Synchronization in Monkey Motor Cortex During a Precision Grip Task. I. Task-Dependent Modulation in Single-Unit Synchrony

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Baker, S. N., R. Spinks, A. Jackson, and R. N. Lemon. Synchronization in monkey motor cortex during a precision grip task. I. Task-dependent modulation in single-unit synchrony. J Neurophysiol 85: 869–885, 2001. Neural synchronization in the cortex, and its potential role in information coding, has attracted much recent attention. In this study, we have recorded long spike trains (mean, 33,000 spikes) simultaneously from multiple single neurons in the primary motor cortex (M1) of two conscious macaque monkeys performing a precision grip task. The task required the monkey to use its index finger and thumb to move two spring-loaded levers into a target, hold them there for 1 s, and release for a food reward. Synchrony was analyzed using a time-resolved cross-correlation method, normalized using an estimate of the instantaneous firing rate of the cell. This was shown to be more reliable than methods using trial-averaged firing rate. A total of 375 neurons was recorded from the M1 hand area; 235 were identified as pyramidal tract neurons. Synchrony was weak (mean \( k^i = 1.05 \pm 0.04 \) (SD) but widespread among pairs of M1 neurons (218/1359 pairs with above-chance synchrony), including output neurons. Synchrony usually took the form of a broad central peak [average width, 18.7 ± 8.7 (SD) ms]. There were marked changes during different phases of the task. As a population, synchrony was greatest during the steady hold period in contrasting to the averaged cell firing rate, which was maximal when the animal was moving the levers into target. However, the modulation of synchrony during task performance showed considerable variation across individual cell pairs. Two types of synchrony were identified: oscillatory (with periodic side lobes in the cross-correlation) and nonsynchronous. Their relative contributions were quantified by filtering the cross-correlations to exclude either frequencies from 18 to 37 Hz or all higher and lower frequencies. At the peak of population synchrony during the hold period, about half (51.7% in one monkey, 56.2% in the other) of the synchronization was within this oscillatory bandwidth. This study provides strong support for assemblies of neurons being synchronized during specific phases of a complex task with potentially important consequences for both information processing within M1 and for the impact of M1 commands on target motoneurons.

INTRODUCTION

Most studies analyzing the function of single CNS neurons have considered a neuron’s output to be its firing rate, averaged over some relatively long, behaviorally relevant time period, such as the time needed to execute a movement. In contrast to this idea, some more recent work has suggested that information may be encoded in the timing of individual neuronal spikes, specifically in the synchronous discharge of small assemblies of neurons (Abeles 1991; Gerstein et al. 1989). As interest in this concept increases, a number of different variants of it has been proposed.

Softky and Koch (1992) suggested that the interspike interval distributions seen for cortical cells are too variable to be explained by the action of integrate-and-fire neurons but were more consistent with neurons acting to detect coincident inputs. A theoretical means by which information could be reliably transmitted over weak synaptic linkages using such short-term synchrony was proposed by Abeles (1991). This “synfire chain” theory provides a rigorous description of how neural synchrony could be used by the brain. It assumes synchrony to within a millisecond or so.

To date, most studies of neural synchrony in cortex have failed to provide evidence for the very high level of temporal precision proposed by the synfire chain hypothesis. Central peaks in cross-correlation histograms between pairs of neurons have a width of around 10–30 ms in visual (Eckhorn 1994; Singer and Gray 1995) or motor cortex (Baker et al. 1994; Fetz et al. 1990; Matsumura et al. 1996; Smith 1989; Smith and Fetz 1989). Several reports have suggested that broader synchrony of this kind may also play a role in neural processing (Baker et al. 1997; Singer and Gray 1995; Vaadia et al. 1995). During performance of the precision grip task, Baker et al. (1997) showed that synchrony in the primary motor cortex (M1) might be of functional importance because it was strongly modulated during different phases of the task and because it was coherent with synchronous activity present in the hand muscles carrying out the task. These findings raise the issue of how neurons become synchronized during such a task; of particular interest is the synchronous behavior of identified output neurons because these may be involved in coherence between activity in cortex and in muscle (Baker et al. 1997; Conway et al. 1995).

The assessment of changes in synchrony during a dynamic task is not easy because the interpretation of the cross-correlation histograms used to detect synchrony is complicated by task-related modulation in firing rates. These nonstationarities can lead to features in the cross-correlation histograms that do not relate to synaptic interactions between the two neurons concerned (Perkel et al. 1967). Existing methods of compensating for this include the “shuffle-predictor” (Engel et al. 1990; Perkel et al. 1967) and the “joint peri-stimulus time histogram” (JSPSTH) (Aertsen et al. 1989), in which the activity
of two units is cross-correlated to produce a predictor of any correlation due to firing rate changes alone. These techniques are unsatisfactory because they assume that stimulus or task-related firing rate changes are stereotyped and resemble the trial-averaged histogram on every component trial. Trial-to-trial variations in firing rates, common in the motor system, then lead to spurious correlations (Brody 1999; Pauluis and Baker 2000).

Grün (1996) proposed a method ("unitary events") for detecting synchronous neural discharges and determining their significance (see Riehle et al. 1997). However, this technique also does not assign significance to synchronous events appropriately if neural firing rates show variation about the trial-averaged mean (Pauluis and Baker 2000), and only a fixed window of synchrony can be investigated unlike cross-correlation-based techniques, which allow the full time course of synchrony to be characterized. Pauluis and Baker (2000) presented a novel means of estimating a neuron’s firing rate in a single trial and showed that this successfully corrected for correlations introduced by firing rate variability.

The objectives of this study were to apply this new method of assessing changes in synchrony during different phases of the task and thereby provide a measure of synchrony that was independent of changes in firing rate. We generated a time-resolved cross-correlation function similar to the JPSTH of Aertsen et al. (1989) but used the instantaneous firing rate estimate of Pauluis and Baker (2000) to correct for firing rate modulation during the period of interest. Using this method, we describe the different forms of synchrony that can be observed between pairs of simultaneously recorded monkey M1 neurons during performance of the precision grip task. We paid particular attention to output neurons [identified pyramidal tract neurons (PTNs) or cortico-motoneuronal (CM) cells] because of their possible involvement in the coupling of synchrony between sensorimotor cortex and muscle referred to above. We used a multiple, 16-channel, single-unit recording method that allowed us to sample cell pairs lying either very close together (about 300 µm apart if on adjacent electrodes) or relatively distant (up to 2.4 mm apart).

By sampling a large number of M1 cell pairs, we demonstrate profound changes in M1 synchronization with task performance, suggesting that synchrony at moderate time scales may play a role in information processing within the motor cortex.

**METH ODS**

Experiments were performed on two adult purpose-bred female *Macaca mulatta* monkeys (6.1 kg, monkey 33; 5.1 kg, monkey 35).

