A simulation study of the effects of activation-dependent muscle stiffness on proprioceptive feedback and short-latency reflex

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Abstract—A biologically-inspired model of the Soleus neuromuscular system was used to study the influences of musculotendon mechanical properties on the proprioceptive feedback and on the short-latency reflex. The model structure comprised: i) stochastic descending drive to a motoneuron pool; ii) a Hill-type muscle model; and iii) a muscle spindle model with its Ia sensory afferents establishing a feedback loop with the motoneurons. H-reflex and short-latency stretch reflex were simulated considering their possible dependence on musculotendon mechanical properties and on the muscle activation level. The main results showed an intrinsic relationship between the Ia response to muscle stretch and the relative stiffness between muscle and tendon. In addition, fusimotor activation and synaptic gain could modulate the short-latency reflex, indicating that these mechanisms may help to maintain reflexes functionally active during different motor tasks. These preliminary results match some experimental data and provide insights on the intricate relationship between muscular mechanics and neuronal activity. Moreover, the adopted model of the closed-loop neuromuscular system has shown its potential as a tool for studies of complex mechanisms involved in motor control.

I. INTRODUCTION

FEEDBACK signals from muscle and tendon sensory receptors modulate the activity of the motoneuron (MN) pool, providing important information for motor control. In fact, several feedback loops, operating at different levels of the nervous system, provide the neuromuscular system with the ability to maintain its performance in a wide range of conditions, not necessarily relying on a direct control from the brain. The most studied of these feedback sources is the muscle spindle (MS), a neuromuscular receptor that lies in parallel with muscle fibers and signals muscle stretch amplitude and velocity [1]. The MS action potentials (“spikes”) travel through afferent axons and activate the MN pool innervating the homonymous muscle either directly or through spinal interneurons (IN). The monosynaptic pathway from Ia afferents to MNs of the homonymous muscle greatly contributes to a sudden increase in the activation of that muscle as a response to an electrical stimulation of the nerve containing those neurons (H-reflex) or as a response to muscle stretch, generating the short-latency reflex (SLR).

When a stretch is imposed to the musculotendon (MT) complex, it is only partly transferred to the muscle, since the in-series tendon has a finite compliance, reducing the movement of the muscle fibers [2]. The distribution of a stretch between muscle and tendinous tissue depends on the relative stiffness between them. It has been suggested that as the muscle force level (or equivalently, the activation level) increases, its stiffness may increase more than the tendon stiffness, leading to a progressive decline in muscle stretch amplitude and stretch velocity in response to the same externally applied stretch. Hence, in the absence of mechanisms to compensate for these effects, an increase in the activation of extrafusal muscle fibers would decrease MS responses, thereby reducing reflex responses [3]. Candidates for this compensation could be the modulation of MS static and dynamic gains by fusimotor activation, and the modulation of the reflex-loop gain by presynaptic inhibition of Ia afferents [4].

SLR has been shown to contribute to force enhancement and muscle stiffness regulation [5]. Yet, a better comprehension of its underlying mechanisms is still necessary to fully understand the role it plays in motor control. In this study, computer simulations were performed in order to evaluate how the relative stiffness between muscle and tendon may affect Ia afferent activity and, consequently, the SLR. In order to better differentiate between the influence of MN pool and muscle dynamics on the reflex activity, simulations of the H-reflex were also performed. Furthermore, a sensitivity analysis was used to investigate how the fusimotor activation and the maximum synaptic conductance between Ia afferents and MNs ($g_{\text{MNa}}$) could modulate reflex responses.

II. METHODS

A. Overview of the simulator

The model developed in this study was implemented in a web-based simulator dubbed ReMoto. This simulator is coded in Java™ programming language and is freely available at http://remoto.leb.usp.br. Currently, it focuses on
the neuronal networks and muscles associated with ankle plantarflexion (Soleus – SOL, Medial Gastrocnemius – MG, Lateral Gastrocnemius – LG) and dorsiflexion (Tibial Anterior – TA). ReMoto may be suitable for non-programmers due to its friendly interfaces, as well as for advanced programmers who may extend or even implement new models. It offers a controlled environment to study aspects of neuromuscular control, which are sometimes impossible to attain in human experiments. Hence, clearer effects or concepts can emerge, without the plethora of confounding factors associated with human experiments. Next, its main features are described.

