Correlation between muscular and nerve signals responsible for hand grasping in non-human primates

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Abstract—**Neuroprosthetic devices that interface with the nervous system to restore functional motor activity offer a viable alternative to nerve regeneration, especially in proximal nerve injuries like brachial plexus injuries where muscle atrophy may set in before nerve re-innervation occurs. Prior studies have used control signals from muscle or cortical activity. However, nerve signals are preferred in many cases since they permit more natural and precise control when compared to muscle activity, and can be accessed with much lower risk than cortical activity. Identification of nerve signals that control the appropriate muscles is essential for the development of such a 'bionic link'. Here we examine the correlation between muscle and nerve signals responsible for hand grasping in the *M. fascicularis*. Simultaneous recordings were performed using a 4-channel thin-film longitudinal intra-fascicular electrode (tf-LIFE) and 9 bipolar endomysial muscle electrodes while the animal performed grasping movements. We were able to identify a high degree of correlation (r > 0.6) between nerve signals from the median nerve and movement-dependent muscle activity from the flexor muscles of the forearm, with a delay that corresponded to 25 m/s nerve conduction velocity. The phase of the flexion could be identified using a wavelet approximation of the ENG. This result confirms this approach for a future neuroprosthetic device for the treatment of peripheral nerve injuries.**

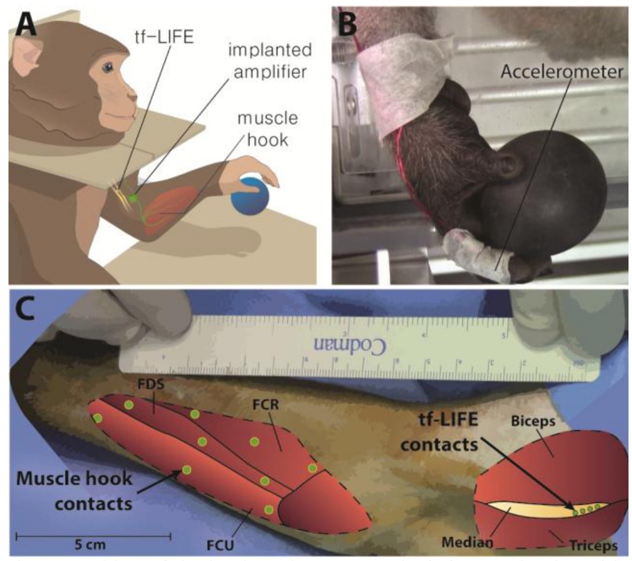

Fig. 1. Position of the implant site composed of tf-LIFE (implanted in the median nerve), amplifier chip, and muscle hooks, and a tri-axial accelerometer on the index finger. The system was connected to an external computer. The task consisted of grasping of ball or metallic instrument. FDS: Flexor Digitorum Superficialis; FCR: Flexor Carpi Radialis; FCU: Flexor Carpi Ulnaris.

I. Introduction

Peripheral nerve injury is a worldwide clinical problem that results in a decreased quality of life due to permanently impaired sensory and motor functions [1]. The outcomes of the current treatments are poor, especially when delayed [2].Although surgical approaches are currently regarded as the gold standard for nerve restoration, recovery of hand function is seldom achieved [3].

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An alternative approach is the use of functional electrical stimulation (FES) to produce contraction of hand muscles [4]. Notably, the use of intra-cortical neural signals to control a FES system might improve the performance [5, 6] but the risks involved in undergoing brain surgery for electrode implantation is not acceptable in most situations. An ideal solution would be then to create a "bionic link" so that information could be relayed from the transected nerve to the denervated muscular groups, bypassing the nerve gap [7, 8]. Direct recording from the nerve has been successfully used for the control of a prosthetic arm in amputees [9], but grasp control of the hand using nerve signals have not been previously attempted. In order to achieve that, a correlation between the activity of the muscles involved in grasping and corresponding nerve signals is required.