**Behavioral task**

The task required that two independently pivoted spring loaded levers were squeezed between index finger and thumb and held in electronically defined position windows (Lemon et al. 1986). Finger and thumb levers both had to be held correctly within their own respective target zones for 1 s, after which a tone (0.2 s) signaled to the monkey that it could release to obtain a reward. The onset of this "end hold" tone was used as a behavioral marker to which analysis was aligned (see following text).

Since the focus of this paper is to investigate task-related effects, it was considered important to ensure that the trials analyzed were as homogeneous as possible. Thus for analysis, we selected only those trials in which the monkey moved the levers directly into the target zone, held steadily for 1 s, and then released the levers immediately after the end hold marker. Such an ideal trial is shown in Fig. 1A. Departures from this ideal were excluded by the selection process illustrated in Fig. 1. We measured the moment when both finger and thumb lever position signals left baseline over the 2-s period before

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**FIG. 1.** Selection of trials from the precision grip task. *A:* position of finger and thumb levers during a single trial. *B:* lever velocity. Dashed line in *B* shows the 0.8-s-long period during which the velocity signal was compared with the threshold indicated by the line; velocity above this limit indicated correction movements during the hold period, leading to the trial being rejected. *C:* histogram of the times of first movement and return to baseline over 367 trials performed in 1 session. All times are relative to the end hold marker (time 0). Vertical dotted lines indicate region within which trials were accepted. *D* and *E:* overlain position signals from 10 accepted trials and from 10 rejected trials, respectively. Asterisks show rapid corrective movements causing trials to be excluded due to high lever velocity. *F* and *G:* averaged position traces for accepted (*n* = 197) and rejected (*n* = 170) trials, respectively, for this recording session. *H:* standard deviation time course of position traces for accepted (*F*) and rejected (*G*) trials. Thick lines, thumb position; thin lines, finger position. Vertical dotted lines in *A* and *B* and *D--G* mark the time of the end hold marker.
end hold, and the moment when the position signals returned to baseline during the 2 s after end hold. Histograms of the distributions of these times for a typical recording session are shown in Fig. 1C. We excluded trials in which either thumb (thick lines) or finger (thin lines) lever left baseline earlier than 1.5 s before the end hold marker; this removed trials in which the monkey failed to enter the target directly. We also excluded trials with a return to baseline later than 0.5 s after end hold, i.e., those in which the monkey did not release the levers promptly after the end hold event. These time limits are shown by vertical dotted lines in Fig. 1C.

Although the target zones were quite narrow (2–3 mm for each lever), they nevertheless allowed some small lever movements during the hold period without transgressing the imposed limits. These movements fell into two categories: first, the monkey often produced a slow drift in lever position during the hold period (see Fig. 1, D and E). We have often observed such behavior on this task. Because all of our published work to date has included such trials in the analysis (Baker et al. 1997; Lemon et al. 1986), we made no attempt to exclude such trials here. While we will refer throughout this paper to the “hold” period of our task, it should be remembered that this period does sometimes include these slow drifting movements. Second, in a few trials, the animal made small, rapid corrective movements to the lever position during the hold period. Examples are marked by asterisks in Fig. 1E. We excluded such trials by calculating the lever velocity signals during the 0.8-s period prior to end hold (Fig. 1B). Trials in which either of the instantaneous lever velocities exceeded 10 mm/s (horizontal dotted line, Fig. 1B) were excluded.

Figure 1D shows lever position signals from 10 trials that were accepted by this protocol, and Fig. 1E shows 10 that were rejected, all from the same recording session as illustrated in Fig. 1C. Figure 1F shows averaged lever position signals for all accepted trials (n = 197) and Fig. 1G for rejected trials (n = 170). Figure 1, H and I, shows the standard deviation time course of the lever position signals for the accepted and rejected trials. The procedure clearly improved the consistency of the timing of the movements relative to the alignment point. This can be seen by the marked reduction in the position standard deviation in the accepted compared with rejected trials before and after the hold period (arrowheads in Fig. 1, H and I).

All subsequent analysis used only the trials which passed the above selection criteria. Data were analyzed in a standard timeframe of 2 s before to 1 s after the end hold marker. This is the period for which lever position signals are shown in Fig. 1, D and F.

Surgical implant and maintenance

Each animal underwent a series of procedures, under deep general anesthesia (2–2.5% isoflurane in 50:50 O₂:N₂O). In the first, a magnetic resonance imaging (MRI) scan revealed the location and orientation of the central sulcus and stereotaxic location of the pyramidal tract. Further details are given in Baker et al. (1999b). The monkeys received an electromyographic (EMG) implant (see Miller et al. 1993); electrodes were routed subcutaneously to a multipin connector on the animal’s back. After re-training, the monkey then received a headpiece and pyramidal tract (PT) electrode implant. A stainless steel headpiece was attached to the skull to allowatraumatic head fixation (Lemon 1984), and two fine varnish-insulated tungsten electrodes were implanted in the medullary pyramid at stereotaxic coordinates A3 and P2. Their location was confirmed during surgery by magnetic resonance imaging (MRI) scan. Further details are given in Baker et al. (1999b). The monkeys (MRI) scan revealed the location and orientation of the central sulcus and stereotaxic location of the pyramidal tract. Further details are given in Baker et al. (1999b). The monkeys received an electromyographic (EMG) implant (see Miller et al. 1993); electrodes were routed subcutaneously to a multipin connector on the animal’s back. After re-training, the monkey then received a headpiece and pyramidal tract (PT) electrode implant. A stainless steel headpiece was attached to the skull to allowatraumatic head fixation (Lemon 1984), and two fine varnish-insulated tungsten electrodes were implanted in the medullary pyramid at stereotaxic coordinates A3 and P2. Their location was confirmed during surgery by the presence of an antidromic field potential recorded from the surface of the motor cortex and at postmortem by histology. After re-training with head restraint, a recording chamber implant operation was carried out over the hand area of M1. The center of the chamber was at stereotaxic coordinates A13, L18. All surgical operations were followed by a full course of antibiotic (oxytetracycline; Terramycin/LA, 20 mg/kg, Pfizer) and analgesic (buprenorphine; Vettegescic, 10 µg/ kg, Reckitt and Colman Products) treatment.

Both hemispheres were investigated in monkey 33, whereas only the right was studied in monkey 35. To maintain the dura mater in a state that could be easily penetrated for recordings, it was treated regularly with an anti-mitotic to depress fibroblastic wound healing (full details are given in Baker et al. 1999b).

Following the end of the experimental period, the monkeys were killed by an overdose of pentobarbitone (50 mg kg⁻¹ ip Sagatal; Rhone Merieux, Harlow, UK) and perfused through the heart. The cortex and brain stem were removed for histological analysis, and the location of the implanted electrode tips within the pyramidal tract confirmed. All procedures were carried out under appropriate licenses from the UK Home Office.

