

Cortical Neural Prosthesis Performance Improves When Eye Position Is Monitored

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Abstract—Neural prostheses that extract signals directly from cortical neurons have recently become feasible as assistive technologies for tetraplegic individuals. Significant effort toward improving the performance of these systems is now warranted. A simple technique that can improve prosthesis performance is to account for the direction of gaze in the operation of the prosthesis. This proposal stems from recent discoveries that the direction of gaze influences neural activity in several areas that are commonly targeted for electrode implantation in neural prosthetics. Here, we first demonstrate that neural prosthesis performance does improve when eye position is taken into account. We then show that eye position can be estimated directly from neural activity, and thus performance gains can be realized even without a device that tracks eye position.

Index Terms—Brain-machine interface, monkey, multielectrode, neural prosthetics, premotor cortex.

I. INTRODUCTION

BRAIN-COMPUTER interfaces that use action potentials recorded from single neurons in the cerebral cortex can now provide limited motor function to paralyzed individuals [1]. To justify the surgical risk of implanting a neural prosthesis, systems must be developed that perform well enough that a human user can control them with reasonable accuracy and speed. To this end, a high performance neural prosthesis was recently demonstrated in nonhuman primates [2].

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We sought to further improve the performance and ease-of-use of neural prostheses. New discoveries about the normal function of the brain areas targeted by prostheses can be used to engineer better systems. We and others recently observed that the direction of gaze influences spatial tuning in the dorsal aspect of the premotor cortex (PMd) [3]–[5], an area known to be involved in reaching [6] and often targeted in prosthetics applications [2], [7]. This paper demonstrates that the accuracy in decoding the desired endpoint from a population of PMd neurons is enhanced when eye position is accounted for by the prosthesis.

Three operating modes for a neural prosthesis are compared. In all three modes, a neural prosthetic decoder is initially trained to associate particular patterns of activity in a population of neurons with the endpoints of intended reaches. Then, the decoder is tested by assessing whether it can accurately estimate the intended reach goal from a novel pattern of neural activity. The three operating modes are distinguished by the manner in which they treat eye position. In operating mode I, eye position is ignored. This reproduces the most common usage of neural prostheses to date. In operating mode II, eye position is instructed to be consistent between training and testing of the decoder. In operating mode III, eye position is instructed during training, but need not be constrained during testing. Instead, eye position is estimated from neural activity, along with target location.

The three operating modes correspond to approaches that might be adopted in a clinical setting. (Training and testing a neural prosthetics algorithm in the laboratory is analogous to calibration and use of a prosthesis in a clinical context.) In the clinical counterpart to operating mode I, eye position is ignored. In the clinical counterpart to operating mode II, eye position is measured via eye tracking glasses during both calibration and use of the prosthesis. In operating mode III, eye position is measured during calibration, but is not tracked during use of the prosthesis. Instead, eye position is estimated from neural activity, and its influence is accounted for algorithmically.

We report here that accuracy in estimating intended reach endpoint is improved in both operating modes II and III, compared to operating mode I. A brief report of this work has appeared [8].

II. METHODS

A. Behavioral Task

Two adult male Rhesus monkeys (*Macaca mulatta*, designated G and H) were trained to perform a delayed reach task (Fig. 1). The animals sat facing a large frontoparallel screen positioned just within arm's reach (27 cm from the eyes), with the

