

Improved decoding of limb-state feedback from natural sensors

J.B. Wagenaar, V. Ventura and D.J. Weber

Abstract—Limb state feedback is of great importance for achieving stable and adaptive control of FES neuroprostheses. A natural way to determine limb state is to measure and decode the activity of primary afferent neurons in the limb. The feasibility of doing so has been demonstrated by [1] and [2]. Despite positive results, some drawbacks in these works are associated with the application of reverse regression techniques for decoding the afferent neuronal signals. Decoding methods that are based on direct regression are now favored over reverse regression for decoding neural responses in higher regions in the central nervous system [3]. In this paper, we apply a direct regression approach to decode the movement of the hind limb of a cat from a population of primary afferent neurons. We show that this approach is more principled, more efficient, and more generalizable than reverse regression.

I. INTRODUCTION

During movement, proprioceptors constantly assess and relay sensory information about the physical state of the peripheral musculature to the central nervous system (CNS). This feedback allows the CNS an indication of the actual state of the limb and consequently to adapt motor drive in order to realize stable and efficient movements. When functional electrical stimulation (FES) is used to restore action to paralyzed limbs, a similar feedback mechanism is required for executing complex movements and adapt for perturbations or fatigue of the muscles. Accessing and decoding the activity in native afferent signaling pathways would be a natural way to determine the kinematic state (i.e. position and velocity) of the controlled extremity [4]. Our initial goal is therefore to predict/decode the kinematic state of the leg using the ensemble activity of primary afferent neurons, recorded with arrays of penetrating micro-electrodes in the dorsal root ganglia (DRG).

Previously, reverse regression methods were used to estimate limb kinematics from ensembles of simultaneously recorded primary afferent neurons in the dorsal root ganglia of anesthetized [1] and alert, locomoting cats [2]. However, direct regression methods are more efficient and flexible than reverse regression approaches. Direct regression methods include population vectors [5], optimal linear estimators [6], maximum likelihood [7], Bayesian [8] methods, and filtering/dynamic Bayesian methods [9]. See [10] for a review and references therein. Our goal for this paper is to determine if

the simplest likelihood method can improve upon reverse regression to decode limb position from the spiking activity of a small ensemble of primary afferent neurons.

II. METHODS AND DATA

A. The experiment

Center-out patterns in a 2-dimensional plane were imposed on the hind limb of an anesthetized cat by a robotic arm (figure 1:b). These movements spanned a significant part of the range of motion for the limb. See Stein et al. [1] for complete details.

The ankle (A_1), knee (A_2), and hip (A_3) angles of the hind leg were recorded at 120 Hz with a high speed video capture system using markers placed at the Iliac Crest (IC), Hip, Knee, Ankle and Metatarsophalangeal (MTP) joints (figure 1:c). Figure 2 shows the recorded joint angles of knee and ankle as functions of experimental time during one trial of the experiment. The trials were repeated to create separate data sets for model fitting (i.e. encoding) and testing (i.e. decoding).

Primary afferent neurons were recorded using penetrating microelectrode arrays with 50 and 40 electrode sites (5×10 and 4×10 , $400 \mu m$ spacing). The arrays were inserted in the L7 and L6 dorsal root ganglion using a high velocity inserter. The neural signals were acquired with a sampling frequency of 30 kHz and bandpass filtered with cutoff frequencies of 100Hz - 3000Hz. Spikes were sorted offline via cluster analysis; figure 1:a shows the raster plot of the spike trains of 15 neurons. We then smoothed the spike trains using a one-sided normal distribution kernel with SD 0.15 sec. We denote by FR_i the resulting firing rate of neuron i .

B. Reverse regression

Reverse regression/correlation was used previously to estimate angular positions and velocities for the hip, knee, and ankle joints [11], [1]. The “reverse” describes the reversal of the natural roles played by the stimulus and spike-activity response. Although in reality, it is the neural activity that varies as a function of joint angular position, reverse regression treats the firing rates as if they were the inputs (the x 's in regression notation), while the joint angles are considered the output (the Y variable). That is, the joint angles A_k , $k = 1, 2, 3$, are expressed as

$$A_k = \beta_{k0} + \sum_{i \in S_k} \beta_{ki} FR_i \quad (1)$$

where FR_i is the firing rate of neuron i , and S_k indexes the set of neurons whose firing rates correlate most strongly with A_k [1]. Then given a training set of angles and firing-rate

