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Modeling Task-specific Neuronal Ensembles Improves Decoding of Grasp

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Abstract

Objective—Dexterous movement involves the activation and coordination of networks of neuronal populations across multiple cortical regions. Attempts to model firing of individual neurons commonly treat the firing rate as directly modulating with motor behavior. However, motor behavior may additionally be associated with modulations in the activity and functional connectivity of neurons in a broader ensemble. Accounting for variations in neural ensemble connectivity may provide additional information about the behavior being performed.

Approach—In this study, we examined neural ensemble activity in primary motor cortex (M1) and premotor cortex (PM) of two male rhesus monkeys during performance of a center-out reach, grasp and manipulate task. We constructed point process encoding models of neuronal firing that incorporated task-specific variations in the baseline firing rate as well as variations in functional connectivity with the neural ensemble. Models were evaluated both in terms of their encoding capabilities and their ability to properly classify the grasp being performed.

Main results—Task-specific ensemble models correctly predicted the performed grasp with over 95% accuracy and were shown to outperform models of neuronal activity that assume only a variable baseline firing rate. Task-specific ensemble models exhibited superior decoding performance in 82% of units in both monkeys ($p < 0.01$). Inclusion of ensemble activity also broadly improved the ability of models to describe observed spiking. Encoding performance of task-specific ensemble models, measured by spike timing predictability, improved upon baseline models in 62% of units.

Significance—These results suggest that additional discriminative information about motor behavior found in the variations in functional connectivity of neuronal ensembles located in motor-related cortical regions is relevant to decode complex tasks such as grasping objects, and may serve the basis for more reliable and accurate neural prosthesis.

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Keywords

Neuronal ensembles; Point processes; Grasp decoding

Introduction

Neurons in motor and premotor cortices in nonhuman primates demonstrate variations in firing activity that correlate with parameters related to motor behavior (Fu et al., 1995; Kalaska, 2009; Stark et al., 2007). Identification of how populations of neurons encode these parameters is of great importance to improving the usability of brain-controlled prosthetic devices and increasing understanding of the brain as a whole (Hochberg et al., 2012; Collinger et al., 2013). Reaching and grasping motions require the activation and coordination of functional networks of neurons. Significant effort has been applied to investigate encoding of motor behavior by neuronal populations, mainly by focusing on how individual neurons in motor and premotor cortices independently encode motor behaviors (Fu et al., 1995; Georgopoulos et al., 1999; Saleh et al., 2010; Panzeri et al., 2015). As recording technologies improve and the number of simultaneously observable neurons grows, so too grows the potential for discovering relevant encoding of behavior in the interactions between neurons (Stevenson and Kording, 2011; Pothof et al., 2016).

Inspection of simultaneous recordings of neuronal activity often focuses upon the existence of apparent interaction among neurons through correlations in firing patterns. This functional (or effective) connectivity (Perkel et al., 1967; Aertsen et al., 1989) is widely incorporated in models of neuronal interactions and demonstrates effectiveness in accounting for spike time variability (Harris et al. 2003; Okatan et al., 2005; Truccolo et al., 2005; 2009; Gerhard et al., 2009; Chen et al., 2011; Panzeri et al., 2015). In some cases, inclusion of ensemble activity has even been shown to result in improved ability to decode sensory stimuli (Pillow et al., 2008) and some motor behaviors (Stevenson et al., 2012, Ma et al., 2017). These studies treat the interactions among neurons in the ensemble as being stationary with regard to changes in stimulus or behavior. Nevertheless, dynamic interactions among neurons in an ensemble may contain important information about a stimulus or behavior that complements the information contained in direct variations in firing rate alone (Riehle et al., 1997; Hatsopoulos et al., 1998, Balaguer-Ballester, 2017). Changes in spike correlation between pairs of motor cortex neurons at short time scales (< 50 ms) have been observed to vary repeatedly during motor tasks (Hatsopoulos et al., 1998; Vaadia et al., 1995; Baker et al., 2001). Other studies observed that short time scale correlations were shown to encode motor information beyond that coded through simple rate modulation (Riehle et al., 1997; Cohen and Newsome, 2008). Changes in firing rate covariance of small groups of neurons at longer time scales have been observed during performance of arm movements (Maynard et al., 1999), prehension (Stark et al., 2008), and motor planning (Hatsopoulos et al., 2003; Zhao et al. 2012). Accounting for these task-related changes in functional connectivity could potentially improve both encoding and decoding models based of neuronal activity.

In this work, we construct models of spiking activity that incorporate ensemble activity from other neurons through task-specific functional connections. Specifically, we investigate whether information about motor behaviors is available within the variation of functional connectivity in neuronal ensembles. We examine two cases, a) where the ensemble weights are static across all grasps being performed, and b) the case in which the ensemble weights are task-specific and assumed to vary with the task being performed. Specifically, we compare the performance of these models within the context of decoding a grasp being performed by monkeys executing a reach-to-grasp task. Through this analysis, we show that additional discriminative information about motor behavior may be found in the variations in functional connectivity of a neuronal ensemble.

