Single-unit activity, threshold crossings, and local field potentials in motor cortex differentially encode reach kinematics

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1Department of Biomedical Engineering, Carnegie Mellon University, Pittsburgh, Pennsylvania; 2Center for the Neural Basis of Cognition, Carnegie Mellon University, Pittsburgh, Pennsylvania; 3Department of Bioengineering, University of Pittsburgh, Pittsburgh, Pennsylvania; 4Systems Neuroscience Institute, University of Pittsburgh, Pittsburgh, Pennsylvania; 5Department of Neurological Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania; and 6Department of Electrical Engineering, Stanford University, Stanford, California and the Department of Neurosurgery, Palo Alto Medical Foundation, Palo Alto, California

Submitted 17 April 2014; accepted in final form 30 June 2015

Perel S, Sadtler PT, Oby ER, Ryu SI, Tyler-Kabara EC, Batista AP, Chase SM. Single-unit activity, threshold crossings, and local field potentials in motor cortex differentially encode reach kinematics. J Neurophysiol 114: 1500–1512, 2015. First published July 1, 2015; doi:10.1152/jn.00293.2014.—A diversity of signals can be recorded with extracellular electrodes. It remains unclear whether different signal types convey similar or different information and whether they capture the same or different underlying neural phenomena. Some researchers focus on spiking activity, while others examine local field potentials, and still others posit that these are fundamentally the same signals. We examined the similarities and differences in the information contained in four signal types recorded simultaneously from multielectrode arrays implanted in primary motor cortex: well-isolated action potentials from putative single units, multiunit threshold crossings, and local field potentials (LFPs) at two distinct frequency bands. We quantified the tuning of these signal types to different spatial scales; and

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METHODS

Behavioral task. Two Rhesus monkeys performed a center-out reaching task in a two-dimensional virtual reality environment. Data analyzed here are from five sessions with monkey J and six sessions with monkey L. The animals were comfortably seated in a primate chair, in front of mirrors for reflecting a computer screen, with one arm restrained and the other free to move behind the screen. A motion-tracking system (Phasespace) was used to track the hand position in real time (resolution: 120 Hz, <1 mm). The recorded hand position was used to animate a cursor on the computer screen in real time, providing the animal feedback about the position of the hand. The workspace was a two-dimensional frontoparallel plane; the depth component of hand movements was ignored. A LabVIEW-based custom computer program controlled the behavioral task progression. At the beginning of every trial, a center target appeared and the animal had to move its hand so that the cursor location on the screen overlapped with the center target. A peripheral target appeared 200–400 ms later, cueing the animal to reach so that the cursor overlapped with the peripheral target. Successful trials ended with a water reward. If the movement took longer than 800 ms, the trial was deemed unsuccessful. Analyses were conducted using only successful trials.

A 96-electrode silicon array (Blackrock Microsystems) was chronically implanted in the arm region of the contralateral M1. Neural activity (SUA, TC, and LFP, see below) was recorded using a PZ2 system (Tucker-Davis Technologies). All procedures were approved by the University of Pittsburgh’s Institutional Animal Care and Use Committee.

Neural data processing. The voltage trace recorded from each electrode was processed to obtain SUA, multiunit TCs, and LFP data. The processing steps are summarized in Fig. 1 and detailed below.

Electrode voltage signals (Fig. 1A) were band-pass filtered (monkey J: 600–6,000 Hz; monkey L: 300–5,000 Hz) to obtain SUA and TC signals (Fig. 1C). Band-pass filtering was performed using a zero-phase filter to eliminate filter delays, and edge effects were minimized by padding signals with their reflection in time. Eliminating filter delays was essential, since we compared how neural signals related to kinematics at various lags. SUA was obtained by spike-sorting the waveforms offline using either window discriminators or principal-component analysis-based clustering (custom software written in Matlab). We used a total of 122 single units in this study, combined across multiple recording sessions. TC event times were obtained using a constant threshold set at three standard deviations below the mean of the voltage trace for each channel. This technique is similar to that used in electromyography studies when relatively few motor units are present in the voltage trace (Viviani and Terzuolo 1973; Soechting et al. 1978; Burton and Onoda 1978). SUA and TC were converted to firing rates by counting TC events in 100-ms bins and dividing by the bin width. We used partially overlapping bins (50-ms overlap) to smooth the data; but results were similar with nonoverlapping bins.

