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Interleaved Multichannel Epimysial Stimulation for Eliciting Smooth Contraction of Muscle with Reduced Fatigue

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Abstract—**Functional electrical stimulation (FES) refers to the method by which sensory or motor functionality is restored through the use of coordinated stimulation of tissue. Our group has developed a mechanically conformable multielectrode array (cMEA) that can stimulate and record from the surface of muscles with high fidelity and low invasiveness, making the device well suited for various FES applications. The research presented here investigates the feasibility of using a cMEA to deliver asynchronous spatiotemporal stimulation patterns epimysially (on the surface of muscles). Specifically, we employ an interleaved stimulation protocol to achieve force responses with less fatigue and less ripple than those produced by standard simultaneous stimulation protocols delivered at high and low frequencies, respectively. This experimentation demonstrates that asynchronous spatiotemporal stimulation protocols delivered epimysially via a cMEA can improve the characteristics of the resulting force profiles.**

I. INTRODUCTION

STIMULATION systems have been developed to restore a wide range of both sensory and motor functionality in patients with such impairments. This technique is known as functional electrical stimulation (FES). The cochlear implant is an example of how FES can be used to treat a sensory deficit, specifically hearing impairment in this case [1]. FES can also be used to activate both voluntary and involuntary muscles and can therefore be used clinically as a treatment for numerous conditions as far-ranging as incontinence, foot drop, and paralysis [1-2]. FES may be delivered to a muscle through electrodes placed on the surface of the skin near the muscle to be activated or by implanting an electrode directly in the muscle, with the latter method providing far greater efficacy but increased invasiveness. Similarly, a multielectrode array (MEA) with penetrating electrodes might be fitted on the muscle in lieu of implanting multiple single electrodes in order to provide multichannel stimulation. However, in addition to the invasiveness, MEAs with penetrating electrodes could also lead to tissue damage and scarring or even damage to the MEA itself if shifting of the device occurs.

One solution to this problem is to make use of epimysial stimulation, meaning stimulation on the surface of the muscle, as a tradeoff between invasiveness and efficacy. To this end, our group has developed a mechanically conformable multielectrode array (cMEA) using a compliant, biocompatible substrate – polydimethylsiloxane (PDMS) [3]. The cMEA can stimulate and record epimysially from muscle tissue with high fidelity and spatiotemporal precision; however, unlike MEAs with penetrating electrodes, the cMEA is less invasive and there is much less of an opportunity for tissue damage due to movement of the device. These properties of the cMEA make it ideal for many FES applications that involve stimulation of muscle. In order for such applications to be realized, however, there is a need for stimulation systems that can accurately and effectively control the force of muscles; this is the over-arching goal of the research presented here. One difficulty in developing such a system is that in order to produce smooth force responses, high frequency stimulation must be delivered, but stimulation of this type causes the muscle to fatigue quickly. Alternatively, lower frequency stimulation generally results in less fatigue, but the force response is not as smooth and will contain ripple at the frequency of stimulation. Therefore, there is a tradeoff between fatigue and ripple.

This problem is not unique to epimysial stimulation, and also occurs with stimulation of nerves to elicit muscle contraction. Previous researchers have addressed this issue by providing interleaved stimulation to nerves [4]. Interleaved stimulation refers to the method by which the frequency of stimulation pulses delivered at any given individual electrode is a fraction of the desired overall frequency; however, electrodes are activated asynchronously rather than simultaneously so that the composite frequency of pulses over all electrodes is equivalent to the desired frequency. The ability to deliver asynchronous spatiotemporal patterns of stimulation is a unique advantage of an MEA, and interleaved stimulation is one of many such possible patterns. In the present study, we adopt this interleaved stimulation technique to examine the effects of epimysial stimulation delivered via a cMEA. We compare

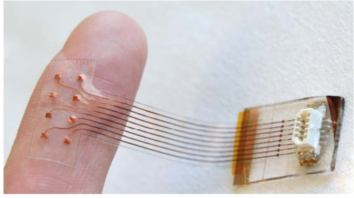

Fig 1. Conformable multielectrode array with eight electrodes.