Methods

Experimental procedure

Two male rhesus monkeys (monkey L and monkey X) were trained to perform a center-out, reach, grasp, and manipulate task. All procedures involving nonhuman primates were approved by the University Committee on Animal Resources at the University of Rochester. The monkey was seated in a primate chair and restrained such that the task was performed only with the right hand and arm. The monkey interacted with an experimental apparatus similar to that depicted in Figure 1A. Four peripheral objects and a central home object were mounted on individual rods extending outward from a vertical plane in front of the monkey. The peripheral objects were arranged along a coplanar arc centered on a central home object. The arc had a radius of 13 cm and each peripheral object was separated by 45° along the arc. The home object was positioned approximately 32 cm in front of, and pointed at, the monkey's right shoulder.

The peripheral objects consisted of 4 unique forms: sphere, coaxial cylinder, perpendicular cylinder, and push button. Each object also had a specific manipulation associated with it. The coaxial and perpendicular cylinders could be pulled toward the monkey approximately 1 cm against a small spring load, the push button could be pressed approximately 1 cm, and the sphere could be rotated 45° clockwise.

A trial began when the monkey grasped and pulled the home object. This initiated a variable hold period requiring the monkey to maintain its pull on the home object for a random duration from 1,000 to 1,500 ms for monkey X and 1,500 to 2,000 ms for monkey L. Following the initial hold period, a blue LED was illuminated next to one of the four peripheral objects. This cued the monkey to release the home object and to reach, grasp and manipulate the indicated object. Successful manipulation of the indicated object resulted in the closure of a microswitch. This illuminated a green LED next to the object indicating successful manipulation and initiating a final hold period. The final hold period required the object manipulation to be maintained for 1,000 ms. Completion of the final hold resulted in a successful trial; the blue and green LEDs were turned off and the monkey received a water reward. Failure to complete any portion of this sequence resulted in a failed trial and no reward.

The mounting rods were attached to a mechanical apparatus that allowed rotation about the central (home) object. Peripheral objects maintained their ordering along the arc and adjacent peripheral objects were always separated by 45°. The apparatus could be rotated to discrete zones separated by 22.5°. In all, eight zones were examined. The first zone positioned the four objects at -90°, -45°, 0°, and 45° relative to the right, horizontal location. The eighth (and final) zone positioned objects at 67.5°, 112.5°, 157.5°, and 202.5°. In each zone, cued trials were limited to only objects located in the range of 0° to 157.5°. This limitation was due to a combination of factors including biomechanical constraints on the shoulder and occlusion of the monkeys' vision by the primate chair. Figure 1B shows all object and location combinations that were examined. Additional details regarding the experiment and kinematics of movement are available in (Rouse and Schieber, 2015).

The experiment was self-paced and the monkey voluntarily initiated each trial by pulling on the central (home) object. Trials were performed in blocks consisting of approximately 10 trials per object with the apparatus fixed in one zone. In the case of failed trials, the following trial would be cued to repeat the same object and location. Failed and repeated trials were not included in this analysis and because of this each block did not always include exactly 10 trials. Within a block, trials were cued in pseudorandom order such that, in general, each object was visited once before being revisited. Following each block of trials in a zone, the apparatus would be rotated to a new zone in pseudorandom fashion. Each zone was visited once before returning to the same zone again. The number of trials included at each experimental condition are summarized in Table 1.

Electrophysiology

Each monkey was chronically implanted with multiple floating microelectrode arrays (FMAs) (MicroProbes for Life Science, Inc, Gaithersburg, MD). Each FMA consisted of 16 recording microelectrodes arranged in a 4 × 4 grid. Microelectrodes within each FMA were of variable length ranging from 1.0 to 6.0 mm. Each electrode had a nominal impedance of 0.5 M at 1 kHz. Recordings were made simultaneously from 8 separate FMAs during performance of the task. In each monkey, recordings were made from arrays implanted in putative primary motor cortex (M1) and premotor cortex (PM) regions of the left hemisphere. In the sessions examined in this study, recordings were made from 6 FMAs in M1 and 2 FMAs in PM. M1 arrays were implanted immediately anterior to the central sulcus spanning the entire upper forelimb representation as verified by intracortical microstimulation. PM arrays were implanted lateral to the superior precentral sulcus and posterior to the genu of the arcuate sulcus. Analog neural recordings were taken from a total of 16 channels per array for a total of 128 channels per monkey. A precise description of electrode placement can be found in Rouse and Schieber (2016).

The signal from each channel was converted to spike snippets online with gains and thresholds set by the experimenter in Plexon's Sort Client software (Plexon Inc., Dallas, TX). Offline spike sorting was performed using Plexon Offline Sorter (v3, Plexon Inc., Dallas, TX). Spike sorting quality was assessed using two metrics. First, the signal to noise ratio (SNR) (standard deviation of mean waveform divided by standard deviation of residual noise waveforms) was calculated. Second, the number of inter-spike interval (ISI) violations

(two spikes occurring within a refractory period of 1 ms) was determined. These violations, together with the total number of spikes, were used to estimate the percentage of true spikes originating from a single unit (Hill et al., 2011). Definite single units were classified as those with no ISI violations (100% true spikes) and SNR greater than 3. Probable single units were those with at least 90% true spikes and SNR greater than 2.5. The present analysis used both single units and multi-units that could not be sorted into separate individual units. For the purposes of this analysis, we do not distinguish between single unit and multi-unit activity. An example trial averaged response for a selected unit across multiple reach and grasp conditions is shown in Figure 2.

