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The Time-Varying Nature of Electromechanical Delay and Muscle Control Effectiveness in Response to Stimulation-Induced Fatigue

Ryan J. Downey, Manelle Merad, Eric J. Gonzalez, and Warren E. Dixon

***Abstract*—Neuromuscular Electrical Stimulation (NMES) and Functional Electrical Stimulation (FES) are commonly prescribed rehabilitative therapies. Closed-loop NMES holds the promise to yield more accurate limb control, which could enable new rehabilitative procedures. However, NMES/FES can rapidly fatigue muscle, which limits potential treatments and presents several control challenges. Specifically, the stimulation intensity-force relation changes as the muscle fatigues. Additionally, the delayed response between the application of stimulation and muscle force production, termed electromechanical delay (EMD), may increase with fatigue. This paper quantifies these effects. Specifically, open-loop fatiguing protocols were applied to the quadriceps femoris muscle group of able-bodied individuals under isometric conditions, and the resulting torque was recorded. Short pulse trains were used to measure EMD with a thresholding method while long duration pulse trains were used to induce fatigue, measure EMD with a cross-correlation method, and construct recruitment curves. EMD was found to increase significantly with fatigue, and the control effectiveness (i.e., the linear slope of the recruitment curve) decreased with fatigue. Outcomes of these experiments indicate an opportunity for improved closed-loop NMES/FES control development by considering EMD to be time-varying and by considering the muscle recruitment curve to be a nonlinear, time-varying function of the stimulation input.**

***Index Terms*—Control Effectiveness, Electromechanical Delay (EMD), Fatigue, Functional Electrical Stimulation (FES), Neuromuscular Electrical Stimulation (NMES)**

I. Introduction

Neuromuscular electrical stimulation (NMES) is a method to evoke skeletal muscle contractions by applying electrical stimuli, thereby activating motor neurons that innervate muscle fibers [1]. NMES is commonly used for postoperative rehabilitation [2], [3] or to increase muscle mass [4], and the technique is referred to as functional electrical stimulation (FES) when the electrical stimuli yield functional limb motion (e.g., walking [5], [6] and cycling [7]–[9]).

Closed-loop control of FES is promising for the further development of rehabilitation procedures and assistive devices; however, closed-loop control of human movement via FES is difficult due to a number of factors. One challenge to closed-loop control is that the passive dynamics of the human limb model (i.e., the dynamics excluding the actuator) are uncertain and nonlinear (e.g., the elastic and viscous effects in the knee joint and musculotendon complex are uncertain, nonlinear functions). Therefore, recent attempts to design FES controllers have utilized nonlinear, Lyapunov-based approaches [7]–[17] to yield limb tracking despite nonlinear passive dynamics. An additional challenge to muscle control is the uncertain and nonlinear muscle response to stimulation (i.e., the actuator dynamics are also uncertain and nonlinear).

The muscle response to electrical stimulation is governed by three stimulation parameters: pulse amplitude, pulse width (i.e., pulse duration), and pulse frequency, as depicted in Fig. 1. Pulse amplitude and pulse width affect the number of recruited motor units whereas pulse frequency affects the rate coding (i.e., firing rate) of recruited motor units [18]. Recruitment curves are often constructed to characterize the muscle response to stimulation by first securing the limb to a fixed apparatus (i.e., the muscle response is tested under isometric conditions) and selecting a constant pulse frequency. One of the two stimulation parameters that affect recruitment is then fixed while the remaining parameter is varied across a range of values and the resulting torque/force is measured. For a linearly increasing stimulation parameter, the recruitment curve is composed of three phases, as shown in [19, Fig. 1]: the dead zone where the stimulation input is low but the torque output is null, the linear zone where the torque increases linearly with respect to the stimulation parameter, and the saturation zone where the torque output remains constant even though the stimulation input is increasing [19]. While the nonlinearities emphasized by the recruitment curve should optimally be considered in the muscle model when developing FES controllers, the recruitment curve is often approximated by a linear curve fit corresponding to the linear portion of the recruitment curve. Recruitment curves represent the total evoked muscle force as a function of stimulation intensity. Therefore, its slope is analogous to the evoked force of individual motor units. The linear slope of the recruitment curve varies (e.g., with respect to the individual, the joint angle, or electrode placement), and therefore, from a control

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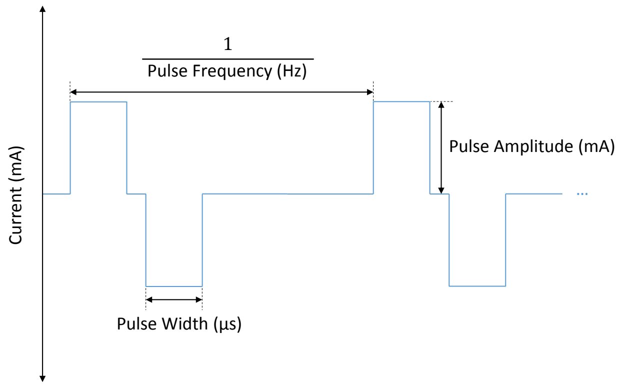

Fig. 1. Stimulation parameters. Depicted are biphasic symmetric pulses (utilized in this study). Monophasic and biphasic asymmetric pulses may also be used to elicit muscle contractions.

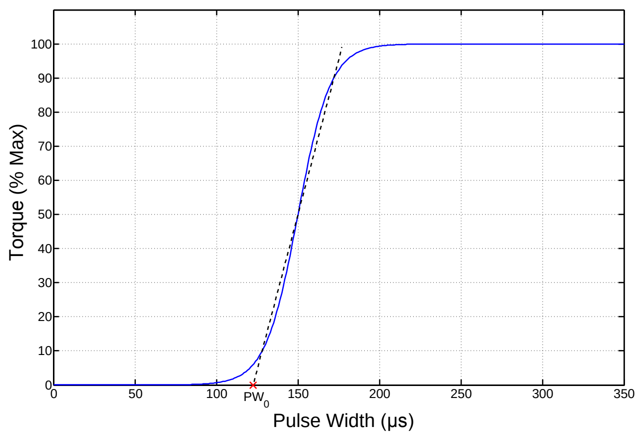

Fig. 2. Example recruitment curve. The recruitment curve is useful for determining the minimum stimulation intensity to evoke nonzero torque (PW_0) and the control effectiveness. The minimum stimulation intensity is often assumed to be a known constant that is added to a computed control law. The control effectiveness is a gain that relates the stimulation intensity (in excess of PW_0) to the evoked torque at a joint (e.g., the knee joint). Muscle contractile force depends on muscle length and velocity. Similarly, the moment arm of the muscle (relating musculotendon force to joint torque) may change throughout the range of motion. Therefore, the control effectiveness varies according to the joint angle and angular velocity. However, under isometric conditions (i.e., fixed joint angle), the control effectiveness simplifies to the recruitment curve slope. As indicated in this study, the recruitment curve changes (specifically, the control effectiveness decreases and PW_0 increases) as the muscle fatigues.

perspective, the muscle control effectiveness is uncertain. A simulated recruitment curve and its linear approximation are depicted in Fig. 2.

An additional difficulty to NMES/FES closed-loop control is muscle fatigue, defined as the decay in muscle force during sustained stimulation [20]. Suggested causes of NMES-induced fatigue are conduction failure due to high potassium ion concentration, decrease in the calcium release during motor neuron depolarization, or slow-down in cross-bridge cycling [21], [22]. Furthermore, fatigue occurs faster with NMES than with voluntary contractions, possibly due to a reversal of the Henneman's size principle [23], stimulation frequency [24]–[26], or the spatially fixed and temporally synchronous muscle fiber recruitment of conventional stimulation [27], [28]. While attempts have been made to slow the onset and rate of NMES-induced fatigue [29]–[33], the onset of fatigue is inevitable, and therefore, its effects should be modeled.