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the muscle force responses to three different stimulation protocols, in which current is delivered at 60 Hz simultaneously to each electrode, at 15 Hz simultaneously to each electrode, and at 15 Hz interleaved to produce a composite frequency of 60 Hz. We hypothesize that the response to the interleaved stimulation will exhibit less ripple than the response to the 15 Hz simultaneous stimulation and less fatigue than the response to the 60 Hz simultaneous stimulation.

II. METHODS

A. Experimental Preparation

The experimentation made use of the Northern Leopard Frog (*Rana pipiens*). Prior to surgery, the animals were anesthetized with tricaine methanesulfonate (MS-222, 1 g L^{-1}) and then double pithed. The leg was then partially skinned so as to expose the plantaris longus muscle. This muscle was chosen because of its accessibility, size, and fatigue properties. The plantaris longus muscle, located in the calf of the frog, is recruited for very short periods of time to generate the frog's powerful leaping motion. The muscle is comprised of a high percentage of fast-fatiguable muscle fibers and is therefore well suited for this test of muscle fatigue [5]. The distal tendon of the muscle was detached from the calcaneus and clamped to a load cell (Strain Measurement Devices S251). A clamp affixed to a stationary support was secured onto the femur at the knee so as to hold the frog leg in place and maintain a constant muscle length. This length was adjusted so that the muscle, when at rest, was still under slight tension. The frog was periodically moistened with Ringer's solution (NaCl, KCl, $CaCl_2$, $NaHCO_3$).

An eight-electrode cMEA (Fig. 1) was wrapped around the exposed plantaris longus muscle. The dispersive adhesive forces associated with the PDMS tend to keep the cMEA affixed to the muscle. Because of the mechanical conformability of the device, the cMEA stays affixed even during and following a contraction, therefore the cMEA was not required to be glued or sutured into place. The cMEA was interfaced to four channels of a stimulator (Multichannel Systems STG2008), connected such that bipolar current stimulation was delivered to four pairs of electrodes. A dSPACE DS1103 PPC real-time controller board was used to trigger the stimulation as well as acquire force readings from the load cell. This force signal was amplified and low-pass filtered (cut-off frequency: 50 kHz) using a Brownlee Precision Model 440 Instrumentation Amplifier. This experimental setup is illustrated in Fig. 2.

B. Stimulation

As shown in Fig. 3, three different stimulation protocols were tested: simultaneous 60 Hz (Sim60), simultaneous 15 Hz (Sim15), and interleaved 60 Hz (Int60). The Sim60 protocol was used because the stimulation frequency was above the fusion frequency for the muscles tested; therefore, we expected very little ripple to be observed. Conversely, the lower frequency Sim15 protocol stimulated below the fusion frequency and was expected to result in a higher degree of ripple but less muscle fatigue. The Int60 protocol was a straightforward implementation of interleaved stimulation and was hypothesized to produce force responses with improved ripple and fatigue characteristics as compared to those of Sim15 and Sim60, respectively.

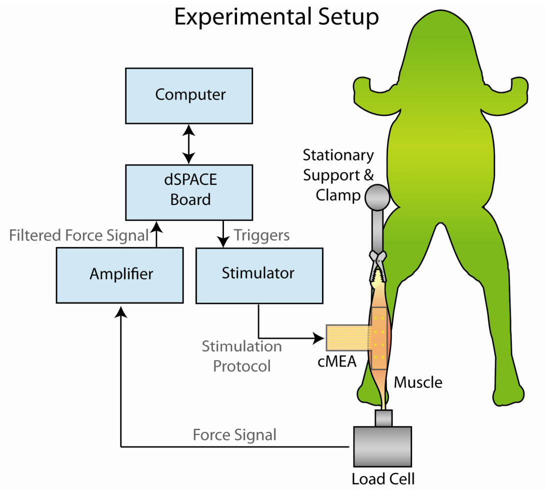

Fig 2. Experimental setup. The appropriate stimulation protocol is chosen by the computer system and is delivered to the frog's plantaris longus muscle epimysially via the cMEA. The resulting contractile force is measured by the attached load cell. This force signal is then amplified and filtered before being recording.