Electrode voltage signals (Fig. 1A) were also band-pass filtered (monkey J: 0.3–500 Hz; monkey L: 10–500 Hz) and stored at a sampling frequency of 1,220 Hz to obtain LFP activity (Fig. 1B). The LFP power-spectral density (PSD) was computed using a 100-ms window, in steps of 50 ms and at frequency resolutions of 1 and 5 Hz (mem library from BCI2000 Project; Schalk et al. 2004). We conducted an Akaike’s information criterion analysis and determined that an autoregressive model order of 30 was appropriate for our data. We verified our selection using both synthetic and real data. Results using 1 Hz were similar to those using 5 Hz, and all further analyses reported here were computed at a 5-Hz frequency resolution. In our encoding analyses, we used linear regression models that make the assumption that errors are normally distributed. To match this assumption as closely as possible, we conducted all analyses on the logarithm of the LFP power values in each frequency band.

We investigated encoding of two PSD frequency bands. For monkey J: 15–40 Hz (LFP_P1, corresponding to the “beta band” in other studies) and 100–300 Hz (LFP_P2); and for monkey L: 15–50 Hz (LFP_P1) and 100–300 Hz (LFP_P2). These bands were chosen based on an examination of both single-channel and channel-averaged normalized PSD plots, since they were the bands that demonstrated similar task-related modulation. We also found that the frequency bands within the LFP_P1 and LFP_P2 bands tended to show similar encoding properties and signal correlation patterns (see Figs. 2 and 3). Because task-related modulation and regression $R^2$ values were significantly lower for the 40- to 90-Hz band, compared with the other frequency bands, it was not included in further analyses. Due to noise artifacts in the frequency band 28–32 Hz for monkey J, these frequencies were notch-filtered before computing the LFP PSD.
When averaging the PSD of individual LFP frequencies, we expect the variance of the resulting signal to behave according to the following calculation. Suppose $X_1, X_2, ..., X_p$ represent the PSD of $M$ individual LFP frequencies, each with variance $\sigma^2$. With the use of the variance properties $\text{Var}(X + Y) = \text{Var}(X) + \text{Var}(Y)$ (when $X, Y$ are independent) and $\text{Var}(cX) = c^2\text{Var}(X)$, a simple calculation shows that the variance of their average should be: $\text{Var}(X_1 + X_2 + ... + X_M/M) = [\text{Var}(X_1) + \text{Var}(X_2) + ... + \text{Var}(X_M)/M]^2 = \sigma^2/M$. Our empirical results match this theoretical calculation (see Fig. 13).

**Encoding models.** Many previous studies have suggested that SUA contains information about hand position, velocity, direction, and speed (for example: Moran and Schwartz 1999; Georgopoulos et al. 1986; Fu et al. 1995; Paninski et al. 2004; Paninski 2004; Riehle and Vaadia 2005). To systematically investigate how SUA, TC, and LFP relate to these kinematic parameters in our data, we regressed neural activity against kinematics and compared how well the kinematics accounted for the variance of the neural activity. We considered 4 encoding models that included 1 model per kinematic variable, and 6 regression models for certain additive combinations, for a total of 10 regression models.

The four basic regression models were:

\[
y = b_0 + b_0p_1 + b_1p_2 + \text{noise} \quad (P: \text{position})
\]

\[
y = b_0 + b_0d_1 + b_1d_2 + \text{noise} \quad (D: \text{direction})
\]

\[
y = b_0 + b_0v_1 + b_1v_2 + \text{noise} \quad (V: \text{velocity})
\]

\[
y = b_0 + b_0s + \text{noise} \quad (S: \text{speed})
\]

where $y$ is one of SUA firing rate (measured in spikes per second), TC firing rate (spikes per second), or LFP power (that is, log-transformed PSD, averaged across a given frequency band, as explained in results); $(p_1, p_2)$ is the hand position; $(v_1, v_2)$ is the hand velocity; $(d_1, d_2)$ is the direction of hand movement; and $s$ is the hand speed. Note that direction differs from velocity in that direction is a unit vector but the magnitude of the velocity vector is the hand’s speed. The six additive combination models we tested were $P + D, P + S, D + S, P + V, V + S, S + P + V + S$.

**Signal and noise correlations.** The variance of a neural signal $y$ can be decomposed to signal and noise, where “signal” is defined as the variance explained by a set of covariates $c$ (in our case kinematics) and “noise” is defined as the variance that remains after accounting for those covariates. This decomposition is given by the law of total variance: $\text{Var}(c) = \text{Var}(E[y|c]) + \text{E}[\text{Var}(y|c)]$, where $\text{Var}(E[y|c])$ is the signal variance and $\text{E[Var}(y|c)])$ is the noise variance. The noise variance may be related to covariates other than the ones we included in $c$. From these quantities, we also computed the signal-to-noise ratio (SNR) as the ratio of the signal variance to the noise variance.

For every encoding model which used a neural signal $y$, we used the encoding model estimate $\hat{y}$ to calculate the signal variance as $\text{Var}(E[y|c]) = \text{Var}(\hat{y})$, and the residuals $y - \hat{y}$ to calculate the noise variance as $\text{E}[\text{Var}(y|c)] = \text{Var}(y - \hat{y})$.