1) Neuron models: Compartmental models are used to represent the dynamics of MNs (two-compartment) and INs (single-compartment). Models of synaptic dynamics yield physiologically appropriate time courses of post-synaptic excitatory and inhibitory potentials and their temporal summation. Descending tracts are driven by non-homogeneous stochastic point processes with gamma interspike interval (ISI) distributions. MNs are subdivided into S-, FR-, and FF-type; INs into Renshaw cells, Ia and Ib inhibitory INs; and afferent fibers into Ia and Ib types. Parameterization is based on human (when there are available data) or cat experimental data.

2) Force and Electromyogram models: A motor unit (MU) twitch is represented by the impulse response of a second-order critically-damped system, so that the muscle force is the algebraic sum of all MU twitches. Similarly, motor-unit action potentials (MUAPs) are modeled as first- and second-order Hermite-Rodriguez functions and the muscle electromyogram (EMG) is the sum of all MUAPs.

3) Inputs and outputs: In the current version, the user may specify three types of inputs: descending commands acting on MNs and INs with chosen ISI statistics; injected currents into the MNs; and electrical stimulation of a mixed nerve comprising efferent and afferent fibers. At the end of the simulation, the time course of any variable of interest may be visualized and exported as ASCII files. Further description of ReMoto may be found at [6].

B. Modeling extensions

In this study only part of the models in ReMoto was used. Other structures were implemented to allow investigations involving muscle mechanical properties and proprioceptor activity (Fig. 1). Instead of a twitch generator representing motor-unit force, as used in the original simulator, a Hill-type model was used to represent the whole muscle mechanics, forming with the tendon model, the musculotendon (MT) complex.

1) Muscle activation: a second-order critically-damped system in series with a non-linear (sigmoidal) function represented muscle activation due to each motor-unit activity. The total activation \( (a) \) was the sum of all MU activations followed by normalization. Proper parameter scaling ensured twitch amplitudes and contraction times along the MN pool consistent with experimental data. Only S-type motor units were considered in this study, since this fiber type is the major constituent of SOL muscle.

2) Muscle contraction dynamics: Four mechanical elements were responsible for the response of the MT complex to activation and length changes (Fig. 1b). The tendinous tissue was modeled as an in-series element with a stress-strain curve obtained following Zajac’s [7] methodology and implementation as in [8]. Muscle fibers were lumped into a representation consisting of one active and two passive elements. A contractile element based on [9] generated active force \( F_{CE} \) as described in (1).

\[
F_{CE} = a \times fl \times f_v
\]  

where \( a \) is the muscle activation level, \( fl \) is the force-length relationship, and \( f_v \) is the force-velocity relationship.

![Fig. 1. Block diagrams representing the neuromuscular model. a) Simplified view of the model. The MN pool containing \( n_{MN} \) MNs receives input from \( n_{DT} \) descending command axons and \( n_{IA} \) afferents. The MT complex is excited by the MNs’ activity and is mechanically constrained by the joint dynamics. b) The MT complex comprises a tendon in series with a pennated muscle fiber. PE represents stiffness and viscosity characteristics and the CE is responsible for the active force. The MS provides the Ia afferent activity due to muscle dynamics.](image-url)
3) Muscle spindle activity: the model described by [12] was implemented in order to predict the Ia mean firing rate of the MS (Ia_{MS}) in response to muscle length, velocity, and fusimotor activation. Static and dynamic fusimotor inputs modulate the sensitivities of the MS to changes in length and/or muscle velocity. This fusimotor activation was assumed to have no direct influence on muscle contraction dynamics. The afferent activity, as described in (3), modulates the intensity of stochastic point processes (ISIs with gamma distributions) representing the spiking activity of each Ia afferent.

\[ Ia_i = Ia_{MS} - RT_i + IFR, \]  

where \( Ia_i \) is the afferent activity, \( RT_i \) is the recruitment threshold and \( IFR \) is the initial firing rate of the i-th afferent Ia; \( Ia_{MS} \) is the muscle spindle model output. \( RT_i \) varies linearly in the Ia pool and \( IFR \) is a Gaussian random number (\( \mu = 5, \sigma = 2.5 \)).