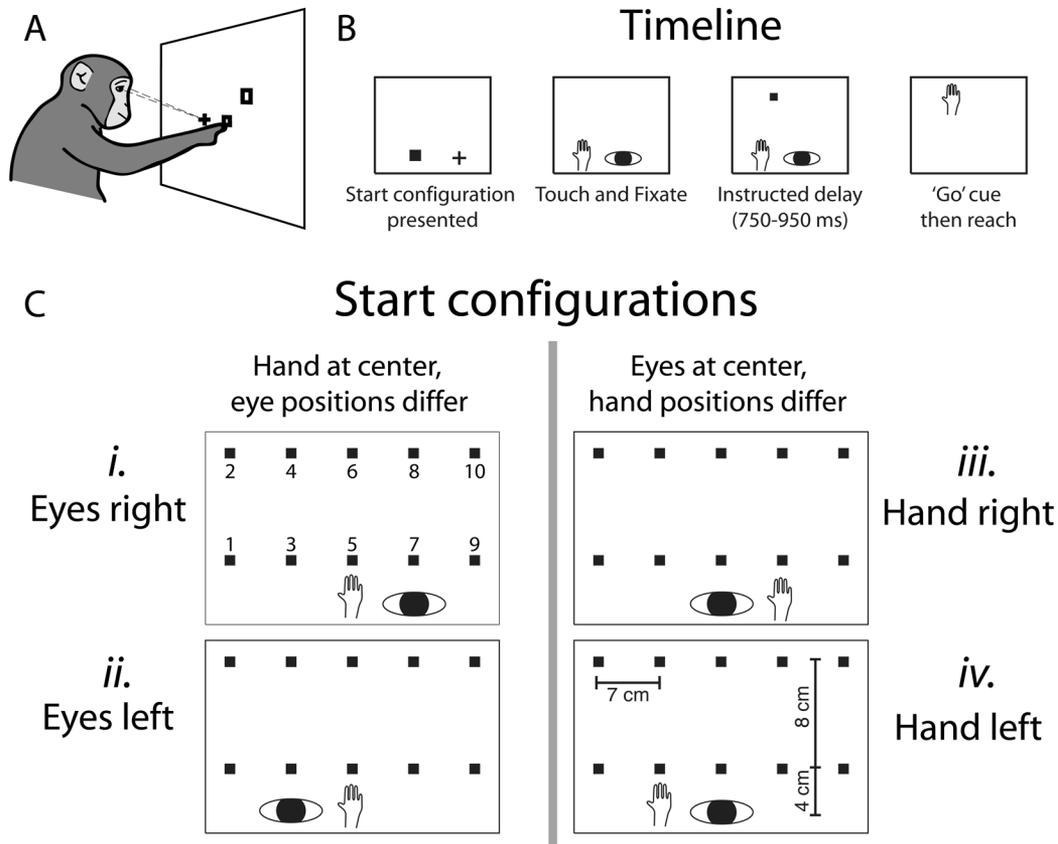


Fig. 1. Behavioral task. (A) Sketch of the monkey performing the task. (B) Delayed reach task timeline. (C) Spatial aspects of the task. Note the numbering scheme for the four start configurations (*i–iv*) and the ten targets (1–10).

head restrained. Hand position and eye position were tracked using infrared sensors (hand position tracked using the Polaris system, NDI, Waterloo, ON, Canada; eye position tracked using the Iscan system, Iscan, Inc., Burlington, MA.) Each trial began with the appearance of a touch point (which instructed the initial position of the contralateral hand) and a fixation point (which instructed the direction of gaze). The locations of the touch and fixation points constitute our main experimental manipulation; they are described in more detail in the next paragraph. Four hundred milliseconds later, a target appeared at one of ten peripheral locations (target locations were arranged in two rows of five targets, subtending on average $55 \times 25^\circ$ of visual angle.) After a delay period of variable duration (750–950 ms), the fixation and touch points were extinguished as a “go” cue, which instructed the monkey to reach to the target. The animal was also free to move his eyes after the go cue. Successful reaches were rewarded during the intertrial interval. All 40 trial conditions (ten targets \times four start configurations) were randomly interleaved, and 26 (monkey G) or 16 (monkey H) successful repetitions were attained per condition.

Four different combinations of initial eye and hand position (termed the start configuration) were instructed, so that we could independently observe the influences of eye and hand position on neural responses in PMd. Fig. 1(C) depicts the start configurations. For two of them (configurations *i* and *ii*), the initial position of the hand is the same, but the eye position differs (gaze is directed to the right in configuration *i*, and to the left in configuration *ii*.) For the other two (configurations *iii* and *iv*)

the direction of gaze is the same, but the initial hand position is either to the right (configuration *iii*) or to the left (configuration *iv*). Reaches are performed to the same ten targets in all four cases. Any differences in neural activity between configurations *i* and *ii* must be due to the difference in the retinal locations of the targets, and/or the position of the eyes. Similarly, differences in neural response between conditions *iii* and *iv* must be due to the difference in the position of the targets relative to the arm, and/or the posture of the arm. If eye and hand position do affect neural activity, then a decoder will perform better if it accounts for these influences. If a decoder ignores these influences, eye and hand position would constitute an unidentified source of variability in the neural activity, which would hinder decode accuracy.

B. Neural Recordings

An array of 96 electrodes (Cyberkinetics Neurotechnology Systems, Inc., Foxborough, MA) was implanted in PMd. Recordings were performed four (monkey G) and seven (monkey H) months after implantation. For monkey G, individual units were isolated using window discriminators during experiments. For monkey H, neurons were identified with an automated procedure [9], [10] summarized here. During the experiment, the background noise on each channel was estimated. Waveforms that exceeded $3 \times$ the root mean square of the noise were saved to disk for sorting. Offline, the saved waveforms were noise-whitened using a modified principal components analysis. Clustering was performed using the expectation-

maximization algorithm. As a final step, the outcome of the algorithm was verified by eye, and only well-isolated single unit isolations were included in the analysis. Sixty-four units collected simultaneously were identified from monkey G, and 91 from monkey H.