Encoding models

The firing of each spiking unit was modeled as a discrete-time point process. Discrete-time point processes are random processes in discretized time with binary observations. Within this context, the spiking activity of a unit can be represented as a time-series with a value of 1 when spikes occur and a value of 0 otherwise. Models of point processes are fully characterized by a conditional intensity function (CIF), $\lambda(t)$, which describes the estimated instantaneous event rate at time t . To represent spiking as a discrete-time point process, we discretized spike trains from each unit to 1 ms bins such that at most one spike could occur in any time bin.

Following this discretization, a valid CIF for a given unit may be any function that produces an estimate of the probability of a spike occurring in a given time bin. Here, we cast this as a binomial logistic regression problem (Chen et al., 2011), which is a specific formulation of a generalized linear model (GLM) (McCullagh and Nelder, 1989). Thorough derivations of this general approach as it applies to modeling spiking have been published previously (Truccolo et al., 2005; Paninski, 2004). Under this model and the limitation of at most one spike occurring in any time bin, the likelihood of an observation in a single time bin t_k for a given CIF is provided by:

$$P(X_i(t_k) | \lambda_i(t_k)) = \exp\{\log \lambda_i(t_k) X_i(t_k) - \lambda_i(t_k)\} \quad (1)$$

where $\lambda_i(t_k)$ is the value of the estimated conditional intensity function or neuron i in time bin t_k and $X_i(t_k)$ is the (binary) spiking activity of neuron i in time bin t_k .

We can extend this likelihood function to account for a sequence of spiking activity under a given CIF by treating the sequence as a collection of conditionally independent Bernoulli trials. For a collection of k sequential time bins, the likelihood of such a sequence, given a CIF, can be expressed as:

$$P(X_i(t_{1:k}) | \lambda_i(t_{1:k})) = \prod_{k=1}^K P(X_i(t_k) | \lambda_i(t_k)) \quad (2)$$

Thus, the task of learning an encoding model can be reduced to providing a valid prototype function for $\lambda_i(t_k)$ and estimating the coefficients through maximum likelihood estimation.

The encoding models we examine here consist of two distinct components: a baseline firing rate and a rate dependent on the recent activity of other neurons in the recorded ensemble. Following the convention applied in Kass and Ventura (2001), Truccolo et al. (2005) and Sarma et al. (2010), we model the firing rate of a unit as consisting of a baseline firing rate combined with a multiplicative term that conditionally modifies the baseline rate. Our general form for the CIF is

$$\lambda(t|g, \mathcal{H}_t) = \lambda^B(t|g)\lambda^E(t|g, \mathcal{H}_t) \quad (3)$$

where $\lambda^B(t|g)$ represents the baseline firing rate dependent on the grasp, g , and $\lambda^E(t|g, \mathcal{H}_t)$ represents a variable gain function dependent on the grasp as well as the past spiking activity of other units in the ensemble, $\mathcal{H}_t$.

Here, we propose three variations on this general form:

I) Baseline Model—The baseline model treats the spiking probability for each unit as constant within trials with a rate that is dependent upon the object being grasped.

$$\lambda_i^B(t|g) = \exp\{\beta_0(g)\} \quad (4)$$

where $\beta_0(g)$ is a functional parameter that represents the baseline firing rate as a function of the discrete grasp, g , being performed. In this case, a neuron's predicted spiking probability is unaffected by the activity of other neurons in the ensemble.

Traditional linear models assume that coefficients are fixed. However, our model requires that coefficients, such as $\beta_0(g)$, behave as discrete functions with values that vary depending on the grasp being performed. We achieve this through the use of indicator functions that are used in conjunction with functional coefficients, as follows:

$$\beta_k(g) = \sum_{g'=1}^G \beta_{k,g'} \cdot \mathbb{1}(g = g') \quad (5)$$

where $g' \in \{1, 2, \dots, G\}$ is a discrete value indicating one of G possible grasps, β is a model parameter and $\mathbb{1}(g = g')$ is an indicator function that is identity during trials when grasp g is being performed and zero otherwise. Here k is a grouping subscript to indicate that the β_k parameters interact as a group with the k^{th} model covariate (or constant, for $k = 0$). Within the context of the baseline model, this functional parameter allows for variations in a unit's average firing rate depending on the grasp being performed.

II) Static Ensemble Model—The static ensemble model augments the baseline model with ensemble terms that modulate the baseline firing probability as a weighted combination of the firing rates of other units. Under this paradigm, the firing of each unit is modeled as:

$$\lambda_i(t|g, \mathcal{H}_t) = \lambda_i^B(t|g) \cdot \exp\left\{\sum_{j \neq i} \beta_{i,j} \cdot r_j(t)\right\} \quad (6)$$

where $r_j(t)$ is the observed number of spikes fired by unit j in the previous 100 ms and $\beta_{i,j}$ is a ensemble coefficient representing the strength of influence of unit j upon the firing of unit i . In this model the ensemble coefficients, $\beta_{i,j}$, are assumed to be constant and not conditional upon the grasp performed. In other words, the influence of spiking from other units is assumed to be stationary with respect to both time and behavior. The 100 ms history window was chosen to incorporate relevant time periods identified in the literature (Truccolo et al.; 2005; 2009; Saleh et al., 2010; Stevenson et al., 2012), while minimizing the total number of parameters in our final model.