Here we show that we were able to classify nerve signals recorded with an intrafascicular electrode placed proximally in the median nerve and the muscle signals leading to hand grasping in a *M. fascicularis*. The experiment involved the acquisition of electrical signals using an implanted amplifier to improve the quality of the recordings, and the offline detection of the different phases of the task being performed. This procedure can be used in future, for developing fully

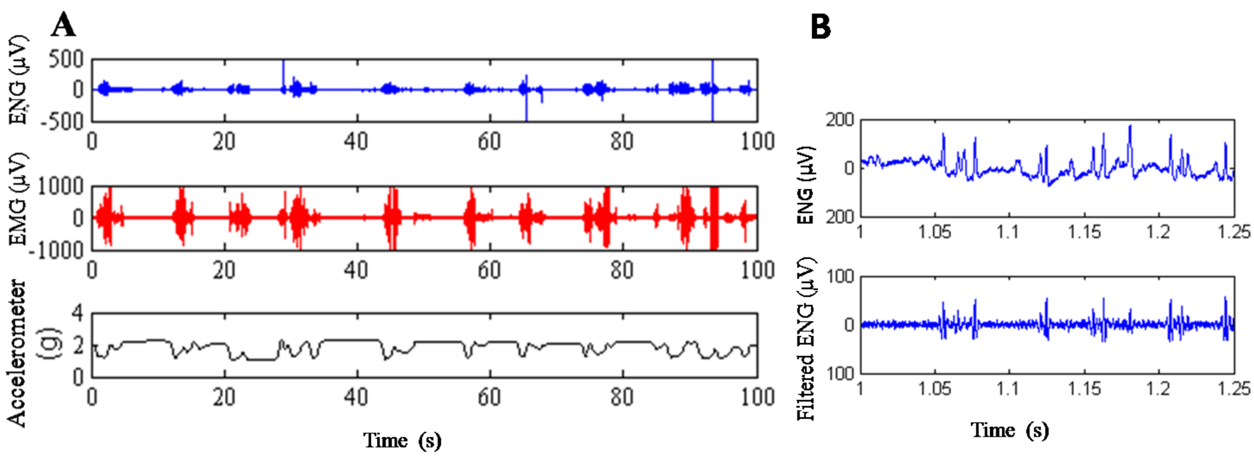

Fig. 2.**A**. Example corresponding to one channel of recordings for ENG (top, blue), EMG (middle, red), and accelerometer (bottom, black) during repetitive grasping tasks. **B.** Detail corresponding to 1.0-1.25 s from A, showing the raw ENG signal and the ENG signal after filtering.

implantable neuroprosthetic devices for treatment of peripheral nerve injuries.

II. MATERIALS AND METHODS

A. Experiment Protocol and Data Acquisition

The procedure was performed in a male *M. fascicularis* according to the guidelines for animal experimentation at the Singapore Institute for Clinical Sciences. A 4-channel intrafascicular electrode (SMANIA, Italy) [10, 11] was implanted longitudinally in the proximal upper portion of the median nerve. Additionally, 9 custom-made endomysial bipolar electrodes were inserted in three different locations of the M. flexor carpi radialis (FCR), M. flexor digitorium superficialis (FDS), and M. flexor carpi ulnaris (FCU) at approximately 10 to 20 cm distal to the nerve electrode (Fig. 1). Impedance measurements were carried out intraoperatively to check the integrity of the electrodes. Recordings were performed 3 weeks after surgery to allow time for recovery. Electroneurographic (ENG) signals picked up by the LIFE electrodes were amplified by a gain of 192 using an Intan Technologies RHD2132 amplifier, implanted next to the recording site. The sampling rate used was 20,000 Hz. Signals acquired during the experiment as illustrated in (Fig. 2) were hardware filtered using a wide band filter with a bandwidth of 10 – 7,500Hz. The amplifier was then connected through a transcutaneous port to an external recording system. The monkey was trained to perform grasping movements involving the flexion of the lateral side of the palm and wrist. The whole task was video-recorded using a hand-held camcorder for visual verification.

