Ascertaining the Importance of Neurons to Develop Better Brain-Machine Interfaces

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***Abstract*—In the design of brain-machine interface (BMI) algorithms, the activity of hundreds of chronically recorded neurons is used to reconstruct a variety of kinematic variables. A significant problem introduced with the use of neural ensemble inputs for model building is the explosion in the number of free parameters. Large models not only affect model generalization but also put a computational burden on computing an optimal solution especially when the goal is to implement the BMI in low-power, portable hardware. In this paper, three methods are presented to quantitatively rate the importance of neurons in neural to motor mapping, using single neuron correlation analysis, sensitivity analysis through a vector linear model, and a model-independent cellular directional tuning analysis for comparisons purpose. Although, the rankings are not identical, up to sixty percent of the top 10 ranking cells were in common. This set can then be used to determine a reduced-order model whose performance is similar to that of the ensemble. It is further shown that by pruning the initial ensemble neural input with the ranked importance of cells, a reduced sets of cells (between 40 and 80, depending upon the methods) can be found that exceed the BMI performance levels of the full ensemble.**

***Index Terms*—Brain-machine interface, cosine tuning, information in neural ensembles, sensitivity-based model pruning.**

I. Introduction

BRAIN-MACHINE INTERFACES (BMIs) interpret and translate neural activity into computer and prosthetic control commands. BMIs have used the firing patterns of the primary motor, premotor, or posterior parietal cortices to reconstruct arm and hand kinematic parameters (i.e., position, velocity, and acceleration) [1]–[14]. Much like a linguist translates language; a BMI model must learn the language of neural firing and translate it into motor commands. Thus far, this translation task has been approached from an adaptive (optimal) signal processing point of view where tools such as Wiener filters [12]–[14], Dynamic Neural Networks [1], [9], [10], [14], and Kalman filters [8], [15]–[17] have been trained to find the functional relationship between neural activity and the kinematic variables. By presenting recordings of neural activity collected simultaneously with behavior and using a statistical learning criterion, it has been shown that arm and hand position, velocity, and acceleration can be reconstructed in a variety of motor tasks [1]–[14].

The performance of BMI neural to motor translation algorithms hinges on the ability to exploit information in chronically recorded neuronal activity. The previous work with linear models mentioned above has revealed that the cellular firing rate is correlated with changes in goal directed behavior. Since during the surgical phase there are no precise techniques to target these modulated cells, the strategy has been to sample as many cells as possible from multiple cortical areas with known motor associations. This approach improves the probability of finding cells modulated to the kinematic variables of interest with the added advantage of enhanced performance due to a more extensive sampling of the motor cortex. However, in terms of modeling there are difficulties associated with a large number of cells.

A significant problem introduced with the use of hundreds cellular inputs is model overfitting. The introduction of extra degrees of freedom not related to the mapping can result in poor generalization, especially in topologies where tap-delay memory structures are implemented in the neural input layer. In fact, with each additional memory delay element, the number of free parameters will scale with the number of input neurons. This explosion in the number of free parameters also puts a computational burden on computing an optimal solution especially when the goal is to implement the BMI in low-power, portable hardware.

As a first step, one could develop and study more parsimonious models such as the recurrent multilayer perceptron [8], [10], [18]. The topology of this model can significantly reduce the number of free parameters by implementing feedback memory structures in hidden network layers. Secondly, during model training, regularization techniques could also be implemented [19] that attempt to reduce the value of unimportant weights to zero and effectively prune the size of the model topology. However, this approach is strictly a statistical modeling technique that requires lots of data and computation, it is not trivial to use, and does not necessarily provide information about importance of neurons. Finally, the number of inputs given to the models could be manually pruned, but it is difficult to know how it will affect BMI performance.

For these reasons, we develop here techniques and compare tools that can be used to assess the utility of recorded neural ensembles in an adaptive modeling framework. Since our ultimate

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goal for BMIs is to design the most accurate reconstructions of hand kinematics from cortical activity using adaptive signal processing techniques, it seems natural to equate here neural importance to sensitivity of inputs to model fitting quality (or its proxy the correlation). Moreover, these measures should be compared with the available neurophysiologic knowledge, with the hope that we can understand better the data, enhance our methodologies and ultimately the performance of BMIs. Therefore, the importance of neurons will be ascertained using the following three techniques.

- Single neuron correlation analysis through a model-based Wiener Filter (the most common linear feedforward model used in the BMI literature).
- Sensitivity analysis through a model-based vector (multi-input) Wiener Filter.
- Cellular directional tuning analysis.

Given a set of data, we would like to evaluate how well these three methodologies are able to find important neurons for building BMI models. Secondly, we would like to use this information to tackle the model generalization issues encountered in BMIs. The goals of the study are formulated in the following questions:

- Can our methods automatically indicate important cells for the prediction of the kinematic variables in the tasks studied?
- In this model-based framework, can better BMIs be built using a subset of important cells?
- Is the model-independent technique a good indicator of cellular importance, and how is it related to sensitivity through the linear model?

It is well known that neurons vary in their involvement in a given task [20]. However, quantifying neuronal involvement for BMI applications is still an ongoing area of research. This is where BMI modeling is an asset, because once trained, the model implicitly contains the information of how cells contribute for the mapping. The difficulty is that the assessment is in principle dependent upon the type of model chosen to predict the kinematic variables and its performance (model-dependent). The linear model will only be addressed in this paper, but the ranking of neural importance is contrasted with the tuning characteristics of each neuron established directly from the data (hence we call this method model-independent). Our second question quantifies the change in performance when only a small subset of cells is used to build the BMI. In principle, one could think that any subset of cells will perform worse than the whole ensemble, but due to the poor generalization of large models, performance may be in fact better in a test set with a reduced number of important cells. Of course, this also makes BMIs more dependent upon the stability over time of these cells, and in the long run performance may suffer, and retraining of the models may be necessary. In this paper, due to the limited data sets, variability over time of the cell importance is not addressed.

The final question seeks to validate ranking of neurons obtained through trained models with directional tuning analysis, which has been used to model the role of motor cortex neurons. First, by picking cells that are highly tuned to the prediction of kinematic variables, BMI performance will be tested. Secondly, the tuning features of the important cells automatically chosen by the linear model will be analyzed. The ultimate goal is to improve understanding of how cells encode kinematic parameters so that better "gray-box" models can be built using the underlying information in neural recordings.

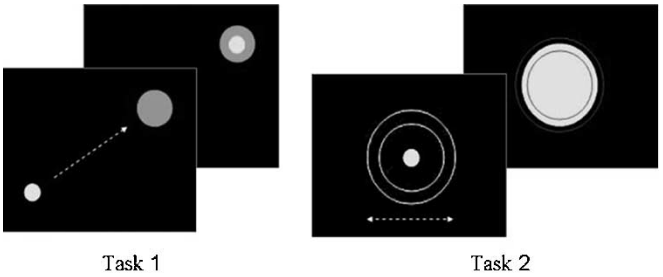

Fig. 1. Using a joystick the monkey controlled the cursor to intersect the target (task 1) and to grasp a virtual object by applying a gripping force indicated by the rings (task 2).