III) Task-specific Ensemble Model—The task-specific ensemble model further extends the baseline and static ensemble models by adding the flexibility to allow for ensemble weights that are conditional upon the task being performed. This model is expressed as:

$$\lambda_i(t|g, \mathcal{H}_t) = \lambda_i^B(t|g) \cdot \exp\left\{\sum_{j \neq i} \beta_{i,j}(g) \cdot r_j(t)\right\} \quad (7)$$

where $\beta_{i,j}(g)$ indicates the task-specific influence of recent spikes from the j^{th} unit. In this paradigm, the ensemble coefficients $\beta_{i,j}(g)$ are assumed to vary with the task and can be expanded, as described in equation (5). Here the functional ensemble coefficients vary with the grasp being performed and allow modeling of task-specific influence from other neurons. Similarly to the static model, ensemble effects for the task-specific model were captured in a single 100 ms history window. Self-history effects were excluded in order to better isolate the role of ensemble effects on encoding and decoding performance.

Estimates for model parameters were obtained using weighted maximum likelihood estimation. This approach follows the same procedure of the standard maximum likelihood estimation procedure for point process GLM models as described in Truccolo et al. (2005), with the exception that each sample in the training data was assigned a weight to account for differences in trial duration. Variations in experimental conditions resulted in trials of different lengths, as can be seen in Figure 2. For instance, trials to the right side of the workspace took longer, on average, than the trials to the left. This results in trials to the right contributing more data samples to the training set than trials to the left. As a result of this imbalance, in regular maximum likelihood, samples from experimental conditions with longer trials on average could contribute a disproportionately large amount to the total likelihood. The weighted maximum likelihood approach compensates for these potential biases by assigning lower weights to samples from experimental conditions that were longer than average and higher weights to samples from experimental conditions that tended to be shorter than average.

The three models have different numbers of free parameters, influenced by two factors: the number of grasps (G) and the number of units in the ensemble (K). The baseline model has

free parameters equal to the number of grasps. The static ensemble has free parameters equal to the number of grasps plus the number of units in the ensemble ($G + K$). The task-specific ensemble model has free parameters equal to the number of grasps plus the size of the ensemble multiplied by the number of grasps ($G + K * G$).

A stratified 5-fold cross-validation approach was used to divide trials into mutually exclusive groups for fitting and evaluating models. In each fold of cross-validation, 20% of trials from each experimental condition were held out for testing. The remaining 80% of trials were used to estimate the parameters of the encoding models. The encoding and decoding performances of these models were evaluated using the trials in the test group. Each of the trials was included in the testing group once across all five cross-validation folds.

Encoding performance of each model for each unit was assessed in terms of spike timing predictability (STP). This measure compares the predictive performance of a proposed encoding model against an uninformed *null model* of spiking (Harris et al., 2003; Pillow et al., 2008; Stevenson et al., 2012; Paninski et al., 2004). The null model is an uninformed model that predicts the unit's firing probability as being constant regardless of experimental conditions or other factors. This constant firing probability is derived from the unit's overall average firing rate across all trials. STP is defined as

$$STP(\lambda) = \mathbb{E}[\log \mathcal{L}(x|\lambda)] - \mathbb{E}[\log \mathcal{L}(x|\lambda_0)] \quad (8)$$

where $\mathbb{E}[\log \mathcal{L}(x|\lambda)]$ is the expected log likelihood of some spiking sequence x under the proposed model and $\mathbb{E}[\log \mathcal{L}(x|\lambda_0)]$ is the expected log likelihood of evaluated under the null model. This measure was calculated in $\log_2$ and normalized over time to return a value in bits per second. As described in Harris et al. (2003) and Cover and Thomas (2012), this value represents the expected number of bits per second saved by a model representing the observed sequence with some additional knowledge such as the grasp being performed or the activity of other neurons. A positive STP indicates that the alternative model's prediction of spiking tends to better match observed spiking than the uninformed null model. A negative STP indicates that the alternative model tends to be less efficient at describing the observed spiking than the null model. We expect that adding informative covariates to the model would result in increased STP, whereas adding non-informative covariates would result in either no change or a decrease to the STP.

Decoding

After encoding models were fit for each unit, the models were applied to the task of decoding the grasp being performed on each trial given observed spiking activity. Using the definition for the probability of a particular sequence conditioned on a grasp type described in equations (1) and (2), the posterior probability over grasp postures can be evaluated using Bayes' Rule. The posterior density over grasps being performed can be expressed as follows:

$$P(g|X_i(t_{1:k}), \lambda(t_{1:k})) = \frac{P(X_i(t_{1:k})|\lambda(t_{1:k}), g)P(g)}{\sum_G P(X_i(t_{1:k})|\lambda(t_{1:k}), g)P(g)} \quad (9)$$

where $P(g|X_i(t_{1:k}), \lambda(t_{1:k}))$ is the posterior likelihood of the grasp being performed given the set of models and the observed population spiking activity, $P(X_i(t_{1:k})|\lambda(t_{1:k}), g)P(g)$ is the likelihood of spiking under some hypothesized task and $P(g)$ is the prior distribution over task probabilities (here assumed to be uniform). Given this estimate of the posterior density, decoding can be performed by identifying the grasp that has the maximum probability under the posterior.

