Computational Models of Populations of Motor Neurons

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1 OBJECTIVES

In this paper, we will provide examples of how computational models of motor neuron and muscle activity can support basic and applied research on human movement. Both examples focus on pathological tremor. Tremor is a rhythmic, involuntary oscillation of a limb and it is the most prevalent movement disorder, symptomatic to e.g. Parkinson's Disease (Wenning et al., 2005). Tremor implies a serious worsening of the quality of life, also because the effect of the current treatments is variable(Rascol et al., 2000).

First, we show how models can be applied in the development of a rehabilitation device for suppressing pathological tremor (Objective 1). The proposed tremor rehabilitation system relied on modulation of spinal neuron excitability of the tremorogenic motor neurons using homonymous excitation and reciprocal inhibition evoked by electrical stimulation of peripheral type Ia nerves. Successful implementation of this strategy implied robust and precise on-line analysis of tremor (Objective 1A) and stimulation parameter selection (Objective 1B). Here, the Iterated Hilbert Transform (IHT) applied to the surface EMG signals were selected for tremor analysis (Dideriksen et al., 2011).

Next, we demonstrate how models can enhance the understanding of the underlying physiological mechanisms of tremor (Objective 2), especially aspects that cannotbe easily assessed experimentally. Specifically, here we will address the contribution of afferent feedback in tremor, which has been debated in the literature (Rack and Ross 1986).

2 METHODS

The neuromechanical models applied to address the two objectives consisted of a number of sub-models and shared the same basic structure; however, the level of model complexity required for addressing each of the objectives determined how the various sub-models were implemented.

2.1 Neuromechanical Models

The model was designed to reflect the characteristics of an antagonist muscle pair acting on one limb in one degree of freedom and consisted of a number of sub-models interacting via one or more variables.

First, the activity of the motor neuron population (spike trains) was determined based on the synaptic input it received. Each motor neuron innervated a set of muscle fibers (the motor unit). Each motor unit was assigned a set of parameters describing its contractile properties. Along with these properties, the discharge rate determined the motor unit force. The force of the muscles (the sum of the force generated by all motor units) evoked the movement of the limb. Proprioceptive activity was determined by limb dynamics (muscle spindle; type Ia) and muscle forces (Golgi tendon organs; type Ib) and provided afferent feedback to the motor neurons. Tremor was simulated by imposing a sine wave to the motor neuron input.

For Objective 1A, a model of the motor unit population and the force it generates was adopted (Fuglevand et al., 1993), while the afferent feedback was simulated as compound signals (Prochazka and Gorassini, 1998). A model of the surface motor unit action potentials(Farina et al., 2004) was used to simulate the surfaceEMG signal (based on the motor unit spike trains), that was used for tremor estimation. For Objective 1B and 2 a more detailed description of the single neuron behaviour (Cisi and Kohn, 2008), a more advanced mechanical model (Oguztoreli and Stein, 1982), as well as models allowing the afferent feedback to be described as spike trains (Mileusnic and Loeb, 2006) were applied. In this way, simulation of axon action potentials generated by surface stimulation was made possible.

2.1.1 Model Validation

The validation for the model used for Objective 1A relied on its ability to generate patterns of motor unit spike trains, as observed in tremor. The key feature for Objectives 1B and 2 were the capability of the model to reflect the true spinal connectivity. For this reason, experimentally used protocols for H-reflex recruitment curves and estimation of reciprocal inhibition strength were simulated.

2.1.2 Simulations

For Objective 1Athe surface EMG signal was simulated in a variety of conditions, including different contraction levels (0-20% MVC), tremor frequencies (4-12 Hz), and tremor intensities. Tremor identification was assessed by comparison with the imposed neural oscillations. For Objective 1B stimulation amplitude, frequency, and timing were varied. Tremor suppression was evaluated by the integral power of the limb movement spectrum with and without stimulation. For Objective 2, simulations were carried out with and without afferent feedback and the power spectra of the neural drive in each situation were compared.

3 RESULTS

The motor unit inter-spike interval histograms in simulated tremor were in agreement to those experimentally observed previously (Christakos et al., 2009) and the simulated H-reflex recruitment curves and the strength of the reciprocal inhibition were comparable to previous experimental results (Wargon et al., 2006) (not shown).