II. Behavioral Experiments and Neuronal Recordings

The data for these experiments was collected in the primate laboratory at Duke University. Using microwire electrode arrays chronically implanted in the dorsal premotor cortex (PMd), supplementary motor area (SMA), primary motor cortex (M1, both hemispheres) and primary somatosensory cortex (S1) [21], the firing times of up to 185 cells[1] were simultaneously collected in an adult female monkey (Macaca mulatta) while performing the two behavioral tasks shown in Fig. 1. The first task, a hand-reaching task, involved the presentation of a randomly placed target (large disk) on a computer monitor in front of the monkey. The monkey used a hand-held manipulandum (joystick) to move the cursor (smaller circle) so that it intersects the target. Upon intersecting the target with the cursor, the monkey received a juice reward. While the monkey performed the motor task, the hand position and velocity for each coordinate direction (HPx, HPy and HVx, HVy) were recorded in real time along with the corresponding neural activity. In the second task, the monkey was presented with the cursor in the center of the screen and two concentric rings. The diameter difference of these two circles instructed the amount of gripping force the animal had to produce. Gripping force (GF) was measured by a pressure transducer located on the joystick. The size of the cursor grew as the monkey gripped the joystick providing continuous visual feedback of the amount of gripping force. Force instruction changed every trial while the position of the joystick was fixed. Neural and behavioral recordings were collected in two independent sessions over two consecutive days for each of the tasks.

For each modeling analysis technique studied, the neuronal spike events were binned (added) in nonoverlapping windows of 100 ms and behavioral datasets, i.e., hand kinematic and force parameters, were digitally low-pass filtered and downsampled to 10 Hz. Both the neural recordings and behavior were time aligned[2] and used directly as inputs and desired signals for

[1]HP, HV Session 1—64 PMd, 56 M1, 39 S1, 19 SMA, 5 M1-ipsiHP, HV Session 2—66 PMd, 57 M1, 38 S1, 19 SMA, 5 M1-ipsiGF Session 1—41 PMd, 33 M1, 22 S1, 16 SMA, 8 M1-ipsiGF Session 2—38 PMd, 28 M1, 21 S1, 16 SMA, 3 M1-ipsi.

[2]We assume that the memory structures in each model can account for the delay between neural activity and the generation of the corresponding behavior.

each model. During each recording session a sample data set was chosen consisting of 8000 data points. This data set was segmented into two exclusive parts: 5000 samples for model training and 3000 samples for model testing (results in [22] showed that models trained with approximately 10 min of data produced the best fit).

III. Methods for Ranking the Importance of a Neuron

In this paper, we would like to obtain an automatic measure of each cell's contribution to encoding motor parameters for a given task, which we call the cell importance. For this reason, a structured approach is taken to ascertaining the importance of neurons with the three methods described above. Our methodological choices however are not free from assumptions. First, all three methods assume stationarity in the data. A snapshot of neural activity is taken and importance is ascertained without addressing time variability in the recordings, which is a shortcoming. Second, in spite of the highly interconnected nature of neural structures, both the cellular tuning and single neuron correlation analysis are computed independently for each individual neuron. With this independence assumption, it is difficult to quantify the importance of pairs, triples, etc. of cells. In contrast, the model sensitivity analysis considers covariations in firing rate among groups of cells in the neural ensemble, but depends on the type of model utilized. Third, the cellular tuning technique only considers the instantaneous neural activity while the modeling techniques include memory structures (tap-delay-lines). Finally, each technique for ascertaining importance focuses on different neuronal firing features. In the case of directional tuning, the local variations of the firing rate are of interest, while in the model sensitivity (as well as the single neuron correlation) variations in firing rate over the analysis interval are quantified.

A. Model-Independent—Cellular Tuning Analysis

Our first method for ascertaining the importance of neurons involves computing the tuning or preferred direction [2] of each cell in the ensemble. Tuning curves convey the expected value of a probability density function indicating the average firing a cell will exhibit given a particular movement direction. In this approach, the data is analyzed in the neural space as compared to using an input-output model that optimizes a set of parameters using a statistical learning criterion to map the neural inputs and desired kinematics.

It has been shown in the literature that a variety of hand trajectories can be reconstructed by simply weighting and summing the vectors indicating preferred directions of cells in an ensemble of neurons [3], [11], [13], [23]. Neurophysiologic evidence suggests that the direction of hand movements is encoded in cells that have cosine shaped tuning curves. Our metric for ranking will be the tuning depth of a cell's tuning curve. This quantity is defined as the difference between the maximum and minimum values in the cellular tuning. For an impartial comparison of the cellular tuning depth, the tuning curves are normalized by the standard deviation of the firing rate. This measurement relates how "peaky" the tuning curve is for each cell and is an indicator of how well modulated the cell's firing rate is to the kinematic parameter of interest.

To use this measurement, the hand direction tuning curves and gripping force histograms must first be computed for each cell. Since this investigation of kinematic parameters exists in different dimensional vector spaces [HP, HV in two dimensional, GF in one–dimensional (1-D) spaces], the differences in the computation are described here. In the multidimensional case, hand direction is determined by using the desired hand position from which the corresponding velocity vector (magnitude and direction) between successive points in the trajectory is computed. The quantity that is commonly used in BMI experiments is the hand movement direction measured as an angle between 0° and 360° [24]. Since cellular tuning can produce properties where the average of angle 0° and 360° is not 180° (this results from the wrap-around effect of the measurements), the mean of each cell's hand direction tuning is computed using circular statistics as in (1)[3] [25]

$$\text{circular mean} = \arg\left(\sum_{N} r_N e^{i\theta_N}\right) \tag{1}$$

where r_N is the cell's average firing rate for angle θ_N where N is from 1 to 360.

In the 1-D case of force, the vector space is restricted to the magnitude of the vector. Typical force histograms are ramp functions that saturate since cells tend to increase their activity proportionally to greater force demands up to the maximum firing rate, so the range is still finite [26]. Moreover, since GF curves are not subject to the wrap-around effect, (1) is disregarded and the maximum value of the firing rate curve of each cell is used to determine the preferred force the cell is tuned to. While the force curves obtained in this analysis do not fit the classical definition of "tuning", for simplicity we will use the term tuning depth for both GF and HV for the remainder of this study. Despite these differences, the depth of tuning of each cell can still be used as a measure of information content provided by the cells[4]. Since computing the tuning depth from finite data is noisy, the curves are smoothened by using a coarse resolution[5] to count the number of times that each cell fires. The sum of neuronal firings is also normalized for each angle/force by the total number of times that the hand visits the angle/force. Essentially with this method the cellular mean firing rate for each angle/force is computed.

