period.** The correlation during a given type of movement was calculated for a time window of 1250 msec, from 250 msec before until 1000 msec after movement onset, an interval that included movement preparation and execution.

The resulting correlogram may be affected both by similar evoked responses (similar mEPs) and by possible trial-wise interactions between the single trial signals. A typical way of distinguishing between these two features is to calculate a “shift predictor” to approximate the correlation between the averages, and then subtract it from the correlograms to estimate the “pure” trial-wise correlation. Examples for such correlograms, obtained from the hold period and from the movement period (during performance of bimanual trials) are shown in Figure 4.14. On the diagonal of each plot are the autocorrelograms of the LFPs in each of the sites. The result depicted in the figure is highly typical in three ways.

![Figure 4.14](image_url)

**FIGURE 4.14** Time-averaged trial-by-trial cross-correlations among all simultaneously recorded LFPs from one recording session, analyzed during the *hold period* (A), and during *bimanual symmetric* movements to the front (B). Autocorrelations are shown along the diagonal. From each correlogram the shift predictor has been subtracted. Straight horizontal lines indicate a confidence limit for significant correlations based on the standard deviation of the shift predictor. Note that the correlations between the hemispheres are much smaller than those within the same hemisphere. As for the correlations within each hemisphere, note that there are clear correlation patterns. Oscillations are in the gamma range in the right hemisphere and in the alpha range in the left hemisphere. However, there are no differences between corresponding correlograms in the different behavioral conditions (A and B). (Reproduced with permission from Reference 28.)
First, the correlations between the hemispheres are significantly smaller than the correlations within the same hemisphere, suggesting that interhemispheric interactions are less intense than intrahemispheric ones. This is in agreement with EEG studies, which have reported only weak interhemispheric correlations. Although weak, many correlations recorded between the hemispheres were statistically significant.

Second, the LFP correlations may show distinct and different correlation patterns. Figure 4.14 shows an extreme example in which all correlograms (auto and cross) in the left hemisphere show oscillatory patterns, while the pattern of correlations in the right hemisphere shows little if any oscillatory activity.

Third, in spite of the clear correlations, the vast majority of the time-averaged correlations were not influenced by behavior, such as the example in Figure 4.14, which fails to show any significant difference between the hold period and the movement period.

4.5.2 Time-Resolved Correlations

In order to address the possibility that movement-related changes in correlation occurred on a faster time scale, and thus may have been averaged out in time-averaged correlations, Cardoso de Oliveira et al. modified the joint–pen–stimulus–time–histogram (JPSTH) technique developed by Aertsen et al. in order to be able to detect short-term modulations of correlations in relation to specific events. The method was adapted to the analog LFP signal using Equation 4.6:

$$CC(t_1, t_2) = \frac{\sum_{n=1}^{N} \left( LFP_{1n}(t_1) - \bar{LFP}_{1}(t_1) \right) \left( LFP_{2n}(t_2) - \bar{LFP}_{2}(t_2) \right)}{\sum_{n=1}^{N} \left( LFP_{1n}(t_1) - \bar{LFP}_{1}(t_1) \right)^2 \cdot \sum_{n=1}^{N} \left( LFP_{2n}(t_2) - \bar{LFP}_{2}(t_2) \right)^2} \quad (4.6)$$