This decoding approach was applied in a synchronous manner in that we assumed the decoder had knowledge of when a trial was initiated. Since the likelihood of a sequence of spiking activity evolves as the number of observations increases, so too does the estimate of the posterior density over grasps. In general, we expect that the posterior density is uniform over all grasps at the beginning of a trial and becomes more peaked around one or more grasps as additional data are observed. Applying the decoder synchronously allows us to examine the evolution of decoder performance over the time-course of a trial.

The decoding approach described so far applies to so-called individual unit decoding as the decoder output is determined by the spiking of an individual unit. Note, however, that the output of the CIF may depend on observed spiking of other neurons. In practice, individual unit outputs are combined within the context of population decoder to overcome the low signal to noise ratio of individual unit spike trains. To extend decoding to incorporate the population activity as a whole, we applied a majority-voting rule. At each time bin during a trial, each observed unit supplied a vote for the grasp with the maximum probability according to its posterior distribution. The grasp receiving the most votes across all observed units was chosen as the output of the classifier.

The posterior likelihood provided by our decoder provides the added benefit of a measure of certainty or confidence in the prediction. Thus, decoding performance was compared in terms of classification accuracy as well as confidence in the prediction as measured by the posterior distribution over grasps. The evaluated model types were compared using a multinomial selection procedure (MSP) to assess differences in decoding performance for each spiking unit (Alsing et al., 2002; Kuncheva, 2004). Rather than just accounting for classification accuracy, the MSP takes into account the posterior probability associated with each model's prediction. In the case where models have similar decoding accuracy, we would generally prefer a classifier that assigns a higher confidence to its prediction. The MSP procedure reflects this preference. Under the MSP approach, the predictions from each model in a set are evaluated against known labeled data. For each sample data point, the model that assigns the highest posterior probability to the correct class is chosen as a winner. This step in particular helps to disambiguate between models that may have similar classification accuracy. Across all samples, we calculate the percentage of times each model

won. The two models with the highest win percentages are identified and we perform a two proportion Z Test to assess statistical significance.

Results

We analyzed a single session of recorded data from each of the two monkeys. The sessions consist of neural recordings made during repetitions of unilateral center-out reach-to-grasp trials to four objects across eight locations, as shown in Figure 1B. The number of trials performed by each monkey under each experimental condition is summarized in Table 1. To account for potential imbalances in the sampled experimental conditions, data from each session was subdivided into two subsets for analysis (encoding and decoding) with three grasps each. Subset 1 consisted of the sphere, push button, and coaxial cylinder trials each at locations 1, 2, 3, and 4 (0° , 22.5° , 45° , 67.5°) and consisted of 377 and 376 trials for monkey X and L, respectively. Subset 2 consisted of push button, coaxial cylinder, and perpendicular cylinder trials each at locations 3, 4, 5, and 6 (45° , 67.5° , 90° , 112.5°) and consisted of 340 trials for each monkey. Trials at locations 7 and 8 (135° and 157.5°) were excluded from the analysis since only two different objects were ever grasped at these locations, whereas other locations included grasps of at least three different objects. Within each subset, all 12 task conditions were included in the encoding and decoding tasks. Grasps were performed at each of 4 locations to dissociate grasp from reach and ensure that the classifier was actually decoding a grasp.

Each subset of trials was analyzed independently. Analysis was isolated to the time period between cue presentation and completion of object manipulation indicated by closure of the associated microswitch. This period had an average duration of 0.79 seconds per trial in monkey X and 0.65 seconds per trial in monkey L. Within each of the subsets, a stratified 5-fold cross-validation approach was used to divide trials into mutually exclusive groups for training and testing.

Firing rate models were estimated only for units with average firing rates greater than 3 Hz. This resulted in inclusion of 58 of 112 units in monkey X and 74 of 104 units in monkey L. For monkey X, of the 58 units with firing rates greater than 3 Hz, there were 2 definite and 17 definite or probable single units. The SNR was 2.8 ± 1.2 (mean $\pm$ standard deviation) for the remaining 39 multi-units. For monkey L, of the 74 units with firing rates greater than 3 Hz, there were 14 definite and 29 definite or probable single units. The SNR was 2.8 ± 1.0 for the remaining 31 multi-units. The included units had mean firing rates of 12.0 Hz and 14.9 Hz for monkey X and monkey L, respectively.

Encoding performance

For each unit in the ensemble, we estimated three encoding models: a baseline model, a static-ensemble model and a task-specific ensemble model. An example of the trial-averaged firing rates predicted by each of these models for an individual unit is shown in Figure 3. In this figure we compare the trial averaged observed firing rate for the indicated unit, as well as the trial averaged conditional predicted firing rate under each grasp type and each model type. As shown, the three model variations exhibit very different predictions for spiking behavior. The predicted firing activity from the baseline models has an average rate that

varies across task conditions but is otherwise constant in time. The static ensemble model allows for some temporal variation that better matches the observed spiking activity. However, because ensemble weights are assumed to be constant across object types, grasp-specific variations in predicted firing rate are limited to changes in offset and the overall shape of the predicted firing rate profile has a similar shape regardless of the grasp the model is conditioned on (Figure 3). Finally, the task-specific model demonstrates greater overall temporal variability in the predicted firing rate as well as object-specific temporal variations in the predicted firing activity.