Signal and noise covariance describe how two neural signals relate to a given set of covariates and are defined exactly the same way, with Cov replacing Var in the equation above. Finally, we also compute the signal and noise correlations by normalizing the signal and noise covariances by the appropriate standard deviations. Thus the signal correlation becomes $\text{Cov}(E[y_1|c], E (y_2|c))/\sqrt{\text{Var}[E(y_1|c)]\times\text{Var}[E(y_2|c)]}$ and the noise correlation becomes $E[\text{Cov}(y_1|c), y_2|c)]/\sqrt{E[\text{Var}(y_1|c)]\times E[\text{Var}(y_2|c)]}$. It should be noted that while the signal and average noise covariances sum to the total covariance, this does not hold true for signal and noise correlations, since they are normalized by different factors. We computed the signal covariance between pairs of neural signals, $y_1$ and $y_2$, as $\text{Cov}(\hat{y}_1, \hat{y}_2)$.

Using the encoding models in the previous section, we computed the following statistics on each signal type: 1) coefficient of determination ($R^2$) per electrode; 2) SNR per electrode; 3) signal correlation between electrodes; and 4) noise correlation between electrodes. For LFP signals, we also computed the signal and noise covariances between individual frequency bands on the same channel and across channels. We used individual LFP PSD frequency bands from 1 to 300 Hz at a 5-Hz resolution (i.e., 1–5, 5–10, ..., 295–300 Hz).

**RESULTS**

Trial-averaged LFP is not representative of single-trial LFP. Previous studies related trial-averaged LFPs to kinematic parameters; hence we begin with a qualitative analysis of encoding properties of the averaged LFP signal. Figure 2 shows the time-resolved PSD for the LFP on one example electrode, averaged across repeated reaches to each peripheral target. Hand positions from representative reaches are plotted at the center, and averaged speed profiles are superimposed on the PSD plots. The LFP on this electrode appears to encode both direction and speed information. The LFP power in the high-frequency range (above ~100 Hz, LFP_H) has a larger increase to rightward targets than in other directions. Across all reach directions, there is a tendency for the LFP_P power to peak just before the peak speed. The LFP_L band shows a clear suppression just before movement onset across all reach directions.

LFP activity during single trials is not necessarily reflective of the mean activity across trials. Figure 3 presents a comparison between trial-averaged (Fig. 3A) and single-trial (Fig. 3B) LFP PSD modulation for one example signal. While the modulation of the trial-averaged LFP power is apparent from visual inspection, it is much harder to detect a significant relationship between LFP power and kinematics in the single-trial data. This illustrates the importance of using a fine timescale when investigating in detail the properties of signals recorded from motor cortex.
Kinematic parameters are encoded differently among the signal types. Our next goal was to investigate how signals of each modality related to the moment-by-moment changes in kinematic parameters (neural signals and kinematics all binned at 100-ms resolution). To quantify our results, we computed the coefficient of determination ($R^2$) between each signal modality (SUA, TC, and both bands of LFP) and a full kinematic model consisting of position, velocity, and speed terms. We computed the $R^2$ at several different lags between kinematics and neural activity, ranging from $-250$ to $300$ ms in 50-ms steps, where the negative sign indicates that neural activity precedes the kinematics. Figure 4 summarizes the resulting regression $R^2$ distributions across signals using data from a typical session. Figure 4, top, shows $R^2$ box plots as a function of lag, across all signals; Fig. 4, bottom, shows the corresponding optimal lags, defined as the lag at which the $R^2$ value was the highest for each channel and neural signal. Only significant regressions (determined by $F$-statistic $P$ values with $\alpha = 0.05$) were included in Fig. 4, with the most common optimal lags occurring around $-100$ to $-50$ ms. The $R^2$ distributions across all neural modalities did not change much when evaluated at lags shifted by 50 to 100 ms backwards or forwards in time relative to the optimal lag, indicating that the regression results were not sensitive to the exact choice of a lag. We therefore chose a fixed $-100$-ms lag for all neural modalities in all following analyses. We also conducted analyses at lags of $-150$ and $-50$ ms. Results were similar, and thus data are shown only for the $-100$-ms lag.

To explore how the different neural modalities encode reach kinematics, we fit 10 regression models to every SUA, TC, and LFP signal. The regression models included one model for each kinematic parameter (position, velocity, direction, and speed) and six more models for their additive combinations (see METHODS for details). Figure 5 summarizes our findings from two representative recording sessions (with a total of 3,694 reach trials). Each box plot describes the $R^2$ distribution.
across all channels, grouped by neural signal modality and organized by regression model, allowing comparisons of the types of information encoded by the different neural modalities. It should be noted that the $R^2$ values in Fig. 5 are lower than we observed with averaged data, because we used single-trial data at 100-ms resolution. The 10 encoding models we considered are ordered on the $x$-axis of Fig. 5 according to their mean $R^2$ for the SUA data; that ordering is preserved for the other three signal modalities to aid visual comparison.