where $t_1$ is the time bin from LFP1, $t_2$ is the time bin from LFP2, and $n$ is the $n$-th trial out of a total of $N$. A bar over LFP1 or LFP2 in Equation 4.3 indicates that the mean should be taken across trials (thus, $\bar{LFP}_1$ and $\bar{LFP}_2$ are $mEP_1$ and $mEP_2$). The result is a matrix of $N \times N$ bins constituting all possible time delays between LFP1 and LFP2. The values corresponding to the simultaneous (zero-delay) correlations fall along the main diagonal of this matrix. Color Figure 4.15 shows joint peri-event time correlogram (JPETC) matrices displayed using a color-coded scale. Time progresses from the bottom-left to the top-right corner such that the value of $t_1$ (the time index of the first LFP) increases along the x-axis and the value of $t_2$ (the time index of the other LFP) increases along the y-axis. The bin-wise significance of the correlation coefficients in the JPETC was determined by testing the hypothesis that the correlation coefficient was 0, using a standard t-test. The JPETC in the figure shows an epoch starting 750 msec before movement onset and continuing to 1000 msec after movement onset. Using a time resolution of 2.5 msec, the matrix dimension size is 700 $\times$ 700 bins.
Unlike the time-averaged correlation, the JPETC revealed movement-related modulation of correlations in a majority of electrode pairs. The example shown in Color Figure 4.15 illustrates a case of two recording sites from different hemispheres, where the LFP correlation at zero-delay (on the main diagonal) increased near movement onset (right-side matrix, increased correlation at just the time of movement onset). Interestingly, the same two sites did not show a similar increase when the movement tested was unimanual (left matrix). (Note that the bimanual and unimanual trials were randomly interleaved in the experiment.) This figure illustrates two main results that were consistent across the whole data sample: (1) unlike the time-averaged correlation, the JPETC method revealed movement-related modulation of correlation; (2) the modulations of correlation strength revealed by the JPETC could be movement-specific.

Color Figure 4.15 shows an example where the correlation increased during the movement period. About half (40 to 60% in different hemispheres and monkeys) of the pairs contained significant increases of correlation in relation to movements. However, in even more cases the correlation decreased. Color Figure 4.16 shows a typical example where the correlation was high during the hold period (lower left part of the diagonal in the matrix) and decreased near movement onset. Decreases
of correlation during movement were detected in the majority of the diagonals tested (60–80% in different hemispheres and monkeys; note that both increases and decreases could occur in the same JPETC at different times).

In contrast to the time-averaged correlations, in which intrahemispheric correlations were stronger than interhemispheric ones, the movement-related modulations of correlations (detected by the JPETC) were as strong and as frequent for interhemispheric as for intrahemispheric sites. The changes in correlations, including correlations across hemispheres, were associated with both bimanual and unimanual movements.

Interestingly, the typical time courses of increases and decreases of correlation differed from each other. Figure 4.17A depicts, for all the JPETCs in one monkey, the total count of occurrences of significant increases (upward) and decreases (downward) of correlation as a function of time around movement onset. Note that the onset of both increases and decreases is similar at approximately 200 msec before movement, corresponding to a time when the targets had already appeared on the screen. Increases in correlation were sharply peaked around movement onset (during movement planning and initiation). In contrast, decreases in correlation were more broadly distributed and occurred preferentially during the movement. Since the decreases were more common and stronger than the increases, the net correlation change after movement initiation was a decrease of correlation, as shown in Figure 4.17B, depicting the grand average of the correlation strength.

**4.5.3 CAN MODULATION OF INTERHEMISPHERIC INTERACTIONS BE RELATED TO BIMANUAL COORDINATION?**

The changes described above were found for interhemispheric as well as intrahemispheric correlations, in all movement types, with similar temporal profiles. They
leave unanswered the intriguing question of whether these changes are related to the level of coupling between the two arms. What, if anything, characterizes neuronal interactions in relation to bimanual movements? We found that two aspects of neuronal interactions could be related to bimanual coordination.

First, decreased correlations are found with relative uniformity in all movement types, and are an oft-reported phenomenon in population activity. The different time course of increased and decreased correlations could explain the behavioral finding that bimanual movements are most closely coupled at their initiation and are progressively desynchronized during movement execution. The fact that this temporal progression of bimanual decoupling occurs both in symmetric as well as in nonsymmetric movements is consistent with our finding that decreased correlations were found for all bimanual movement types.