Model encoding performance was assessed by evaluating how well each model's predicted firing activity compared to the observed firing activity. We examined the spike timing predictability (STP) of each model, which is the ratio of the expected log-likelihood of spiking activity under the proposed model compared to a null model based on average spiking across all trials. The null model is a constant-rate model representing the average firing rate across all trials irrespective of experimental condition. STP is described in terms of bits per second and positive values correspond to a more descriptive encoding model. The average encoding and decoding performance of each unit is shown in Figure 4.

The baseline model significantly improved upon the STP of the null model in 52% of neurons in monkey X and 55% of neurons in monkey L (paired t-test at single-unit level, $p < 0.01$). The mean STP score of the baseline model was 0.48 ± 0.17 bits per second in monkey X and 0.42 ± 0.15 bits per second in monkey L. These results indicate that over half of our observed units in each monkey demonstrate grasp-dependent changes in their baseline firing rate.

The addition of static ensemble terms improved the STP compared to the baseline model. Static ensemble models had higher STP scores compared to baseline models in 83% of units in monkey X and 74% of units in monkey L (paired t-test at single-unit level, $p < 0.01$). The mean STP among units under the static ensemble model was 2.29 ± 0.42 bits per second in monkey X and 3.67 ± 0.56 bits per second in monkey L.

Task-specific ensemble models tended to have superior encoding performance compared to the baseline model but do not generally outperform static ensemble models. Task-specific ensemble models improved upon baseline models in 62% (57%) of units and improved upon static ensemble models in 10% (8%) of units in monkey X (monkey L) ($p < 0.01$). The mean STP under the task-specific ensemble models was 2.18 ± 0.49 bits per second in monkey X and 3.16 ± 0.62 bits per second in monkey L. The STP for each unit under the static and task-specific ensembles was strongly correlated in both monkeys (Pearson's r of 0.997 in monkey X, 0.991 in monkey L).

The average STP scores for each model type were aggregated across all units and a Friedman test with post hoc analysis was applied to compare encoding performance for each of the model types. In both monkeys, task-specific and static ensemble models had higher STP than baseline models ($p < 0.01$) and the static ensemble model had higher STP than the task-specific ensemble model ($p < 0.01$).

Decoding performance

Decoding was performed by synchronously evaluating the maximum likelihood estimate of grasp being performed using the learned encoding models. Decoding performance was evaluated using both classification accuracy as well as prediction confidence as accounted for by the use of the posterior distribution in the multinomial selection procedure. Each trial was evaluated sequentially, allowing the predicted class estimate to be updated with each time step. Because of the trials subset approach (as shown in Figure 1b) decoding was always evaluated for three grasps at four locations. The evolution of average individual unit accuracy over the time course of a trial is shown in Figure 5.

Differences in individual unit decoding performance were evaluated using the multinomial selection procedure (MSP), which is based on the posterior distribution of the classifier rather than accuracy. Task-specific ensemble models exhibited superior decoding performance in 82% of units in both monkey X and monkey L (averaged over both data subsets, $p < 0.01$). Baseline models had the best classification accuracy in 1% of units in each monkey. The remaining units did not have superior performance under any one model according to the MSP. Static ensemble models were never identified as having the best decoding performance.

Individual unit decoding performance was also assessed based on average classification accuracy at the end of each trial (switch closure). In monkey X (monkey L) individual units achieved a mean accuracy of $43.7\% \pm 1.2\%$ ($43.6\% \pm 0.9\%$) under the baseline model, $41.6\% \pm 0.9\%$ ($41.0\% \pm 0.7\%$) under the static ensemble model and $50.0\% \pm 1.6\%$ ($50.2\% \pm 1.5\%$) under the task-specific ensemble model. Overall individual unit classification accuracy under the three models was compared using a Friedman test with post hoc analysis. In both monkeys, individual unit classification accuracy was significantly higher for the task-specific ensemble model than both the static ensemble and baseline models ($p < 0.01$). The baseline model had higher classification accuracy than the static ensemble model in monkey L ($p < 0.01$), but not in monkey X ($p > 0.05$).

Within a model type, units showed a strong correlation between STP and individual unit classification accuracy. In monkey X (monkey L), the Pearson's correlation between the mean STP and mean individual unit decoding performance for each unit had a value of 0.66 (0.58) for the baseline model, 0.79 (0.80) for the static ensemble, and 0.80 (0.76) for the task-specific ensemble. This suggests that within a model type, units with better encoding performance relative to the population also tend to have better decoding performance.