Muscle fatigue is expected to cause the uncertain control effectiveness to vary with time (specifically, it is expected to decrease), and therefore, the uncertain nonlinear dynamic model is also time-varying. Efforts have been made to design FES controllers that yield limb tracking despite an uncertain control effectiveness that varies with the knee angle (modeling muscle force-length properties) [8]–[16], the knee angular velocity (modeling muscle force-velocity properties) [8], [9], [11]–[14], and time (modeling muscle fatigue) [10], [14]–[16]. However, the time-varying changes in the control effectiveness in response to fatigue has not been examined in previous closed-loop control literature. Therefore, one objective of the present study was to evaluate the time-varying nature of the muscle control effectiveness during repeated fatiguing NMES-evoked contractions.

In addition to muscle fatigue, closed-loop control of FES is difficult due to the fact that skeletal muscle exhibits an electromechanical delay (EMD) between the onset of muscle activation and the onset of force production. While EMD is often measured during volitional contractions (e.g., to assess knee safety after harvesting tendons for ligament reconstruction [34]), muscle also exhibits EMD in response to externally applied electrical stimuli. From a control perspective, EMD appears as an input delay in the dynamics. Input delays can lead to instability of the closed-loop system, and therefore, EMD should be considered when designing controllers for FES. While there have been some attempts to account for EMD, the delay is often assumed to be constant [11], [13], [17]. Meanwhile, there is evidence to suggest that EMD changes with volitional fatigue [35], [36], but the time-varying nature of EMD due to NMES-induced fatigue is presently unclear. Since this knowledge could guide future control designs, the second objective of the present study was to evaluate the time-varying nature of EMD during repeated fatiguing NMES-evoked contractions.

The overall objective in this paper is to highlight areas of improvement for NMES modeling, thereby motivating future development of improved closed-loop NMES control designs. Specifically, the effect of NMES-induced fatigue on two major muscle parameters, the control effectiveness and the EMD, was examined. Transcutaneous electrical stimulation was delivered to the quadriceps femoris muscle group in isometric conditions. The resulting knee-joint torque was measured and analyzed to determine the EMD and control effectiveness. Two protocols (high-fatiguing and low-fatiguing)[1] were examined to elucidate the fatigue-induced variations in the EMD and control effectiveness. The results indicate that EMD and the control effectiveness vary as the muscle fatigues. Specifically, EMD increased with contraction number while the control effectiveness decreased. Furthermore, the rates of change for both variables were greater for the high-fatiguing protocol.

[1]To facilitate presentation of the following results, the term "low-fatiguing" refers to a stimulation pattern whereby 5 seconds of stimulation is delivered every 15 seconds while "high-fatiguing" refers to 10 seconds of stimulation every 15 seconds, as depicted in Fig. 4.

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II. Methods

Transcutaneous electrical stimulation was applied to the quadriceps femoris muscle group and the resulting knee-joint torque was recorded during isometric conditions to examine the time-varying nature of the EMD and control effectiveness in response to NMES-induced fatigue. Current amplitude (90 mA) and stimulation frequency (30 Hz) were fixed while the pulse width was varied in an open-loop manner (i.e., the stimulation pattern was predetermined). The pulse width pattern was designed to enable repeated EMD measurements throughout the trial while simultaneously fatiguing the muscle. To further elucidate the effect of fatigue, high-fatiguing and low-fatiguing stimulation protocols were separately tested where the two protocols utilized pulse width patterns of the same general design but differed in their duty cycles (33% versus 67%).

A. Subjects

Five able-bodied individuals (male, aged 20 to 27) participated in the study. Prior to participation, written informed consent was obtained from all participants, as approved by the University of Florida Institutional Review Board. All five individuals had prior experience with NMES.

B. Apparatus

All testing was performed using an apparatus that consisted of the following:

- A current-controlled 8-channel stimulator (RehaStim, Hasomed GmbH, operating in ScienceMode)
- A data acquisition device (Quanser Q8-USB)
- A personal computer running Matlab/Simulink
- A leg extension machine (depicted in Fig. 3) that was modified to include force sensors as well as boots to securely fasten the shank and foot
- Force transducers to measure knee-joint torque (Transducer Techniques)
- Electrodes (Axelgaard Manufacturing Co., Ltd.)[2]

C. Stimulation protocols

Biphasic symmetric electrical stimulation was delivered from a current-controlled stimulator (Hasomed GmbH, RehaStim) to a pair of 7.5 cm $\times$ 13 cm rectangular surface electrodes (Axelgaard, Valutrode®, CF7515) placed medial-distal and lateral-proximal over the quadriceps femoris muscle group according to Axelgaard's electrode placement manual.[3] Each trial lasted five minutes, and the current amplitude and stimulation frequency were set to 90 mA and 30 Hz,[4] respectively. Meanwhile, the pulse width was varied in an open-loop manner according to a predefined signal consisting of short bouts of nonfatiguing[5] stimulation and longer, fatigue-inducing sections that repeated every 15 seconds. The shape of the signal was designed to facilitate the measurement of the control effectiveness and EMD in addition to inducing muscle fatigue. To further examine the effect of fatigue, high-fatiguing (HFat) and low-fatiguing (LFat) protocols were tested with the only difference being the duration of the fatigue-inducing sections (33% versus 67% duty cycle). A visual depiction of the two fatiguing protocols is provided in Fig. 4.

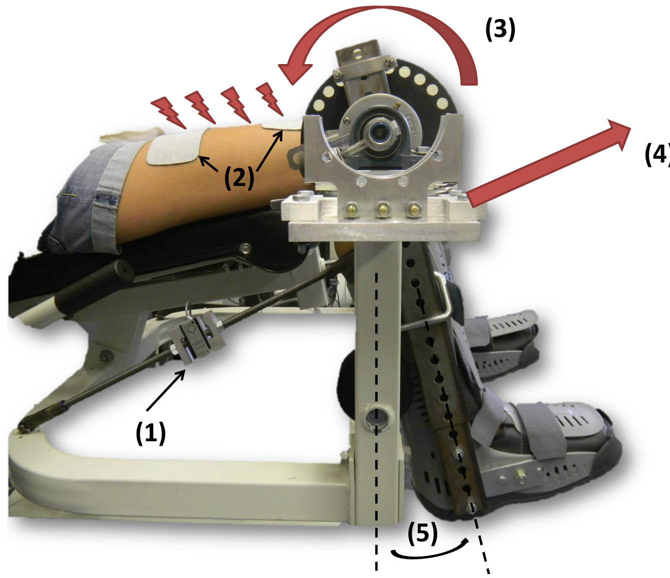

Fig. 3. The experimental testbed was a modified leg extension machine with boots to securely fasten the shank. Force transducers (1) were attached between the base of the machine and the boots to fix the knee-joint at a constant angle (5). Stimulation was applied via surface electrodes (2) and the measured force (4) from the force transducers was converted to isometric knee-joint torque (3) for subsequent analysis.

D. Precautions

The order of the two stimulation protocols (HFat and LFat) was randomized for each leg. To prevent any layover effect of fatigue, each leg received only one stimulation protocol per day. A minimum of 48 hours of rest was required before the individual completed the remaining stimulation protocol for each leg. Due to the nonselective nature of NMES [27], [28], fatigue should be similar across intensity levels. However, as a precautionary measure, a test was conducted to determine the appropriate range of pulse width values (i.e., A and B in Fig. 4) before executing the stimulation protocols. During this test, two seconds of stimulation was delivered every 25 seconds, and the pulse width was increased between contractions until stimulation evoked 15 $\mathrm{N \cdot m}$. This value of pulse width was recorded and the process was continued until the evoked torque reached 25 $\mathrm{N \cdot m}$.