A fatigue trial consisted of delivering a given stimulation protocol for a 20 second duration and examining how the force response of the muscle evolved over that time period. After stimulating, the muscle was given 10 minutes to rest before the following fatigue trial would begin. The different stimulation protocols were delivered in a pseudorandom order.

From trial to trial, the size of the muscle force in response to the same stimulation protocol can vary greatly. This is especially true when comparing across muscles from different frogs, as factors such as variations in the size of the muscles can obviously cause variations in force response. However, the size of the force response can also vary to a large degree even within the same preparation. For example, our preliminary experiments with this preparation showed that the peak force achieved during trials tended to decrease as the time into the experiment progressed. This decline in force was not dependent on the duration of the rest period between fatigue trials (provided that this rest period was at least 10 minutes long). The particular current amplitudes chosen for each stimulation protocol were selected because, despite the inter-trial force variation, preliminary experiments showed that, at the given current amplitudes, the average peak force produced during a fatigue trial was statistically the same between the three protocol types.

C. Data Analysis

The efficacy of the stimulation protocols were evaluated by examining the resulting muscle fatigue and ripple in the

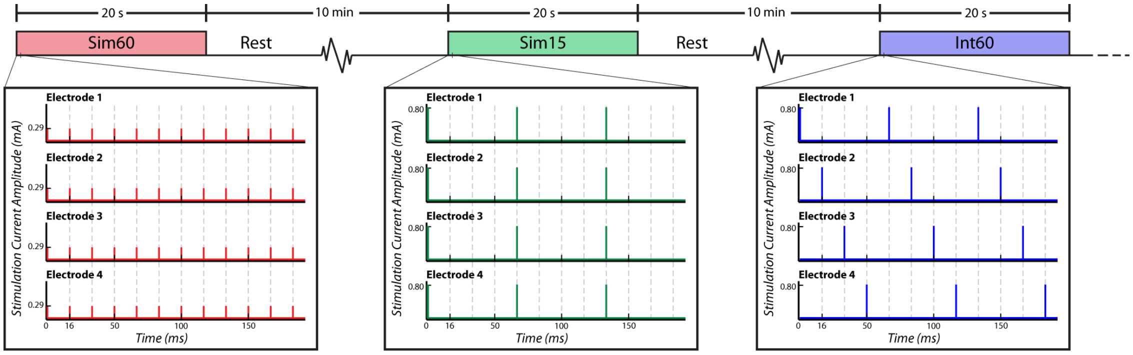

Fig 3. Stimulation protocols. During a fatigue trial, the Sim60, Sim15, or Int60 stimulation protocol was randomly selected and delivered for a 20 s duration. The muscle was then given 10 min to rest before the next trial began. For the Sim60 and Sim15 protocols, stimulation pulses were delivered simultaneously to each electrode pair at 60 Hz and 15 Hz, respectively. For the Int60 protocol, stimulation pulses were delivered asynchronously to each electrode pair at 15 Hz. Each successive pair of electrodes was out of phase with the previous electrode pair by 16.66 ms such that the composite frequency of all four electrode pairs was 60 Hz. The amplitude of the current delivered to each electrode pair for the Sim60 protocol was 0.290 mA, while the Sim15 and Int60 protocols were both delivered at 0.800 mA to each pair. The stimulation pulse width was 200µs for all three protocols.

force responses. Before analyzing these properties, the force response from each fatigue trial was normalized such that the baseline force of the resting muscle was at zero and the peak force produced during a fatigue trial was at one. This normalization allowed us to better compare fatigue and ripple between trials, as these are relative properties.

If different protocols cause fatigue at different rates, then the average normalized force profiles associated with the different protocols should differentiate as trial time progresses. Therefore, fatigue was analyzed by testing for statistical differences between the average normalized forces produced by the different stimulation protocols at given points in time during the fatigue trial.