C. Analysis

An offline neural prosthetic decode algorithm [2], [11]–[13] was used to estimate target endpoint (and, for operating mode III, start configuration) from the activity of the PMd population. The algorithm consisted of two stages: In the first stage, a model of the relationship between neural activity and behavior is learned through training. In the second stage, the model is tested by estimating behavior from neural activity, and comparing that estimate with the actual behavior. The training and testing procedures are first described in general, then the specific procedures employed in each of the three operating modes are detailed.

The data record used for each trial consisted of the task condition (target location and start configuration) and the population neural response: the average number of action potentials during a 500 ms interval from 250 ms after appearance of the target till the time of the earliest go cue, for each neuron. We focused our analysis on this delay period preceding the movement because the eyes and arm are not moving, so the reach target is at a constant location relative to them, and because neural activity during the delay period is correlated with reach endpoint [6].

The model of the relationship between neural activity in the PMd population and task condition (target location and/or start configuration; see below) was trained by assuming the spike count during the delay period obeys a Poisson distribution. That is

$$x_i | m \sim \text{Poisson}(\lambda_{i,m}) \quad (1)$$

where x_i is the spike count for the i th neuron and m is the task condition. The maximum-likelihood estimate for each Poisson parameter $\lambda_{i,m}$ is the mean spike count for the i th neuron in task condition m . Thus, training the model consisted of computing the mean for each combination of neuron and task condition.

Each trial in the experimental dataset was set aside in turn to serve as the test data. The decoder was trained using data from all of the other trials. (To equalize the number of trials per task condition in the training set, one trial was dropped at random from each of the conditions to which the training trial did not belong.) Then, the decoder was tested using the excluded trial. This procedure, known as leave-one-out cross-validation, provides the largest possible training set without duplicates while ensuring that test data are not included in the training data.

The model was tested by determining the task condition m that makes the observed spike counts \bar{x} most likely. That is

$$\hat{m} = \arg \max_m (p(\bar{x} | m)) \quad (2)$$

where the likelihood $p(\bar{x} | m)$ is given in (1) above.

The estimated task condition was compared to the actual task condition, and scored as either correct or incorrect.

The decode algorithm was trained and tested in three different operating modes. The modes differed only in how the 40 task conditions were grouped. In operating mode I, the decoder was trained to estimate target location, and initial eye and hand position were ignored. All four start configurations were combined, and 26 (monkey G) or 16 (monkey H) trials were selected at random for each of the ten targets (about one quarter of trials came from each start configuration). In operating mode II, the decoder was also trained to estimate target location, but training and testing were performed with a consistent eye and hand position. Four separate decodes were performed, one for each of the four start configurations (all 26 or 16 repetitions were used for each condition). In operating mode III, the decode algorithm was trained to estimate start configuration as well as target location. In this case, the decoder was trained using 40 separate conditions (ten targets times four start configurations; all 26 or 16 trials were used for each condition). During testing in this operating mode, the decode algorithm estimated both target location and start configuration from the neural activity.

In a separate analysis, we trained the decode algorithm using one start configuration, and then tested it using another start configuration. This allowed us to separately quantify the consequences of ignoring eye position and hand position. To measure the effect of ignoring eye position, the decoder was trained using configuration i and tested with configuration ii [and vice versa; see Fig. 1(C)]. To measure the effect of ignoring hand position, the decoder was trained using configuration iii and tested using configuration iv , and vice versa. This analysis was performed alongside a neuron-dropping analysis. Subsets of the neural population were selected (without replacement), and analyzed in this manner. For each subset size, the neural selection and analysis was repeated 25 times, to construct error bars. By performing repeated draws, we ensure that spurious results due to a random subset consisting of the most (or least) discriminating neurons did not bias the results.

III. RESULTS

A. Comparing Three Operating Modes for a Neural Prosthetic System

We measured the performance of a neural prosthetic decode algorithm in three distinct operating modes. Operating mode I estimated the intended reach target while ignoring eye position and initial hand position. Operating mode II estimated the intended target using an eye and initial hand position that were consistent between training and testing. In operating mode III, the decoder was trained to estimate intended target location as well as eye and initial hand position. Results for each of these operating modes are described in turn.