[2]Surface electrodes for the study were provided compliments of Axelgaard Manufacturing Co., Ltd.

[3]http://www.axelgaard.com/Education/Knee-Extension

[4]The pulse train was delivered at 30 Hz since literature suggests this frequency is a good compromise between slowing the rate of fatigue and eliciting strong contractions. The pulse amplitude was selected as 90 mA based on preliminary experiments which indicated the resulting pulse width to target 15-25 $\mathrm{N \cdot m}$ would have sufficient range across individuals.

[5]Although it's possible that the short bouts (0.25 seconds) of stimulation may also induce some level of fatigue, the term "nonfatiguing stimulation" is used to facilitate presentation of the results.

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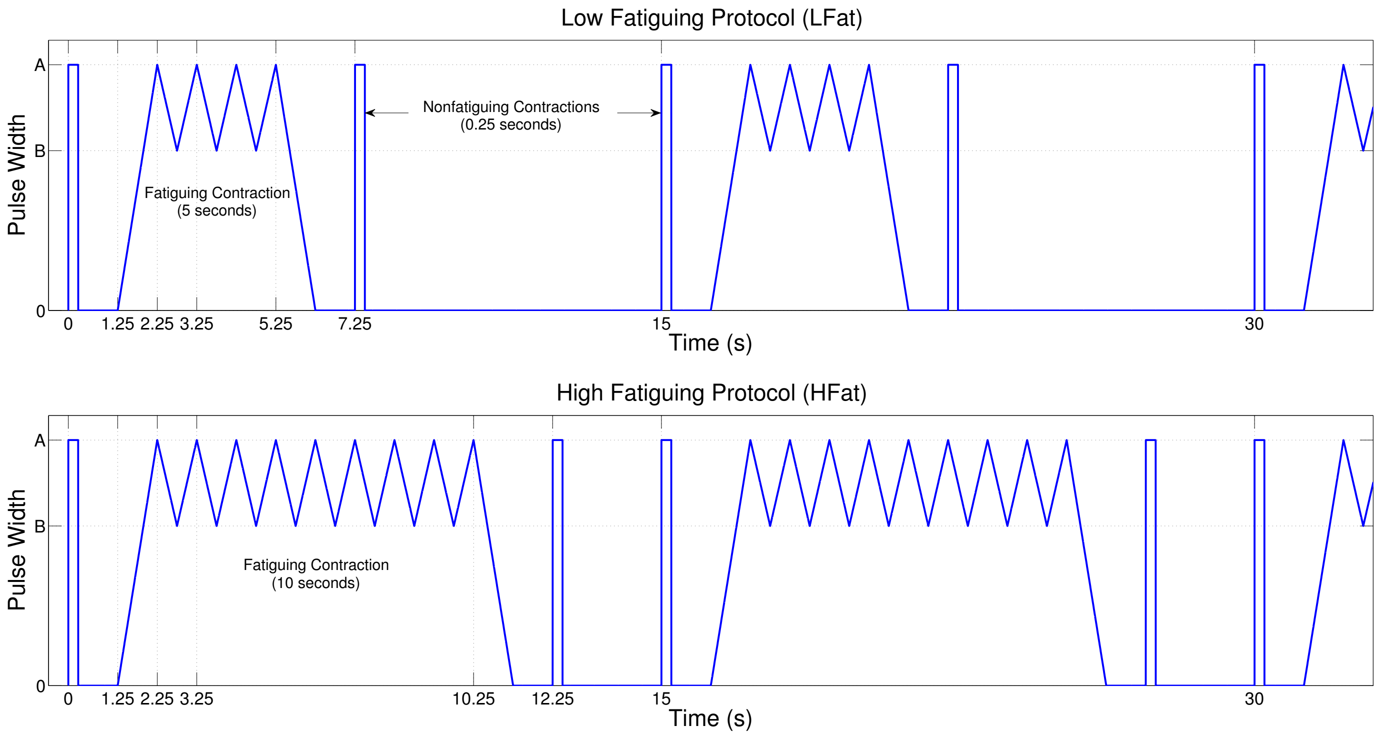

Fig. 4. Open-loop pulse width profiles for the low-fatiguing and high-fatiguing protocols. Short bouts of nonfatiguing stimulation (0.25 seconds) were delivered before and after longer, fatiguing bouts of stimulation (five seconds for low-fatiguing and ten seconds for high-fatiguing). The short bouts of stimulation enabled fatigue to be quantified by the peak torque and EMD to be measured with a thresholding method. By delivering nonfatiguing stimulation before and after each fatiguing contraction, the immediate effect of NMES-induced fatigue on EMD (i.e., pre/post contraction) could be determined in addition to the effect of the fatiguing contraction number. Fatigue was also quantified during the fatiguing bouts of stimulation according to the mean evoked torque during the triangle wave section. The triangle wave shape of the fatigue-inducing sections was designed to enable a second type of EMD measurement (via a cross-correlation method) and to measure the control effectiveness by relating the pulse width input and torque output after correcting for the delay between the two signals. The pattern of short bouts of nonfatiguing stimulation before and after fatiguing stimulation repeated every 15 seconds with each trial lasting a total of five minutes (i.e., there were 20 fatiguing contractions for each protocol). The pulse width values A and B were determined based on tests conducted beforehand to target specific values of torque (25 $\mathrm{N \cdot m}$ and 15 $\mathrm{N \cdot m}$ for A and B, respectively).

E. Measurements

Pulse width and torque data were recorded at a sampling frequency of 1000 Hz. The recorded torque was forward and reverse filtered (i.e., the filter did not introduce a delay) with a Butterworth lowpass filter. Two types of torque and three types of delay measurements were then calculated throughout the trial. Linear fits relating pulse width and torque were calculated within the triangle wave sections of each fatiguing contraction, where the slope of the linear fit (i.e., the control effectiveness) and the zero-crossing point (i.e., the minimum required pulse width to evoke knee-joint torque) were used to characterize the time-varying muscle response to stimulation.

1) Torque: Peak torque ($\mathrm{Torque_{peak}}$) is defined as the peak value of torque reached during the short bouts of nonfatiguing stimulation. These measurements occurred before and after each fatiguing contraction. Average torque ($\mathrm{Torque_{avg}}$) is defined as the mean value of torque evoked during the triangle wave section of each fatiguing contraction (i.e., the central eight seconds of each fatiguing contraction for HFat and the central three seconds for LFat; Fig. 4).

2) Delay: Three types of delay measurements were made: contraction delay ($\mathrm{EMD_{thres,contr}}$), relaxation delay ($\mathrm{EMD_{thres,relax}}$), and cross-correlation delay ($\mathrm{EMD_{x-corr}}$). The contraction delay measurement uses a thresholding method and corresponds to the short bouts of nonfatiguing stimulation. This delay was calculated as the difference between the time that the first electrical pulse was delivered and the time that the torque increased to 0.3 $\mathrm{N \cdot m}$ above the baseline (i.e., the torque resulting from no stimulation). Similarly, the relaxation delay also corresponds to the short bouts of nonfatiguing stimulation and was calculated as the difference between the time that the last electrical pulse was delivered and the time that the torque fell to 0.3 $\mathrm{N \cdot m}$ above the baseline. Example delay calculations using the thresholding method are provided in Fig. 5. The cross-correlation delay measurement corresponds to the fatiguing contractions. This measurement was completed by first selecting the torque and pulse width data over the window where the pulse width is a triangle wave. The first second of data (i.e., the first sub-contraction) was then removed.[6] The cropped torque and pulse width signals were then detrended (i.e., the best linear fit was removed to center the signals about zero). The delay between

[6]There were instances where the torque increased during the first sub-contraction (e.g., due to potentiation), rather than immediately reaching a peak and subsequently decaying due to fatigue. Since this nonlinear effect (upward and then downward trend) could not be removed by a linear detrend, the first sub-contraction was removed to obtain more reliable measurements.