FIGURE 4.17 Movement-related modulations of correlation. Plots A and B show results from all JPETC diagonals in all movement types. (A) Rate of occurrence of increases (upward plot) and decreases (downward plot) of correlation as a function of time around movement onset. Deviations were detected by comparing each time bin in the JPETC diagonals to the hold period. The number of significantly deviating correlations in each time bin is plotted on the y-axis. The vertical dashed line at time 0 indicates movement onset. The horizontal dashed line indicates the average level of randomly occurring deviations in correlation during the hold period. (B) Grand average of the correlation at different time bins around movement onset expressed in correlation coefficients. The graph shows that the result of the increases and decreases shown in A is a net decrease in correlation during movement execution. The vertical dashed line indicates the time of movement onset. The horizontal dashed line shows the average level of correlation during the hold period. (C) Average normalized size of significant increases of correlation between hemispheres revealed within the JPETC diagonals during different unimanual (open bars) and bimanual (black bars) trial types. Note that increased correlations in bimanual symmetric movements are higher than in all other types of movements (marked by three stars; Wilcoxon rank sum test, $a < 0.001$). Lines at the end of each bar represent the standard error of the mean.
Second, comparing the statistics of significant increases in correlations in inter-hemispheric versus intrahemispheric pairs revealed that interhemispheric correlations were consistently related to the degree of bimanual coupling, whereas the intrahemispheric correlations were not. Figure 4.17C shows a comparison of the normalized average of interhemispheric correlation increases in unimanual, bimanual symmetric, and bimanual nonsymmetric movements. The figure clearly demonstrates that symmetric bimanual movements were accompanied by significantly greater increases in interhemispheric correlations than asymmetric bimanual or unimanual movements. This was not true for pairs from the same hemisphere. At the same time, we found that the velocities of the two arms were more strongly correlated with each other in symmetric than in asymmetric bimanual movements (see Cardoso de Oliveira et al.28). This finding suggests that interhemispheric correlations in particular contribute to interlimb coupling and aid in the production of similar movements of the two arms (bimanually symmetric movements). By the same token, interhemispheric coupling may underlie the difficulties we have in producing asymmetric movements. The significantly weaker correlation increases that we found during asymmetric movements may be the result of an active process that reduces coupling, and the residual correlations may be a neural correlate of our inability to completely decouple our arms.

The idea that interhemispheric correlations are related to bimanual coupling has also recently been supported in a study by Serrien et al.,53 who showed that the stability of bimanual cyclic movements is related to the strength of interhemispheric correlations. This idea is also in line with the finding that split-brain patients (in which the callosal connections have been destroyed) are better than normal individuals in highly asymmetric bimanual tasks.35,36 Thus, the findings are consistent with the view that interhemispheric correlations reflect neuronal interactions that serve to generate coordinated motor plans for the two hands. The strength of “cross-talk” between the hemispheres may determine the level of coupling between the arms. The time course of correlation changes lends further support to this notion. Correlation increases usually began before movement onset. It is thus feasible that they are related to movement programming or preparation rather than execution. This would be consistent with the observation that motor cortical, but not cerebellar, areas are activated during imaginary bimanual movements.54 Also, interlimb cross-talk occurs even when a movement is not actually executed, such as when it is only imagined,55 or when a limb has been amputated.56 Like the increased correlations described here, cross-talk between two simultaneously planned movements occurs during a transient phase associated with the process of movement preparation.57

4.6 CONCLUSION

While we have a long way to go before we can fully understand how the coordination between simultaneous bimanual movements takes place in the brain, the work summarized here provides insights into the neuronal mechanisms involved. It demonstrates that single neurons and the population of neurons in motor cortical fields contain activity evoked specifically when bimanual movements are performed. This modulation of directionally tuned cells during bimanual movements does not interfere with the population rate-code of movement directions, since the population still
faithfully predicts both components of a bimanual movement. In addition to rate modulations, our findings indicate specific temporal patterns of activity that are related to the coordination between arm movements. Transient increases of activity correlations are consistently related to the symmetry and correlation of the movements of the two arms. This relation was found solely for sites in different hemispheres. We conclude that flexible interhemispheric correlations may be a neuronal basis for achieving appropriate coordination of the individual movement components.

REFERENCES