In operating mode I, eye position and initial hand position are ignored. This recreates the standard operating mode for most current neural prosthetics systems: eye position is commonly not monitored or accounted for in neural prosthetics (e.g., [1], [7], [14]). Fig. 2(A) and (C) depicts the results of a neural prosthetic system used in this manner. The system exhibited reasonable accuracy in estimating reach endpoint (45% correct for

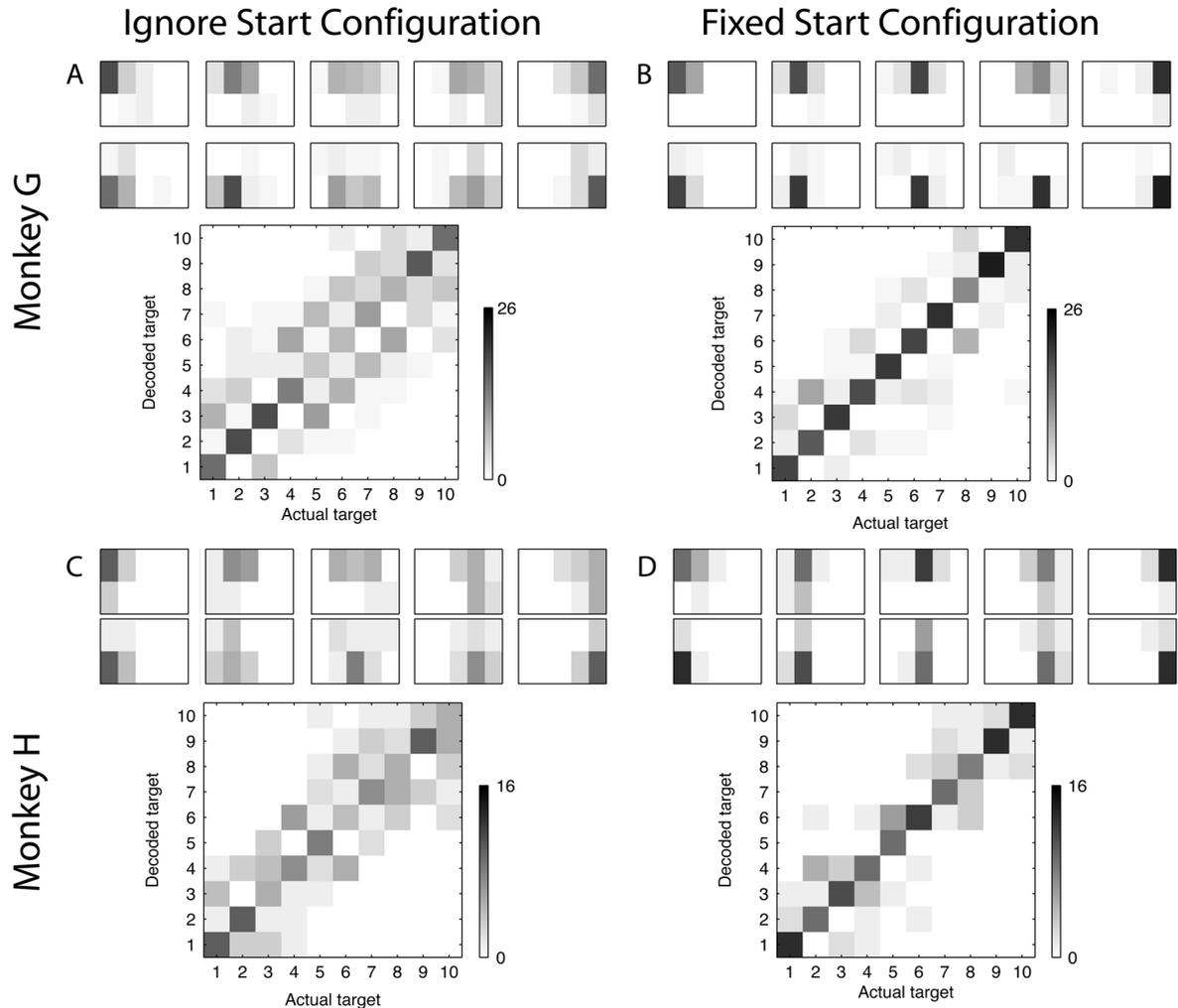


Fig. 2. Confusion matrices depict decode accuracy. (A), (C) Decode performance in operating mode I, when start configuration is ignored. (B), (D) Decode performance in operating mode II, when start configuration is constrained between training and testing (results for the best of four start configurations tested are shown). Panels A and B show data from monkey G; C and D are for monkey H. Within each panel, the same data are shown in two formats. Top: Ten subpanels are arranged to correspond to the location of the ten targets on the screen. Each subpanel indicates decode performance when the actual target is at that relative location. Within each subpanel, the ten targets are again represented at their relative locations. The grayscale indicates the number of trials for which that particular combination of actual and decoded target occurred. Bottom: In this format, correctly decoded trials lie along the unity diagonal. Target-numbering scheme as illustrated in Fig. 1(C).

monkey G [Fig. 2(A)], and 44% correct for monkey H [Fig. 2(C)].