Recordings

Cortical recordings were made from up to 14 separate microelectrodes using the Eckhorn microdrive (Eckhorn and Thomas 1993) (Thomas Recording, Marburg, Germany). Glass-insulated platinum electrodes (diameter, 80 µm) were inserted into the cortex in a 4 × 4 grid with interelectrode spacing of 305 µm. The height of each electrode could be independently adjusted to record the clearly isolated activity of a single neuron (Baker et al. 1999b). Following preamplification, the signals from each electrode were filtered to split it into local field potential (LFP, 10–250 Hz) and single-unit activity (1–10 kHz). Sampling rates were 500 Hz and 24 kHz for LFP and spikes, respectively. Only spike data are analyzed in this paper; the relationship of spikes to the LFP will be the subject of a future paper. All data were recorded onto digital tape using a 32-channel tape recorder (RX832, TEAC). The data were transferred off-line to a personal computer, where single units were discriminated by principle component analysis on spike waveforms and cluster cutting (Eggermont 1990) using custom-written software. Considerable care was taken to ensure that all trigger events were derived from action potentials from one and the same neuron throughout the analysis period. In particular, we confirmed that the interspike interval histogram did not contain any counts in the first 1–2 ms (see Fig. 2A). The refractory period of neurons means that such short intervals are physiologically impossible and are thus a sign that the discharge of more than one cell has been included in the discriminated events.

Neurons were identified during the experiment as PTNs by antidromic activation following stimulation through the electrodes implanted in the pyramidal tract (Lemon 1984); antidromic thresholds varied from 10 to 400 µA (biphasic current pulse, each pulse, 0.2 ms). The same PTN was re-identified accurately by means of the antidromic collision test several times during the session (Baker et al. 1999b).

Analysis

The basis of the analysis to be presented here is the time-resolved cross-correlation of spike activity in a pair of cortical neurons. This is a function of two variables: the time during task performance relative to a behavioral marker, t, and the lag of a cross-correlation histogram, τ. We designate activity from one of the two cells as the trigger spike and that from the other, the response spike. Let the times of these spikes that occur during the jth trial be represented as T₁ and T₂, where the indices i, k identify the particular spike. Times are assumed to be referenced to the behavioral marker used to align analysis. The binned time-resolved cross-correlation histogram X is then generated by incrementing the contents of bin (Xₘₙ) for all possible pairs of spikes (T₁, T₂), where

\[
\begin{align*}
  n & = \frac{T_1}{w} \\
  m & = \frac{(R_k - T_1)}{w}
\end{align*}
\]
and \( w \) is the bin width used for the histogram. This procedure is repeated for all \( N \) available trials. In practice, \( X_{n,m} \), is computed over a limited grid bounded by the interval before and after the behavioral marker of interest (which determines the range of \( n \)) and the maximum cross-correlation lag to be measured (which determines the range of \( m \)).

If there is no synaptic interaction between the neurons, the form of \( X \) will be determined solely by the co-modulation of firing rate of the two units. On this null hypothesis, \( X \) should therefore tend toward \( \bar{X} \), a predictor formed by cross-correlating the instantaneous firing rates (IFRs) of the two neurons

\[
\hat{X}_{n,m} = \sum_{j} wF_{j}(nw) \cdot F_{j}[n + m]w
\]

where \( F_{j} \) and \( F_{j}' \) are the IFRs for the trigger and response neurons, respectively, during trial \( j \), determined using the technique of Pauluis and Baker (2000). The basis of this technique is to estimate the IFR at a given time as the reciprocal of the interval between the preceding and succeeding spike. The estimate is smoothed by convolution with a Gaussian kernel (a standard deviation of 10 ms was used here). Moments when the firing rate shows an abrupt change are explicitly detected, and care is taken not to smooth across them so as to avoid blurring rapid rate changes. The result is a low-noise estimate of the IFR, which contains no information on the precise timing of the underlying spike train. Features that are present in \( X \), but not \( \bar{X} \), are therefore related to short-term synchronization of the two neurons not to co-modulation of their firing rate (Pauluis and Baker 2000).

This IFR approach has two differences from the JPSTH technique of Aertsen et al. (1989). First, the time-resolved cross-correlation is expressed in terms of time relative to the behavioral marker and cross-correlation lag. The JPSTH is instead expressed in terms of two indices, indicating a time during task performance at which each cell fired. We prefer the present convention since it permits the examination of different time scales for lag (of interest typically to around \( \pm 100 \) ms) and time relative to task performance (here of the order of seconds). Second, the predictor used by Aertsen et al. (1989) is produced by multiplying together the firing rates \( \bar{F} \) of the cells estimated by averaging across trials (the JPSTH)

\[
\bar{X}_{n,m} = w^2 F_{j}(nw) \cdot F_{j}[n + m]w
\]

The essential difference between \( X \) and \( \bar{X} \) is the order of operations: \( \bar{X} \) forms the product, and then sums, whereas \( X \) sums over trials before calculating the product (Pauluis and Baker 2000).

If the binwidth \( w \) is chosen to permit good resolution of cross-correlation peaks, it is likely that each bin of \( X \) will have only a small number of counts (see Fig. 3B). To visualize the time-resolved cross-correlation and make comparisons with the predictor, we therefore smooth \( X \) using a Gaussian kernel (Silverman 1986); in general, the amount of smoothing in the lag and task-time direction should differ due to the different time scales of features in these two directions. Defining \( \sigma_{n} \) and \( \sigma_{m} \) as the widths of the smoothing kernels in each direction, the smoothed time resolved cross-correlation is given by

\[
X'_{n,m} = \sum_{j} \sum_{j'} X_{n+1,m+1} k_{i,j}
\]

where

\[
k_{i,j} = \frac{1}{2\pi\sigma_{n}\sigma_{m}} e^{-i(2\pi x_{n})^2/2\sigma_{n}^2 - i(2\pi x_{m})^2/2\sigma_{m}^2}
\]

and the prime (‘) is used to indicated the smoothed value.