[3]In computing the circular mean, we used the four quadrant inverse tangent.

[4]We have observed that the tuning of a cell can vary as a function of the delay between the generation of the neural activity and the physical movement of the hand. Since we are interested in tuning depth, we are looking for cells that have the smallest variance in their tuning function. After computing tuning variance across all cells for delays up to 1 second, we found that the sharpest tuning occurs at the 0th delay or the instantaneous time alignment. This was the delay chosen for the remaining sections of this study.

[5]For hand direction, 45 degree bins were chosen. In the case of force, the dynamic range of the measurement was divided into 10 nonoverlapping bins.

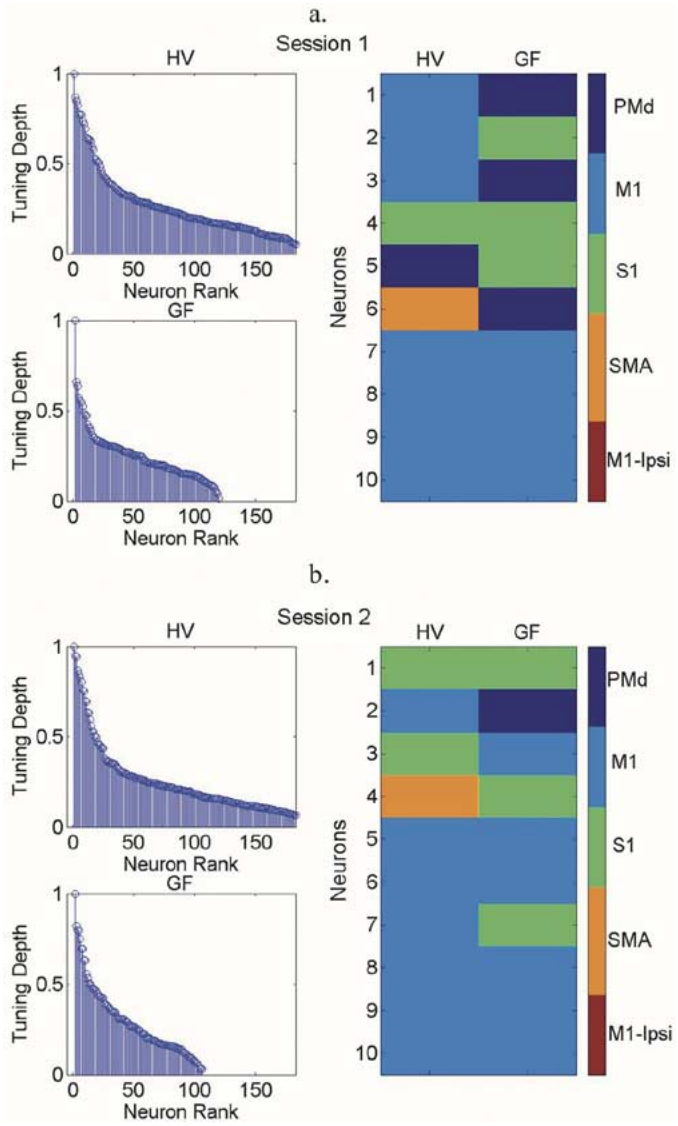

Fig. 2. Neuronal ranking based upon the depth of the tuning for each cell. The cortical areas corresponding to the most sharply tuned cells is given by the colormap.

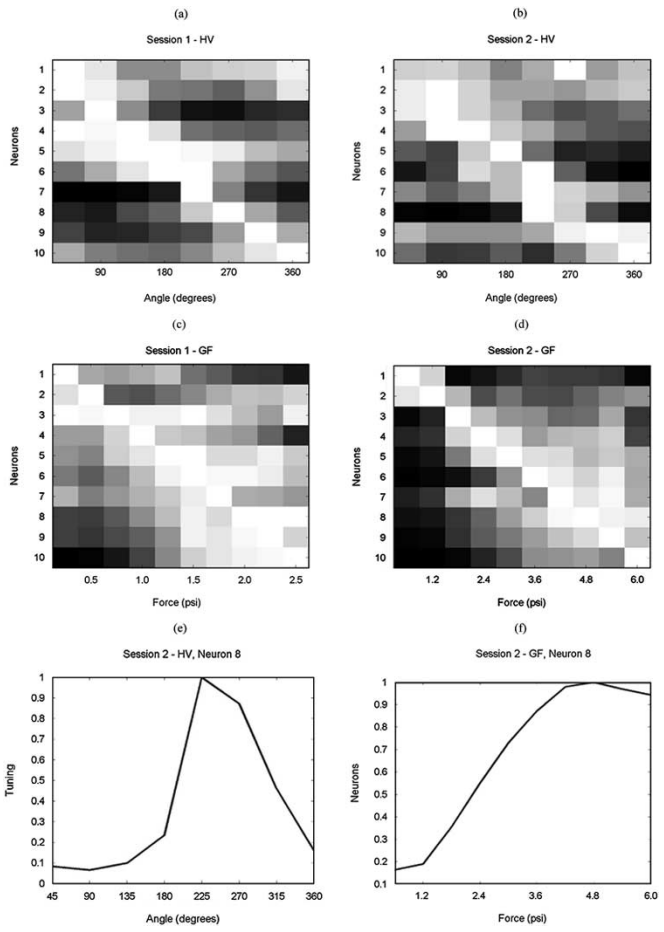

Fig. 3. (a)–(d) Cellular tuning curves for hand direction and gripping force using a model independent ranking method, (e)–(f) Tuning curves for two representative cells from plots (b) and (d).

In Fig. 2(a) and (b) (left subplots) a plot of the ranked list of cells is given for hand direction and gripping force based upon the normalized depth of their tuning. From the plots of both sessions, we can see that the histograms have a knee between 10 and 40 (depending on the kinematic variable) suggesting that the cells can be divided into two groups according to tuning depth.

One can expect that for model building, these highly tuned cells will be more relevant. But tuning depth is not the only parameter of interest for a BMI since the input must also supply sufficient information to reconstruct all of the HPs, HV, and GFs desired trajectories, that is, the set of deeply tuned neural vectors must span the space (i.e., angles 0°–36°, 37°–72°, ...) of the desired kinematic variable. Therefore, each cell was ranked by the tuning mean angle and the corresponding depth of tuning was used to select cells to cover the space. For simplicity and robustness, the hand direction space is divided into 10 equally spaced bins, and in each bin, the cell that exhibits the deepest tuning is selected.