Ripple is a periodic aberration that occurs at the frequency of stimulation. The amplitude of the force profile decays gradually during a fatigue trial; subsequently, the energy of this signal is concentrated at very low frequencies. We can therefore consider the ripple to be noise and quantify the ripple as the energy in the normalized force response at frequencies above 10 Hz. Therefore, for a given fatigue trial, we have defined the metric *ripple energy* as the integral from 10 to 5000 Hz of the power spectral density of the normalized force profile associated with this trial. These values were examined to determine if the average ripple energy associated with the three stimulation protocols differed from one another with statistical significance.

III. RESULTS

Data were acquired for 17 fatigue trials in all. Of these 17 trials, the Sim60 protocol was delivered during six of the trials, the Sim15 protocol during five, and the Int60 protocol during six. The two-sample Student's t-test was used to show that the average of the peak forces (before normalization) was statistically the same between each group of protocols (Sim60 to Int60: p=0.0068, Sim60 to Sim15: p=0.0320, Int60 to Sim15: p=0.0366). The force data were then normalized and compared.

A. *Comparison of Fatigue*

As shown in Fig. 4a, the Sim60 protocol was associated with the greatest amount of muscle fatigue, while the Sim15 protocol resulted in the least amount of fatigue. As hypothesized, the force response associated with the Int60 protocol exhibited more fatigue than the Sim15 results, but less than the Sim60. Fig. 4b shows the p-values corresponding to two separate t-tests performed on the distribution of normalized forces at various points in time during the fatigue trial. The first t-test (p-value shown in red) tests the null hypothesis that the average normalized force at a particular point in time is less for Int60 stimulation than it is for Sim60 stimulation. The second t-test (p-value shown in green) tests the null hypothesis that the average normalized force is less for Sim15 stimulation than Int60 stimulation. We see that after approximately two seconds into the trial, the first null hypothesis can be rejected with statistical significance (a=0.05), and the second null hypothesis can be rejected after approximately 4.25 seconds. At 20 seconds, the end of the trial, we find that Int60 is significantly greater than Sim60 ($p=8.5\times10^{-5}$), and significantly less than Sim15 ($p=3.5\times10^{-5}$).

B. *Comparison of Ripple*

Ripple was quantified and compared by analyzing the noise frequency band (10 Hz to 5000 Hz) of the normalized force data. The amplitude spectrum of the mean normalized force curves associated with each stimulation protocol are shown in Fig. 4c. Clearly, the amplitude of the frequency response in the noise band is largest for the Sim15 protocol, smaller for Int60, and smallest for Sim60. The Student's t-test was used to show that the ripple energy (as defined in methods) for the Int60 trials was significantly smaller than that of the Sim15 trials (p=0.0049). Similarly, the ripple energy for the Sim60 trials was significantly smaller than that of the Int60 trials (p=0.0048).

IV. DISCUSSION AND CONCLUSION

The ultimate goal of this research is to design a control system so that muscle force can be accurately controlled through stimulation delivered epimysially via the cMEA. Such a system would have definite applications in the field