The next stage is to determine the significance of any deviations of \( X \) from \( \bar{X} \). Following Aertsen et al. (1989), on a single trial the number of counts in an unsmoothed bin \( X_{n,m} \) will be either zero or one (if the bin size \( w \) is sufficiently small). It can be easily shown, therefore that the variance of the counts in a single bin of \( X'_{n,m} \) on one trial is

\[
\hat{X}_{n,m}(1 - \hat{X}_{n,m})
\]

Hence summing over all \( N \) available trials, the variance of \( X_{n,m} \) is given by

\[
\hat{s}_{n,m}^2 = N\hat{X}_{n,m}(1 - \hat{X}_{n,m})
\]

However, the situation is complicated by the smoothing operation of Eq. 4. Under the assumption that the adjacent bins are independent, the expected value of \( X_{n,m} \), is given simply by smoothing the predictor \( \bar{X}_{n,m} \) in a similar way to Eq. 4. The variance of this smoothed predictor \( s_{n,m}^2 \) will be given by smoothing \( s_{n,m}^2 \) using weights which are the squares of the weights of Eqs. 4 and 5

\[
s_{n,m}^2 = \sum_{j} \sum_{j'} s_{i,j}(n + m)w
\]

where \( X_{n,m} \) will have an approximately Gaussian distribution (central limit theorem). We can therefore compute

\[
Z_{n,m} = \frac{X_{n,m} - \bar{X}_{n,m}}{s_{n,m}}
\]

which will be normally distributed, with mean zero and standard deviation one, on the null hypothesis that \( X_{n,m} \) equals \( \bar{X}_{n,m} \). Following Aertsen et al. (1989), we then compute a composite “Surprise” measure by

\[
S_{n,m} = \log \left( \frac{\Phi(Z_{n,m})}{1 - \Phi(Z_{n,m})} \right)
\]

where \( \Phi(\cdot) \) represents the cumulative probability for a standard normal distribution. This permits the display on one graph of both periods where there is an excess, and a deficit, of synchronous activity relative to the expected chance level.

Data from one recording session were therefore preprocessed by computing all possible cross-correlation histograms between all cells recorded. Histograms were then inspected for the presence of a correlation peak. For cell pairs showing such features, time-resolved analysis was carried out as in the preceding text with a binwidth \( w \) of 1 ms and smoothing constants of \( \sigma_{n} = 100 \) ms and \( \sigma_{m} = 2 \) ms. The maximum cross-correlation lag computed was \( \pm 125 \) ms. A period of 2 s before to 1 s after the end hold task marker was used. It was often possible to record pairs of clearly discriminable cells on the same electrode. The cross-correlation histogram then exhibited an artificial central trough, due to failure to detect overlapping spikes. In this case, the time-resolved cross-correlation \( X \) was linearly interpolated over the artificially reduced bins.

The Surprise measure \( S \) was displayed for each analyzed neuron pair. Those pairs with no central correlation peak rising above a significance threshold of \( P < 0.001 \) were not analyzed further. The unusually low significance threshold was used to account for the multiple comparisons implicit in testing a two-dimensional Surprise map. Since we used a 3-s-long time axis for the task and a 100-ms-wide smoothing kernel in the time direction, around 30 independent tests were made on the zero-lag row. Using a \( P < 0.001 \) significance level, thus yielded a Bonferroni corrected significance for the entire zero-lag row of at least \( P < 0.05 \).

For cell pairs that did show significant features, we determined lags that enclosed the peak using interactive cursors. In a number of plots, the central peak altered its location during the task period analyzed. In these cases, the cursors were placed to encompass all such sub-peaks.

The strength of short-term synchrony as a function of task performance was assessed from the \( k' \) measure (Ellaway and Murthy 1985). If \( m_{1} \) and \( m_{2} \) are the bins chosen to encompass the central peak, \( k' \) is given by the ratio of the number of synchronous spikes seen to those expected.
The subscript $n$ denotes the dependence on time during task performance.

It was of interest to determine how much of the synchrony between cells was due to rhythmic activity in the bandwidth 18–37 Hz since a number of studies have reported field potentials oscillations in this range (Conway et al. 1995; Kilner et al. 1999b; Murthy and Fetz 1996a,b). The difference between the time-resolved cross-correlation and its predictor, $X_{n,m}^{*} - X_{n,m}$, was treated as an array of cross-correlations, being vertical cross-sections through the two dimensional plot. These individual cross-correlations were filtered using fast Fourier transforms to remove all frequencies between 18 and 37 Hz. This frequency range was chosen based on previous reports (Baker et al. 1997; Kilner et al. 1999b; Murthy and Fetz 1996b) and on frequency domain analysis of the current dataset (E. M. Pinches, S. N. Baker, and R. N. Lemon, unpublished observations). Subtraction of this filtered correlation from the original produced a correlation with only 18- to 37-Hz signals present. These two time-resolved cross-correlations could then be processed in the usual way to measure $k'$ and generate a Surprise display resulting from only nonsynaptic or only oscillatory synchrony.

All analysis was carried out using programs custom written in MATLAB (Mathworks) and Pascal (“Delphi,” Borland).

**RESULTS**

**Database**

Quantitative analysis in this paper is based on recordings from 375 neurons in the hand representation of M1 (175 and 133, respectively, from the left and right hemisphere of *monkey 33* and 67 from *monkey 35*). Most recordings were made in the anterior bank of the central sulcus. Of these 375 cells, 235 (63%) were antidromically identified PTNs with antidromic latencies ranging from 0.7 to 3.7 ms; most had short latencies (less than 1.2 ms). Fourteen neurons in *monkey 33* were further identified by spike-triggered averaging as cortico-motoneuronal cells (E. M. Pinches, S. N. Baker, and R. N. Lemon, unpublished observations). A total of 1,359 cross-correlations were calculated, and of these, 218 (16%) showed significant synchrony between neurons in the task-related Surprise plots. Of the correlated pairs, 33 were recorded on the same electrode; the others were recorded with inter-electrode distances ranging from 305 to 2,400 μm (median, 656 μm). Pairs recorded on the same electrode were significantly more likely to show excess synchrony than those on distant electrodes ($\chi^2$ test, $P < 0.001$). The predominant type of synchrony was a broad peak [mean width, 18.7 ± 8.7 (SD) ms], straddling the origin of the cross-correlation (see Fig. 3A). These peaks, similar to those reported by Smith (1989), were probably due to common synaptic inputs to the neurons (Perkel et al. 1967). When summed over all spikes occurring 2 s before to 1 s after the end hold marker, the strength of synchrony $k'$ was 1.05 ± 0.04. There was a slight, but significant, difference in the strength of synchrony between the two animals (mean $k' = 1.052$ in *monkey 33*; mean $k' = 1.069$ in *monkey 35*; $t$-test $P < 0.05$). Synchrony was significantly stronger between cell pairs recorded on the same, compared with different, electrodes (mean $k' = 1.08$ vs. 1.05, $t$-test $P < 0.001$). Task-related analysis used between 17 and 488 trials selected as described in METHODS; during the period of the task analyzed, the cells with significant synchrony fired between 588 and 37,200 spikes (mean, 10,200).

**Effect of different normalization methods**

Considerably different results were obtained from time-resolved cross-correlation of unit pairs using the two different normalization schemes described in METHODS. Figures 2–4 illustrate this. A single pair of cells is shown that had a clear central peak in the cross-correlation histogram (see Fig. 3A). Figure 2A presents overlaid spike waveforms for these neurons and inter-spike interval histograms, confirming the single-unit nature of the recordings. Both were identified PTNs and both showed an typical pattern of activity during the precision grip task with a phasic increase in firing during the initial movement phase of the task, followed by a period of tonic firing during the task hold phase (Fig. 2, B and C) (cf. Bennett and Lemon 1996).