Parameters for the MN pool and EMG may be found in [6]. In general, MS parameters were the same as those in [12], and MT parameters were the same as in [10]. However, some parameter modifications are listed in Table 1.

### Table 1

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
<th>Value</th>
<th>Unit</th>
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<td>( n_{MN} )</td>
<td>number of motoneurons</td>
<td>800</td>
<td>---</td>
</tr>
<tr>
<td>( n_{ax} )</td>
<td>number of Ia afferent axons</td>
<td>400</td>
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<td>30</td>
<td>Hz</td>
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<tr>
<td>( \gamma_{DStic} )</td>
<td>gamma static nominal value</td>
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<td>Hz</td>
</tr>
<tr>
<td>( F_0 )</td>
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<td>N</td>
</tr>
<tr>
<td>( RT_i )</td>
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</tr>
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<td>m/degree</td>
</tr>
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<td>( a_5 )</td>
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<td>( L_0 )</td>
<td>optimal muscle fascicle length</td>
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<td>sensory region stretch to afferent firing in bag1 fiber</td>
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<tr>
<td>( G_{bag2/Chain} )</td>
<td>Same as ( G_{bag1} ) for bag2 and chain fibers</td>
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<td>Hz/L_0</td>
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</table>

C. Simulation protocols

The scenarios and analyses used in this study are described in what follows.

1) Muscle and tendon stiffness: In order to evaluate this characteristic the MT model was simulated at different activation levels. Dorsiflexion (8° amplitude at 250°/s) was applied to the ankle joint, as in Fig. 2. Muscle and tendon stiffness were measured and compared, along with pre-stretch fascicle lengths, stretch amplitudes and stretch velocity of muscle fascicles.

2) H-reflex: Assessing H-reflex is valuable to differentiate between the effect of MN pool excitability and the effects of MT and MS dynamics on the stretch-reflex response. To simulate an H-reflex, an electrical stimulation of 10 mA was applied to the posterior tibial nerve. In order to quantify the reflex response, the EMG signal was re-sampled at 2 kHz, low-pass filtered (first-order zero-phase Butterworth filter with a 40 Hz cut-off frequency), and normalized by the maximum evoked M-wave (\( M_{max} \)).

![Fig. 2. Simulation example of an 8° dorsiflexion of the ankle (stretching the SOL muscle). Time courses of the EMG (a), #spikes of MNs (b), #spikes of Ia afferents (c), muscle fascicle length (d), force (e), and the ankle angle (f).](image)

3) Stretch-reflex: An 8° dorsiflexion at 250°/s was simulated, as illustrated in Fig. 2f, resulting in force response (Fig. 2e) and stretch of the SOL (Fig. 2d). This stretch led to a raise in Ia activity (Fig. 2c) and, consequently, in the MN pool activity (Fig 2b), which caused a SLR in the EMG (Fig 2a). The EMG signal was re-sampled, filtered, and normalized by \( M_{max} \).
4) Effect of fusimotor drive and maximum synaptic conductance: In order to evaluate the sensitivity of the SLR with respect to the fusimotor drive, the static and dynamic fusimotor levels were varied from 0 to 90 Hz. Additionally, $g_{Ia-MN,max}$ was varied from 300 to 1200 nS. Simplistically, the variation of $g_{Ia-MN,max}$ gives a qualitative idea of the effect of presynaptic inhibition of Ia fibers. The SLR was measured as previously described.

III. RESULTS

Muscle fiber pre-stretch length decreased monotonically with activation (Fig. 3a), whereas muscle stretch amplitude and velocity first increased and then decreased (Fig. 3b, c). As activation level increased, muscle and tendon stiffness changed as shown in Fig. 3d. This relation determined the relative stretches in these elements at a given force. The reduction in the muscle pre-stretch length with activation caused an increase in tendon pre-stretch length and, consequently, an increase in its stiffness. At about 30 to 40% of maximum activation, tendon stiffness reached a maximum value and remained approximately unchanged for higher activation levels. The ascending regions in Fig. 3b and Fig. 3c were coincident with a relative increase in tendon stiffness compared with the muscle stiffness. Accordingly, muscle stretch amplitude and velocity decreased with activation in the region where muscle stiffness increased more than tendon stiffness.