Operating mode II employs a consistent eye and hand position between training and testing of the decoder. This resembles the systems used in [2], [13], [15], wherein eye position is held constant between training and use of the device. Fig. 2(B) and (D) illustrates performance gains when eye position and initial hand position are matched between training and testing the decoder. Performance increases dramatically (66% correct estimates of target on average across all four start configurations, range 63%–73% for each start configuration for monkey G; for monkey H, 59% correct on average, range 51%–66% correct.) This indicates that a substantial improvement in decode accuracy is attainable (with the same number of training trials) if eye position and initial hand position are matched between training and testing the neural prosthetic system.

An ideal neural prosthetic system would incorporate the flexibility of the first operating mode with the accuracy of the second mode. We designed operating mode III to balance these specifi-

cations. In this operating mode, the start configuration (eye position and initial hand position) is incorporated into the decode algorithm during training. The decoder is trained to distinguish the 40 task conditions (ten targets times four start configurations). Then, during testing, the decoder estimated both target location and start configuration. Fig. 3 illustrates decode accuracy in this operating mode. Percent correct performance was 48% for monkey G and 47% for monkey H (chance = 2.5%). Target alone was estimated correctly for 61% of trials for monkey G, and 56% of trials for monkey H (chance = 10%). Start configuration alone was estimated correctly for 67% and 74% of the trials for monkeys G and H (chance = 25%).

B. Distinguishing Impacts of Eye and Hand Position on Decode Accuracy

The four start configurations differed systematically in the position of both the eyes and the hand. By accounting for both of these factors in operating mode II, decode accuracy improved, in comparison to operating mode I. We compared the relative