Figure 3B shows the unsmeared time-resolved cross-correlation between these two PTNs. The small size of the bin-width (1 ms square) means that most bins contain only zero or one spike, and it is impossible to reach any conclusions on the task dependence of the synchronization of the cells based on this plot. However, a good estimate of the underlying spike density can be obtained in the presence of such sparse data using a kernel estimator, which is more efficient than using large rectangular bins (Silverman 1986). The extent of the two-dimensional Gaussian kernel used in the present work is shown in Fig. 3C. Ninety-five percent of the support of this kernel is contained within a box 400 × 8 ms in extent; the relatively large region over which this kernel smooths allows noise-free estimates of the spike density. Following such processing, several features become apparent, as shown in Fig.

**FIG. 2.** A: inter-spike interval histograms, and overlain waveforms of 20 spikes from each of 2 simultaneously recorded pyramidal tract neurons (PTNs), indicating the unitary nature of the recordings. Only discharges falling 2 s before to 1 s after the end hold task marker were used for this analysis. Calibration bars, 200 μs, 100 μV. B and C: dot raster display of cell firing during 50 trials of the task and firing rate, respectively, averaged over all 120 trials available for analysis, smoothed with a Gaussian kernel (standard deviation, 100 ms). The abscissa (which is the same for B and C) represents time relative to the end hold marker of the precision grip task. Both cells showed a phasic burst of firing during the movements just prior to the hold period. PTNs had antidromic latencies (ADLs) of 0.9 and 1.0 ms, respectively, and were recorded 680 μm apart. Analysis based on 6,326 and 9,280 spikes from the 2 cells, and 120 trials selected according to the criteria illustrated in Fig. 1.
There are two regions of high spike density at all lags: one during the initial movement phase (from $-2$ to $-1$ s relative to the end hold marker), and a smaller one at the end of the time frame analyzed (1 s). These regions correspond to periods when the firing rate was elevated (Fig. 2C) and reflect the concomitant increase in chance synchronous discharge. However, in addition to these rate-related effects, a clear peak in spike density around zero lag can be seen, and this was present for all times displayed.

Figure 3, E and F, displays the two predictors for the
time-resolved cross-correlation histogram that were described in METHODS. Both capture the broad changes in spike density, in particular the band of high-density in the initial 1 s displayed. However, there are subtle differences in the magnitude and shape of the features between these two plots.

Figure 4 compares the use of the two predictors in normalizing the time-resolved cross-correlation for the same cell pair as used in Figs. 2 and 3. The left column presents analysis using the predictor $\hat{X}$ of Aertsen et al. (1989), the right column presents analysis using the predictor $\hat{X}$ developed in this paper and based on the neuron instantaneous firing rate (IFR). Figure 4, A and B, shows the difference between the actual time-resolved cross-correlogram and the predictors, divided by the predictor. It can be seen that use of the predictor $\hat{X}$ failed to remove all of the firing-rate-related features such that large areas of the plot are nonzero even at large lags. By contrast, the IFR method successfully removed the correlogram features at large lags such that only the relatively narrow peak around zero lag, reflecting short-term neuronal synchronization, remained. The difference between the two techniques is accentuated by the significance calculation of the Surprise plot (Fig. 4, C and D); wide regions of the time-resolved cross-correlation are above significance at $P < 0.001$ using the predictor based on trial-averaged firing rate (Fig. 4C), whereas only the central peak is consistently significant using the IFR method (Fig. 4D).

Figure 4E plots the differences in the time course of synchrony across the task using the $k'$ measure. This depends on the area above baseline within a measurement window around zero lag (shown by the bracket to the right of the color plots). We expect this measure to be less affected by noise than relying simply on the peak height, which is represented in Fig. 4, A and B, by the color of the zero-lag bins. In addition, if synchrony is detected by coincident excitatory postsynaptic potentials (EPSPs) in downstream neurons, a small “jitter” will be allowable. The peak area, rather than the peak height that represents only temporally precise coincidences, will then be the more functionally meaningful measure. Figure 4E shows that the relatively subtle differences in the features plotted in Fig. 3 lead to major discrepancies in $k'$, with profound implications for the estimated extent of task-related synchrony. Measurements of $k'$ derived from Fig. 4, A (red, JSPTH method) and B (black, IFR method), are superimposed. The magnitude of synchrony relative to background was consistently overestimated by the trial-averaged firing-rate predictor. In addition, the two methods revealed modulation in synchrony with task performance that had a very different time course: in particular, the trial-averaged method shows a sharp increase in synchrony around 1 s before the end hold marker (arrow in Fig. 4E) that is not present with the IFR normalization.

Figure 4F indicates why the trial-averaged firing rate method yields unreliable results in this case. The firing rate of the two PTNs on single trials is displayed as a scatter plot. The firing rate was measured over the period 2 to 1 s before the end hold marker, which included the phasic discharge at trial onset (see Fig. 2, B and C), i.e., the region where features relating to firing rate modulation could be seen in the time-resolved cross-correlation plots (Fig. 3, D–F). The firing rate of both cells varied over more than a twofold range from trial to trial; this was the case even though analysis was restricted to trials with a similar movement profile using the methods described in Fig. 1. This variability in discharge rate was weakly, but significantly, correlated between the two cells ($r^2 = 0.12, P < 0.001$).

The firing of the two neurons was thus not independent. This nonindependence of single trial firing rates leads to erroneous assignment of significance to regions of the time-resolved cross-correlation. By contrast, the IFR method removes this effect, leaving above significance only genuine synchronization due to synaptic interactions between the cells.

Population changes in firing rate and synchrony with task

Figure 5 shows population data for each of the two animals in which experiments were carried out. Figure 5A shows a normalized time-resolved cross-correlation, calculated using the sum of the actual and predicted measures for all cell pairs that showed significant features. Figure 5B gives a display of Surprise similarly calculated. In both animals, it is clear that synchronization is strongest during the hold period (−1 to 0 s relative to the end hold marker); however, there is a clear peak at zero lag for all parts of the task. Additionally, synchrony during the hold period appears to be oscillatory in nature with the zero-lag peak flanked by troughs and subsidiary peaks. The oscillation period (c. 40 ms), agrees with our previous finding of 20- to 30-Hz oscillations in LFPs during this phase (Baker et al. 1997). Further investigation of this oscillatory synchrony is carried out in Figs. 7 and 8.

Figure 5C plots the average firing rate of all cells recorded in the two animals as a function of task performance. The pattern of discharge was similar in both animals: firing rate was highest during the initial movement phase, reduced during the hold phase, and then rose again as the monkey released the levers (cf. Bennett and Lemon 1996; Davis and Lemon 1997; Lemon et al. 1986) (see Fig. 2B).