The brain areas corresponding to the deepest tuned cells that span the kinematic space are presented in the right subplots of Fig. 2. Notice the different brain areas that contribute deepest tuned cells for GF and HV. In the first session, the top cells for hand direction are primarily from M1 while gripping force involves not only M1, but also S1, and PMd. In session two, hand direction is still dominated by M1, but two of the top PMd cells for gripping force are replaced with M1 cells. In both figures, it is interesting to observe that S1, a somatosensory cortical area, was ranked highly in the cell ordering for motor tasks.

The corresponding tuning curves for the top ten cells are shown in Fig. 3. Here the maximum and minimum values for each tuning curve are represented by white and black respectively. In both sessions, for hand direction and gripping force, we could find cells that span the kinematic variables (i.e., have their maximum values approximately on the diagonal). Fig. 3 also depicts the differences in the tuning between hand direction and gripping force where in (e) a representative neuron's tuning curve shows a bell-shape while in (f) the neuron exhibits a (left to right) graded increase in the tuning curve from smaller to maximum force. The latter organization is consistent with a threshold of firing arranged by force level.

B. Model-Dependent—Single Neuron Correlation Analysis

Fig. 4 shows the topology of the multiple output Wiener filter (WF) where the output y_j is a weighted linear combination of the 10 most recent values of neuronal inputs $\mathbf{x}$ (i.e., the dimension of $\mathbf{x}$ is $5000\times185*10$) given by (2), [27]. The optimal MSE solution is given by (3), where $\mathbf{R}$ and $\mathbf{P}_j$ are the autocorrelation and cross correlation functions, respectively, and $\mathbf{d}_j$ is one of the following: hand trajectory, velocity, or gripping force.[6]

$$y_j(t) = \mathbf{x}(t)\mathbf{W}_j \tag{2}$$

$$\mathbf{W}_j = \mathbf{R}^{-1}\mathbf{P}_j = E(\mathbf{x}^T\mathbf{x})^{-1}E(\mathbf{x}^T\mathbf{d}_j). \tag{3}$$

The goal of the linear correlation analysis is to quantify how much of the variance in the output of the linear model is captured by each cell. Therefore, only one input is used in Fig. 4. Our metric of performance will be the correlation coefficient (CC) between the outputs of the model and the desired HP, HV, or GF. The method involves first training separate WFs for each cell (and each output variable) of the entire neural ensemble.

Using each cell's correlation coefficient, a ranked list of single cells can be created based on their contribution to reconstructing the kinematic variables. In Fig. 5 (left subplots), the cellular ranking is presented for position, velocity, and gripping force for two sessions. The general shape of these curves is very similar to Fig. 2. In the right subplots the brain areas associated with the top 10 cells for each ranking is presented. The highest ranked HP and HV cells for Sessions 1 and 2 are primarily from M1 as expected, but 3 cells from areas other than M1 are also included (10% SMA, 20% S1). However, in the first GF recording session 40% of the highest ranked cells are from PMd. Interestingly (as in the model-independent ranking) in the second GF recording session these cells disappear and are replaced with other M1 cells. It is also interesting that nonmotor S1 cells appear high in the ranking for Session 2 for this model-dependent analysis.

Again, the ranked brain areas are supplemented with the corresponding tuning curves for HP, HV, and GF in Fig. 6. For all three kinematic parameters, the correlation analysis still prefers cells that span the space (roughly have maximum along the diagonal[7]), in spite of the fact that this is not explicitly imposed by the method. For HP and HV, the curves show slightly more emphasis on 270° angles. We would like to also point out the differences in cellular tuning for GF across recording sessions. In the first session, the top cells tend to split the space with two strategies; one set of tuning curves (cells 1–3) ramps down from maximum for lower forces and the other set (cells 4–6) that ramps up to maximum for larger forces. In the second session the majority of the cell tuning curves ramp up, with maximum values occurring at different force levels.

C. Model-Dependent—Model Sensitivity Analysis

The last method of inferring cell importance is through sensitivity analysis of the trained vector Wiener filter, which is a multiple input, multiple output (MIMO) system. When the fitting error is small, the desired response can be approximated by the output of the model. This approximation yields a significant savings in computing the correlation between the input and the output. In fact, for each coordinate direction, a sensitivity analysis can be performed by computing the Jacobian of the output vector with respect to each neuronal input i, which for the linear model, yields directly

$$\frac{\partial \mathbf{y}_j}{\partial \mathbf{x}_i} = \mathbf{W}_{10(i-1)+1:10(i-1)+10,j}. \tag{4}$$

Hence, a neuron's importance can be determined by simply reading the corresponding weight value[8] in the trained model, if the input data for every channel is power normalized. Since for neural data this is not the case, the neuron importance is estimated in the vector Wiener filter by multiplying the absolute value of a neuron's sensitivity with the standard deviation of its firing computed over the dataset[9] as in (5). To obtain a scalar sensitivity value for each neuron, the weight values are also averaged over the 10 tap-delays and output dimensions

$$S_i = \sigma_i \frac{1}{2}\sum_{j=1}^{2}\frac{1}{10}\sum_{k=1}^{10}\left|\mathbf{W}_{10(i-1)+k,j}\right|. \tag{5}$$

The sorted position, velocity and griping force sensitivities of the neuron population for each session's are plotted in Fig. 7(a) and (b) for two sessions. Like the model independent and single neuron correlation analysis, an initially sharp decrease from maximum indicates that there are a few neurons that are significantly more sensitive than the rest of the ensemble. For HP and HV, the most important neurons are again mostly located in the primary motor cortex (M1). For the GF the same trends can be seen as with the model-independent and WF; initially during first session multiple brain areas are contributing but many of these cells are replaced during Session two with cells from M1.

To complete our cellular ranking analysis, the cortical rankings are again supplemented with the corresponding tuning curves in Fig. 8. The same trends on tuning for the kinematic variables of HP, HV, and GF are found here. Even the selections

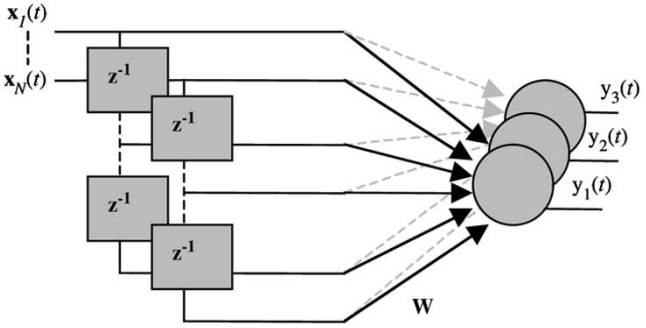

Fig. 4. Wiener filter topology. Each neuronal input $\mathbf{x}_N$ contains a tap-delay line with 10 taps.

[6]Each neuronal input and desired trajectory for the WF was preprocessed to have a mean value of zero.

[7]Cellular tuning curves are plotted in order of increasing circular mean.