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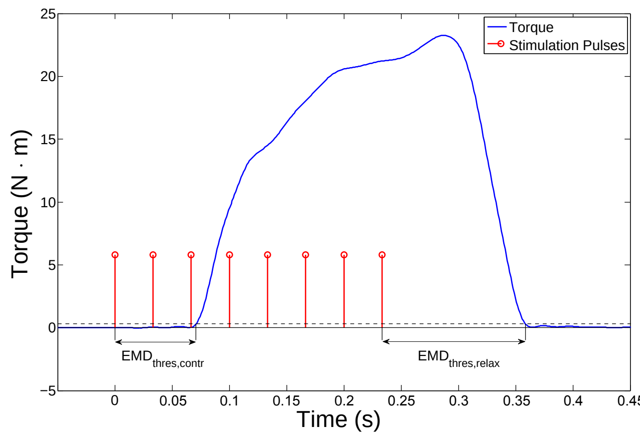

Fig. 5. Thresholding delay measurements. Depicted are example measurements of EMD using the thresholding method during the short (0.25 seconds) bouts of stimulation. The horizontal dashed black line indicates the threshold (0.3 $\mathrm{N \cdot m}$). Stimulation pulses are presented for timing information only (i.e., the height is arbitrarily drawn).

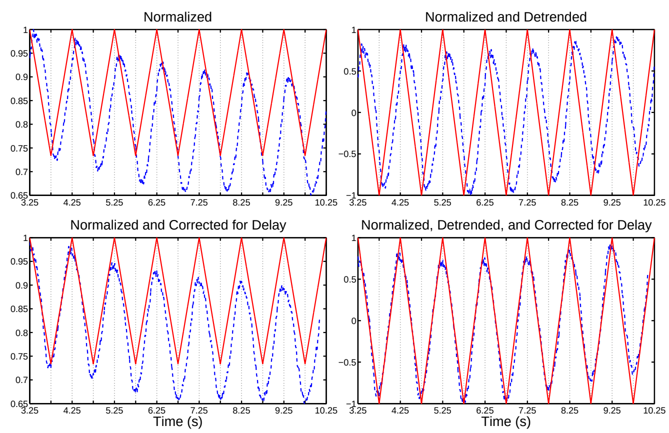

Fig. 6. Cross-correlation delay measurement, $\mathrm{EMD}_{\mathrm{x-corr}}$. Depicted is an example measurement of EMD using a cross-correlation method during the fatiguing bouts of stimulation. $\mathrm{EMD}_{\mathrm{x-corr}}$ was calculated by first detrending the pulse width (solid) and torque signals (dashed). The detrended signals were then sent as inputs to the *finddelay* function in Matlab which shifts the two signals relative to each other across a range of delay values, calculates the correlation coefficient at each delay, and then returns the delay value for which the correlation coefficient is maximized. In the present example, the signals are normalized for illustrative purposes.

the resulting signals was then calculated with the *finddelay* function in Matlab (a function which uses cross-correlation to find the delay between two signals). An example calculation of $\mathrm{EMD}_{\mathrm{x-corr}}$ is depicted in Fig. 6.

3) Control Effectiveness and Minimum Pulse Width: After the delay was calculated using the cross-correlation method for each fatiguing contraction, the torque signals were shifted with respect to the pulse width signals to remove the effect of delay. Scatterplots were then constructed with the recorded torque as a function of the input pulse width. Similar to the example recruitment curve in Fig. 2, linear curve fits were then used to estimate the control effectiveness (i.e., the slope) and the minimum required pulse width to evoke nonzero torque (i.e., the zero-crossing point, PW_0). Rather than fit a single line to the entire scatterplot of pulse width-torque data during the entire fatiguing contraction, the fatiguing contraction was split into multiple segments (three segments for LFat and eight segments for HFat), where each segment corresponds to a single traversal of the pulse width on a downward and then upward trajectory. By segmenting the data, the effect of fatigue was able to be examined within each fatiguing contraction as well as between contractions.

F. Statistical Analysis

1) Overview: Multiple linear regression[7] was performed separately on $\mathrm{EMD}_{\mathrm{thres,contr}}$, $\mathrm{EMD}_{\mathrm{thres,relax}}$, $\mathrm{EMD}_{\mathrm{x-corr}}$, the control effectiveness, and PW_0 measurements to examine the effect of repeated fatiguing NMES-evoked contractions on their values. All regression analyses utilized the following predictors: fatiguing contraction number (ContrNum; quantitative predictor ranging from 1 to 20), stimulation protocol (Protocol; HFat or LFat), the individual being tested (Subject; S1, ..., S5), and leg side (Side; Left or Right). To further elucidate the effect of fatigue, the interaction term ContrNum$\times$Protocol was also included in all regressions. Other interaction terms were initially included in the model but they were subsequently removed when they were determined not to be significant (P-Value > 0.05). For $\mathrm{EMD}_{\mathrm{thres,contr}}$ and $\mathrm{EMD}_{\mathrm{thres,relax}}$, an additional predictor was utilized to indicate whether or not a measurement was made immediately before or after a fatiguing contraction (Pre/Post Contr; Pre or Post). Similarly, regressions on the control effectiveness and PW_0 utilized an additional predictor corresponding to the sub-contraction number (SubContrNum; quantitative predictor ranging from 1 to 3 for LFat and 1 to 8 for HFat) within a fatiguing contraction. Reference levels for the categorical predictors Protocol, Subject, Side, and Pre/Post Contr were selected to be LFat, S1, Left, and Pre, respectively. Therefore, coefficients do not appear in the subsequently presented regression tables for LFat, S1, Left, and Pre since their effects are already encapsulated in the constant term of the regression.

2) Interpretation: The effect of fatigue on the variables of interest were inferred via the predictor coefficients and their statistical significance, with coefficients for quantitative predictors representing slopes and coefficients for categorical predictors representing vertical shifts. For example, if ContrNum (quantitative) was a statistically significant predictor of $\mathrm{EMD}_{\mathrm{thres,relax}}$ and the value of the coefficient for ContrNum was 1.5, then $\mathrm{EMD}_{\mathrm{thres,relax}}$ increased on average by 1.5 ms per fatiguing contraction (and this effect is significantly different from zero). Similarly, for categorical predictors, statistically significant coefficients indicate significant effects; however, proper inference requires the additional step of considering the reference levels. For example, significant differences between LFat and HFat conditions are evidenced by the coefficient for HFat being significantly different from zero since LFat is considered the reference level. Furthermore, if for example, the fitted coefficient for HFat was 20 and statistically significant, then that would indicate that the stimulation protocol has a significant effect on EMD and the

[7] Multiple linear regression is regression on one continuous dependent variable with ≥ 2 independent variables (continuous, discrete, or both).

EMD was 20 ms longer on average (across all contractions) than LFat (note that it is 20 ms longer than the reference level of LFat, not simply 20 ms). Finally, on the interpretation of the cross-term ContrNum×Protocol, if HFat is statistically significant for this interaction, then it indicates that the effect of ContrNum on EMD depends on the protocol. For example, if ContrNum×Protocol is significant with an HFat coefficient of 2 (note this coefficient is specific to this interaction, not to be confused with the other HFat coefficient), then this would indicate that EMD increases 2 ms more per contraction than LFat (i.e., the linear effect of ContrNum on EMD has a steeper slope for the HFat protocol).