Six trends are evident. 1) In agreement with previously published results, SUA signals encode all kinematic parameters, with the highest $R^2$ for velocity, followed by speed, position, and direction. 2) All signal modalities exhibit a pronounced improvement in model fit when speed is added to the model (box plots for models including speed are colored blue in Fig. 5). 3) Based on the ordering and magnitude of the model fits, TC more closely resembles LFPH than SUA. Indeed, when we compared the $R^2$ distributions for the full model (position, velocity, and speed) across SUA, TC, and LFPH, visual inspection of the quantile-quantile plots showed that the TC $R^2$ distribution was more similar to the LFPH distribution than to the SUA distribution: a two-sample Kolmogorov-Smirnov test showed that the TC $R^2$ distribution was significantly different from the SUA distribution ($P = 0.008$), but not significantly different from the LFPH distribution ($P = 0.06$). 4) TCs signals provide the best encoding among the four neural modalities, at least when speed is included in the model. 5) LFP$_H$ provides the poorest encoding. Finally, 6) most of these distributions exhibit long tails and have means that are higher than medians. This indicates that a subset of channels ($\sim 20\%$) provide the best encoding of kinematics.

Figure 6 displays the same $R^2$ distribution box plots, now grouped by model type and organized by signal modality. We wish to highlight two trends evident in the data when viewed in this manner. First, for the position, direction, and velocity models, the mean $R^2$ was highest for SUA and decreased in this order: TC to LFP$_H$, then LFP$_L$. The median $R^2$ showed a different trend, and this difference between mean and median indicates that the SUA $R^2$ distributions are skewed in the positive direction compared with TC and LFP$_H$. In other words, the top 25% of single units have higher $R^2$ compared with the top 25% of TC or LFP$_H$ signals and therefore encode kinematics better. Second, the speed model showed a different trend, with the best encoding for LFP$_H$ (judged by either mean or median), with TC a close second, and both SUA and LFP$_L$ showing poorer encoding of speed. These trends were quantified using Kolmogorov-Smirnov tests: SUA and TC $R^2$ distributions for position, direction, and velocity models were not significantly different ($P = 0.26, 0.12, and 0.62$); but both were significantly different from the LFP$_H$ distributions ($P = 0.003, 0.007$, and $0.001$) and had higher means than the means for LFP$_H$ signals. In contrast, mean $R^2$ values for the speed model increased from SUA to TC and LFP$_H$, and comparison of the $R^2$ distributions of the speed model across all neural modalities showed statistically significant differences.

To study if SUA, TC, and LFP$_H$ encode the same directional information, we compared their preferred directions (PDs). We used the full model (position, velocity, and speed) to account for the prominent speed encoding present in all neural modalities. We estimated PDs by normalizing the velocity coefficients ($b_v$, $b_{v'}$) and representing this vector as an angle around the unit circle (between $-180$ and $+180^\circ$). Figure 7, **diagonal plots**, shows the estimated PDs for SUA, TC, and LFP$_H$, with one radial line for each channel. PD grey scale intensities vary by the regression $R^2$ values from light gray (low $R^2$) to black (high $R^2$). Figure 7, **bottom triangular portion**, compares the...
similarity of PDs for the different signal modalities. It contains scatter plots of PDs for different neural modalities on the same electrodes. To allow proper comparisons, we wrapped the PDs so that every data point lies as close to the equality line as possible, and therefore, some PDs extend beyond the $-180^\circ$ to $+180^\circ$ range. These scatter plots demonstrate that TC PDs are better correlated with LFP_H PDs ($\rho = 0.77$) than with SUA PDs ($\rho = 0.41$). A comparison of the regression $R^2$ from which PDs were estimated can be found in Fig. 7, top triangular portion. These demonstrate that TC regression $R^2$ are better correlated with LFP_H $R^2$ ($\rho = 0.79$) than with SUA $R^2$ ($\rho = 0.35$).

The signal types are correlated differently across cortical tissue. We examined how different signal types were organized across the cortical tissue. To do this, we computed the correlation between signals across electrodes. Figure 8 shows histograms for correlations computed for all pairs of SUA-LFP_H and TC-LFP_H originating from the same electrode. The mean
Figure 8. SUA and TC signals show different noise correlations with LFP$_{H}$ signals on the same electrode. Histograms of noise correlations between TC and LFP$_{H}$ signals (A) and SUA and LFP$_{H}$ signals (B). All signal pairs originated on the same electrode. Correlations were computed using the full model that included position, velocity, and speed. The mean noise correlation for SUA-LFP$_{H}$ was smaller than the mean TC-LFP$_{H}$ noise correlation but not significantly different.