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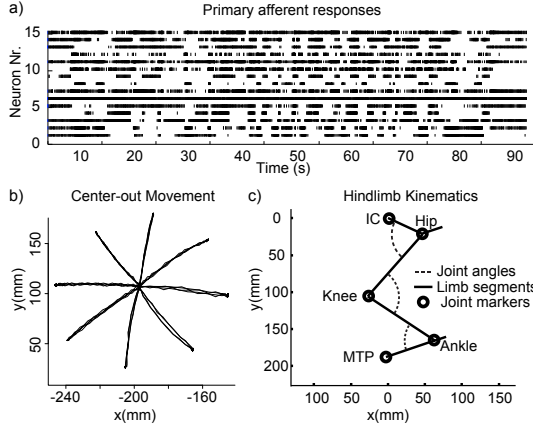


Fig. 1. a) Responses of different neurons to passive movement of the leg. Each vertical line represents an action potential. b) The endpoint kinematics of the hindlimb during passive center-out movement. This movement is imposed on the hindlimb using a robotic manipulator. c) Schematic of the hindlimb; joint angles are being decoded to represent the kinematic state of the limb.

combinations, one computes the usual least-squares estimates $\hat{\beta}$ of the β 's; this step is usually referred to as encoding. In the decoding stage, given the firing rates FR_i^* of all neurons in a small window of time, the predictor of joint angle k is then

$$A_k^* = \hat{\beta}_{k0} + \sum_{i \in S_k} \hat{\beta}_{ki} FR_i^*$$

To allow for the possibility that the relationships between neurons' firing rates and joint angles are not linear, we will consider in place of Eq.1 the more flexible non-parametric generalization

$$A = \beta_0 + \sum_{i=1}^N s_i(FR_i)$$

where the $s_i(\cdot)$ are taken to be moving lines with 4 non-parametric degrees of freedom (DOF).

C. Direct regression methods

Direct regression methods include population vectors, optimal linear decoding, as well as likelihood-based and dynamic decoding. Firing rates are considered random variables whose distributions, often just the means, vary with joint angles. Assuming that firing rates are approximately normal with constant variances σ_i^2 , the simplest relationship one could consider for neuron i is

$$FR_i = \alpha_{0i} + \alpha_{1i}A_1 + \alpha_{2i}A_2 + \alpha_{3i}A_3 + \sigma_i^2 \epsilon_i, \quad (2)$$

$i = 1, \dots, N$, where ϵ_i are standard normal random errors. Note that Eq. 2 specifies one relationship per neuron, whereas Eq. 1 specifies one relationship per angle. Then given a training set of angles and firing-rate combinations, encoding consists of computing the maximum likelihood/least-squares estimates of the α_{ji} and σ_i^2 . In the decoding stage, the observed firing rates FR_i^* of all neurons in a small window of time are each assumed to have distributions specified by Eq. 2, where the α_{ji} and σ_i^2 are now taken to be equal to their

estimates from encoding. The predictor of joint angle is then the least square/maximum likelihood estimate of (A_1, A_2, A_3) obtained from the set of N models in Eq. 2, $i = 1, \dots, N$.

Eq. 2 is the simplest firing rate model we could consider. To allow for non-linear relationships between firing rates and angles, we will instead use $s_{ji}(A_j)$ in place of $\alpha_{ji}A_j$, $j = 1, 2, 3$, where $s_{ji}(\cdot)$ are splines with 4 non-param. DOF. Our model will also include interactions between pairs of joint angles, to allow for the possibility that relationships between firing rates and a particular angle vary with another angle. The data supports this possibility, as illustrated by Figure 3. We also considered hind limb biomechanics and physiology to guide our choice of physiologically plausible firing rate models: muscle afferents (i.e. primary and secondary muscle spindles, tendon organs) encode maximally two out of the three joint angles (bi-articulate muscles span either hip/knee or knee/ankle). Therefore, each neuron is modeled to encode either for one angle (hip, ankle or knee), or for two angles (hip and knee or ankle and knee). That is, for each neuron i , we considered the two families of firing rate models

$$FR_i = \alpha_{0i} + s_{ji}(A_j) + s_{ki}(A_k) + s_{ji}(A_j) : s_{ki}(A_k) + \sigma_i^2 \epsilon_i, \quad (3)$$

for $j, k = 1, 2$ (ankle/knee) and $j, k = 2, 3$ (knee/hip), where $s_{ji}(A_j) : s_{ki}(A_k)$ denotes an interaction between angles j and k , and within these two families of models, we determined the statistical significance of each term using the Bayesian information criterion (BIC) and selected the best model based on this measure.

