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A Mathematical Model That Incorporates The Force-Intensity Relationship Of Human Skeletal Muscle

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Abstract

We have previously reported the development of a force-model system that accurately predicts the force-frequency relation of human skeletal muscle. The ability to also predict the effects of stimulation intensity on muscle force can enable a more precise prediction of muscle forces and allow a better control of FES-elicited movements. The model presented here incorporates the force-intensity relationship to predict the effects of stimulation intensity and frequency on skeletal muscle forces. The current model was developed and tested on quadriceps femoris muscles (N=7) of healthy subjects. Our model successfully predicted the forces produced when the muscle was activated with stimulation trains of different pulse durations (100 ~ 600 μs) and frequencies (12.5Hz ~ 80 Hz). The successful addition of an intensity component to our model system further supports its potential use for the design of subject-specific stimulation patterns for FES applications.

1. INTRODUCTION

1.1. Mathematical Models and FES

Mathematical modeling is a powerful tool for accelerating the development of better FES systems. Models can help predict the best stimulation strategy (i.e., frequency, intensity and pattern) to obtain the targeted forces during FES to help minimize fatigue. However, the stimulation strategy that optimizes skeletal muscle performance may vary from person to person[2] and, even for the same individual, varies with the physiological condition of the muscle, such as level of fatigue or muscle length[3]. Numerous measurements would therefore be needed experimentally to identify the best stimulation strategy for each patient and each task. Mathematical models that predict force responses to stimulation trains of different frequencies and intensities can speed up this process and decrease the number of measurements required to determine the best pattern for each subject. In addition, as an integral part of optimal control, mathematical models can help design subject-specific and task-specific stimulation strategies[5]

1.2. Isometric Force Model

A mathematical model system has been developed in our laboratory to predict muscle force of human quadriceps femoris in response to stimulation trains of different frequencies and patterns[1]. In addition, our model predicts the force responses at different muscle lengths[4].

The model is composed of two simple differential equations; the first equation describes the activation dynamics at each stimulation pulse and the second describes the force activation driven by the calcium-troponin complex produced by the first equation[1] (see Table 1 for the definitions of symbols used in equations below).

a. Calcium Dynamics

$$\frac{dC_N}{dt} = \frac{1}{\tau_c}\sum_{i=1}^{n} R_i \exp(-\frac{t-t_i}{\tau_c}) - \frac{C_N}{\tau_c}$$

$$R_i = 1 + (R_0 - 1)exp[-(t_i - t_{i-1})/\tau_c]$$

b. **Force Dynamics**

$$\frac{dF}{dt} = A\frac{C_N}{K_m + C_N} - \frac{F}{\tau_1 + \tau_2\frac{C_N}{K_m + C_N}}$$

1.3. Addition of the Intensity Component

Our modeling work has thus far focused only on the temporal aspect of muscle stimulation. This study extends our previously developed force model system by adding the intensity component to enable prediction of the effects of changing the stimulation frequency and intensity (by changing pulse width of the stimulation pulses) on muscle force.

To account for intensity modulation, parameter A, the scaling factor, was modulated as a function of pulse duration:

$$A = a'[1-\exp(-(pd - pd_0)/pd_t)]$$

2. METHODS

2.1. Subjects

Quadriceps femoris muscles of 7 healthy subjects were tested at 65° knee flexion angle. Subjects signed informed consent forms approved by the Human Subject Review Board of the University of Delaware.

2.2. Apparatus

An electromechanical dynamometer (KINCOM, Chattanooga Corp., Chattanooga, TN) was used to measure knee joint torques. A Grass electrical stimulator (Grass Instrument Company, Quincy, MA), controlled by custom written LabVIEW software, was used to deliver electrical stimulation to the muscle.

2.3. Testing Procedure

The subject was informed about the testing procedure and acquainted with the apparatus at the beginning of the testing session. Next, the subject's maximum voluntary isometric contraction (MVIC) was determined. Then, the pulse amplitude was set to elicit a force equal to 80% of the subject's MVIC, using a 1-sec 100-Hz train with a pulse duration of 600µs. After the stimulation amplitude was set, the muscle was potentiated with a series of eleven 14-Hz trains (resting time 5-s, train duration 770-ms, pulse duration 600-µs). Following potentiation, a series of 48 trains (each 1-sec in duration) were delivered at the rate of 1 train every 10 second. These 48 trains included 4 pairs of 50-Hz constant-frequency trains (CFTs) (pulses equally spaced) and variable-frequency trains (VFTs) that consisted of two closely spaced pulses (a doublet) inserted in the beginning of a 12.5Hz CFT. These 8 trains were delivered at pulse durations of 100, 200, 300, and 600µs and used to determine the parameter values of the model. The other 40 trains, containing 5 different frequencies (12.5, 20, 33, 50, 80 Hz), 2 patterns (CFTs and Doublet Frequency Trains (DFTs) that contain doublets separated by longer constant intervals) at 4 different pulse durations (100, 150, 250, 500µs) were used to test the accuracy of the model's predictions.

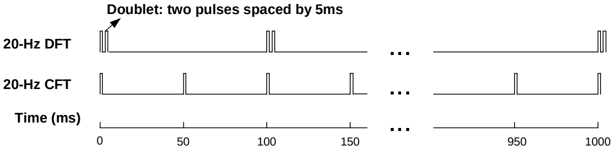

Fig.1 Examples of stimulation train patterns used for testing. The figure shows 20-Hz CFTs and DFTs.