To understand the spatial integration properties of our signals, we examined the signal and noise correlations between similar modalities recorded on all pairs of electrodes across the recording array. Figure 9 shows the signal and noise correlations for all TC and LFP$_{H}$ signal pairs. Every color matrix contains all correlations (either noise in Fig. 9A or signal in Fig. 9, B and C) between all pairs of signals on the array, sorted by their distances from one of the array corners. We observed that LFP$_{H}$ recordings have higher noise correlation than do TC recordings. Because most signal types encode speed in a positive-going manner (i.e., increases in speed tend to lead to increased SUA, TC, and LFP$_{H}$ activity), we computed signal correlations for models with speed ($P + V + S$) as well as for models without speed ($P + V$). With the use of a position and velocity only encoding model, LFP$_{H}$ pairs also show higher signal correlation compared with TC pairs (Fig. 9B). TC pairs show a more heterogeneous correlation pattern compared with LFP$_{H}$ pairs. That trend is even stronger when speed is added to the encoding model (Fig. 9C), as the LFP$_{H}$ signal correlation map becomes even more uniform.

We extended our spatial correlation analysis to all LFP frequencies between 1 and 300 Hz. Results are shown in Fig. 10. We computed the signal and noise correlations between all pairs of electrodes for each frequency band. Instead of displaying one color matrix per frequency band, we summarize the data with one curve for every frequency band. Each point on a curve represents the average correlation between all electrodes that are at a certain distance from each other. Correlation strength is inversely related to frequency: correlations are strong at low frequencies and weaken as the frequency increases. Noise correlations decay with distance, while signal correlations do not.

Figure 10 shows that TC noise correlation is very low (<0.1), while noise correlations for all frequencies in LFP$_{H}$ (100–300 Hz) range from 0.1 to 0.4. Signal correlations for TC are also low (0.2), compared with 0.3 to 0.8 for LFP$_{H}$ frequencies. TC signal and noise correlations are as low as or lower than the ones for the highest LFP frequency we examined (290–300 Hz). We further evaluated the fidelity of encoding by SUA, TC, and LFP$_{H}$ on the same electrode by quantifying the SNR of the full linear model fit ($P + V + S$). These SNR values are plotted against one another in Fig. 11. We found that 92% of TC and 77% of SUA signals showed better SNR than the LFP$_{H}$ signals on the same electrode. More TC signals have better SNR compared with SUA signals due to the more robust TC speed encoding. It is also important to note that for all signal modalities, noise variance was much higher than signal variance. The mean ($\pm$SE) percentages of noise variance out of the total variance were 93 ± 0.8% for SUA, 92 ± 0.6% for TC and 93 ± 0.4% for LFP$_{H}$.

LFP can be averaged across frequencies to improve SNR. Because trial-averaged LFPs usually exhibit correlated modulations in neighboring frequency bands (see Fig. 3A), it is common practice to average the LFP across frequencies, presumably to smooth and “clean” the signal. Single-trial LFPs appear by eye to be more heterogeneous across frequency than trial-averaged LFPs (e.g., Fig. 3B). We examined whether LFP should be averaged across frequency bands. Averaging LFP across frequency bands would only be beneficial if those frequency bands encoded similar information but did not have correlated noise. We computed the signal and noise correlation between individual frequency bands of every LFP signal. For this analysis we used the position-velocity ($P + V$) encoding model and data from an entire session. We show an example of correlations for a typical electrode in Fig. 12. It is clear that noise is mostly independent across frequencies, exhibiting weak correlation for frequency bands >10 Hz apart. On the other hand, the signal correlation is high across the two frequency bands we used in this study: LFP$_{L}$ (15–40 Hz) and LFP$_{H}$ (100–300 Hz). These results indicate that it should be beneficial to average single-trial LFP across these two frequency bands, rather than treat all frequency bands independently when studying how kinematic information is encoded in cortex.

If averaging across frequency bins boosts signal, then averaging the LFP across several 10-Hz frequency bins will show an enhanced SNR compared with the 10-Hz bins taken individually. We tested this separately for the LFP$_{L}$ and LFP$_{H}$ bands (Fig. 13). In the LFP$_{H}$ band, averaging the LFP power across frequency bins before computing the SNR (ordinate) yields higher values than computing the SNR in each frequency bin first and then averaging (abscissa), by roughly a factor of $\sqrt{21}$ (the square root of the
When we repeated this analysis at 5-Hz resolution, the SNR of the average band did not continue to improve at the same rate (data not shown). This indicates that in the frequency range of LFPH neural noise is correlated at frequency bins of 10 Hz or wider. For the LFPL band, averaging across frequency bins did not boost the signal as much. Inspection of the data indicate this is primarily because there is some heterogeneity in the LFPL band edges: while many (~40%) channels exhibit common signal modulation from 10 to 40 Hz, in other channels these edges are slightly higher or lower. The LFPL band heterogeneity is interesting, but due to its relatively poor kinematic encoding, we did not pursue it further here.