D. Contrasting methods

Direct regression offers several theoretical advantages over reverse regression. In direct regression, all angles are allowed to contribute to explaining the firing rates of each neuron, whereas in reverse correlation, angles are each decoded separately, using different groups of neurons. From a physiological view point, direct regression is more appropriate because Eq. 2 attempts to model how each neuron encodes joint angles, whereas there is no physiological basis for Eq.1.

From an efficiency view point, if all neurons encoded single joint-angles, both methods should predict approximately similar trajectories. As most muscles span multiple joints, responses from muscle afferents code for multiple angles simultaneously. Fig. 3 shows an example of a neuron whose firing rate depends not only on the hip angle but also on the knee angle. Reverse regression decodes each angle separately so it cannot properly extract the information in firing rates about several angles. In contrast, direct regression makes efficient use of this information provided the firing rate model in Eq. 3 is accurate. For example, if one of the joint angles is consistently better represented in the afferent data set, the weaker contributor will be poorly estimated by a reverse regression method. On the other hand, direct regression combines the information of strongly and weakly encoded angles to improve the prediction of both.

III. RESULTS

We first selected the best 25 neurons, encoded using the first center-out movement sequence of the experiment,

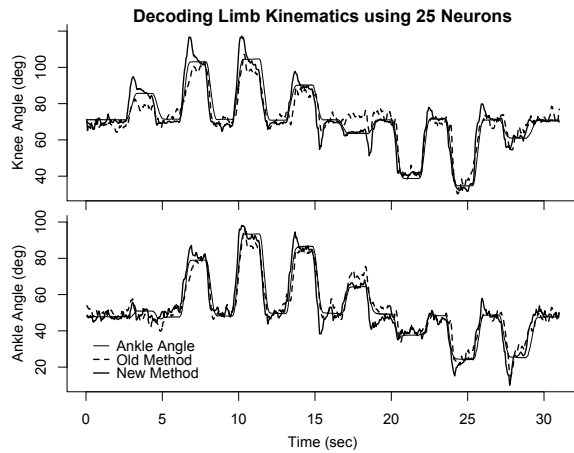


Fig. 2. True knee and ankle trajectories (solid thin curves), along with decoded trajectories using reverse regression (dashed) and direct regression (solid). Decoded trajectories are based on the 25 neurons which are best explained by the kinematic variables (highest R^2) during the training phase.

and decoded with the second center-out movement trial. Fig. 2 shows true knee and ankle trajectories, along with the decoded trajectories using reverse and direct regression. Ankle and hip angles gave similar results so we do not show the latter. The two decoding methods produce visually comparable results.

The integrated squared error (ISE) provides a more quantitative assessment of efficiency. For a particular data set, the ISE is the squared difference between the decoded and actual trajectories, integrated over all time bins. For this particular experiment, the time bins corresponding to the rest position account for over half of all bins. We therefore downweighted these bins so that their contribution would be comparable to the contribution of each of the 8 angle configurations. The ISE is a useful efficiency measure because it typically decreases proportionally to the inverse of the number of neurons. Therefore, based on this measure, the accuracy of a method based on N_1 neurons will be comparable to the accuracy of another method based on N_2 neurons when $N_2 = N_1 \times R$, where $R = ISE_1/ISE_2$ is the ratio of the ISEs of the two methods.

The ISE ratios for knee and ankle in Fig. 2 are 1.12 and 0.97 respectively which indicates both methods are approximately equally efficient. This is somewhat surprising because most neurons actually encode more than one joint angle. Indeed, when we consider Figure 3, which shows the firing rate of a typical neuron versus hip angle: the relationship is not random, which suggests that this neuron encodes for hip angle. Note also that the + and o plotting symbols correspond to small and large knee angles respectively: the two sets of symbols hardly overlap, which suggest that the neuron also encode information about knee angle. Moreover, the relationship between firing rate and hip angle varies with knee angle, which suggests an interaction between hip and knee angles. These characteristics are common to most afferent neurons we examined.