3. RESULTS

Subjectively, the model predicted the shapes of the force profiles very well for stimulation trains of different frequencies at the 4 different pulse durations tested (fig 2)

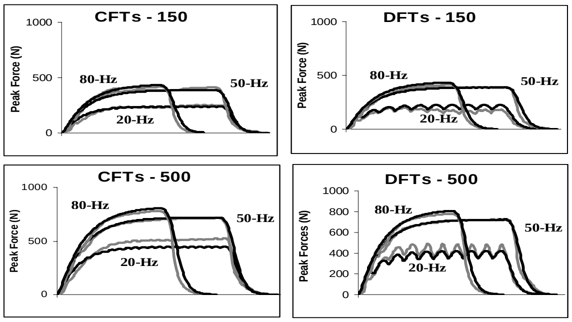

Fig 2- Predicted (black lines) and experimental (gray lines) force profiles for CFTs (left column) and DFTs (right column), at 150-µs and 500-µs pulse durations. Forces in response to 3 stimulation frequencies are shown for each pattern and pulse duration: 20-Hz, 50-Hz, and 80-Hz.

The r^2 values and slopes of the trendlines for the correlation between the modeled and experimental force-time integrals (FTIs) and peak forces (PKs) were close to 1 (Fig. 3).

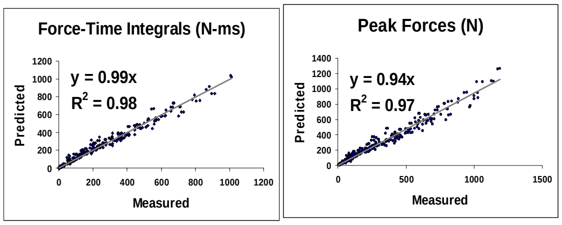

Fig.3: Predicted vs. measured force-time integrals and peak forces for all testing trains for all subjects (N=7).

The percent errors between the predicted and measured forces were within ±15% range for most of the stimulation trains (Fig. 4), with the exception of the lowest frequency train, i.e., the

12.5-Hz train, which showed percent errors slightly greater than ±15%.

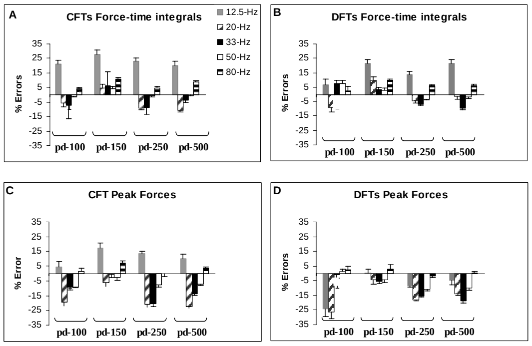

Fig.4 Percentage difference in force-time integral (A, B) and peak force (C, D) between the experimental and predicted forces (N=8).

Finally, the ANOVAs used to compare the predicted and measured PK forces produced at 60Hz for each of the four intensities showed no significant difference (Fig.5).

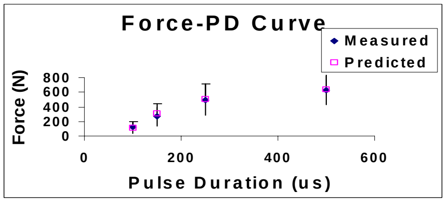

Fig. 5 Predicted and measured peak force versus intensity (pulse duration) relationships plotted at 60-Hz (N=7).

4. DISCUSSION AND CONCLUSIONS

A mathematical model that incorporated the force-intensity relationship for human quadriceps femoris muscles was developed and tested. The model successfully predicted isometric forces in response to stimulation trains with two different pulse patterns (CFT and DFT), a wide range of frequencies (12.5Hz ~ 80Hz) and stimulation intensities (100us~500us).

Similar to the frequency-modulation and recruitment-modulation used by the nervous system to control muscle force output, the current model accounts for the effects of both stimulation frequency and pulse duration on muscle force output. The model has the ability to predict peak forces and force-time integrals in response to stimulation trains with a wide range of frequencies, pulse durations, and patterns; thereby providing a multi-dimensional prediction of muscle responses.

By predicting the forces in response to an arbitrary pattern of stimulation and stimulation intensity, we envision that the present model may help to identify the optimal stimulation scheme for activation of skeletal muscle, and can be incorporated into a feedback control system during FES.

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Acknowledgements

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Table 1: Definition of symbols used in equations

Symbol	Unit	Definition
C_N	---	normalized amount of Ca^{2+}-troponin complex
R_0	---	mathematical term characterizing the magnitude of enhancement in C_N from the following stimuli
τ_c	ms	time constant controlling the rise and decay of C_N
n	---	total number of stimulus in the train before time t
t_i	ms	time of the ith stimulation
F	N	instantaneous force
A	N/ms	scaling factor for the force and the shortening velocity of the muscle
K_m	---	sensitivity of strongly bound cross-bridges to C_N
τ_1	ms	time constant of force decline at the absence of strongly bound cross-bridges
τ_2	ms	time constant of force decline due to the extra friction between actin and myosin resulting from the presence of cross-bridges.
a'	N/ms	scaling factor for parameter A as a function of pulse duration
pd	µs	pulse duration
pd_0	µs	offset for pulse duration
pd_t	µs	time constant controlling parameter A as a function of pulse duration