INTRODUCTION
Tremor, which is one of the most common movement disorders, makes activities of daily living difficult or impossible [1]. Although tremor is widespread, current treatment options are unsatisfactory; a recent survey of persons with Essential Tremor (ET) found that one of the things most lacking in their treatment was an effective, alternative treatment option—something other than medication or neurosurgery [2]. Peripheral tremor suppression devices could provide such an option. However, the development of effective peripheral tremor suppression devices faces an obstacle: we do not currently know where to intervene (which muscles or degrees of freedom (DOF)) because we do not know where in the upper limb the tremor originates mechanically (which muscles), how it propagates (i.e. spreads) throughout the upper limb, and where it manifests the most (which DOF). To investigate these questions, we need a model capable of simulating how tremor propagates from tremorogenic muscle activity to tremulous joint displacement. Since both inputs (muscle activity) and outputs (joint displacement) can be measured experimentally, such a model could be subjected to experimental validation. Ultimately, such a model could enable one to determine which muscles to target (e.g. through injection of Botulinum toxin type A or electrical stimulation) to suppress tremor in an optimal manner. To create this model, we expanded a prior, limited model that focused on tremor propagation only from joint torques to joint displacement [3].

METHODS
Model Structure: As this is the first simulation of tremor propagation from muscle activity to joint displacement, we deliberately chose a simple model to capture first the most fundamental effects. This model consists of three sub-models that successively transform muscle activity into muscle force, muscle force into joint torque, and joint torque into joint displacement (Fig. 1). The inputs to the model are the neural drives to the 15 major superficial muscles that actuate the 7 main DOF from the shoulder to the wrist.

Model Parameters: Model parameters include the 15-by-15 diagonal matrices of time constants representing the dynamics of excitation ($t_1$) and contraction ($t_2$) of the muscles and the conversion from steady-state muscle activity to muscle force ($C$); the 7-by-15 moment-arm matrix ($M$); and the 7-by-7 impedance matrices representing inertia, damping, and stiffness ($I$, $D$, and $K$). These parameters were painstakingly gathered from a large number of past studies, but a subsequent sensitivity analysis showed that the conclusions drawn from the simulations were quite robust to variations in parameter values.

Input-Output Relationships: Since the model is linear, the relationship between each input and each output is fully described by the associated transfer function. For our model, this means the response of the whole system can be described by a 7-by-15 matrix of transfer functions.

Fig 1: The model transforms tremorogenic activity in a given muscle (here: triceps longus, a.u.) into tremulous displacement throughout the upper limb. SFE, SAA, SIER: shoulder flex-ext, abd-add, int-ext rot; EFE: elbow flex-ext; FPS: forearm pro-sup; WFE, WRD: wrist flex-ext and rad-uln dev.
Simulation Protocol: To determine how tremor propagates from tremorogenic muscle activity to tremulous joint displacement, we simulated tremorogenic input in each muscle and observed the resulting tremor in all DOF. Since the system is fully described by its matrix of transfer functions, we simulated steady-state behaviour by evaluating the magnitude ratio and phase shift of each transfer function in the tremor band (4-12 Hz).

RESULTS AND DISCUSSION
Tremor propagation patterns (how tremor distributes from input in a given muscle to output in multiple DOF) were quite independent of tremor frequency. Importantly, all 15 muscles produced the greatest tremor in one of the three most distal DOF (Fig. 2). The greatest contributor in a given DOF depended on the DOF, but distal muscles were most prominent: the greatest contributor in each of the seven DOF was (from proximal to distal, as listed in the caption of Fig. 2): BRA, PECM2, FCU, FCU, BIClong, FCU, and FCU. Summarizing these results, we concluded that (assuming equal inputs in all muscles, i.e. equal proportion of the maximum force in each muscle): 1) tremor increases proximal-distally, and 2) the importance of muscles (to tremor) increases proximal-distally.

The spreading of tremor from a given muscle to various DOF is caused by neural coupling (shared descending neural pathways and reflex activity) and physical coupling (musculoskeletal geometry, i.e. moment arms, and coupled joint inertia, damping, and stiffness). To determine which of these physical coupling effects (our model did not include neural coupling) was most responsible for spreading the tremor, we compared the output from the model based on default parameter values to the outputs of models in which coupling was suppressed in some of the $M$, $I$, $D$, and $K$ matrices. We found that joint inertia contributed more to spreading than musculoskeletal geometry, and joint damping and stiffness hardly contributed at all (not shown).

CONCLUSIONS
The goal of this work was to understand the propagation of tremor from muscle activity to joint displacement. To this end, we 1) determined the extent to which the original tremor propagation principles [3] established for propagation from joint torque to joint displacement held true for propagation from muscle activity to joint displacement, and 2) modified the original principles where necessary to reflect propagation from muscle activity to joint displacement. Thus, the following revised principles govern simulated tremor propagation from muscle activity to joint displacement: 1) The distribution of tremor depends strongly on musculoskeletal dynamics. 2) The spreading of tremor is due to inertial coupling (primarily) and musculoskeletal geometry (secondarily). 3) Tremor spreads narrowly; tremorogenic activity in a muscle does not spread significantly to many DOF—instead, most of the tremor caused by a muscle occurs in a small number of DOF. 4) Assuming uniform distribution of tremorogenic activity among upper-limb muscles (i.e. an equal proportion of the maximum force in each muscle), tremor increases proximal-distally, and the contribution from muscles increases proximal-distally. 5) Increasing inertia can decrease or increase tremor. 6) Increasing viscoelasticity can decrease or increase tremor.

REFERENCES

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