III. Results

Descriptive statistics of the variables of interest (previously described in Section II-E) are provided in Table I. The effect of contraction number and protocol on $\mathrm{Torque}_{\mathrm{peak}}$, $\mathrm{EMD}_{\mathrm{thres,contr}}$, and $\mathrm{EMD}_{\mathrm{thres,relax}}$ (i.e., the measurements made during the short bouts of stimulation) is depicted in Fig. 7. Similarly, Fig. 8 depicts the effect of contraction number and protocol on $\mathrm{Torque}_{\mathrm{avg}}$ and $\mathrm{EMD}_{\mathrm{x-corr}}$ (i.e., the measurements made during the fatiguing contractions), and Fig. 9 depicts the effect of contraction number and protocol on the control effectiveness and PW_0. Regression results on $\mathrm{EMD}_{\mathrm{thres,contr}}$, $\mathrm{EMD}_{\mathrm{x-corr}}$, the control effectiveness, and PW_0 are provided in Tables II, III, IV, and V, respectively. Although data was collected in only five individuals, the study design allowed for 400-2200 samples of each variable of interest (Table I), and normality of the residual errors were confirmed visually with normal probability plots. Statistical significance of the fitted coefficients is noted by *, **, and *** for P-Value≤0.05, 0.01, and 0.001, respectively, with ns used to indicate coefficients that were not significant (P-Value > 0.05).

A. Delay

1) $EMD_{\mathrm{thres,contr}}$: Protocol, ContrNum, and Pre/Post Contr were all statistically significant predictors of $\mathrm{EMD}_{\mathrm{thres,contr}}$, indicating that fatigue has a significant effect on EMD. Specifically, $\mathrm{EMD}_{\mathrm{thres,contr}}$ increased with each contraction, was longer for the high-fatiguing protocol, and was longer when the measurement was taken immediately after a fatiguing contraction (compared to immediately before). Furthermore, the interaction term ContrNum×Protocol was found to be statistically significant, with $\mathrm{EMD}_{\mathrm{thres,contr}}$ increasing at a rate of 4.090 ms per contraction for the high-fatiguing protocol (cf., increasing at a rate of 0.776 ms per contraction for LFat; Table II).

2) $EMD_{\mathrm{thres,relax}}$: Although regression analysis was originally conducted on $\mathrm{EMD}_{\mathrm{thres,relax}}$, the results are not presented since poor fitting was obtained (R^2_{adj} = 36%). Moreover, Fig. 7 depicts a sudden and unexpected change in the relaxation delay for HFat from a sharp upward trajectory to a sharp decrease with contraction number after the fifth contraction. The sudden change in direction was determined to be a measurement artifact rather than indicative of the true EMD. Since $\mathrm{EMD}_{\mathrm{thres,relax}}$ represents the time it takes for the torque to fall below 0.3 $\mathrm{N \cdot m}$ (measured from the time

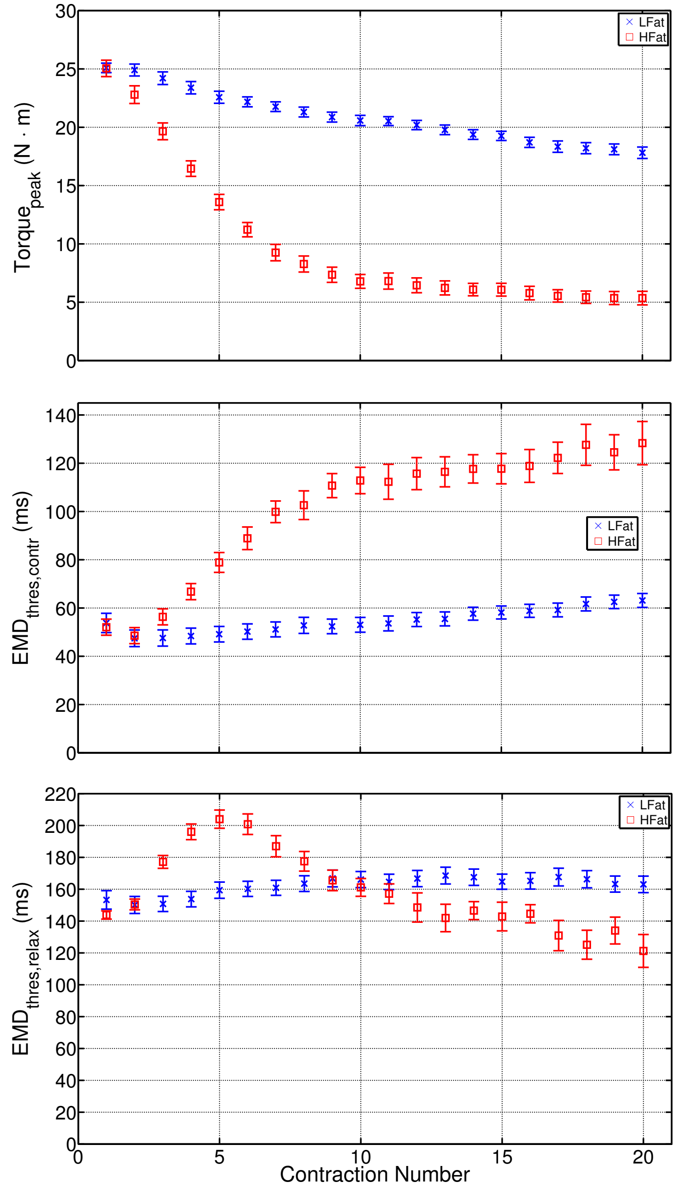

Fig. 7. Torque and delay measurements corresponding to the short bouts of nonfatiguing stimulation (0.25 seconds) that were delivered before and after longer, fatiguing contractions. Values presented are the mean across all subjects (as well as across Pre/Post fatiguing contraction) ± the standard error of the mean. protocol. Note that the sudden change in $\mathrm{EMD}_{\mathrm{thres,relax}}$ for HFat following the fifth contraction is considered to be a measurement artifact and not indicative of the true relaxation delay (Section III-A2).

that the last electrical pulse is delivered), then when there is significant fatigue, the evoked torque (at the moment stimulation terminates) is too close to this threshold for the delay measurement to be meaningful. Therefore, $\mathrm{EMD}_{\mathrm{thres,relax}}$ in Fig. 7 is considered to be invalid after the fifth contraction for the HFat protocol.

3) $EMD_{\mathrm{x-corr}}$: Protocol, ContrNum, and ContrNum×Protocol were all found to be statistically significant predictors of $\mathrm{EMD}_{\mathrm{x-corr}}$. Although ContrNum was negatively correlated to $\mathrm{EMD}_{\mathrm{x-corr}}$ (in contrast to its expected effect), there was a strong effect of Protocol. Specifically, HFat resulted in $\mathrm{EMD}_{\mathrm{x-corr}}$ measurements 39

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TABLE I
DESCRIPTIVE STATISTICS

Variable	Units	N	Mean	SD	Min	Q1	Median	Q3	Max
$\mathrm{EMD}_{\mathrm{thres,contr}}$	ms	800	77.766	36.045	22.004	53.998	67.921	97.025	233.985
$\mathrm{EMD}_{\mathrm{thres,relax}}$	ms	800	159.960	32.144	1.266	143.849	156.983	175.985	253.976
$\mathrm{EMD}_{\mathrm{x-corr}}$	ms	400	139.613	29.457	65.000	116.000	135.000	163.000	204.000
$\mathrm{Torque}_{\mathrm{peak}}$	$\mathrm{N \cdot m}$	800	15.417	7.491	0.482	7.809	17.707	21.358	29.736
$\mathrm{Torque}_{\mathrm{avg}}$	$\mathrm{N \cdot m}$	400	11.322	5.141	2.670	6.362	12.353	15.323	24.314
Control Effectiveness	$\mathrm{N \cdot m \cdot \mu s^{-1}}$	2200	0.241	0.097	0.076	0.165	0.218	0.297	0.606
PW_0	μs	2200	66.525	41.820	-65.799	42.657	60.124	79.044	201.875