B. Cross Correlation

Cross correlation was performed between the acquired ENG and EMG signals as a measure of similarity. Pearson's linear correlation coefficient, *r*, was calculated for each of the raw ENG and EMG channels. Time difference between the first ENG and 9 EMG contacts were analyzed to observe the expected distance dependent causality between these

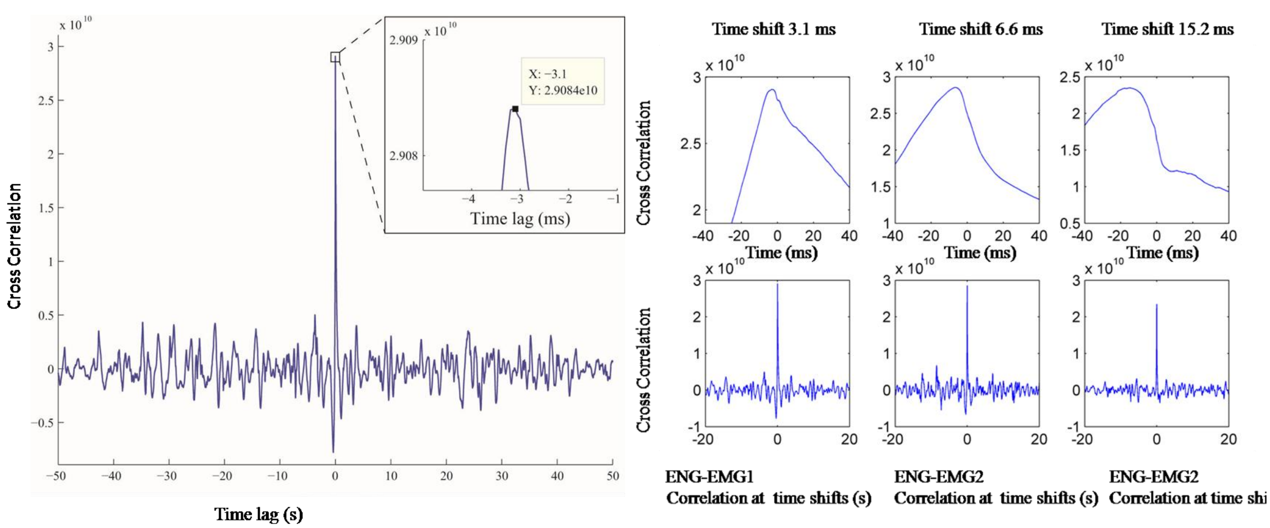

Fig. 3. Left Panel : Example of a correlation plot between ENG and EMG showing a time shift of -3.1 ms (ENG happening before EMG). Right panel:Example of the time shifts along three EMG contacts spaced in the muscle. The increasing time shift is proportional to the distance between the muscle hook and the nerve electrode resulting in a estimated velocity of propagation of about 25 m/s.

signals (Fig. 3).

C. Wavelet Approximation

Raw ENG signals were band-pass filtered between 300-3,000Hz using a 4th order Butter-worth filter. Time-invariant wavelet transform [12] was applied to ENG signals.

Wavelet decompositions were obtained at different levels and using Symmlet 7 as the mother wavelet since its morphology helps in detecting neural activity. Let 'Ψ' denote the mother wavelet. The transformed signal is given by the following equation:

$$X(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} \Psi\left(\frac{t-b}{a}\right) x(t)dt$$

Here '*a*' is the dilation parameter, which corresponds to frequency information, and '*b*' is the translation parameter, which corresponds to the location of wavelet in time [13]. The integration here can be viewed as convolution performed to achieve time invariance.

