Extraction of Muscle Synergies in Spinal Cord Injured Patients

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***Abstract*— Muscle synergies encode motor activity as a linear superposition of multiple motor units composed of a temporal command exciting a specific network of muscles. This study examines muscle synergies derived from simple standing studies of a complete spinal cord injury (SCI) patient under epidural spinal stimulation. A popular technique for extracting these synergies from EMG data is non-negative matrix factorization (NNMF). However, standard NNMF algorithms do not allow for physiological delays for a neural signal to reach different muscles. These delays are prevalent in SCI patients under spinal stimulation, and so we propose a new algorithm (regularized ShiftNMF) to extract muscle synergies which account for signal delays. We find muscle synergies extracted by the regularized ShiftNMF algorithm are significantly better at reconstructing EMG activity, and the resulting features are physiologically consistent and more useful in describing patient behavior.**

I. INTRODUCTION

Motor activity requires a complex mapping from the brain to the spinal cord and then to individual muscles. In 1994, Mussa-Ivaldi et al. observed that in frogs, total muscle activity was encoded as a linear superposition of a few motor primitives, suggesting a low-dimensional, linear representation of motor output [11]. *Muscle synergies* capture this low-dimensional, linear motor behavior, and are defined as the coordinated recruitment of a group of muscles with a specific activation waveform. Similar results in other animals have provided substantial evidence of muscle synergies in the central nervous system (CNS) [2], [17], [9]. Statistical analysis from previous experiments with animals and humans have shown that many motor behaviors can be described by the combination of a few muscle synergies [4], [16], [1], [13], [5]. Figure 1 shows the concept of muscle synergies and how muscle synergies linearly combine to produce overall EMG activity. The idea is that each muscle synergy represents a network of interneurons activated by a neural command; each interneuronal network excites a specific pattern of motoneurons, resulting in fixed patterns of muscle activity following a similar temporal waveform. A current theory is that the spinal cord controls functional motor activity, in large part, by modulating activity of these muscle synergies – as opposed to directly controlling individual muscles.

This study explores the use of muscle synergies in patients with complete spinal cord injury (SCI). Until recently, it was believed that motor function could not be recovered after complete SCI, but studies have shown that complete SCI patients can recover motor function under spinal cord stimulation (SCS) [6], [12]. However, the muscle activity resulting from SCS is significantly different from healthy muscle activity. By examining muscle synergies elicitied from SCI patients under SCS, we will be able to better quantify these differences, understand the effects of SCS on motor activity, and design better rehabilitation strategies.

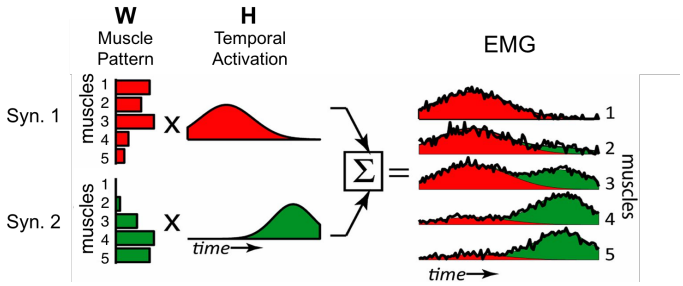

Fig. 1. Illustration of two muscle synergies composed to reconstruct some EMG activity. W represents the activation pattern of muscles, and H represents the activating neural signal. Figure adapted from [3].

Non-negative matrix factorization (NNMF) is a common method for extracting muscle synergies from EMG data [8]. Using this method, studies indicate that muscle activity from animals and humans can indeed be accurately decomposed into the linear superposition of a few muscle synergies, which are associated with specific movement kinematics [16], [2], [1]. However, a significant issue with this method is that it is not shift-invariant with respect to the different EMG channels – it assumes that each muscle is activated simultaneously by the central nervous system without differential delays.

It is known that neural signals take differing times to reach different muscles, based on the distance these signals must travel and the finite speed of neural signals along axons. For example, a neural signal originating from the spinal cord will reach proximal muscles before distal muscles. In healthy subjects, it is assumed that the CNS accounts for these signal delays when processing and sending the appropriate motor signals (e.g. it may properly synchronize the activation of interneurons in a muscle synergy). However, in patients with SCI under spinal stimulation, an activating signal is externally induced at a specific area of the spinal cord at a fixed frequency. This induced neural response must propagate down the limbs, resulting in significantly different delays in the EMG response at distal muscles. Therefore, extracted muscle synergies must account for these delays, which NNMF cannot do. In this work, we utilize a variant of NNMF which accounts for these delays, named regularized ShiftNMF, and observe how these extracted muscle synergies better capture the motor behavior of a complete SCI patient under SCS.