TABLE II
REGRESSION ON $\mathrm{EMD}_{\mathrm{thres,contr}}$ (ms)

Term	Coef	SE Coef	P-Value	Sig.
Constant	48.33	2.69	0.000	***
ContrNum	0.776	0.172	0.000	***
Pre/Post Contr				
Post	4.08	1.40	0.004	**
Protocol				
HFat	11.58	2.92	0.000	***
Subject				
S2	-0.94	2.22	0.673	ns
S3	2.26	2.22	0.309	ns
S4	-18.42	2.22	0.000	***
S5	-14.77	2.22	0.000	***
Side				
Right	4.87	1.40	0.001	***
ContrNum×Protocol				
HFat	3.314	2.444	0.000	***

S = 19.8692, R^2_{adj} = 69.61%

TABLE III
REGRESSION ON $\mathrm{EMD}_{\mathrm{x-corr}}$ (ms)

Term	Coef	SE Coef	P-Value	Sig.
Constant	110.93	2.79	0.000	***
ContrNum	-0.452	0.186	0.015	*
Protocol				
HFat	39.42	3.14	0.000	***
Subject				
S2	7.26	2.39	0.003	**
S3	9.84	2.39	0.000	***
S4	1.44	2.39	0.548	ns
S5	-4.60	2.39	0.055	ns
Side				
Right	13.89	1.51	0.000	***
ContrNum×Protocol				
HFat	0.760	0.262	0.004	**

S = 15.1301, R^2_{adj} = 73.62%

TABLE IV
REGRESSION ON CONTROL EFFECTIVENESS ($\mathrm{N \cdot m \cdot \mu s^{-1}}$)

Term	Coef	SE Coef	P-Value	Sig.
Constant	0.22725	0.00472	0.000	***
ContrNum	-0.00216	0.00034	0.000	***
SubContrNum	-0.00263	0.00051	0.000	***
Protocol				
HFat	-0.00089	0.00488	0.856	ns
Subject				
S2	0.20990	0.00320	0.000	***
S3	0.01099	0.00320	0.001	***
S4	0.01758	0.00320	0.000	***
S5	0.07859	0.00320	0.000	***
Side				
Right	0.01407	0.00202	0.000	***
ContrNum×Protocol				
HFat	-0.00306	0.00039	0.000	***

S = 0.0474081, R^2_{adj} = 76.19%

TABLE V
REGRESSION ON PW_0 (μs)

Term	Coef	SE Coef	P-Value	Sig.
Constant	97.54	2.01	0.000	***
ContrNum	0.520	0.143	0.000	***
SubContrNum	1.437	0.215	0.000	***
Protocol				
HFat	-2.53	2.08	0.223	ns
Subject				
S2	-71.69	1.36	0.000	***
S3	-71.52	1.36	0.000	***
S4	-86.79	1.36	0.000	***
S5	-85.50	1.36	0.000	***
Side				
Right	18.478	0.860	0.000	***
ContrNum×Protocol				
HFat	1.799	0.167	0.000	***

S = 20.1756, R^2_{adj} = 76.73%

ms longer on average than LFat (Table III). Indeed, a visual comparison of Figs. 7 and 8 shows that while $\mathrm{EMD}_{\mathrm{thres,contr}}$ was similar across protocols for the first two contractions, $\mathrm{EMD}_{\mathrm{x-corr}}$ was different between protocols across all contractions.

B. Control Effectiveness

ContrNum and SubContrNum were found to be statistically significant predictors of the control effectiveness. Specifically, the control effectiveness decreased as ContrNum and SubContrNum increased. Although Protocol was not found to be statistically significant, the cross term ContrNum×Protocol was statistically significant, with the control effectiveness decreasing at a rate of 0.0052 $\mathrm{N \cdot m \cdot \mu s^{-1}}$ per contraction for HFat (cf., decreasing at a rate of 0.0022 $\mathrm{N \cdot m \cdot \mu s^{-1}}$ per contraction for LFat; Table IV).

C. PW_0

ContrNum, SubContrNum, and ContrNum×Protocol were found to be statistically significant predictors of PW_0 while Protocol was not. Specifically, PW_0 increased with ContrNum as well as SubContrNum, and PW_0 increased at a higher rate for HFat than LFat (2.319 μs per contraction versus 0.520 μs per contraction; Table V), indicating that the minimum

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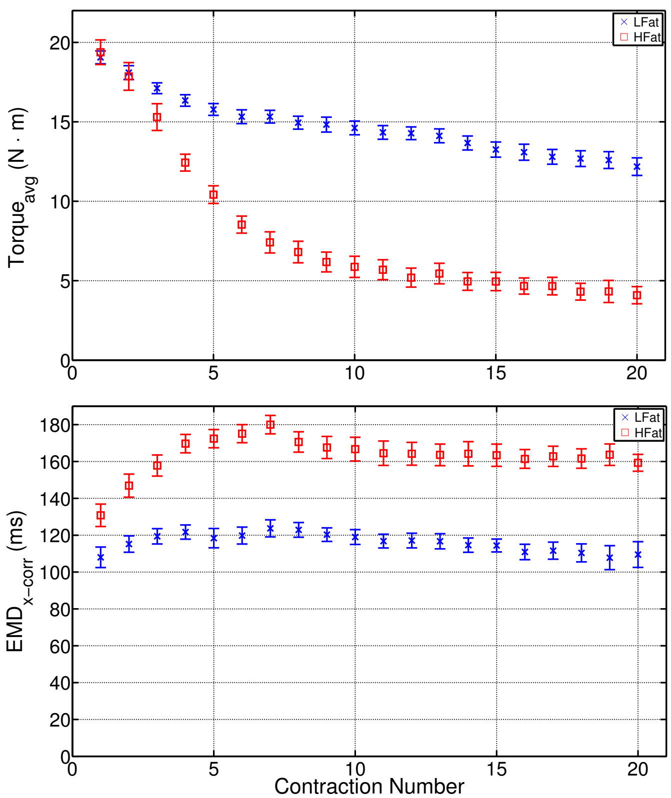

Fig. 8. Torque and delay measurements corresponding to the longer, fatiguing contractions. Values presented are the mean across all subjects ± the standard error of the mean.

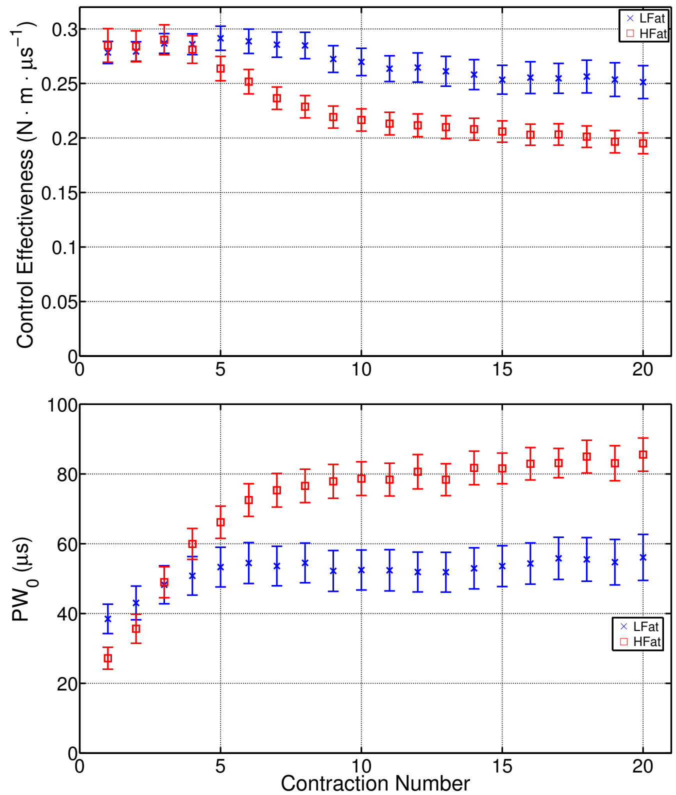

Fig. 9. Control effectiveness and minimum pulse width to evoke nonzero torque (PW_0) corresponding to the longer, fatiguing contractions. Values presented are the mean across all subjects (and across all sub-contractions within a fatiguing contraction) ± the standard error of the mean.

pulse width to evoke nonzero torque increased with fatigue. It should be noted that some calculations of PW_0 were negative (70 instances out of the 2200 measurements). While the true minimum pulse width to evoke nonzero torque cannot be negative, PW_0 and the control effectiveness can still be used to characterize the time-varying nature of the recruitment curve. Therefore, these data were not removed from regression analysis.