[8]In this analysis we consider the absolute values of the weights averaged over the two output dimensions and the *ten* tap-delays per neuron.

[9]By multiplying the model weights by the firing standard deviation we have modified the standard definition of sensitivity; however, for the remainder of this paper we will refer to this quantity as the model sensitivity.

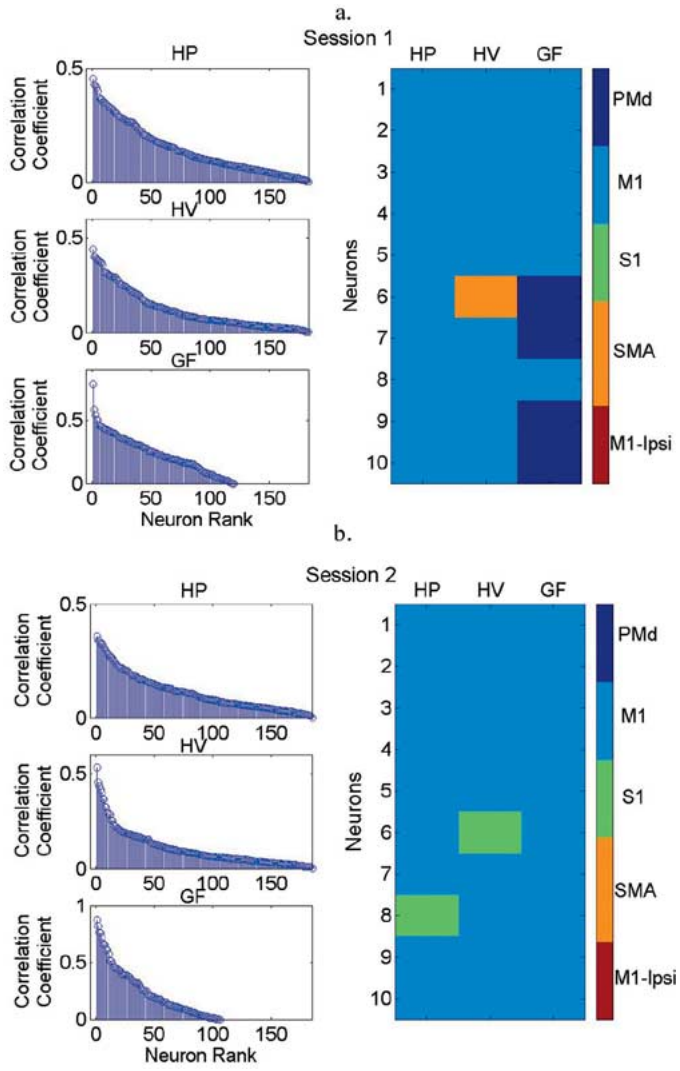

Fig. 5. Single neuron correlation-based neuronal ranking for HP, HV, and GF for two sessions. The cortical areas corresponding to the ten highest ranking HP, HV, and GF neurons are given by the colormap.

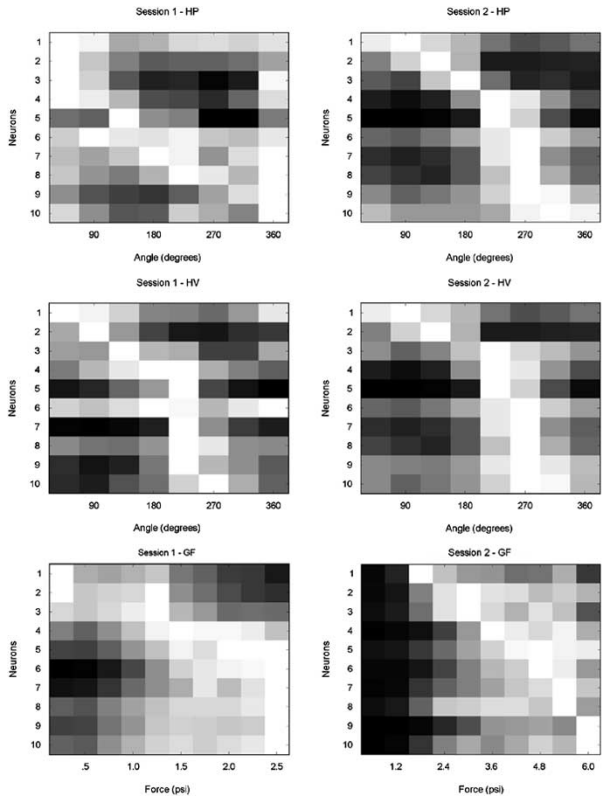

Fig. 6. Cellular tuning curves for HP, HV, and GP using single neuron correlation analysis through a linear model.

of ramp up and ramp down cells for GF in the first session are similar to the linear correlation analysis.

IV. Relative Ranking of Neurons

All three approaches utilized to ascertain the importance of cells for reconstructing hand kinematics lead to very similar distributions of cell rankings, and consistently point to similar brain areas for the important neurons. We now quantify in more detail the relative ranking of cells given by each method.

The pair wise ordering of cells from all three methods is compared by plotting the normalized[10] rank value of each cell as in Fig. 9. Ideally, if both methods contained the same order in ranking, all points would lie on the line $y = x$. In these figures, we did observe differences in the rankings produced by the three methods. Principal component analysis (PCA) revealed that the eigenvector corresponding to the largest eigenvalue roughly aligns with the diagonal. Additionally, the ratio of first and second eigenvalues was large for each scatter plot (Tuning Depth versus Single Neuron Correlation -7.90, Single Neuron Correlation versus Sensitivity -4.88, Sensitivity versus Tuning Depth -3.15). This can be interpreted as meaning that the 3 methods tend to pick the same top ranked cells. Table I shows in bold the common cells in the group of the 10 top-ranked cells.

[10]The ranking values for each method were normalized by the maximum.

V. BMI Performance

For uniformity with the tuning curve method, only the ten most important cells were picked from each ranking and used them as model inputs. Again, the same 8000 data points were chosen for evaluating the models (5000 pts training, 3000 pts testing).

The performance of each model was evaluated by computing the correlation coefficient between the model output and the desired kinematic trajectory. In Table II, the average (computed over 60 s) and best test set correlation coefficients for both sessions, coordinates (x, y), and kinematic variables (HP, HV, and GF) are presented when all the 185 neurons are used in the modeling. By evaluating the CC over windows of various sizes, the variability of the correlation coefficient over the session was assessed. One can see from the table that the best CC values can be much higher than the mean value, meaning that the fit is not equally good across the test session.