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The main two contributions of this work are:

- The first examination of muscle synergies in SCI patients under spinal stimulation,
- The first use of regularized ShiftNMF algorithm to enable extraction of muscle synergies which account for signal delays in the CNS.

II. METHOD

A. SCI Subjects and Task

Data was collected from a complete, paraplegic SCI patient implanted with a Medtronic 5-6-5 epidural electrode array for SCS with a Medtronic RestoreAdvanced Neurostimulator. Experiments were performed over two non-consecutive weeks, and a total of 104 trials of stimulation/EMG data were gathered from the patient. For each trial, the patient attempted to stand with minimal support for ≈ 5 minutes. The experimental procedures involving the human subject were approved by the UCLA Institutional Review Board.

The choice of stimulating electrodes recruited on the array and their polarities were modified between trials. This choice was determined by a machine learning algorithm which proposed different "safe" stimuli (high probability of non-painful response), and tested good ones against each other to search for the best stimulation patterns [14], [15].

Stimulation frequency and pulse width were kept constant across trials at 25 Hz and 200 μs, respectively. For each trial (fixed stimulation pattern), the SCS amplitude was ramped up until reaching a well-performing value. The patient achieved full weight-bearing standing with minimal assistance when empirically-optimal stimulating configurations were used.

We utilized measurements from 8 muscles (left and right muscles of 4 muscle groups) taken using surface EMG at a sampling frequency of 2000 Hz. The 4 muscle groups were: MH (medial hamstring), MG (medial gastrocnemius), TA (tibialis anterior), and SOL (soleus). The EMG was low-pass filtered at 55 Hz, rectified, and then high-pass filtered at 1 Hz using a 3rd order butterworth filter.

For each trial, clinicians scored the patient's quality of standing on a 1-10 integer scale. For scores in the range 1-5, the standing is not independent but as the score increases, the patient requires less assistance. From 6 to 10, the standing is independent and full-weight bearing; as the score increases, the standing is more natural, stable, and of greater duration.

B. Muscle Synergy Extraction Algorithm

Muscle synergies can be extracted from EMG data using existing efficient algorithms for NNMF [8] by solving the following optimization problem:

$$\underset{W,H}{\text{minimize}} \quad ||EMG - \sum_k W_{n,k} H_{k,t}||_2^2$$

This is solved using alternating least squares with multiplicative updates to find a local optimum. Here EMG refers to the measured EMG response, W represents the activation pattern of each muscle synergies (each column represents the relative muscle activation pattern for synergy k), and H represents the activating signal for each muscle synergy (each row represents the activation waveform for synergy k). This is illustrated in Figure 1.

As mentioned previously, this formulation does not account for delays between different muscles. The implicit assumption when using NNMF for muscle synergy extraction is that the neural signal generated by the spinal cord must reach every muscle simultaneously. To account for delays in SCS, we can reformulate the problem as follows:

$$\underset{W,H,\tau}{\text{minimize}} \quad ||EMG - \sum_k W_{n,k} H_{k,t-\tau_{n,k}}||_2^2$$

By adding a delay parameter, τ, to the original optimization problem, we can now allow each neural signal (represented by a row, k, of H) to be shifted by a small delay $\tau_{n,k}$ before being sent to each individual muscle, n. The optimization problem is solved by first doing a Fourier transform on the parameters W, H, τ to conveniently represent the delay as a complex exponential, and then using alternating least squares with multiplicative updates to iteratively converge on parameter estimates. Details can be found in [10].

We also must ensure that the calculated delays are consistent with neurophysiology. Consider that a generic 10Hz periodic signal would be equally likely to have a 10ms delay and a 110ms delay. Hence, the optimization problem above may lead to non-physiological estimates of delay τ, since many delays τ can lead to similarly good factorizations. However, based on the physiology of the CNS, we can estimate the order of magnitude of expected delays. For example, neural signals travel down motor nerves at speeds on the order of $100\frac{m}{s}$, and the length of a lower limb is $\approx 0.5 - 1m$, so a signal sent from the spinal cord should take order of magnitude $10ms$ longer to reach a thigh muscle than a shank muscle with variations from patient to patient.

Given these order of magnitude estimates of expected delays, we can modify the algorithm to incorporate a prior, T_0, on the delays to ensure that they remain physiological consistent. If we assume the synergy reconstruction error is gaussian (i.e. $\mathbb{P}(EMG|W,H,\tau) = \mathcal{N}(\sum_k W_{n,k} H_{k,t-\tau_{n,d}}, \Gamma)$), then adding a gaussian prior, T_0, on the delay, τ in a bayesian formulation is equivalent to adding L_2 regularization to the underlying optimization problem, as shown below:

$$\underset{W,H,\tau}{\text{minimize}} \quad ||EMG - \sum_k W_{n,k} H_{k,t-\tau_{n,d}}||_2^2 + \lambda||\tau - T_0||_2^2$$

This new optimization problem can be solved by alternating least squares as before, and only the update law for the delay τ must be modified by linearly adding in the gradient/Hessian corresponding to the regularization term.