Population decoding was performed using majority vote during each step of a trial. Typical trial-averaged performance is shown in Figure 6. Population classification accuracy was greatest for the task-specific ensemble models, though all three models performed significantly better than chance with average accuracy of at least 75% by the time of switch closure. In monkey X (monkey L) the final mean population classification accuracy was $79.6\% \pm 2.8\%$ ($87.8\% \pm 1.1\%$) for the baseline model, $77.3\% \pm 1.3\%$ ($75.8\% \pm 1.6\%$) for the static ensemble model and $95.4\% \pm 1.5\%$ ($96.6\% \pm 0.6\%$) for the task-specific ensemble model. In both monkeys, classification accuracy for population decoding was significantly higher for the task-specific ensemble model than both the static ensemble and baseline

models ($p < 0.001$). Population decoding performance under the baseline model was significantly greater than the static model in monkey L ($p < 0.001$) but not in monkey X ($p > 0.05$).

Discussion

In this study, we examined the impact of modeling task-specific encoding, a measure of effective connectivity, among an ensemble of simultaneously recorded cortical neurons in motor and premotor regions during performance of a motor task. We constructed point process encoding models of neuronal activity recorded from motor cortical areas of non-human primates during a reach to grasp and manipulate task. Three different models of neuronal firing were constructed, evaluated and compared: a *baseline* model, in which each neuron was modeled as having a baseline firing rate dependent on the object being grasped; a *static ensemble* model, in which the baseline model was augmented with ensemble interaction terms that were fixed across all grasp types; and a *task-specific ensemble* model, in which the influence of the ensemble interaction varied with the grasp performed. Model performance was assessed both in terms of the ability to predict spiking activity (encoding) as well as the ability to discriminate between different grasp types (decoding).

The relative encoding and decoding performance of the three model types was consistent in both data subsets in both monkeys. Inclusion of ensemble activity in both the static and task-specific ensemble models improved encoding performance compared to the baseline model as can be seen in Figure 4. Compared to the baseline model, the ensemble models are more flexible and allow for time-varying estimates of firing rate that are influenced by the activity of other units.

This result is consistent with several previous studies (Truccolo et al., 2005; Pillow et al., 2008; Stevenson et al., 2012) that found that ensemble interactions can be especially predictive of spiking activity given even a modestly-sized ensemble. Modeling task-specific ensemble interactions did not generally improve spike-timing prediction beyond that achieved by static ensemble models. Decoding performance was significantly improved compared to baseline in task-specific ensemble models but not in static ensemble models. This difference in decoding performance was observed in the case of both individual unit and population decoding, as shown in Figures 5 and 6. We thus observe that inclusion of ensemble activity generally improves prediction of spiking, but significant improvements in decoding performance due to ensemble activity require the model to account for task-specific variations in functional connectivity. In the case of static ensembles, object-specific firing may be masked by the activity attributed to the constant influence of other units, resulting in poorer decoding performance. Therefore, increasing the number of parameters in the model, as in the case of the static ensemble model compared to baseline, does not necessarily increase classification accuracy.

We observed that task-specific ensemble models do improve decoding performance compared to baseline while the static ensemble models do not. If there were no variation in ensemble effects with object, we would expect to see no difference in decoding performance

between the static and task-specific ensemble models. Those results suggest that there are potentially small but significant variations in functional connectivity across objects.

The task-specific ensemble model did not generally outperform the static ensemble model in terms of encoding. Under the task-specific ensemble model, estimates of ensemble parameters corresponding to a particular grasp are improved only by observations of trials involving that grasp. In the event that task-specific ensemble effects are small or zero, differences in precision of model parameter estimates could account for lower STP performance by the task-specific ensemble model compared to the static ensemble. If object-specific ensemble effects were sufficiently large, we would expect to see the task-specific model to have better encoding performance compared to a static ensemble model. This was the case for some units, but not the majority.

Decoding of grasping activity from neuronal data has been demonstrated previously (Carpaneto et al., 2011; Townsend et al., 2011; Aggarwal et al. 2013; Hao et al., 2014; Schaffelhofer et al., 2015; Vargas-Irwin et al., 2015). Although our study did not necessarily consider as many task conditions as those earlier works, the results show decoding performances consistent with those previous efforts. Our underlying model is a generative model that continually assesses the likelihood of spiking activity in one millisecond time bins given recently observed activity from the neural ensemble. Though this approach makes the common assumption that the time of cue presentation was known, transitioning to purely asynchronous decoding could be facilitated through a separate state classifier or other heuristic to detect the onset of a new trial or intention to move (Kemere et al., 2008; Aggarwal et al., 2008; 2013; Velliste et al., 2014). Another advantage is that our method relies on modeling functional interactions with other neurons with time-varying behavior. This allows our model to account for significant task-specific temporal variability in firing rates without explicit modeling of a tuning function or state-transition models (Shenoy et al., 2003; Kemere et al., 2008; Kang et al., 2015, Rouse and Schieber, 2016). Finally, the underlying application of a generalized linear model-to-model firing facilitates introspection of the model and further investigation of its behavior.

In this study, we introduced a novel methodology that incorporates the influence of an ensemble of neurons into a point-process decoding model. The analyses were performed over a single session of recorded data from each of two monkey subjects. Our results for both encoding and decoding proved similar across both monkey subjects over a number of trials and task conditions. Therefore, if on the one hand, an increase in the number of sessions would reinforce our claims, on the other hand, we believe that the data is adequate to support the main aim of this paper. It is worth noting that, even though variation in neural activity and recording properties would be significantly greater across monkeys than variation within a single monkey across multiple sessions (Mollazadeh et al., 2014; Rouse and Schieber, 2015; Rose and Schieber, 2016), our model showed consistent results for both monkeys.