IV. Discussion

EMD has been often studied in previous literature with a wide range of reported values. Specifically, contraction EMD has been reported to range from 4.84 ± 0.31 ms in [37] to 125.9 ± 30.7 ms in [38], and relaxation EMD has been reported to be as long as 300 ± 59 ms in [39]. This discrepancy in values may be due in part to the method used to evoke contractions. Specifically, EMD has been examined during *i) volitional contractions* [34]–[36], [38]–[53], *ii) NMES-evoked contractions* [11], [37], [43], [52]–[60], *iii) magnetically-evoked contractions* [44], and *iv) tendon reflex-evoked contractions* [45], [52], [53], [61]–[63]. While EMD is typically studied with only one type of contraction, Zhou *et al.* compared EMD in volitional, reflex-evoked, and NMES-evoked contractions [52]. The authors found that the EMD of involuntary contractions (i.e., tendon reflex and NMES) was shorter than that of volitional contractions (17.2, 22.1, and 38.7 ms for NMES, reflex, and volitional, respectively). The wide range of reported EMD values may also be due in part to different measuring techniques. Specifically, previous studies have utilized *i) electromyography* [34]–[55], [57], [59]–[63], *ii) mechanomyography* [35], [54], [55], [59], *iii) force/torque recordings* [34]–[37], [39]–[63], *iv) ultrasound* [56], [58], and *v) joint angle recordings* [11], [38], [48], in combination with *i) thresholding* methods [11], [34]–[36], [38], [39], [41]–[44], [48]–[51], [53]–[55], [57]–[63], *ii) cross-correlation* methods [40], [46], [47], and *iii) manual determination* [37], [56] to calculate the EMD. In the present study, isometric knee-joint torque was recorded during repeated fatiguing NMES-evoked contractions, and the mean EMD across all contractions was found to be 77.8 ± 36.0 ms, 139.6 ± 29.5 ms, and 160.0 ± 32.1 ms for $\mathrm{EMD}_{\mathrm{thres,contr}}$, $\mathrm{EMD}_{\mathrm{x-corr}}$, and $\mathrm{EMD}_{\mathrm{thres,relax}}$, respectively (Table I).

Previous research has examined the effect of contraction intensity [35] and stimulation intensity [52], [56], showing that EMD is shorter for stronger intensities. EMD has also been shown to be dependent on muscle fiber velocity: Cavanagh *et al.* found EMD to be 49.4, 53.0 and 55.4 ms for eccentric, isometric, and concentric contractions, respectively [41]. EMD varies with tendon slack: Muraoka *et al.* examined EMD at multiple joint angles with percutaneous NMES and found that EMD depends on the joint angle until the slack is fully taken up, and then EMD is constant for further changes in joint angle [57]. EMD has been shown to increase after passive stretching [37], [55]. EMD differs between populations: Granata *et al.*

examined EMD in individuals with spastic cerebral palsy and found that EMD in patients with spasticity was significantly shorter compared to normally developing individuals (40.5 ms versus 54.7 ms) [61]. Kaneko *et al.* examined EMD in individuals following ACL reconstructions by delivering supramaximal electrical stimulation to the femoral nerve, and the involved leg had prolonged EMD [43] compared to the uninvolved leg and the control group. EMD can also be dependent on sex: Winter *et al.* found EMD was longer in women (44.9 ms versus 39.6 ms) [48].

One objective of the present study was to examine the time-varying nature of NMES-evoked EMD following NMES-induced fatigue since it has direct implications on the design of feedback controllers for FES. While previous studies have examined the effect of fatigue on EMD (e.g., EMD increased from 39.6 ms to 51.9 ms in [49] and from 96.7 ms to 125.9 ms in [38]), studies have primarily focused on measuring the volitional EMD following a volitional fatiguing task [35], [36], [38], [42], [44], [45], [49]–[51], [53]. The effect of fatigue on EMD has also been examined by measuring EMD during NMES-evoked [53], [60], tendon reflex-evoked [45], [53], [62], [63], and magnetically-evoked [44] contractions; however, these studies also utilized a volitional fatiguing task. Meanwhile, NMES is well known to rapidly induce fatigue compared to volitional contractions.

Two related studies examined the effect of NMES-induced fatigue on NMES EMD [54], [59]. Rampichini *et al.* found contraction EMD to increase after two minutes of NMES delivered to the gastrocnemius medialis [59]. Specifically, EMD increased from 26.85 ms to 31.74 ms while peak force decreased from 687 N to 639 N. The data in [59] was then reanalyzed, and relaxation EMD was found to increase from 20.7 ms to 29.0 ms [54]. In the present study, where stimulation was delivered to the quadriceps femoris muscle group over the course of five minutes, the HFat protocol caused EMD to increase significantly. Specifically, $\text{EMD}_{\text{thres,contr}}$ increased from 52.06 ms in the first contraction to 128.34 ms in the final contraction while $\text{Torque}_{\text{peak}}$ decreased from 25.05 $\text{N}\cdot\text{m}$ to 5.35 $\text{N}\cdot\text{m}$. Meanwhile, $\text{EMD}_{\text{thres,relax}}$ increased from 148.81 ms in the first contraction to 203.98 ms in the fifth contraction, after which the measurement was determined to be invalid (Section III-A2).

The results of the present study highlight that EMD is time-varying. Specifically, EMD increases with fatigue during repeated NMES-evoked contractions. Moreover, the increase in EMD is not only statistically significant but also of significant magnitude during prolonged NMES (e.g., $\text{EMD}_{\text{thres,contr}}$ increased by a factor of 2.47 for HFat). This is an important finding since EMD has been often assumed to be constant when developing NMES/FES controllers [11], [13], [17]. Sharma *et al.* developed a controller to compensate for EMD where the EMD is assumed to be constant [11]. Although the controller yielded limb tracking, the experiments lasted only 20 seconds since the authors' main goal was to quantify the added value of the delay compensation term in the controller. Therefore, the trials may not have been long enough for EMD to increase significantly. Similarly, the controller in [13] was tested for 30 seconds at a time, and experimental results were not provided for the controller in [17]. Therefore, future efforts could extend the work in [11], [13], [17] by considering EMD to be time-varying rather than constant when developing controllers. Similarly, the developed controllers could be tested for extended durations to verify robustness to time-varying EMD since prolonged durations are desired for rehabilitative treatments and assistive devices.