D. Event Annotation and Identification

Wavelet approximation of ENG was used to identify flexion movement. Event annotations were made from the accelerometer recordings along the axis corresponding to the direction of the movement after filtering (10 Hz low pass Butter-worth filter, phase shift adjusted using filt-filt function in MATLAB). Corresponding EMG, ENG annotations were calculated from the accelerometer taking into account an approximate of the expected delay due to the causality between each of these signals. Annotations were verified using the video recorded during the experiment. Using these annotations, templates of ENG signal were formed with windows of width 100 ms (Fig. 4) and labeled to represent flexion and relaxation phase of hand movement. Following this the ENG signals were tested during the entire recording period (11 trials, ~ 60 s). The detection algorithm considered 100 ms of ENG signal each time for testing and returned the label of the template with which it produced best match. Dot product was computed on normalized values between the created templates and the tested ENG signal. The result of this dot product was used to determine closeness of match. Results are presented in the form of mean ± std.

III.RESULTS

A. Correlation between ENG and EMG

The surgical procedure was performed without any complications. Recordings were initiated after 3 weeks of recovery. Nerve electrode impedances increased from intra-operative (105.5 ± 93 kΩ) to a 3-week post-operative (726.2 ± 250 kΩ) and remained unchanged hereafter.

All correlation values were obtained with a p-value less than 0.01. Most of the channels showed a high degree of relationship ($r > 0.6$) and were considered for analysis. Cross correlation was maximum when time shift was applied. This shift depended on the position of the electrode in muscle and

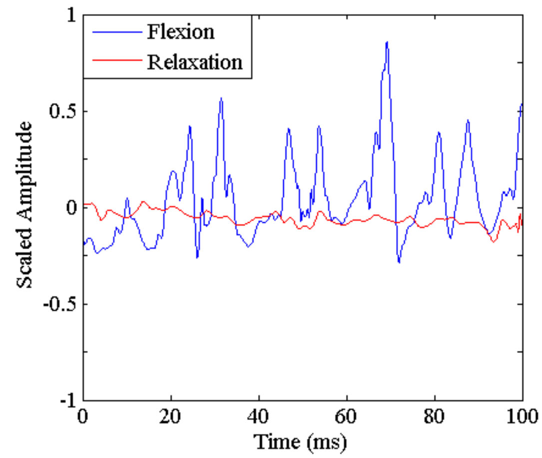

Fig. 4. Template of relaxation state (red trace) and flexion state(blue trace) of wavelet approximation of one of the ENG signals. These normalized windows were considered for categorizing ENG recordings.

its distance to the nerve electrode (Fig. 3), ranging from -3.02 ± 0.10 ms at the proximal portion of the FCR (~ 10 cm) to -15.09 ± 0.10 ms at the distal portion of the FDS (~ 20 cm). This may represent the time between an observed ENG and the onset of the EMG elicited by it and can be considered as an estimate of the delayed motor latency (DML). Due to the experiment characteristics, no exact measurements between the nerve and the muscle electrodes were obtained. Using approximated values of the distance, the DML was calculated to be 25.0 ± 5.5 m/s, which is consistent with previous results [14, 15].

B. Flexion Identification.

In order to see whether the windowed energy based analysis could be used for discrimination of hand movement, the animal was trained to perform an extension followed by a grasp (Fig. 5). The grasping consisted of gripping a metallic tool ("flexion") and relaxing ("relax").

Using dot product energy measure, it was possible to identify the flexion phase of gripping. The with-in class Euclidean distance for "flexion" phase was found to be 201.9 ± 36, for "relax" phase this was found to be 250.4 ± 206. Between-class Euclidean distance was found to be 308.6 ± 242 between "flexion" and "relax". These values are computed for n = 11 trials. This analysis could be used in future for control of a prosthetic device.

CONCLUSIONS AND DISCUSSION

In this work we recorded simultaneously nerve and muscle signals during a grasping task in the NHP and correlated the activity pattern between both. Owing to this, it was possible to infer hand movement from the ENG. Interestingly, we observed that our recorded nerve signals were larger in amplitude than those reported previously [16]. One possibility would be that the use of an implanted amplifier besides the recording electrodes prevented signal degradation due to distance and improved the SNR.