C. Determination of Number of Synergies

Note that in the above muscle synergy extraction formulations, the number of muscle synergies k must be predefined. Most work on muscle synergies utilize the variance accounted for (VAF) metric defined below to estimate the proper number of muscle synergies:

$$VAF = 1 - \frac{||EMG - \sum_k W_{:,k} H_{k,t-\tau_{n,k}}||_2}{||EMG||_2}$$

This is a measure of how well the muscle synergies reconstruct the underlying EMG activity. In the NNMF formulation, we will have $\tau = 0$ (no delays).

Typically the number of synergies is defined as the minimum k such that VAF rises above some threshold, or the slope of VAF decreases significantly. However, this makes the number of synergies highly dependent on the threshold values used and the pre-process filtering of the EMG. Other work has attempted to improve on these methods by cross-validating over several trials [7], or utilizing different likelihood measures and information criterion [18]. We utilize the curvature of the VAF vs. synergy number curve as applied in [18] to define the number of synergies.

Note that since the regularized ShiftNMF algorithm uses 8 more free parameters per synergy (for 8 muscles) compared with NNMF, it is expected to better fit to the data. To address this, we run the algorithm on training data to obtain proper delays τ for the synergies, and then cross-validate by running the algorithm with the same fixed delay parameters, τ, on test data. Then we can directly compare the ShiftNMF fit results with NNMF, since they utilize the same free parameters – see Figure 2(a).

For further cross-validation of results, we run the regularized ShiftNMF algorithm on training data, then fix *both* the activation pattern W and delays τ, and run the algorithm on test data. This helps avoid overfitting to the data – see Figure 2(b). Because the underlying EMG data is not stationary due to natural fluctuations in the muscle activity and patient's stance, we do not fix the activating signal, H.

III. Results and Analysis

A. EMG Reconstruction and Number of Synergies

We were able to obtain a significantly better EMG reconstruction (higher VAF) using the regularized ShiftNMF algorithm versus the NNMF algorithm across all trials, as reflected in Figure 2. When cross-validating with respect to both the activation pattern W and delay τ, the synergy extracted by ShiftNMF is able to account for $\approx 70\%$ of the variance in the EMG signals, whereas NNMF achieves less than 60% reconstruction accuracy even with more synergies. Furthermore, the performance of regularized ShiftNMF remains high with cross-validation, whereas NNMF performance degrades considerably with cross-validation (fixing activation pattern W). Based on the curvature of the VAF curve, we conclude that there is a single muscle synergy obtained through regularized ShiftNMF.

B. Analysis of neural signal delays, T

As validation of our extracted muscle synergy, we note that the algorithm's calculated delays, τ, are consistent with expected values based on the speed of neural signals, as discussed in Section II(b). The delays when considering a single synergy are shown in Figure 3.

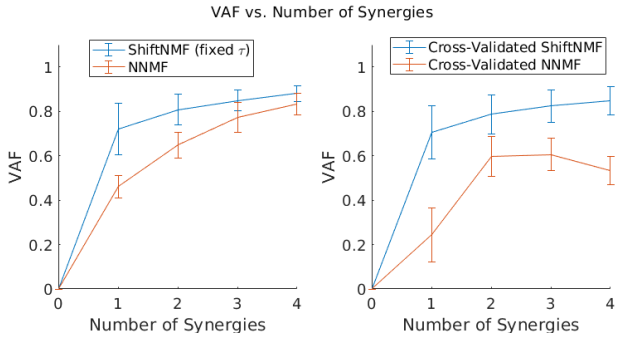


Fig. 2. VAF plotted against the number of synergies extracted. The mean VAF across the 104 trials was used for each data point. (a) ShiftNMF is cross-validated by fixing the delay τ, whereas NNMF is not cross-validated. (b) ShiftNMF is cross-validated by fixing the delay τ *and* activation pattern W. NNMF is cross-validated by fixing activation pattern W.