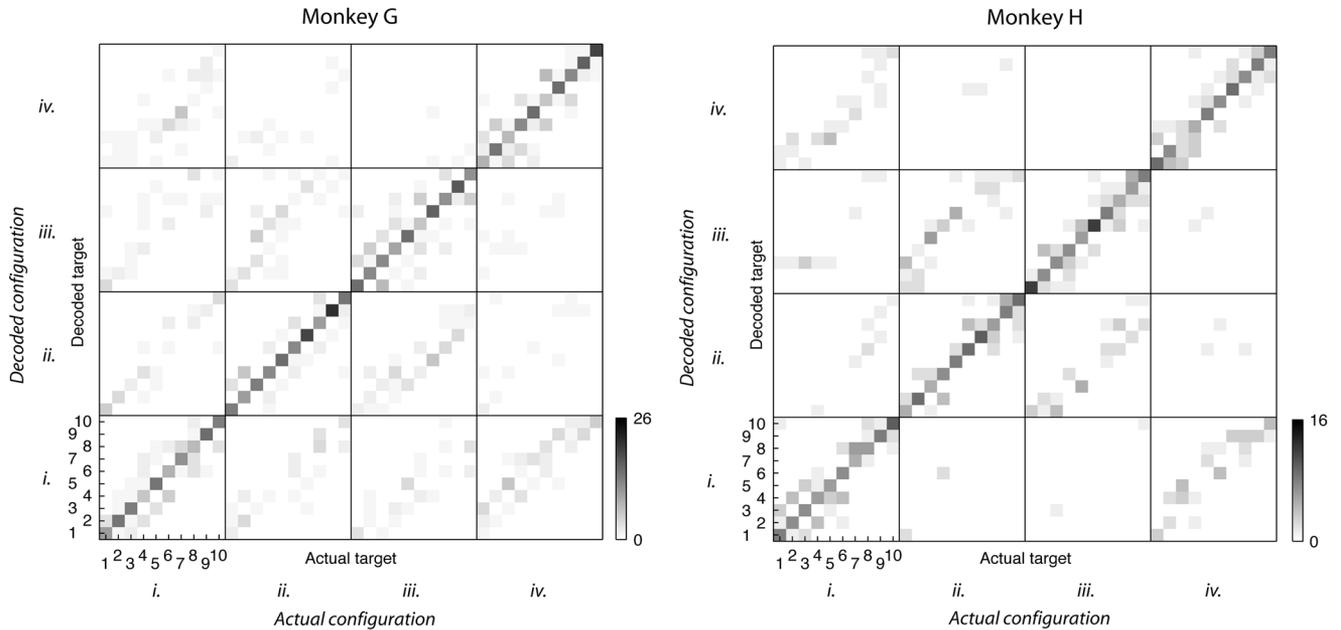


Fig. 3. Confusion matrices depicting decode accuracy in operating mode III, when the decoder must estimate both target location and start configuration. Horizontal axis: the 40 different task conditions: ten targets for each of four start configurations. Vertical axis: the decoded target and start configuration, for each trial. Grayscale indicates the number of trials where that combination of actual and decoded task conditions occurred.

importance of controlling eye and initial hand position for decode accuracy. As illustrated in Fig. 1(C), start configurations *i* and *ii* differ from one another by eye position, but not initial hand position. Start configurations *iii* and *iv* differ by initial hand position, but not eye position. We measured the consequences of ignoring eye position by training the decode algorithm using start configuration *i*, then testing with configuration *ii*, and vice versa. As a baseline, we trained and tested the decode algorithm using the same start configuration. When training and testing were performed using the same start configuration, decode accuracy was 68% and 60% correct, for the two animals (average for start configurations *i* and *ii*.) When training and testing were performed using different start configurations, accuracy dropped to 48% and 26% correct, on average [Fig. 4(A) and (C), rightmost data points].

Using start configurations *iii* and *iv*, the influence of initial hand position on decode accuracy was quantified. When the decode algorithm was trained and tested using the same start configuration, average accuracy was 63% and 59% for the two monkeys. When training and testing were performed using different start configurations, average accuracy was 25% and 28%, respectively [Fig. 4(B) and (D), rightmost data points].

C. Effects of Neural Population Size

Perhaps the deleterious consequences for decode accuracy of ignoring eye position could be mitigated by recording from more neurons. To explore this, we conducted a neuron-dropping analysis (Fig. 4). We conducted the analyses described in Results section B above for a range of neural population sizes. It is evident in Fig. 4 that the trends described in section B for the full population are also manifest in smaller population sizes. The consequences of ignoring eye and hand position are fairly consistent at least across the neural population sizes we could test.

IV. DISCUSSION

Recent neurophysiology studies show that the direction of gaze influences neural activity in cortical areas commonly targeted for neural prosthetics applications, including the dorsal aspect of the premotor cortex (PMd) [3]–[5], and the parietal cortex [4], [16], [17]. Most current neural prosthetic systems do not account for the position of the user's eyes. Here, we demonstrate that prosthesis system performance can be improved by incorporating the position of the eyes into the decode algorithms. Furthermore, eye position need not be exogenously measured: it can be estimated from neural activity along with target location.

We conducted offline implementations of neural prostheses operating in three modes. In operating mode I, eye position and initial hand position were ignored. This recreates the usage mode of many current neural prosthetics systems. This system was about 45% accurate in estimating reach endpoint. While this exceeds chance levels of 10%, overall decode accuracy is lower than other systems described in the literature (e.g., [2], [13]) presumably because in our study targets were not spaced to maximize discriminability.

Operating mode II maintained a consistent set of eye positions and initial hand positions between training and testing the device. Decode accuracy improved substantially in this usage mode. This indicates that constraining or tracking eye position can improve neural prosthesis performance. We propose two clinical applications of this concept. First, in direct analogy to operating mode II, patients can be instructed to direct gaze at a consistent location when using their neural prosthesis, especially when precise control is desired. This location should be the one where gaze was directed while the prosthesis was calibrated. Ideally, however, gaze and reaching would be dissociable, as is the case for healthy human beings. A second clinical approach to matching eye position during calibration and use