3.1 Tremor Identification

Figure 1 shows an example of the simulated surface EMG signal during an 8-Hz tremor. Furthermore, the oscillations imposed on the motor neuron population (Figure 1B, black line) are shown, superimposed with the estimation of the tremorogenic input signal obtained from the surface EMG using the IHT algorithm. The two signals were similar, except the delay, caused by the delays of the nervous system. Across all simulated conditions, the estimation of the tremor amplitude was correlated with the imposed amplitude (r^2=0.52), and the RMSE in estimation of frequency was 2.6 Hz, mostly due to errors at high frequencies in conditions with low tremor. This efficiency was maintained in windows down to 500 ms, showing the capability of the algorithm to drive tremor suppression on-line (Dideriksen et al., 2011).

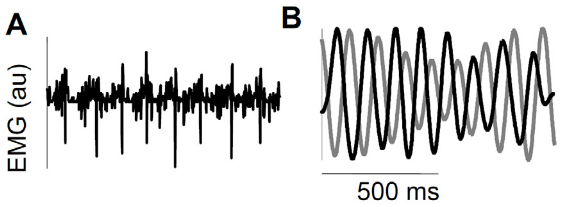

Figure 1: Simulated surface EMG (A) and imposed and estimated tremor (black, grey respectively; B).

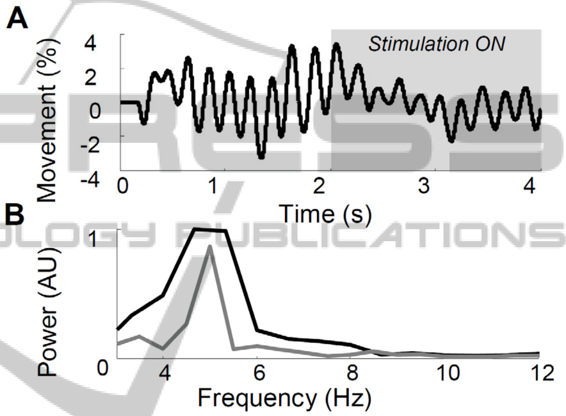

Figure 2: Simulated tremor with and without afferent stimulation (grey box; A). Power spectrum (B) indicates tremor suppression (grey line).

3.2 Tremor Suppression

Figure 2 depictsthe simulated tremor suppression approach applied in a 2-s window during 5-Hz tremor. The tremor amplitude was decreased by 63%, as also shown in the power spectrum represented in the lower panel. The optimal suppression was obtained at 60 Hz stimulation at an intensity recruiting 22% of all Ia axons and no motor neuron axons. Stimulation efficiency was highly sensitive to the timing of the stimulation bursts with respect to the imposed oscillations. Optimally a 15-ms delay should be used, while deviations of more than 25 ms involved tremor amplification, implying the need for accurate tremor estimation algorithms.

3.3 Afferent Contribution to Tremor

Figure 3 shows the power spectra of the motor neuron population output in simulations performed with and without afferent feedback. At 6 Hz, the afferent feedback enhanced the oscillations by up to

80%, while afferent feedback reduced tremor at 2 Hz by 40%. This difference can be explained by the neural delays. At low frequencies, the afferent feedback arrives at the motor neuron almost exactly out of phase with the imposed oscillations, and vice versa at higher frequencies, due to faster contractions. This observation may explain the common occurrence of tremor in the 4-6 Hz range.

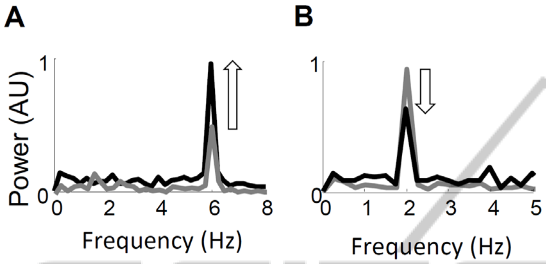

Figure 3: Power spectra of neural drive in simulations with (grey) and without (black) afferent feedback with 6 Hz (A) and 2 Hz (B) imposed.

4 DISCUSSION

Two examples of applications of neuromechanical models were given, each highlighting different advantages of using simulations to support experimental tests. The first example demonstrated how models can be applied to test the robustness of rehabilitation techniques when experimental data is sparse and when full parameter sensitivity analysis in patients is not feasible. Last, the sensitivity of internal physiological parameters on the motor output was assessed, for neuromuscular properties that cannot be measured experimentally.

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