**DISCUSSION**

Our ability to simultaneously record the activity of single neurons has increased steadily with time (Stevenson and Kording 2011) and multielectrode recording arrays currently allows us to record from several hundred neurons at the same time (Collinger et al. 2013; Ifft et al. 2013; Schwarz et al. 2014). However, this still only represents a small fraction of the total number of neurons in any given brain area. We are far from the...
ultimate goal of recording from all the neurons in a complete mammalian neural circuit (Insel et al. 2013). It is therefore of critical importance to extract as much information as possible using the available recording resources.

Extracellular electrodes inserted in the cerebral cortex measure a voltage signal composed of spikes and dendritic potentials. Some spikes are large, originating from larger neurons that are close to the electrode tip, and are easily discriminated as SUA. Smaller neurons, and neurons further away from the electrode tip, contribute smaller spikes which are harder to discriminate and are commonly analyzed together as multiunit activity. In our data, TCs surely included contributions from well-isolated single neurons, nonisolatable multiunit activity, and fluctuations that could not be clearly identified as multiunit activity. Dendritic potentials likely also contribute to the voltage trace, mostly at low frequencies (Buzsáki et al. 2012). Our goal was to characterize the differences and similarities between signals that can be extracted from the extracellular voltage trace during a behavioral task. In this discussion, we focus on the implications of our results for our understanding of encoding (that is, the native tuning properties of primary motor cortex), the biological underpinnings of extracellular voltage signals, and decoding (that is, the use of motor cortex signals for BMI control).

Fig. 11. SUA and TC signals have higher signal-to-noise ratio (SNR) compared with LFP signals. SNR comparison between SUA/TC and LFP signals on the same channels for the P + V + S model: 95 (77%) SUA signals show better SNR compared with LFP signals; 177 (92%) TC signals show better SNR compared with LFP signals. This difference is likely due to the more robust speed encoding in TC compared to SUA.

Kinematic parameters in M1 are encoded differently by different neural signal modalities. We compared the encoding properties of three types of signals commonly extracted from intracortical electrode recordings in M1: SUA, TC activity, and LFP activity in two distinct frequency bands. To investigate how they represent kinematic parameters on a moment by moment basis, we fit a set of encoding models that included the hand’s position, direction, velocity, speed, and their additive combinations. We fit these models to single-trial neural and kinematic data binned at 100-ms resolution.

We observed a progression in the encoding properties from SUA through TC to LFP (100 – 300 Hz), with directional signals showing stronger encoding among the single units and speed signals showing stronger encoding in LFP. SUA is the only modality for which the median $R^2$ for velocity was larger than the median $R^2$ for speed. Of all the signal types we considered, LFP shows the strongest encoding of speed relative to velocity. TC is intermediate between these two. Progressing from SUA through TC to LFP, the median $R^2$ for all models that include directional signals (velocity, direction, and position) shows a gradual decrease, while the median $R^2$ for models that include speed shows a gradual increase. For all signal modalities, the majority of the information about any particular kinematic feature is best represented by a relatively
A single electrode. LFPL showed a high correlation across the sessions as a function of distance across the cortical tissue under whiskers in the box plots of Figs. 5 and 6. (Fig. 4).

between neural activity and kinematic variables was 100 ms (e.g., Moran and Schwartz 1999), the average optimal lag distributions in Fig. 6. Also in agreement with previous studies across our population, as evident by the long upper tails for the is heterogeneous encoding of all of the kinematic variables of velocity in SUA and a weaker representation of speed. There

Paninski et al. 2004). Our results are in overall agreement with 1999; Alexander and Crutcher 1990; Hatsopoulos et al. 2007; Schwartz 1999; Churchland and Shenoy 2007; Kakei et al.

distances tested (3 mm). We interpret these results to mean that these signal modalities convey information that is present at different spatial scales within the cortex.

We further evaluated the decay in noise and signal correlations as a function of distance across the cortical tissue under the recording array and, in the case of LFP, frequency within a single electrode. LFP showed a high correlation across the cortical tissue. At higher frequencies, LFP correlation decayed more sharply across the cortical tissue. TC activity shows relatively weak noise correlation even on neighboring electrodes, indicating a very local signal (<200-μm radius) source. In contrast, LFP showed a more gradual decline in noise correlation with distance: in the 50- to 100-Hz range, LFP noise correlations were still >0.2 even at the largest distances tested (~3 mm). We interpret these results to mean that these signal modalities convey information that is present at different spatial scales within the cortex.