Table III shows the average and best CC for the models trained with the 10 most important cells picked by each of the criteria. Even with a gross subsampling (10 cells out of 185) of the ensemble, these models produced correlation coefficients close to our best performing models which were trained on

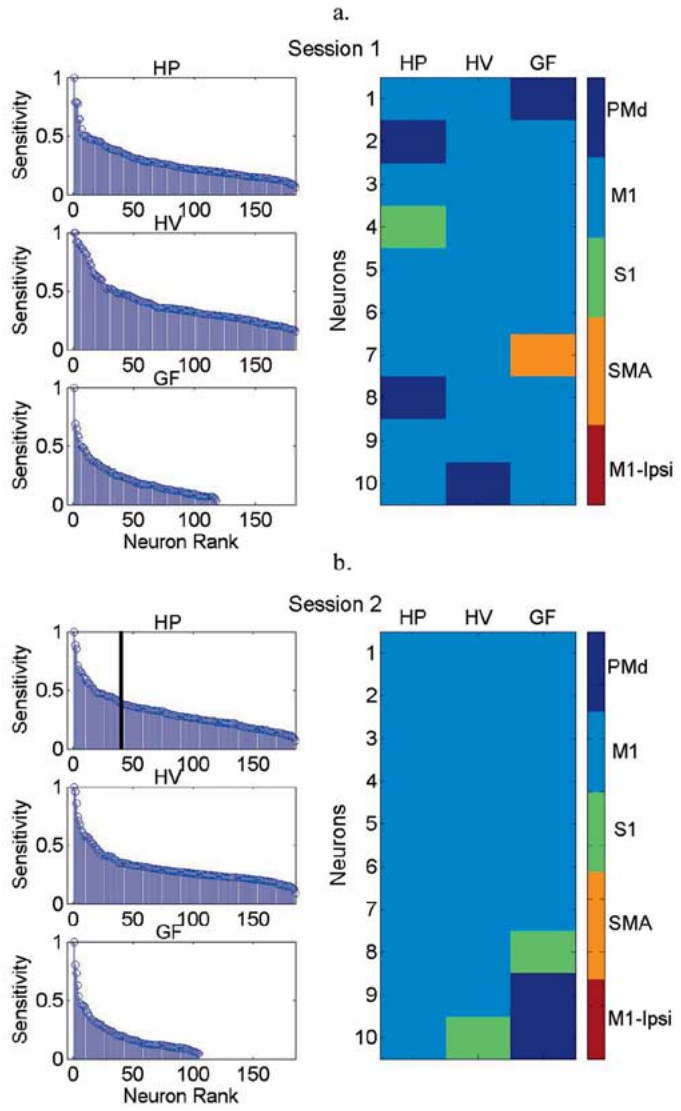

Fig. 7. Sensitivity-based neuronal ranking for HP, HV, and GF for two sessions using WF sensitivity analysis. The cortical areas corresponding to the ten highest ranking neurons are given by the colormap.

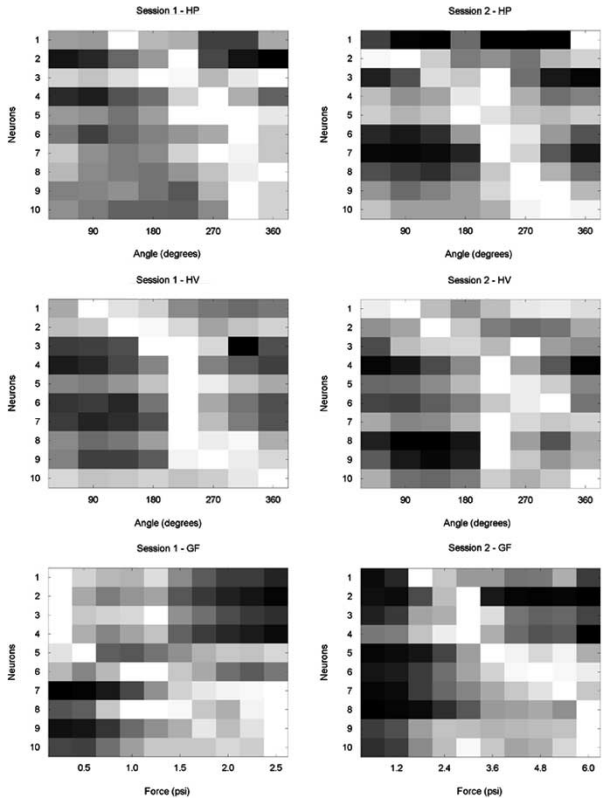

Fig. 8. Cellular tuning curves for HP, HV, and GP using WF sensitivity analysis.

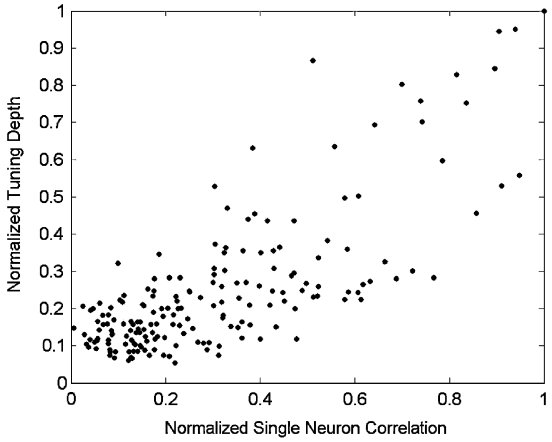

Fig. 9. Scatter plot of neuron ranking for tuning depth and single neuron correlation analysis.

the full ensemble. This observation provides confidence in the methodologies for selecting cellular importance. Statistically, a significant decrease in performance was observed in several of the kinematic variable predictions when the Kolmogorov-Smirnov (K-S) significance test ($p = 0.05$) was applied to 60-s windowed correlations between the ensemble and subsets, as shown in Table III (1 means significantly different). Performance between the models that used model-independent and dependent cellular ranking techniques only differed by 0.03 ± 0.03 for position, 0.02 ± 0.01 for velocity, and 0.03 ± 0.04 for force. The cells picked using model sensitivity, when compared to the other methods, produced more models that are not significantly different from the ensemble as indicated by the K-S significance test.