Figure 5D shows the time course of the measure $k'$ (ratio of synchronous spikes seen to those expected by chance) averaged over the population of cells with significant features in their time-resolved cross-correlations. This showed a pattern that was almost the exact opposite of the change in firing rate. Synchrony was low during both movement phases of the task but increased to a high level during the hold period (−1 to 0 s). The overall pattern of modulation was similar in the two animals, although it was stronger and more deeply modulated in monkey 35. Similar results to Fig. 5D, with a peak of synchrony in the hold period, were obtained when analysis was confined to cell pairs recorded on the same or on different electrodes (analysis only performed in monkey 33 due to the small number of same-electrode pairs available in monkey 35).

Since many of our neurons were identified as PTNs, it was of interest to compare these cells with those that could not be antidromically activated and were classified as unidentified neurons (UID). Figure 5, E and F, presents an analysis of both the firing rate and the level of synchrony, separately for these two classes of cell. Figure 5E shows the result for firing rate: PTNs discharged between 2.5 and 9.5 Hz faster than the unidentified neurons. Although a similar trend was present in both animals, the smaller number of cells recorded in monkey 35 meant that there was a significant difference only in monkey 33 (black bar indicates times when difference was significant,
FIG. 4. Comparison of the use of different predictors to normalize the time-resolved cross-correlation. A and B: normalized time-resolved cross-correlation, using either the $\tilde{X}(A)$ or $\hat{X}(B)$ predictor. C and D: Surprise plots, derived from the normalized time-resolved cross-correlations shown in the preceding text. E: measure $k'$ calculated using trial-averaged predictor $\tilde{X}$ (red) or instantaneous firing rate predictor $\hat{X}$ (black). $k'$ was measured over the region indicated by the bracket to the right of A–D, a peak in $k'$ seen only when using the trial-averaged predictor. F: scatter plot of firing rate of the 2 neurons analyzed in this figure during the period 1–2 s before the end hold marker. The line shows the significant linear regression fit ($P < 0.001$). Same neuron pair as Fig. 2.
Figure 5: A: normalized time-resolved cross-correlations, computed from the population averages of 180 cell pairs in monkey 33 and 38 pairs in monkey 35. B: Surprise calculated from the measures in A. C–F: comparison of statistics of firing rate and synchronization (measured by $k'$) over the cell population recorded as a function of time during the task for the 2 different monkeys. C and D: mean of all measurements. E and F: means constructed separately for PTNs or unidentified cells (UIDs), respectively, for pairs where both cells were PTNs compared with pairs where 1 cell was UID. In E and F, * indicates a significant difference between the populations ($t$-test, $P < 0.05$).

test, $P < 0.05$). Figure 5F shows the population mean of the $k'$ measure separately for pairs where both neurons were PTNs and for pairs where one or both neurons were unidentified. The curves overlapped considerably, and only for a brief part of the hold period in monkey 35 were they significantly different (black bar, $t$-test, $P < 0.05$).
Task-related modulation in synchrony in individual cell pairs

While the analysis of Fig. 5 presents an overall view of how population synchrony changes in motor cortex during performance of the precision grip task, it masks the more complex patterns that were often visible in individual cell pairs. Figure 6 illustrates three cell pairs that had features in their time-resolved cross-correlation not indicated by the averages of Fig. 5.

The pair of PTNs (recorded on the same electrode) in the left column (Fig. 6, A–E) had significant correlation around zero lag for the entire time of task performance analyzed as shown by the time-resolved cross-correlation in Fig. 6B, and this was significant (Surprise plot, Fig. 6C). During the hold phase of the task, synchrony between these two cells was oscillatory in nature so that side lobes could be seen in a section taken through the time-resolved cross-correlation (Fig. 6Eb). Finally, at the end of the hold, the synchroniza-
tion returned to a nonoscillatory form (Fig. 6D). The mod-
ulation of near zero-lag synchroniza-
tion, as assessed from the k’ measure (Fig. 6D), was similar to the population average (Fig. 5D), although unlike the average, the level of synchrony between this cell pair continued to rise during and just after the hold period.

The cell pair (both PTNs, recorded on electrodes 420 μm apart) shown in the middle column (Fig. 6, F–J) showed a rather different pattern of synchroniza-
tion. The noise level in the time-resolved cross-correlation and k’ displays (Fig. 6, G and J) is quite high. It is therefore important to view the Surprise plot (Fig. 6H) at the same time to assess which features are statistically significant. The level of synchrony rose sharply at the onset of the hold period and remained high for the first part of this period before declining to nonsignificant values. In this case, the synchronization did not appear to have an oscillatory component as judged from the lack of side lobes in the cross-correlogram of Fig. 6Jb.

The cell pair shown in the right column (Fig. 6, K–O) comprised two CM cells. Both produced postspike facilitation in the extensor carpi radialis muscle EMG. They were recorded on electrodes 1.3 mm apart and displayed a complex pattern of synchrony only superficially similar to the mean illustrated in Fig. 5. First, the magnitude of synchrony showed three clear peaks (Fig. 6N), which were separated by periods of low excess synchroniza-
tion (compare cross-correlograms in Fig. 6O, a–c). Second, the form of the cross-correlation peak changed during the task. At the point marked by d in Fig. 6, L–N, the single, central peak appeared to split into two separate peaks either side of zero lag (Fig. 6Od). A small proportion (approximately 13/218 = 6% as judged by eye) of the significantly synchron-
ized cell pairs exhibited such complex effects involving a shift in lag of the cross-correlation peak, or the splitting of the peak into two, during task performance.

Two types of synchronization could be distinguished from the analysis presented above: oscillatory synchrony, char-
acterized by side lobes in the cross-correlograms, and non-oscillatory synchrony, showing a central peak without side lobes. The former is presumably associated with the c. 25-Hz oscillations in LFP that we have previously shown to be a prominent feature of cortical activity in this task (Baker et al. 1997).

To distinguish these two forms of synchronization, we filtered the time-resolved cross-correlations to exclude frequencies between 18 and 37 Hz or all higher and lower frequencies; further details are given in METHODS. These two filtered time-
resolved cross-correlations could then be processed in the usual way to measure k’ and generate a Surprise display.

An example of this analysis for a pair of PTNs recorded from monkey 33 is shown in Fig. 7; the electrode separation was 305 μm. The left column presents the unprocessed time-
resolved correlation data, the middle column shows data where the 18- to 37-Hz frequencies have been removed, and the right column shows data containing only the 18- to 37-Hz frequencies. The normalized time-resolved cross-correlations and the Surprise plots (Fig. 7, A and B) show that the total synchrony exhibited side lobes that appeared around the central peak during the hold period. Nonoscillatory synchrony was main-
tained weakly throughout the task, while oscillatory synchrony was most pronounced during the last part of the hold period.