Conclusion

Our findings suggest that task-specific functional interactions between neuronal spike trains recorded from motor-related cortical regions provide information about motor behavior. By using point process models of spiking, we were able to model these interactions and compare against traditional assumptions of independent variation of firing rate with motor behaviors. Both static and task-specific ensemble interactions explained a significant amount of spiking behavior in many neurons. Task-specific variations in ensemble interactions carried a significant amount of discriminative information about the grasp being performed, and may form the basis of more accurate and discriminative sources of decoding of movement for controlling neural prosthesis. These results also warrant further investigation into encoding of information by the functional interactions of neural ensembles beyond typical assumptions of independent encoding of motor behavior.

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Figure 1.

Experimental apparatus and analyzed experimental conditions. (A) Trials consisted of cued reach, grasp and manipulate behaviors from a home object (indicated with darker shading) to one of four objects located at 45-degree intervals along an arc centered on the home object. Moving clockwise along the arc, the objects were: perpendicular cylinder, coaxial cylinder, push button and sphere. (B) The apparatus could be rotated and allowed for objects to be presented at 8 possible locations. During a single experimental session, trials were performed at a total of 24 unique object-location combinations. We subdivided these conditions into 2 sets for analysis (Subset 1 and Subset 2, as indicated). Subsets were constructed to include 3 objects presented at each of 4 locations. In this figure, objects are denoted by shapes and possible positions are indicated by number. The apparatus setting depicted in (A) shows the objects in positions 2, 4, 6 and 8.

Figure 2.

Spike rasters and trial averaged firing rates for an individual unit from Monkey L grouped by (A) grasp, and (B) reach conditions. Trials were aligned to the onset of movement (thick vertical line) and order within task conditions by increasing trial duration. Times of completion of object manipulation in each trial are indicated with thick black marks. Spike trains were smoothed with a Gaussian kernel with standard deviation of 50 ms before averaging.

Figure 3.

Example of trial-averaged predicted spiking activity for an individual unit versus observed spiking activity under each of the object conditioned model paradigms. The black trace shows the trial-averaged observed firing rate for all trial repetitions of a particular object type. The colored traces show the predicted firing rates ($\lambda(t|\cdot)$) that were predicted by each of the models under different assumptions regarding the object being grasped. In each row, the predicted firing corresponding to a match between the assumed object being grasp and the actual object being grasped is indicated as a solid colored trace. Predicted firing rates for a mismatch between model assumptions and actual object are shown with dashed traces. For illustrative purposes, both observed and predicted spiking activities were convolved with a Gaussian kernel (std. dev. 25 ms) before averaging. Trials were time-normalized within each experimental epoch before averaging. Vertical lines indicate cue presentation (Cue), onset of movement (OM), object contact (OC), and static hold (SH).

Figure 4.

Relationship between spike timing predictability and accuracy. The average classification accuracy for each unit and each model is plotted against STP (main panel). Values represent the average across both data subsets. The left panels show the box plots for the marginal distribution of classification accuracy for each model. The bottom panels show the box plots for the STP for each model. In the box plots, the tick mark corresponds to the median and the thicker region of each colored trace indicates inter-quartile range.

Figure 5.

Trial averaged classification accuracy for individual unit decoding across all trials for both monkeys averaged across both subsets. Classification accuracy averaged across units is indicated for each of the three model types. Shaded region denotes standard error. Classification at each time step was performed by selecting the class corresponding to the maximum under the posterior distribution given observations prior to that time step. Vertical lines indicate cue presentation (Cue), onset of movement (OM), object contact (OC), and static hold (SH). Decoder output was time-normalized within each epoch (Cue to OM, OM to OC, OC to SH) before averaging. The horizontal dashed line indicates threshold for chance decoding performance at $p = 0.05$ significance level.

Figure 6.

Trial averaged classification accuracy for population decoding across all trials for both monkeys averaged across both subsets. Average classification accuracy is indicated for each of the three model types. Shaded regions denote standard errors. Classification at each time step was performed using majority vote with each spiking unit contributing a single vote for the most likely grasp given the observations prior to that time point. Vertical lines indicate cue presentation (Cue), onset of movement (OM), object contact (OC), and static hold (SH). Decoder output was time-normalized within each epoch (Cue to OM, OM to OC, OC to SH) before averaging. The horizontal dashed line indicates threshold for chance classification performance at $p = 0.05$ significance level.

Table 1

Number of trials included in analysis at each object and location for monkey X (monkey L).

	0°	22.5°	45°	67.5°	90°	112.5°	Total
Sphere	34 (30)	33 (30)	39 (27)	24 (29)	–	–	130 (119)
Push button	28 (25)	26 (26)	29 (27)	30 (26)	37 (27)	29 (29)	179 (160)
Coax. cylinder	33 (29)	33 (30)	33 (29)	35 (29)	33 (29)	31 (31)	198 (177)
Perp. cylinder	–	–	25 (28)	29 (29)	31 (29)	34 (31)	119 (117)
Total	95 (84)	92 (86)	126 (114)	118 (113)	101 (85)	94 (91)	626 (573)