VI. Implications of Sensitivity Analysis for Model Generalization

In both our correlation and sensitivity analyzes, 10 cells were chosen to match the model-independent cell ranking. However, the optimal number of cells required for the maximum model performance remains unknown. Previously, Wessberg et. al. have shown through neuron dropping analysis that increasing the size of the neural ensemble as the inputs to a WF will lead to the best HP test set CC values [14]. In this paradigm, the WF was initially trained with the entire neural population and test set CC values were computed. A single neuron was then *randomly* removed from the population, the model was retrained, and the new CC values were computed. This process was then repeated until a single cell remained. We have reproduced this analysis for HP using the data from Session 2 of our

TABLE I
THE 10 TOP RANKED CELLS

HP		HV			GF		
CC	*Sens.*	*CC*	*Sens.*	*TD*	*CC*	*Sens.*	*TD*
80*	**73***	**80***	**104***	126*	**44***	**41***	82*
110	104	**99**	**80**	67	**53**	**44**	20
99	**69**	**84**	**110**	**149**	**57**	62	**41**
69	108	81	**84**	167	**55**	**53**	76
84	107	**77**	108	106	**49**	61	**49**
81	**80**	**149**	120	**104**	45	**56**	**57**
106	**84**	**76**	**99**	**76**	**41**	**57**	71
149	68	**110**	**77**	**80**	**56**	27	**53**
77	**99**	85	92	69	46	72	**44**
73	123	73	**149**	72	63	14	**56**

*Neurons are listed from most important to least important
CC-Single Neuron Correlation Analysis, Sens.-Sensitivity Analysis, TD-Cellular Tuning

TABLE II
TEST SET CORRELATION COEFFICIENTS USING THE FULL ENSEMBLE

		HP		HV		GF
	CC	x	y	x	y	n/a
Session 1	Average	0.76 ± 0.04	0.67 ± 0.08	0.71 ± 0.03	0.70 ± 0.05	0.83 ± 0.02
	Best	0.84	0.81	0.79	0.78	0.87
Session 2	Average	0.63 ± 0.05	0.77 ± 0.03	0.67 ± 0.07	0.75 ± 0.02	0.84 ± 0.02
	Best	0.73	0.83	0.78	0.79	0.94

TABLE III
TEST SET CORRELATION COEFFICIENTS USING 10 MOST IMPORTANT NEURON CELLS

			HP		HV		GF
			x	y	x	y	n/a
Session 1	Model-Independent	Average	0.67 ± 0.06	0.46 ± 0.04	0.67 ± 0.04	0.67 ± 0.03	0.83 ± 0.02
		Best	0.78	0.55	0.73	0.73	0.88
		K-S test	1	1	1	1	0
	Single neuron Correlation	Average	0.69 ± 0.04	0.47 ± 0.09	0.69 ± 0.05	0.65 ± 0.03	0.84 ± 0.03
		Best	0.76	0.62	0.76	0.72	0.89
		K-S test	1	1	1	1	0
	Vector WF Sensitivity	Average	0.68 ± 0.03	0.60 ± 0.07	0.64 ± 0.04	0.67 ± 0.03	0.84 ± 0.03
		Best	0.74	0.71	0.69	0.73	0.89
		K-S test	1	1	1	1	0
Session 2	Model-Independent	Average	0.62 ± 0.06	0.67 ± 0.05	0.65 ± 0.08	0.69 ± 0.04	0.91 ± 0.01
		Best	0.72	0.75	0.77	0.74	0.94
		K-S test	0	1	0	1	1
	Single neuron Correlation	Average	0.62 ± 0.06	0.73 ± 0.04	0.63 ± 0.10	0.77 ± 0.03	0.91 ± 0.02
		Best	0.75	0.81	0.77	0.81	0.94
		K-S test	0	1	1	1	0
	Vector WF Sensitivity	Average	0.65 ± 0.05	0.65 ± 0.05	0.64 ± 0.10	0.76 ± 0.03	0.92 ± 0.02
		Best	0.74	0.75	0.78	0.80	0.95
		K-S test	0	1	0	1	0

neural/behavioral recordings and the corresponding curves for both the x and y coordinates are shown in red (ND) in Fig. 10.[11]

The neuron dropping analysis was repeated but now removing the neuron that is *least sensitive* according to the vector WF sensitivity. The CC in the test set obtained with the modified neuron dropping analysis in blue (SA) for the x and y coordinates is presented in Fig. 10. In this figure, one can see that using the ten most sensitive cells high CC values are quickly achieved. As more cells are added, the performance increases further, peaking above the performance of the full ensemble once 41 cells have been added as inputs. Beyond 41 cells, a *decrease in model performance* especially in the x-coordinate can be observed. The optimal number of cells (41) was determined by taking the maximum of the average CC over the two coordinate directions and yielded CC of $0.70/0.77$ for $\mathrm{x/y}$ HP and $0.72/0.78$ for $\mathrm{x/y}$ HV.

Referring back to the HP sensitivity curves Fig. 7(b), this threshold of peak performance (black vertical line) for the ranked list of cells appears where the slope of the sensitivity curve changes. The curves in blue resemble the generalization curves reflecting the bias variance dilemma of model fitting [28]. Using this sensitivity-based neuron dropping analysis, a similar behavior is obtained by pruning the input from cells that were less important. Using the 41 most sensitive cells the vector WF obtained a 6% and 5% increase in CC on the test set for HP and HV, with respect to the WF with 185 neurons. By repeating this analysis technique using rankings from single neuron correlation analysis and tuning depth, we have observed differences in the number of cells needed to achieve the maximum average correlation (Single Neuron Correlation max avg $\mathrm{CC} = 0.74$ for 69 cells, Tuning Depth max avg $\mathrm{CC} = 0.74$ for 81 cells). Once again, the ranking by sensitivity finds a smaller cell subset that generalizes well.

VII. DISCUSSION

We have chosen to ascertain the importance of neurons in BMIs for two reasons:

- to build better engineered BMIs systems;
- to better understand neural activity.

[11]Neuron dropping curves obtained are the average CC values from 30 Monte Carlo simulations. This method is consistent with that used by Wessberg, et. al.

A reduction in the number of free parameters without affecting performance leads directly to BMI systems that require less power, bandwidth, and computational demands. Solving these challenges will bring us one step closer to real, portable BMIs. Analysis of the most important neurons in both the model-independent and model-dependent methods has opened up directions to better understand how neural activity can be effectively used for BMI design. Having now evaluated and verified the three different methods, the questions posed in the introduction will now be addressed.

Can our methods automatically indicate important cells for the prediction of the kinematic variables in the tasks studied?

Since the work of Wessberg *et al.*, it is known that the performance of linear models for BMIs improves as more neu-

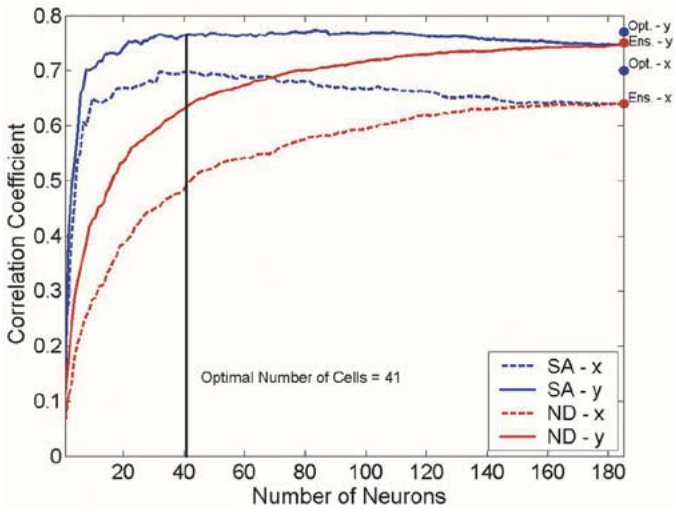

Fig. 10. Model performance as a function of the number of cells utilized. Cells were removed from the analysis either by randomly dropping cells (neuron dropping—ND) or by removing the least sensitive cell in an ordered list (computed from a sensitivity analysis—SA).