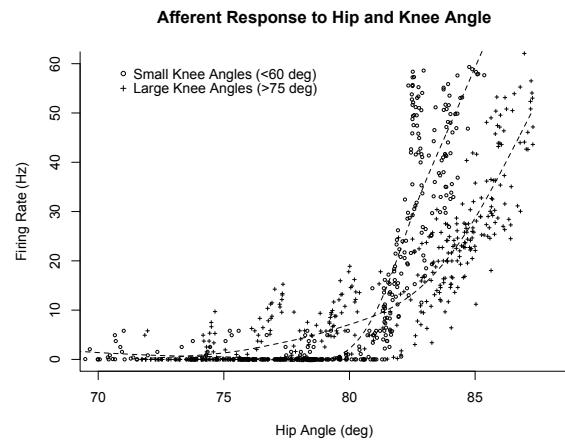


Fig. 3. Firing rate of a typical neuron varies with hip angle, in response to passive movement of the leg. The + and o plotting symbols correspond to large and small knee angles resp. A spline was fitted through each of the two subsets and is plotted as a dashed line. The clear separation between the lines indicate that the neuron encodes for knee angle as well as hip angle.

Because direct regression models how each neuron encodes information about joint angles, it makes better use of the information about angles in the neurons' firing rates. The comparatively good efficiency of reverse regression might be due to robustness against model misspecifications: while reverse regression uses one model per angle, direct regression specifies a different model for each neuron, so that even minor model misspecifications can add up across neurons. It also might be attributed to the number of neurons used and the careful selection of the neurons used to predict limb kinematics. The results in Fig. 2 used 25 neurons from 2 recording sites. We are unlikely to have that many well defined neurons in practice, so we are interested in the performance of the two methods given neuron populations of different sizes.

Fig 4 shows the result of the following analysis. We first selected a pool of neurons encoding "well" for knee and ankle angles: we regressed the firing rates of all neurons on a smooth function of knee and ankle angles, and retained only the neurons for which the two angles explained more than 40% of firing rate variations. We thus retained 64 of the 153 total neurons. We then selected m neurons at random out of this pool of 64 neurons, decoded knee and ankle trajectories using these m neurons using reverse and direct regression, and calculated the ISE ratio of the two methods. We repeated this 99 more times to obtain 100 ISE values, which we plotted versus m as a violin in Fig. 4. We repeated this simulation for several values of m .

Direct regression has clear advantages over the inverse regression methods for all number of included neurons for the knee and up to 20 neurons for the ankle. This agrees with the fact that most neurons primarily encode ankle angle and that only direct regression can extract knee information from those neurons. However, when using higher neuron counts, the sensitivity of the direct regression approach to

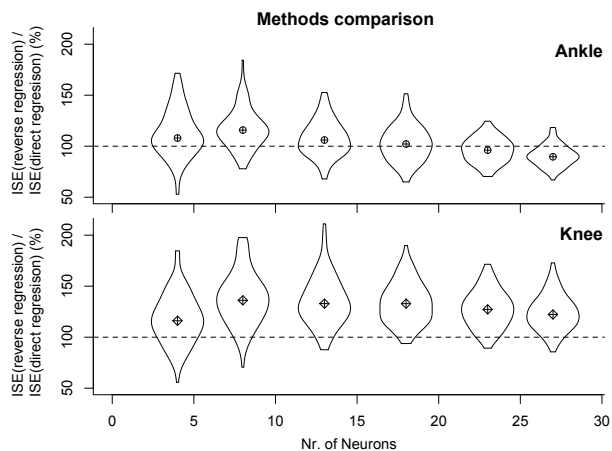


Fig. 4. Violin plots of 100 ISE ratios for several neuron population size m . The mark at the center is at the median. Violin plots are similar to boxplots but they provide more information: they show the full smooth histogram of the data (here the 100 ISEs) whereas boxplots would only show quartiles and outliers. Independent of the available neural population, reverse regression would need approx 25% more neurons to be as efficient as direct regression to decode knee angle.

inaccuracies in the individual firing rate models becomes problematic, giving reverse regression methods an advantage.

IV. DISCUSSION

The results show that direct regression methods are more efficient in using all information from afferent firing rates which is predominantly due to the ability to include multiple joint angles in a single model. Being more efficient, this method requires fewer neurons to predict limb kinematics accurately. Although the CNS might not be sensitive to confounding information due to the large redundancy in the primary afferent population, the implications are more severe for neuroprosthetics which have access to a limited subset of the neural population. For practical reasons, it is desirable to use a decoding method that extracts the information as efficiently as possible.

Reverse regression treats each kinematic parameter as an independent decoding problem and will therefore suffer due to confounded information. The ability of direct regression to use this information results in a better effective use of the afferents predominantly in the kinematic variables that are poorly represented in the neural population (i.e. A_2).