Recently, Merad *et al.* developed a controller that allowed for isometric torque tracking despite a time-varying EMD [64]; however, the control design required EMD to be known. By focusing on isometric torque tracking (rather than limb trajectory tracking as in [11], [13], [17]), it becomes more feasible to estimate EMD in real time since the torque signal is readily available. However, given the wide range of reported EMD values in literature, the difficulty of determining EMD in real-time during limb trajectory tracking, and estimation inaccuracy, future efforts on FES control could also consider EMD to be uncertain. Along these lines, in the present study there were differences between the thresholding and cross-correlation measures of EMD. Specifically, $\text{EMD}_{\text{x}-\text{corr}}$ was greater than $\text{EMD}_{\text{thres,contr}}$ in general. One plausible explanation for this discrepancy is that the $\text{EMD}_{\text{x}-\text{corr}}$ measurement took place during a fatiguing contraction. Meanwhile, there were periods of rest before the short bouts of nonfatiguing stimulation used to measure $\text{EMD}_{\text{thres,contr}}$ (Fig. 4). This may also explain why there were differences in the initial $\text{EMD}_{\text{x}-\text{corr}}$ between the two fatiguing protocols (Fig. 8) since the cross-correlation method represents an average EMD for the entire fatiguing contraction (and EMD is expected to increase with time during a fatiguing contraction). Meanwhile, $\text{EMD}_{\text{thres,contr}}$ was similar for the first two contractions for both protocols (Fig. 7). A second plausible explanation for the discrepancy between measurement methods is that the cross-correlation method requires the pulse width signal to be composed of upward and downward segments to find the delay. Therefore, $\text{EMD}_{\text{x}-\text{corr}}$ is expected to lie somewhere between the contraction and relaxation EMD measurements.

Another objective of the present study was to examine the time-varying nature of the muscle control effectiveness following NMES-induced fatigue. The results of the present study indicate that the control effectiveness decreases over time and is dependent on the level of fatigue. While it was expected that the control effectiveness would decrease, the results of the present study emphasize that the control effectiveness should be modeled as a time-varying, nonlinear function rather than a static, nonlinear function. Along these lines, the results of the present study indicate that the minimum pulse width to evoke nonzero torque, PW_0, increases with fatigue. Although this result is not surprising, it highlights some deficiencies in a commonly used model for muscle control.

Specifically, the evoked knee-joint torque in response to NMES is often modeled as[8]

$$T_m(t) = \Omega\big(q(t), \dot{q}(t), t\big)u\left(t\right), \tag{1}$$

[8]The effect of EMD is temporarily ignored for clarity of exposition. Previous FES control studies have also modeled the control effectiveness as $\Omega\left(q, t\right)$ and $\Omega\left(q, \dot{q}\right)$; however, the most general version that captures muscle force-length, force-velocity, and fatigue properties is $\Omega\left(q, \dot{q}, t\right)$.

where T_m is the active muscle torque, u is the applied electrical stimulation input,[9] and Ω (i.e., the control effectiveness) is an unknown, strictly positive, nonlinear function of the knee-joint angle (q), knee-joint velocity ($\dot{q}$), and time (t). The structure of (1) is able to model muscle force-length and force-velocity properties as well as fatigue; however, it implicitly states that torque will be evoked for any nonzero stimulation input. Therefore, a deficiency of (1) is that it does not model the time-varying minimum stimulation input needed to cause a muscle contraction (i.e., PW_0 in the present study). If this minimum needed amount of stimulation were constant, then it could easily be measured in a pretrial test and subsequently added to the stimulation input calculated by the controller. In other words, if the minimum stimulation to evoke muscle force were constant, then a change of variables could be used so that the implicit assumption of nonzero torque for nonzero stimulation in (1) is valid (cf., [11, Section IV-B]). However, the results of the present study have shown that the minimum required stimulation increases over time. Therefore, unless this value can be estimated in real-time, it is unclear how the implicit assumption in (1) can be satisfied as the muscle fatigues. Therefore, future work could focus on developing new approaches that theoretically guarantee limb tracking despite an unknown, time-varying minimum required stimulation.

A related deficiency of the model in (1) is that, although it can be used to model the nonlinear muscle force-length and force-velocity properties, it linearly approximates the nonlinear muscle recruitment curve. Specifically, if the knee-joint was fixed (i.e., q is a constant and $\dot{q} = 0$) and if muscle fatigue was temporarily ignored (removing the effect of time), then it is clear that Ω would be constant and torque would linearly increase with the stimulation input. Meanwhile, the muscle recruitment curve is known to have a sigmoidal shape [19, Fig. 1]. Therefore, to model the nonlinear recruitment curve, (1) could be modified to

$$T_m(t) = \Omega\big(q(t), \dot{q}(t), t, u\,(t)\big), \tag{2}$$

where $\Omega\,(q, \dot{q}, t, u) \geq 0$ (i.e., positive torque) when stimulation is delivered to the agonist muscle group (i.e., $u > 0$) and $\Omega\,(q, \dot{q}, t, u) \leq 0$ when stimulation is delivered to the antagonist muscle group (i.e., $u < 0$). Furthermore, $\Omega\,(q, \dot{q}, t, u)$ is a non-decreasing function of u (i.e., greater absolute value of the evoked torque at higher stimulation intensities), and $\Omega\,(q, \dot{q}, t, u) = 0$ when the stimulated muscle is already contracting at its maximum shortening velocity or when the stimulation intensity is within the deadzone of the stimulated muscle. Therefore, (2) can be used to model the nonlinear force-length and force-velocity properties as well as the time-varying, nonlinear recruitment curve (although it still neglects EMD).

Another limitation of the model in (1) is that it does not account for EMD. This model has recently been modified in [11], [13], [17] to account for delay as[10]

$$T_m(t) = \Omega\big(q(t), \dot{q}(t), t\big)u\big(t - \tau_c\big), \tag{3}$$

where τ_c is a constant EMD. Efforts have been made to develop controllers for a constant, known delay in [11], [13], [17]; however, the results of the present study have shown that EMD is time-varying and increases with fatigue. Therefore, future efforts could develop controllers for the following modified version of (3)

$$T_m(t) = \Omega\big(q(t), \dot{q}(t), t\big)u\big(t - \tau(t)\big), \tag{4}$$

where τ is an uncertain, time-varying delay. Finally, to account for both a time-varying delay and a time-varying nonlinear recruitment curve, (4) could be modified to

$$T_m(t) = \Omega\Big(q(t), \dot{q}(t), t, u\big(t - \tau(t)\big)\Big).$$

V. Conclusion

The results of the present study have highlighted areas of FES control to be improved upon in future work. Specifically, EMD was shown to be time-varying and increase significantly with NMES-induced fatigue, motivating future efforts to develop controllers that guarantee tracking despite a time-varying, uncertain EMD. Furthermore, the control effectiveness was shown to be time-varying and decrease significantly with fatigue, motivating the development of controllers that are robust to the fatigue-induced decline of the control effectiveness. Finally, the minimum required stimulation to evoke muscle force (PW_0) was shown to be time-varying and increase significantly with fatigue, motivating future efforts to either develop methods that estimate PW_0 in real-time or to develop controllers that consider the muscle recruitment curve to be nonlinear, uncertain, and time-varying. Future efforts leveraging the results of the present study may lead to improved NMES/FES rehabilitative treatments and assistive devices.

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[9] u is referred to simply as the stimulation input since it can represent either the pulse amplitude or the pulse width, with corresponding changes to the scale of Ω. It is the user's choice to decide which stimulation parameter to fix and which parameter to vary during feedback control.

[10] Technically, the control effectiveness was previously modeled as $\Omega\,(q, \dot{q})$ rather than $\Omega\,(q, \dot{q}, t)$; however, the explicit dependence of Ω on time was added in (3) to model the effect of fatigue on the control effectiveness, as evidenced in the present study.

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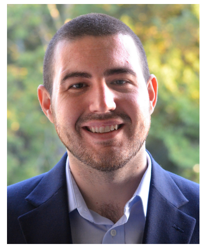

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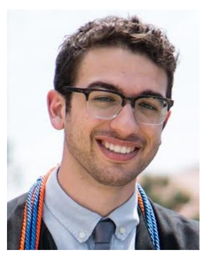

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