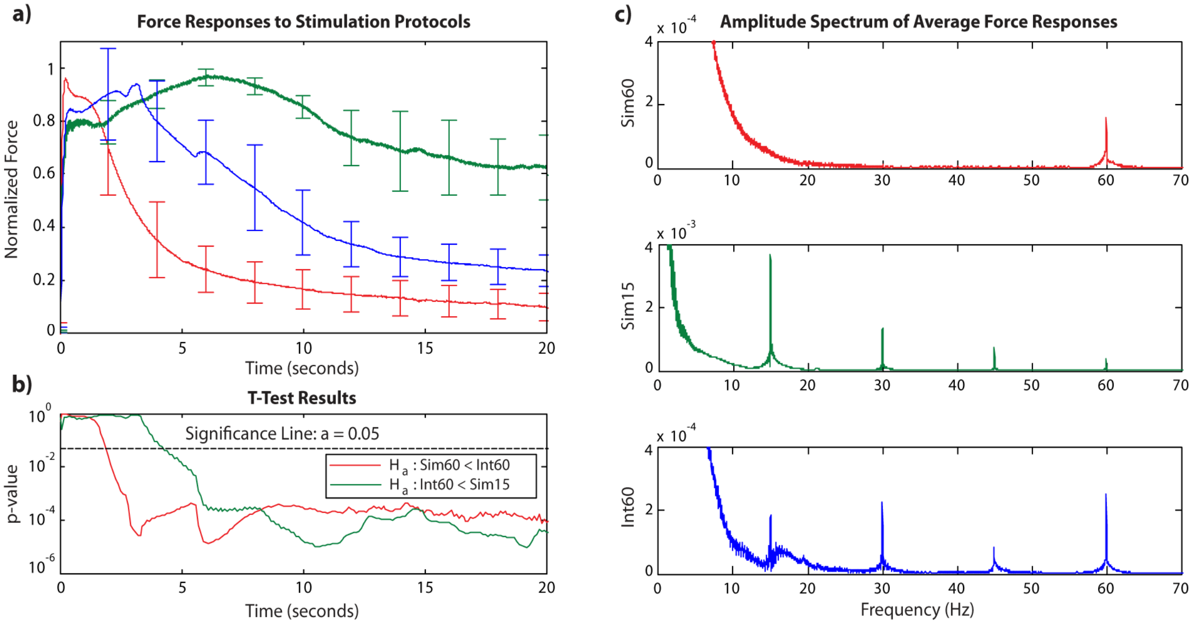

Fig 4. Results of fatigue trials. a) The average normalized force responses to each stimulation protocol during fatigue trials are plotted (red: Sim60, green: Sim15, blue: Int60). This figure shows qualitatively that the force responses to different stimulation protocols fatigue at different rates, with Sim60 fatiguing fastest, Int60 fatiguing slower, and Sim15 fatiguing slowest. b) Analysis with the Student's t-test quantitatively shows that after two seconds into the fatigue trial the Sim60 response is significantly less than the Int60 response, and after 4.25 seconds the Int60 response is significantly less than the Sim15 response, thereby confirming the qualitative results in (a). c) The amplitude spectrum of the average normalized force response to each stimulation protocol is plotted (**note** that for visibility the Sim15 y-axis is scaled ten times larger than that of Sim60 or Int60). For each response, the majority of the signal is concentrated at low frequencies, and energy in the frequency band above approximately 10 Hz is simply noise, primarily caused, in this case, by ripple. For Sim60 there is a small amount of noise concentrated at 60 Hz, while there is a somewhat larger amount of noise concentrated at multiples of 15 Hz for the Int60 protocol. The Sim15 protocol has an order of magnitude more noise at frequency multiples of 15 Hz.

of FES. The development of stimulation protocols, such as the interleaved protocol presented here, that achieve smooth force responses and that do not excessively fatigue the muscle is an important aspect of this overall design process.

The present study illustrates that simultaneous epimysial stimulations of both low and high frequency have benefits and weaknesses, namely the tradeoff between increased muscle fatigue and increased ripple. As we hypothesized, interleaved epimysial stimulation offers a compromise between these two protocols, generating less fatigue than the simultaneous high frequency stimulation and a reduction in ripple over the simultaneous low frequency stimulation.

It should be noted that the interleaved protocol tested here is still merely a compromise and not a clear cut solution to the fatigue/ripple tradeoff. Ideally, we would like to identify a spatiotemporal stimulation protocol that achieves a force response with fatigue characteristics that are the *same* as those of the Sim15 protocol while maintaining the *same* amount of limited ripple as the Sim60 protocol. Future experimentation should explore other more complex asynchronous spatiotemporal stimulation patterns in an attempt to achieve this goal. For example, in this experiment, the same amount of current was delivered to each electrode pair. If, however, the charge delivered was balanced so that each electrode pair individually produced an equivalent force response, it is possible that ripple and fatigue properties could be improved further still. Additionally, one could experiment with various different orders and timing characteristics of electrode activation. Nevertheless, though there is room for improvement, this work provides an important proof-of-concept. A key benefit of MEA technology is its ability to deliver asynchronous spatiotemporal stimulation and we have shown that such stimulation delivered epimysially can provide unique improvements to the force response.

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