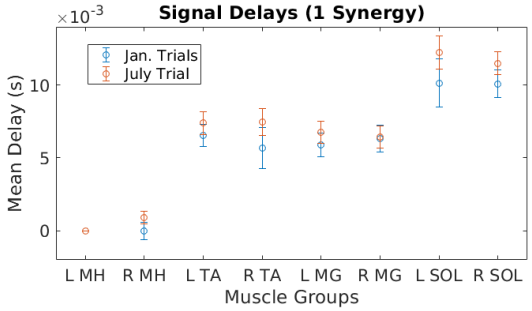


Fig. 3. Muscle activation delay for each muscle in the muscle synergy (normalized to left MH) from 56 trials in January and 48 trials in July.

Note that left/right muscles within each muscle group have similar delays, and that delays increase as we go from MH to TA/MG muscles to SOL, which reflects an ordering based on distance from the spinal cord. We also note that the observed delays are in line with the order of magnitude delay expected ($\approx 10ms$) as discussed in Section II(b). This consistency with physiological models is further evidence that regularized ShiftNMF muscle synergies capture physiological phenomenon that would be missed by NNMF.

C. Prediction of Standing Score from Synergy Features

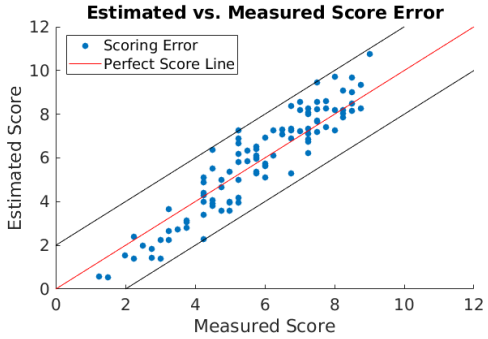
To further validate the utility of regularized ShiftNMF for muscle synergy extraction, we look for correlations between muscle synergy features and standing ability of the SCI patient. We also want to compare muscle synergies extracted with regularized ShiftNMF versus NNMF, and see which are better indicators of motor deficits. To find correlations between muscle synergies and standing ability, we attempted to "predict" the patient's standing ability score (from 1-10) based on EMG power and muscle synergy features, using Linear Regression, SVMs, or Random Forests – all with 3-fold cross-validation. For features of the muscle synergies, we consider the activation pattern W, activation coefficient H, and VAF for a given synergy number.

Figure 4(a) shows prediction accuracy based on linear regression with EMG power and muscle synergy features. We found that using these features for the 104 trials, 74% of the

estimates are within ± 1 of the true score, and 97% are within ± 2 of the true score. In comparison, if we do not include the muscle synergy features, only 59% of the estimates are within ± 1 of the true score, and 91% are within ± 2 of the true score. Thus adding muscle synergy features leads to significant improvements in prediction accuracy. Figure 4 (b) compares score classification accuracy – independent standing (score ≥ 6) vs. non-independent standing – using synergy features from either NNMF or regularized ShiftNMF.

One of the most interesting findings was that VAF extracted by ShiftNMF (a single scalar feature) had a significant linear correlation with the patient's standing ability, and was the most important synergy feature in predicting standing ability. Thus the patient's standing ability depends on how well the muscle activity follows a low-dimensional muscle synergy structure. This suggests that good SCS for standing should excite one (or more) well-defined muscle synergy in the spinal cord, and that activation of synergy structures could be important to human motor function under SCS.

We also note that features of muscle synergies extracted with regularized ShiftNMF were better correlated with standing ability than synergy features extracted with NNMF. More importantly, the linear correlation between VAF and standing ability was much weaker with synergies extracted by NNMF. The significant correlations between synergy features and standing ability, in combination with the improved EMG reconstruction and accurate modeling of physiological delays, suggest that regularized ShiftNMF provides a better description of muscle synergies for SCI patients.



	Classification with all Synergy Features	Classification with VAF	Regression with VAF (% trials predicted within ±2)
NNMF	72.00%	54.50%	69.20%
Regularized ShiftNMF	84.60%	77.70%	76.90%
Prediction Method	Random Forest	Random Forest	Linear Regression

Fig. 4. Top figure shows error in score prediction by linear regression on muscle synergy features and EMG power. Bottom table shows error of standing score prediction based on synergy features, on scoring scale between 1-10. First column in table utilizes activation pattern W, muscle delays T, activation coefficient H, and VAF as features (18 features), whereas the second/third column uses only VAF as a predictor (1 feature).

IV. CONCLUSIONS

We have seen that regularized ShiftNMF allows us to identify muscle synergies in SCI patients under SCS by accounting for signal delays. The patient's standing ability is significantly correlated with the presence of muscle synergy structure and the features of that muscle synergy. Our results suggest that muscle synergies extracted by regularized ShiftNMF can be a useful lens through which to examine motor activity. We hope a better understanding of these synergies, and how they map to the spinal cord, can guide design of better stimulation by helping us to (1) identify good motor activity and (2) optimally excite important synergies.

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