Figure 7C plots k’ measured from each of the three time-
resolved synchronization plots separately. The total k’ has two sharp maxima at the beginning and end of the hold period, superimposed on a sustained rise during the hold. When this is decomposed, it is seen that the nonoscillatory component contributed mainly to the initial peak. By contrast, the increase in synchronization during the hold period and the sharp rise just before the end hold marker (time 0) is accounted for entirely by oscillatory components. Figure 7D shows cross-sections through the time-resolved cross-correlation at the times indicated by the dashed lines in Fig. 7, A–C, so that the effect of decomposing the cross-correlation in this way can be clearly seen.

Population data on this analysis are shown in Fig. 8. Figure 8, A and B, shows normalized time-resolved cross-correlations, constructed from summing together all time-resolved cross-correlations from cells with significant synchronization. Data from both animals have been combined together. Figure 8A shows the results of removing the 18- to 37-Hz band; Figure 8B shows the results when only this band was permitted to remain.

Figure 8, C and D, shows the corresponding Surprise calculations. It is clear from the plots of oscillatory synchrony that this form is strongest during the hold period of the task (−1–0 s). The broader band synchrony is also strongest during the hold period.
phase, although this modulation is less marked. Interestingly, the “nonoscillatory” plot (i.e., excluding 18- to 37-Hz signals) shows a marked oscillation in this population average at a higher frequency, with a period of approximately 20 ms. Such higher-frequency oscillations rarely reached significance for individual cell pairs (e.g., Fig. 7B) but are significant in this average constructed over 218 cell pairs.

Figure 8, E and F, shows the mean of $k'$ across all cell pairs with significant synchrony. In the case of the monkey, for the total synchrony (black), and the nonoscillatory (blue) and oscillatory (red) components. All three curves show a rise during the hold period. In monkey 33, the peak of the total population synchrony occurred 0.13 s before the end hold marker; the mean $k'$ was then 1.091, and 51.7% of the excess synchrony ($k'>1$) was generated by components in the 18- to 37-Hz bandwidth. In monkey 35, the peak in total population synchrony occurred 0.53 s before end hold, with $k'=1.25$, and 56.2% of the excess synchrony was contained in the 18- to 37-Hz band.

Figure 8G plots the standard deviation of $k'$ for the population of cell pairs analyzed in monkey 33. The peaks in variability clearly correspond to points just before or after movements, and the majority of this variability is contributed by the nonoscillatory component. The smaller number of pairs in monkey 35 precluded a similar analysis.


discussion

The results presented here demonstrate a significant extent of synchrony between M1 neurons active during the precision grip task. Using a new method, we have been able to distinguish genuine changes in synchrony from those that arise from co-activation of neurons during the task. Our results suggest that, as a population, synchrony among M1 neurons is maximal during the hold period of the task at a time when most of them are firing at much lower rates than during movement phases. However, inspection of a large number of neuron pairs also shows that synchrony can occur during any phase of the task. Finally, we demonstrate that synchrony between spike trains has both oscillatory and nonoscillatory components, which contribute to the total synchrony present to different degrees during the time course of the task. All of these features suggest that synchrony may reveal important underlying mechanisms for task control by primary motor cortex.

Time-resolved cross-correlation technique

The steep changes in firing rate exhibited by M1 neurons during the precision grip task create considerable difficulties for distinguishing and measuring the extent of genuine short-term synchrony. The time-resolved cross-correlation method that we have developed here has a number of advantages over previous approaches. The data in Figs. 2–4 show that serious errors of interpretation can occur if trial-averaged firing rate measures are used in the normalization of measures of synchrony. The same point has been made, although from a theoretical standpoint, by Brody (1999) and Pauluis and Baker (2000). The present work is the first to demonstrate that experimentally recorded spikes can have sufficient trial-by-trial covariation in firing rate to render inappropriate methods such as the JPSTH (Aertsen et al. 1989) or unitary event analysis (Grünewald 1996; Riehle et al. 1997), which rely on the trial-averaged firing rate for their normalization. By contrast, use of an IFR measure (Pauluis and Baker 2000) represents a considerable improvement.

The time-resolved cross-correlation has an additional advantage over unitary event analysis, which imposes a fixed width of synchronization (5 ms in Riehle et al. 1997). This fails to recognize the considerable variability in the width of the cross-correlation peak between cell pairs and is likely either to dilute the peak by including additional lags surrounding it or to underestimate it. By contrast, the time-resolved cross-correlation displays the full correlation peak, allowing a detailed examination of its evolution with task performance. As shown in Fig. 6, both the time course and strength of the correlation peak between two cells can change during task performance; both parameters are likely to be important for the functional role of synchrony in the cortex.

Finally, the display convention differs from that used in the JPSTH of Aertsen et al. (1989). Instead of presenting spike density in a two-dimensional map whose axes are both time relative to task performance, we choose to rotate the display by 45° such that the abscissa still shows time, but the ordinate shows cross-correlation lag. Such a display convention is more appropriate when, as in motor cortex, synchrony between spikes occurs on a time scale of tens of milliseconds, whereas task performance takes several seconds. Similar displays have been used by Schneider et al. (1983), Nowak et al. (1995), Gerstein (1998) and Castelo-Branco et al. (1998).

Nature of task-related changes in synchrony

When synchrony within a large population of M1 neurons was examined, a clear pattern of modulation with task performance was apparent. Synchrony was maximal during the hold period of the task, but also present, at lower levels, during the movement phases at the onset and termination of the trials (Fig. 5, A, B, and D). This is in striking contrast to the neuronal population firing rate with phasic bursts during the movement phases and a lower discharge rate in the hold period (Fig. 5C) (Bennett and Lemon 1996; Lemon et al. 1986).

In motoneurons, the strength of synchronization as measured by $k'$ can vary with firing rate of the cells whose discharge is cross-correlated (Ellaway and Murthy 1985) and depends in part on the time course of the afterhyperpolarization and spiking threshold (Matthews 1996; Olivier et al. 1995; Segundo et al. 1968). At high firing rates, the membrane potential of pyramidal neurons accelerates toward threshold (increasing slope), whereas at low firing rates, it rises more linearly or even levels off as threshold is reached (Schwindt et al. 1997;
FIG. 8.  A and B: normalized time-resolved cross-correlations calculated over the population of 218 cells in both monkeys filtered to exclude frequencies between 18 and 37 Hz (A) or to include only these frequencies (B).  C and D: Surprise calculation based on the data in A and B.  E and F: mean of k’ measure as a function of time during the task, over all cell pairs analyzed (black), and its separation into nonoscillatory (blue) and oscillatory (red) components. This has been calculated separately for monkeys 33 and 35.  G: standard deviation time course computed across the population recorded in monkey 33 separated as in E.
Stafstrom et al. 1984). Thus slowly firing cortical pyramidal cells will spend more time close to firing threshold than fast firing ones and therefore are more likely to respond to synchronous common input when driven at lower rates.