The correlation between hand movement, muscle activity, and nerve signal was relatively high but not absolute. It is

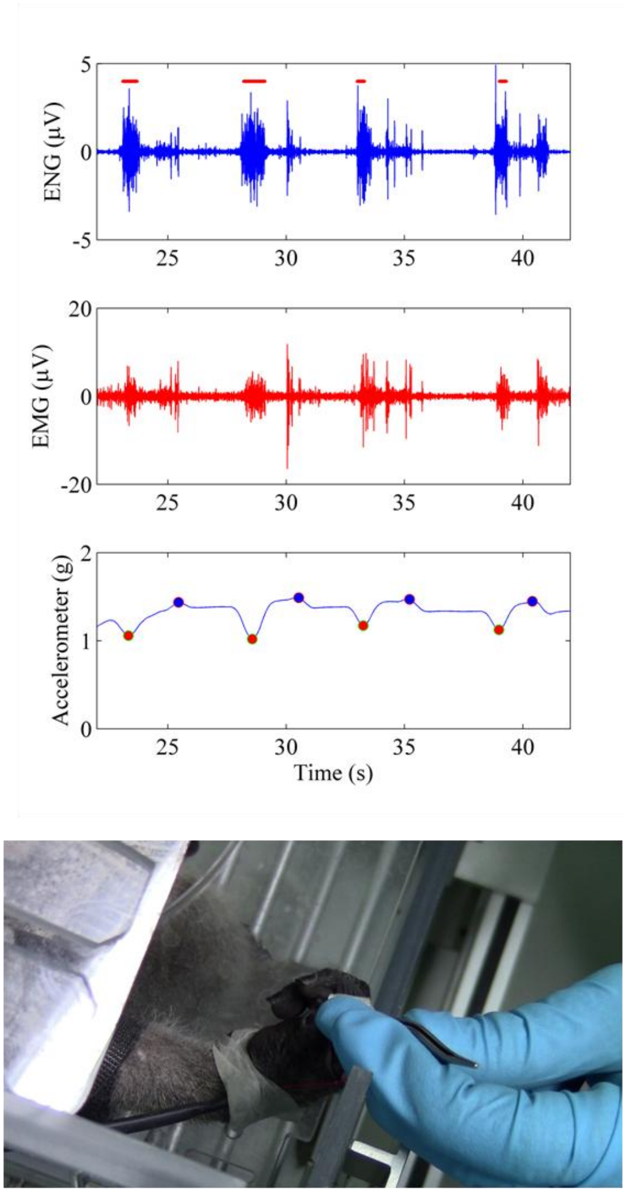

Fig. 5. Top panel showing wavelet approximation of an ENG (blue) used for decoding. Here, the detected flexion phase, is indicated with a red bar. Middle panel shows the corresponding EMG signal (red).Bottom panel shows annotated accelerometer recordings corresponding to the movement. Red dot indicates the beginning of flexion and the blue one indicates end. The screen shot shows flexion during one trial.

worth noting that, due to the design of the implant, it is possible that some motor nerve signals had no corresponding muscular activity since grasp movement involves more muscles than the three muscles with implanted electrodes. Considering this fact, the correlation obtained might be good for neuroprosthetic applications. Importantly we could identify flexion phase of the event, which would help us to use similar signals to bring about this kind of movement which might correspond to different motor pathways involved in flexion.

This work confirms the possibility of using a similar system for a future neuroprosthetic device for hand rehabilitation in proximal peripheral nerve injuries such as brachial plexus injuries. The main advantage of this system over other existing devices is the possibility of using signals from the nerve directly, which allows recording an increased number of different signals for prosthetic control and provides a natural way for the patient to communicate with the implant. A further refinement of our device would be to achieve a fully implantable system that would prevent the use of a transcutaneous connection.

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