The direct regression method also truly models the stimulus-response encoding properties of each neuron. In contrast to reverse regression, where model coefficients are arbitrary, direct regression coefficients convey information to what is encoded by each individual neuron. Insight into what the neurons encode is therefore apparent from the fitted models. Classification of the origin of a particular neuron can theoretically be extracted from the model parameters. Although, as noted in the results section, model selection should include more complex and afferent modality specific models to predict neural type accurately.

Because of its flexibility, it is possible to improve the estimate accuracy by improving the firing rate models. Although a basic model was chosen to demonstrate the possibilities in this paper, there are several more sophisticated models of muscle spindles suggested in the literature. [12], [13], [14] Any of those models can theoretically be implemented using direct regression methods and will contribute to the prediction accuracy. Fig. 2 shows large overshoots during the reaching movements. It is believed that the dynamic component of primary muscle spindles is one of the leading causes for this behavior. Including a velocity component is only possible when decoding using direct regression methods and will likely improve the accuracy of the estimated kinematic limb state.

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REFERENCES

- [1] R. B. Stein, D. J. Weber, Y. Aoyagi, A. Prochazka, J. B. M. Wagenaar, S. Shoham, and R. A. Normann, "Coding of position by simultaneously recorded sensory neurones in the cat dorsal root ganglion." *J Physiol*, vol. 560, no. Pt 3, pp. 883–96, 2004.
- [2] D. J. Weber, R. B. Stein, D. G. Everaert, and A. Prochazka, "Limb-state feedback from ensembles of simultaneously recorded dorsal root ganglion neurons." *J Neural Eng*, vol. 4, no. 3, pp. S168–80, 2007.
- [3] R. E. Kass, V. Ventura, and E. N. Brown, "Statistical issues in the analysis of neuronal data." *J Neurophysiol*, vol. 94, no. 1, pp. 8–25, Jul 2005.
- [4] K. Yoshida and K. Horch, "Closed-loop control of ankle position using muscle afferent feedback with functional neuromuscular stimulation." *IEEE Trans Biomed Eng*, vol. 43, no. 2, pp. 167–176, 1996.
- [5] A. P. Georgopoulos, A. B. Schwartz, and R. E. Kettner, "Neuronal population coding of movement direction." *Science*, vol. 233, no. 4771, pp. 1416–1419, Sep 1986.
- [6] E. Salinas and L. F. Abbott, "Vector reconstruction from firing rates." *J Comput Neurosci*, vol. 1, no. 1-2, pp. 89–107, Jun 1994.
- [7] E. N. Brown, L. M. Frank, D. Tang, M. C. Quirk, and M. A. Wilson, "A statistical paradigm for neural spike train decoding applied to position prediction from ensemble firing patterns of rat hippocampal place cells." *J Neurosci*, vol. 18, no. 18, pp. 7411–7425, Sep 1998.
- [8] T. D. Sanger, "Probability density estimation for the interpretation of neural population codes." *J Neurophysiol*, vol. 76, no. 4, pp. 2790–2793, Oct 1996.
- [9] K. Zhang, I. Ginzburg, B. L. McNaughton, and T. J. Sejnowski, "Interpreting neuronal population activity by reconstruction: unified framework with application to hippocampal place cells." *J Neurophysiol*, vol. 79, no. 2, pp. 1017–1044, Feb 1998.
- [10] A. Brockwell, R. Kass, and A. Schwartz, "Statistical signal processing and the motor cortex," in *Proceedings of the IEEE*, vol. 95, 2007, pp. 881–898.
- [11] D. J. Weber, R. B. Stein, D. G. Everaert, and A. Prochazka, "Decoding sensory feedback from firing rates of afferent ensembles recorded in cat dorsal root ganglia in normal locomotion," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 14, no. 2, pp. 240–243, 2006.
- [12] A. Prochazka and M. Gorassini, "Models of ensemble firing of muscle spindle afferents recorded during normal locomotion in cats." *J Physiol*, vol. 507 (Pt 1), pp. 277–291, 1998.
- [13] M. P. Mileusnic and G. E. Loeb, "Mathematical models of proprioceptors. ii. structure and function of the golgi tendon organ." *J Neurophysiol*, vol. 96, no. 4, pp. 1789–1802, 2006.
- [14] M. P. Mileusnic, I. E. Brown, N. Lan, and G. E. Loeb, "Mathematical models of proprioceptors. i. control and transduction in the muscle spindle." *J Neurophysiol*, vol. 96, no. 4, pp. 1772–1788, 2006.