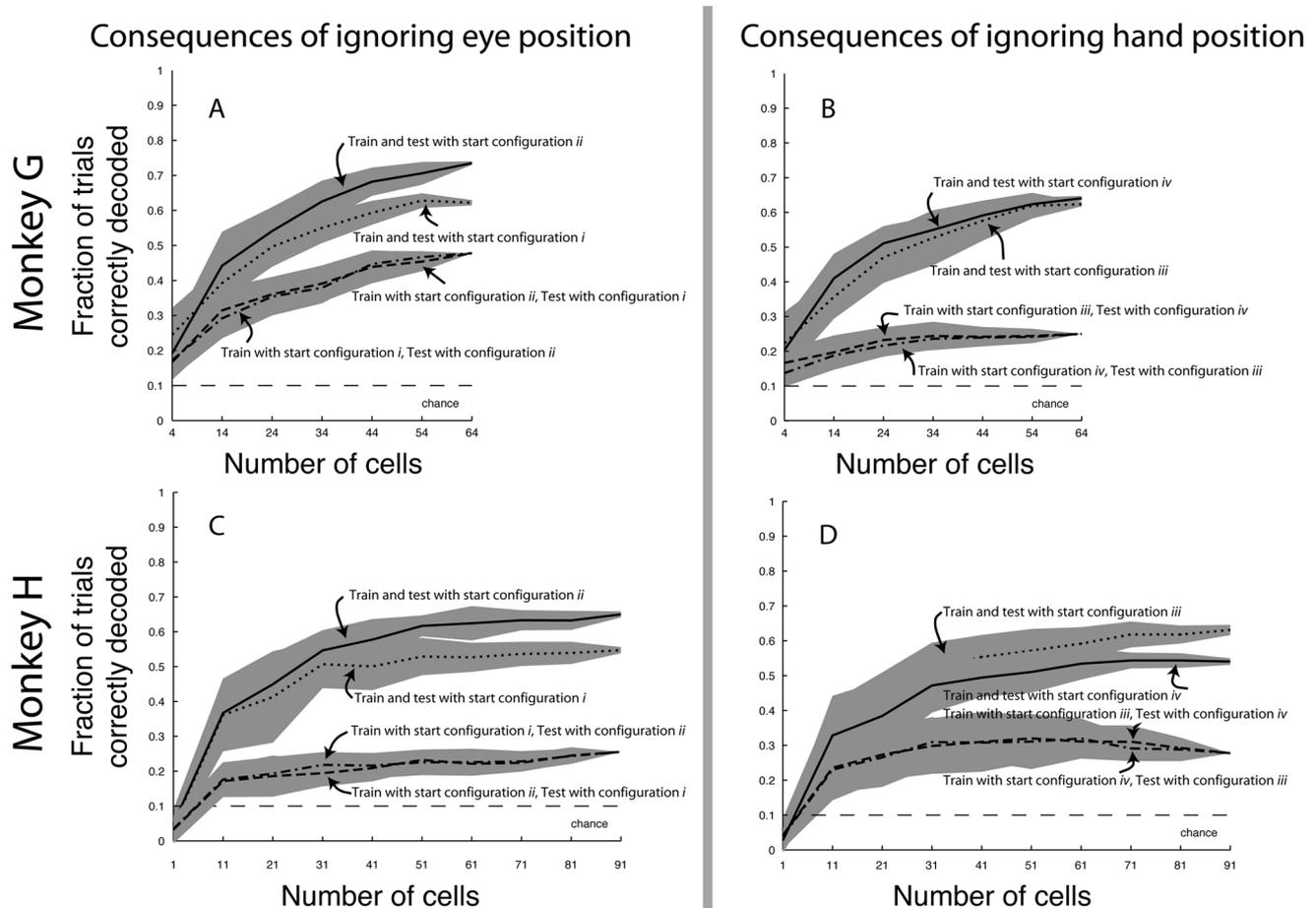


Fig. 4. Consequences of ignoring either eye or hand position, and neuron-dropping analyses. Decode performance is measured for various neuron pool sizes. Grey regions indicate the standard deviation of decode accuracy for 25 repeated draws of a subset of neurons (without replacement) from the full population. Note that these error bars indicate the variability in decode accuracy due to repeated draws of random subsets of neurons; they should not be interpreted as confidence ranges to the estimated decode accuracy. (A), (C) Consequences of ignoring eye position. Start configurations *i* and *ii* (which differ in eye position, see Fig. 1) are compared. Four traces are shown. For two of them (solid and dotted curves), training and testing is performed using the same start configuration. For the other two (dashed and dot-dashed), training is performed with start configuration *i* or *ii*, and testing is performed with the other start configuration. The drop in the percentage of trials correctly decoded exhibits the effect of ignoring eye position. (B), (D) Consequences of ignoring hand position. Start configurations *iii* and *iv* are compared. Four traces are shown. For two of them (solid and dotted), training and testing is performed using the same start configuration. For the other two (dashed and dot-dashed), training is performed with start configuration *iii* or *iv*, and testing is performed using data from the other start configuration. This exhibits the decrement in decode accuracy due to ignoring hand position. (A), (B) monkey G. (C), (D) monkey H.

of a prosthesis is to measure eye position with an eye tracking system. The eye position can be supplied to the decode algorithm along with neural data to determine the intended movement more accurately. While the system is being calibrated, a range of fixation positions should be instructed, to span the range of gaze directions the user is likely to perform. Then, during use of the prosthesis, eye position can be unconstrained, as long as it is tracked.