A vast body of literature relates motor cortex SUA to various kinematic parameters during reaching movements (e.g., Georgopoulos et al. 1982; Scott and Kalaska 1995; Moran and Schwartz 1999; Churchland and Shenoy 2007; Kakei et al. 1999; Alexander and Crutcher 1990; Hatsopoulos et al. 2007; Paninski et al. 2004). Our results are in overall agreement with these findings. In particular, we see a prominent representation of velocity in SUA and a weaker representation of speed. There is heterogeneous encoding of all of the kinematic variables across our population, as evident by the long upper tails for the distributions in Fig. 6. Also in agreement with previous studies (e.g., Moran and Schwartz 1999), the average optimal lag between neural activity and kinematic variables was 100 ms (Fig. 4).

Different neural origins for different neural signal modalities. Movements are ultimately driven by action potentials conveying the collective activity of millions of cortical neurons. Voltage traces recorded using extracellular electrodes comprise a mixture of spiking activity and the postsynaptic potentials that give rise to spiking. We processed those voltage traces using two different nonlinear filters, the first to extract SUA/TC and the second to extract LFP (see Fig. 1). These two processing procedures provide us with two different, complementary views of the underlying neural process.

SUA activity, by definition, stems from the action of single neurons. TC signals likely reflect that activity of very local neurons, almost certainly numbering <10, given the thresholds used in this study. The source of the LFP signal is not yet agreed upon. Historically, LFPs have been considered to represent mainly synaptic activity and membrane-potential-derived voltage fluctuations (reviewed in Buzsáki et al. 2012). However, recent evidence suggests that spiking activity can affect the LFP power at all frequencies and that these effects cannot be simply removed by low-pass filtering the raw voltage signal (Waldert et al. 2013). We believe that our LFP signals included both spikes from local neurons and spikes from very distant neurons. The spatial scale of LFP signals is not well known and is likely to depend on frequency (Leopold et al. 2003; Einevoll et al. 2013). However, given that the 95th percentile of the R² distribution for velocity of the LFP signals is nearly half that of the TC signals (Fig. 6), it is likely that LFP integrates information over a substantially broader range than TC, sufficient to dilute the velocity tuning.

In addition to being tuned to movement direction, most neurons in motor cortex are also positively (albeit weakly) tuned to speed, meaning that increased movement speed will result in increased average firing rate (Moran and Schwartz 1999). However, the directional tuning of nearby neurons is only weakly correlated (Naselaris et al. 2006). Therefore, as signals from multiple neurons are combined (as is the case for TC and LFP), directional tuning should weaken while speed tuning strengthens. Indeed, we found that LFP signals encoded mostly speed information, with the exception of a subset of channels that also encode directional information. LFP PDs were most correlated with TC PDs, suggesting that LFP activity in the 100- to 300-Hz band contains some information from action potentials included in TC. LFP has both higher noise and signal correlations compared with TC, indicating that LFP signals are more homogeneous and tend to modulate similarly. TC signals recorded from two neighboring electrodes even just 400 μm apart have very low correlation. Our findings support the interpretation that SUA, TC, and LFP integrate information at increasing spatial scales within the cortex. Their neural origins are likely not identical: SUA is composed purely of spikes from one nearby neuron, TCs are probably a few neurons near the electrode tip, and also some more distant large neurons, with perhaps a contribution from postsynaptic potentials; LFP is probably a large-scale (approaching millimeters) aggregate of spiking activity and postsynaptic potentials; LFP is probably a generalized signal shared across a large swath of cortical tissue, far larger in spatial scale than our array could sample and perhaps also with a subcortical component. These interpretations are consistent with the trends in our data, although other explanations may not fully account for all of the observations.
also fit the data, and verifying these interpretations is well beyond the scope of this work.

It is known that the beta band of LFP activity (here, LFPL), roughly between 10 and 40 Hz, is suppressed during movement (Rickert et al. 2005). We confirmed this in our data. However, when assessing the encoding of kinematic features during a reach, at 100-ms resolution, we find that the moment-by-moment LFPL activity is not well correlated with the moment-by-moment kinematic parameters. The already relatively small $R^2$ values for speed that we observe in the LFPL band further decrease when we window our data to include only those hand speeds that are $>$ 10% of the maximum speed of the reach (data not shown). Thus, while LFPL can be used to distinguish intended movement epochs from nonmovement epochs (e.g., Hwang and Andersen 2013), it does not appear to be useful for inferring instantaneous features of the reach. This supports our view that LFPL signals reflect a nonspecific signal that arises from a much broader or more distant neural origin than LFP$_H$.