A further influence on the size of cross-correlation peaks is the magnitude of noise fluctuations in the membrane potential. Theoretical (Kirkwood 1979) and experimental (Polikov et al. 1996) results indicate that the higher the membrane noise is, the lower is the probability of a cell firing in response to an EPSP of given amplitude. Assuming that the larger inputs necessary to drive the neuron at high rates will result in greater membrane noise, this would also lead to a reduced response to any common input at high rates of firing. Synchrony would then be weaker at high firing rates than at low rates.

Some of the changes in synchrony reported here might therefore be a simple consequence of firing rate modulation. However, this is unlikely to provide a complete explanation since not only the strength but also the form of synchrony varied during the task, with an increase in oscillations during the hold period. Additionally, changes in synchrony in individual cell pairs were not simply related to their firing profile (Fig. 6).

It is likely therefore that the changes in synchrony that we have observed during the precision grip task reflect changes in the underlying network state between hold and movement phases. The finding that synchrony is maximal during the hold phase agrees with our previous finding that 20- to 30-Hz phases. The finding that synchrony is maximal during the hold period. Additionally, changes in synchrony in individual cell pairs were not simply related to their firing profile (Fig. 6).

The population data (Fig. 5) should not obscure the important finding that there was great variability in the nature, strength, and task-related time course of neural synchrony between individual cell pairs. Thus not every neuron pair participated in synchronous oscillations (Fig. 6, middle), and the parts of task performance when synchrony was maximal varied widely. In addition, the duration and lag of correlation peaks could change depending on task phase, presumably reflecting activation of different sets of common inputs. In some cases, it appeared that a central peak was joined, for part of task performance, by peaks at nonzero lag (Fig. 6, L, M, and O). This may also reflect additional common input recruitment but with different delays to reach the two cells (Moore et al. 1970), differential gating of transmission through serial connections between the sampled neurons (Larkum et al. 1999), or rate-dependent mechanisms (Thomson et al. 1993).

Similarly to the work of Smith (1989), we found that neighboring cells recorded on the same electrodes were more likely to be synchronized than cells further apart and that the mean levels of synchrony were higher for same-electrode versus different-electrode pairs. However, it should be emphasized that synchrony was seen between cells recorded as far as 2.4 mm apart. This is in keeping with the results of Matsumura et al. (1996), who found synchronous excitatory potentials in spike-triggered averages of intracellular recordings even when cells pairs were separated by up to 4 mm. Synchrony has also been measured in both motor and visual cortices between hemispheres (Engel et al. 1991; Murthy and Fetz 1996a), so that it is clearly not confined to within single cortical columns but occurs over a relatively large spatial scale.

Functional role of synchronization

Much recent work has proposed that synchronization between neurons could form the substrate for information processing by the cortex (Abeles 1991; Riehle et al. 1997; Vaadia et al. 1995). Attention has been recently focused mainly on oscillatory synchrony (Singer and Gray 1995). In motor cortex, oscillations predominantly occur at somewhat lower frequencies (20–30 Hz) than the 40-Hz activity observed in visual
true: only neurons with long time constants are capable of the temporal summation necessary to extract information on synchronization. The values of $k'$ in this study were always relatively small ($\sim 1.05-1.2$), such that only around 1 in 5 to 1 in 20 synchronous spikes could be attributed to nonchance events. If information is carried by these synchronous spikes, it is buried in a high noise level. The signal could only be extracted by sampling over an assembly of neurons all of which fired together in synchrony at defined times. Thus temporal codes and the more familiar firing rate codes both equally require population averaging to permit low noise processing (Lee et al. 1998; Shadlen and Newsome 1998).

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Cortex (Conway et al. 1995; Jasper and Penfield 1949; Pfurtscheller et al. 1996). Oscillatory activity in the LFP of awake monkeys or MEG from human motor cortex is most pronounced during steady contractions and disappears during movements (Conway et al. 1995; Kilner et al. 1999a,b). The findings presented here on synchrony between single neurons are consistent with those deduced from global measures of cortex activity, where oscillatory synchrony is strongest during the steady contraction of the hold period. Thus if oscillatory synchrony is involved in information processing, this is confined to periods of stable motor set when the pattern of muscle activation is predominantly one of co-contraction and when presumably the processing load on the cortex is least (Baker et al. 1997).

Here we show that synchrony outside the 18- to 37-Hz band is also maximal in the hold period, although it could be seen at all phases of the task and generally shows considerably more variation in its timing and strength between cell pairs than the oscillatory kind (Fig. 8G). This suggests that the two types of synchrony may subserve different functional roles. Nonoscillatory synchrony was present during phasic movements when the requirement is to produce a highly fractionated pattern of muscle activity by activating appropriate subsets of the corticomotoneuronal cells (Bennett and Lemon 1996; Porter and Lemon 1993). Nonoscillatory, broadband synchrony could therefore be a plausible substrate for the information processing required to produce such complex movements.

While there may be different underlying reasons for the generation of the two types of synchrony, it is important to note that all forms of synchrony between PTN discharges will act as an increased drive to motoneurons. We have previously proposed that motor cortical oscillations might operate to generate a synchronous descending command that recruits motoneurons more efficiently, i.e., with a lower input firing rate (Baker 1997; Baker et al. 1997, 1999a; Kilner et al. 1999b). Further work is needed to assess the relative importance of such synchronization, versus changes in firing rate, in motoneuron recruitment. Recruitment is also likely to depend on higher-order (greater than pairwise) (Bohte et al. 2000) correlations between corticospinal inputs to motoneurons. However, additional statistical methods will be required before the extent of such higher-order correlations can be determined in experimental data given the difficulties of normalizing appropriately for variable neuronal firing rate.

Our cross-correlation peaks were often considerably broader than the sharp peaks assumed in “synfire chain” models (Abeles 1991) but in agreement with previous work (Baker et al. 1994; Matsumura et al. 1996; Smith 1989; Smith and Fetz 1989). If temporal coding by neuronal synchronization does occur in the cortex, it may work on a broader time scale than has previously been assumed. Synchronization with large jitter would be capable of efficient temporal summation only if neuron time constants were long, as reported for both cortical pyramidal cells and motoneurons (see Koch et al. 1996 for review). Softky and Koch (1992) challenged these values by suggesting that active dendritic conductances (Stuart et al. 1997) could shorten effective time constants. Softky and Koch (1992) considered that small time constants would make neurons more like coincidence detectors, promoting temporal coding. However, if synchrony has high jitter, the exact reverse is true: only neurons with long time constants are capable of the
TASK DEPENDENCE OF SPIKE SYNCHRONY IN THE MOTOR CORTEX