rons are recorded, but that the performance improvement does not increase linearly with the number of neurons. Motivated by their work, this paper takes a closer look at the neuron importance for modeling. For the sample set of up to 185 neurons collected from five cortical areas of a rhesus macaque, we have shown using three techniques that these methods can automatically choose important cells for reconstructing the kinematic parameters of HP, HV, and GF (see Figs. 2, 5, and 7). The similarity in the shape of the ranking curves regardless of the methodology leads us to believe that there may be an underlying principle governing the kinematic contribution of randomly selected cells in the motor cortex. To quantify the shape similarity, we fit two exponentials to the ranking curves and found that all three method's (for the HP, HV, and GF) ranking curves can be explained ($R^2 = 0.99$) by a function of the form $y = Ae^{Bx} + Ce^{Dx}$ where the values of A, B, C, and D ranged respectively from 0.3–0.6, -0.1–(-0.2), 0.5–0.8, and -0.01–(-0.02).

The linear model trained with only the 10 most important cells was able to achieve on average 89%, 96%, and 101% of the CC of the full model for HP, HV, and GF, respectively (Table III). It was verified that BMIs performance is statistically inferior to the full ensemble for some of the kinematic variables and sessions, but from an implementation point of view, this slight reduction in performance (except for force where there is an actual improvement) is coupled with huge savings in number of training parameters (from 3700 to 200) that simplifies the real-time implementations.

One must remember that this reduced number of cells makes BMIs more sensitive to the instability of neuronal firings over time. In this short data set, some variability was observed in the importance of neurons among PMD and M1 for GF. Recent studies are showing that the activity of individual neurons and cortical areas used in BMI experiments can vary considerably from day to day [22], therefore, the variance over time of the importance of neurons must be quantified in future studies. Moreover, this neuron selection requires long records, and it is done off-line from trained models or tuning curves. It is, therefore, not clear how practical the neuron selection techniques will be to the surgery stage. For these reasons, we advocate the use of a higher sampling of the cortical activity to help improve this ratio until other models are proposed that take advantage of the information potentially contained in the spike trains and not exploited by linear models.

In this model-based framework, can better BMIs be built using a subset of important cells?

This question is rooted in our goal to build models for BMIs that generalize optimally. The problem is the well-known bias-variance dilemma of machine learning [28], and it is related to the number of free parameters of a model. The MIMO structure of BMIs, with thousands of free parameters, makes this problem particularly critical, and excludes the traditional Akaike or BIC criteria [29]. The previous sensitivity analysis is an attractive alternative because it ranks the importance of neurons; however, it does not give any indication on where to start excluding neurons for better generalization. Inspired by the neuron dropping methodology, but excluding the least sensitive of the neurons instead of a random one, we were able to find a set of 41 important neurons that performs better than the full set of neurons (Fig. 10). It is very interesting that such a small change in the model dropping methodology can provide an answer to this important question for BMI design. However, it should be noted that the other ranking methodologies found different sets of neurons for best generalization. Therefore, it remains to be seen if alternative methods (possibly combining regularization theory) are able to find smaller combinations of neurons that improve performance even further. At this point of the research, we suggest the use of sensitivity analysis (or correlation analysis which is basically sensitivity for a neuronal independence assumption) as an indicator of neurophysiologic cellular importance combined with a neuron dropping scheme for each modeling task so that an estimate of the appropriate model order can be obtained.

Is the model-independent technique a good indicator of cellular importance, and how is it related to sensitivity through the linear model?

The previous two questions were successfully answered by both sensitivity and correlation analysis through the model, but it should not be forgotten that model-based sensitivity is biased by the type of model chosen, its performance level and by noise in the data. Therefore, it is important to pursue a model independent approach to establish the importance of neurons. We hypothesized from a combined neurophysiologic and modeling point of view that highly modulated neurons spanning the space of the kinematic parameter of interest should be chosen. Intuitively these constraints make sense for the following reasons.

- If a cell is modulated to the kinematic parameter, the adaptive filter will be able to correlate this activity with the behavior through training. Otherwise, neural firing works as a broadband excitation that is not necessarily related to better performance.
- If a group of cells are highly modulated to only a part of the space, the adaptive filter may not be able to reconstruct data points in other parts of the space.

After choosing cells based upon these considerations, the hypothesis was validated by achieving performance levels that are akin to using the model-based techniques of choosing cells (see Table III). It is also gratifying that all the 10 most sensitive cells picked by the two model-based methods display tuning curves that span the space (peaks lie roughly on the diagonal of Figs. 6 and 8). Therefore, we conclude that the three methods pick many common cells as their top 10, and this is what matters for model performance, since the WF is not sensitive to the ordering of the cells. However, as can be seen in Table I (and Fig. 9) the cells picked by the three methods do not exactly coincide; 50% of cells are common for HP, 60% and 60% of the cells are common for HV and GF respectively. We are in fact surprised that many cells coincide when recalling the different assumptions behind each method: correlation and sensitivity are computed by averaging cell firings over the training interval, while tuning relates to instantaneous cell firings. Moreover, correlation assigns importance one cell at a time, while sensitivity assigns importance to cells within the whole cell assembly. We can imagine many cases where a cell is important for a given metric but not important in another. Therefore, this coincidence in cell importance is either a feature of the spatio-temporal organization of the motor cortex, or is a byproduct of using a linear model and correlation coefficients to implement and assess performance in the BMI model. Further research is needed to fully understand this important issue.

A final comment goes to the overall performance of the BMI system built from adaptive models. Although it is impressive that an optimum linear (or nonlinear) system is able to identify the complex relations between spike trains in the motor cortex and hand movements/gripping force, a correlation coefficient of ~ 0.8 may not be sufficient for real world applications of BMIs. Therefore, further research is necessary to understand what is limiting the performance of this class of adaptive linear and nonlinear systems. Another issue relates to the unrealistic assumption of stationarity in neural firings over two sessions that is used to derive results presented in this study about neuron sensitivity and tuning curves. In future studies, it will be necessary to assess the time variability of the neuronal rankings and determine its effect on model generalization.

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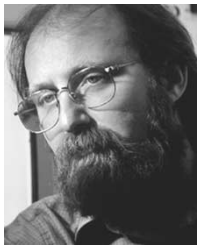

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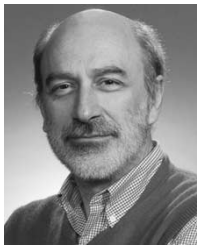

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