**Implications for BMI decoding.** Our results have implications for BMIs, devices that use recorded neural signals to actuate some device, such as a computer cursor (Taylor et al. 2002; Suminski et al. 2009; Ganguly and Carmena 2009; Hochberg et al. 2006; Mullen et al. 2008; Schalk et al. 2007; Gilja et al. 2012; Ifti et al. 2013), robotic arm (Collinger et al. 2013; Hochberg et al. 2012; Wang et al. 2013), or muscle stimulator (Ehther et al. 2012; Moritz et al. 2008). TC activity is often thought to convey similar information as SUA. Several researchers have used TCs in place of SUA during BMI tasks (Santhanam et al. 2004; Fraser et al. 2009; Chestek et al. 2011; Saddler et al. 2011; Hochberg et al. 2012; Christie et al. 2014). The general conclusion from that work has been that decoding performance can be just as good with TCs as with SUA. We find that although velocity encoding models fit to TC and SUA span a similar range of $R^2$ values (Figs. 5 and 6), there is more prominent speed encoding in our TC signals compared with SUA. In fact, it is in part because of this that TC signals encode information more similarly to LFP$_H$ than to SUA. This indicates an avenue to improving BMI design: velocity information could be extracted from SUA, and TC could provide speed information. We note that it is likely that the prominent speed tuning we see also depends on our choice of threshold, which was set to be three times the root mean square value of the intertrial band-pass-filtered voltage trace. This is slightly more inclusive than is used in many BMI settings (e.g., Hochberg et al. 2012 and Chestek et al. 2011 used a setting of 4.5 times root mean square). Because of this, the speed tuning in TC in those studies may be somewhat less pronounced than it was in our data.

While the majority of BMIs rely on either sorted spikes or TC activity, there is an increasing recognition that LFP activity also carries useful information and may actually provide a more stable long-term signal for clinical applications (Flint et al. 2013; Markowitz et al. 2011; Bansal et al. 2012; Hwang and Andersen 2013).

Although it is sometimes dangerous to draw conclusions about online decoding performance from offline data (Chase et al. 2009; Cunningham et al. 2011), the prominent speed tuning we observe in our TC and LFP$_H$ signals suggests that decoders that utilize these signal types would likely benefit from taking speed tuning into account. Unfortunately, since speed is a nonlinear transform of velocity, this implies that linear decoders such as the Kalman filter (Wu and Hatsopoulos 2008) may not actually be optimal when based on TC or LFP$_H$ inputs. However, nonlinear state-space algorithms abound and have proven fruitful in decoding applications (e.g., Koyama et al. 2010; Li et al. 2009; Brockwell et al. 2004; Shpigelman et al. 2008; Dethier et al. 2013). Another approach to accounting for speed in improving BMI control would be to treat it as a “nuisance variable,” and use latent variable approaches to mitigate its effect on decoding (Lawhern et al. 2010; Paninski et al. 2010). Speed control, especially in terms of stopping stability, is known to be poor in BMI control (Carmena et al. 2003; Hochberg et al. 2006; Kim et al. 2006; Ganguly and Carmena 2009; Gilja et al. 2012; Golub et al. 2014). It is possible that speed and stability could be improved by the addition of LFP$_H$ and LFPL signals to existing decoding algorithms.

Given the differential encoding of reach kinematics across the three signal types, we suggest that a hybrid approach may prove optimal for BMI decoding. This approach could rely more on the well-isolated single units to infer direction and more on the LFP$_H$ signals to infer speed. The LFPL signals could serve as an on/off switch to initiate movement. In a hybrid decoding scheme, SUA would be used whenever well-isolated neurons were available, and TC could be taken from the other electrodes. Together, they could provide direction and velocity information. LFP$_H$ could provide speed information. Since LFPL is so similar across electrodes, only a few electrodes would be needed. Of course, the same electrodes could be processed differently (Fig. 1) to attain signals of different modalities. Then, a signal to turn on and off neural control of the device could be taken from LFPL (again, a few channels would be sufficient). In this way, a BMI could be designed that provides continuous use, eventually allowing such devices to be used outside of the laboratory setting.

**GRANTS**

Funding was provided by National Institute of Child Health and Human Development “Collaborative Research in Computational Neuroscience” Grant 1R01-HD-071686, National Institute of Neurological Disorders and Stroke Grant 5R01-NS-065065, the Burroughs Wellcome Fund, the Craig A. Nielsen Foundation, the DARPA Reliable Cortical Interfaces (RCI) Program, and the Pennsylvania Department of Health Research Formula Grant SAP#4100057653 under the Commonwealth Universal Research Enhancement Program.

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

**AUTHOR CONTRIBUTIONS**

Author contributions: S.P., P.T.S., E.R.O., A.P.B., and S.M.C. conception and design of research; S.P. analyzed data; S.P., E.R.O., A.P.B., and S.M.C. interpreted results of experiments; S.P. prepared figures; S.P., A.P.B., and S.M.C. drafted manuscript; S.P., A.P.B., and S.M.C. performed experiments.

**REFERENCES**

Differential Encoding of Reach Kinematics in Motor Cortex