Operating mode III was designed to combine the accuracy of operating mode II with the flexibility of operating mode I. In this operating mode, some performance gains can be achieved even if eye position is not tracked during use of the system. PMd neural populations convey information about the direction of gaze; thus, if patients are instructed to look at a range of fixation positions while forming reach plans during training, then during use of the system, information can be extracted from PMd about both the intended direction of movement, and also the direction of gaze. Although accuracy will not be as high as when eye position is exogenously tracked, it should improve over existing

systems where eye position is not considered at all. The key intuition is, if while using the prosthesis the patient directs gaze at a location where he or she never gazed during calibration, a pattern of neural activity will occur in PMd that was never presented to the decode algorithm during training, even if the intended target location did appear during training. It will be less likely for the desired target to be correctly decoded from this unfamiliar pattern of activity.

Note that the third operating mode utilized more training trials overall than did the first operating mode (Twenty six or 16 repetitions for 40 conditions were used in operating mode III, versus 26 or 16 repetitions for ten conditions in operating mode I.) In most clinical situations, it is probably feasible to devote additional time to calibrate a neural prosthesis using a range of eye positions.

We directly compared the consequences of ignoring eye position and initial hand position on decode accuracy. The effects of ignoring hand position were strong [39% and 31% decrements in performance for the two animals compared to when hand po-

sition is not ignored; Fig. 4(B) and (D)]. This is to be expected: since PMd is involved in reaching, it is reasonable that it conveys information about the position of the hand. However, the effects of ignoring eye position were comparably strong (for the two animals, 20% and 34% decrements in performance resulted from ignoring eye position.) This is perhaps surprising in an area as close to the motor periphery as is PMd [18], but is consistent with recent neurophysiological findings in PMd [3]–[5].

In intact animal subjects, neural activity in PMd is correlated with arm position [19], [20]. Patients in need of a neural prosthesis will lack a sensory representation of the arm's position. The absent or inaccurate signal about arm position will have unknown effects on neural responses in PMd, and may impair prosthesis performance [cf. Fig. 4(B) and (D)]. This concern is magnified by a recent report demonstrating that neurons in a portion of PMd rostral to our recording sites employ a reference frame defined by the combined position of the eyes and hand [4]. If eye and hand position are not independent, the best achievable accuracy of a neural prosthesis based on PMd signals in amputees or paralyzed individuals might be limited. Fortunately, we observed a subpopulation of neurons within PMd that encode reach goals relative to the eyes only, and are unaffected by the position of the hand [3], [5]. These cells could sustain an accurate encoding of target location, even in the face of absent or variable signals about arm position.

Perhaps by recording from more neurons, the consequences of ignoring eye position can be overcome. To explore this idea, we conducted a neuron-dropping analysis (Fig. 4). We found that across a range of neuron pool sizes, the consequences of ignoring eye position are comparable. These curves suggest that even with larger neural populations beyond the size we were able to record here, the influence of eye position may persist. Thus, ignoring eye position, even for any population size of premotor or parietal neurons, is likely to be detrimental to prosthesis performance.

A limitation to the system proposed here is that eye position must remain stable while the reach is being planned. Natural saccades are spaced by a dwell time of several hundred milliseconds, so the 500 ms integration window we employed in this study is not dramatically longer than what occurs naturally. However, this window could be shortened without sacrificing much accuracy, especially if more neurons were available [2]. The period of fixation between saccades could define the neural integration window over which target location is computed.

In our experiments, we held head position constant. Head position may also influence neurons involved in controlling reaches. If so, it could potentially also be estimated from neural activity. This would allow both eye and head position to be unconstrained, providing a prosthetic system that is both accurate and easy to use.

Although this study focuses on the premotor cortex, we anticipate that neural prostheses that extract signals from many cortical regions will benefit from monitoring eye position. It is known that neurons in the Parietal Reach Region and area 5 of the parietal lobe—other cortical fields that have been successfully targeted for neural prostheses—are modulated by the direction of gaze [4], [16], [17]. Possibly, primary motor cortex may also exhibit an influence of the direction of gaze (albeit

we anticipate weaker than that observed in premotor cortex.) Thus, estimating eye position from neural responses affords a simple adjustment to neural prosthesis decode algorithms that will probably enhance the performance of any neural prosthesis that extracts signals from cortical neurons.

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