Fig. 3. Muscle and tendon properties as a function of activation level when the MT complex is stretched by an 8° dorsiflexion of the ankle. Muscle fascicle length before the stretch (a), stretch amplitude (b) and velocity (c), and the dynamic stiffness for the muscle and the tendinous tissue (d) are depicted.

The variation of H-reflex with muscle force is shown in Fig. 4. The maximum force ($F_{max}$) the muscle could generate with the ankle angle at 0° was 0.78$F_g$. The amplitude of the H-reflex corresponding to the smallest simulated force level (here adopted as reference and shown with an arrow in Fig. 4) was 0.19$M_{max}$. From this point to about 30% of $F_{max}$ the amplitude remained approximately constant. About 37% increase in the reflex amplitude was observed from 30% to 50% $F_{max}$ and, for higher contraction levels, the amplitude progressively decreased down to 15% below the reference value (at $F_{max}$). A quadratic curve was adjusted, leading to a coefficient of determination ($R^2$) of 0.57.

Fig. 4. Variation of H-reflex amplitude with muscle force. The resulting reflex was normalized by the maximum evoked M-wave response. Muscle force is normalized by the maximum force that the muscle can produce with the joint angle at 0°.

Similarly to the H-reflex, the SLR increased and then decreased with muscle force. Fig. 5 shows the relationships between SLR amplitude and muscle force (Fig. 5a) and between Ia afferent response and muscle force (Fig. 5b). For the SLR, there was an increase in reflex amplitude as the force increased from the resting condition to approximately 20% $F_{max}$. For mid-to-high contraction levels the reflex amplitude decreased slightly. Adjusting the SLR simulated data with a quadratic curve resulted in $R^2 = 0.58$. An analogous relationship was observed for Ia responses. It had ascending and descending regions, with a peak at ~23%. For contraction levels above 85% of $F_{max}$, the Ia response was significantly decreased and the reflex could not be distinguished in the EMG signal.

Fig. 5. Variations of SLR and Ia response with muscle force. SLR is normalized by the maximum evoked M-wave ($M_{max}$). The Ia responses shown were measured as the difference between its peak response to the stretch and its basal value. Muscle force is normalized by the maximum force that the muscle can produce with the joint angle at 0°.

Fig. 6 shows the sensitivity of SLR with respect to fusimotor activation and $g_{Ia-MN,max}$ for a fixed force level (~20% of $F_{max}$). SLR increased with dynamic fusimotor activation up to 45 Hz and remained at about the same level thereafter, but with a marked increase in its variability (Fig. 6a). A similar effect was observed when varying $g_{Ia-MN,max}$.
On the other hand, the SLR did not show an expressive change with static fusimotor activity (Fig. 6a). With muscle activation (or force) is an important feature [2] and seems to be well captured by the MT model.

In order to gain some insights into the role of MN pool excitability on the reflex activity, H-reflex simulations were performed. H-reflex generated by nerve stimulation bypasses the natural Ia afferent activity from the MS so that the measured EMG signal may be used to evaluate MN pool excitability regardless of MS dynamics. However, in human experiments there are still some methodological considerations regarding the extent to which the H-reflex could be related to MN pool excitability [15]. For instance, low-intensity stimulation tends to recruit only Ia afferents, which have large diameter axons, whereas high-intensity stimulus tends to recruit other afferents, such as Ib and cutaneous, which could affect the net synaptic activity on the MN pool [16]. In the simulated scenario, low-intensity stimulation was used in order to recruit only Ia afferents (and not MN efferents) and to avoid the saturation of the reflex pathway. H-reflex amplitude (shown in Fig. 4) had a similar behavior to the experimental results. For instance, some experiments have shown that H-reflex increases up to 40 to 60% of MVC (measured as an ankle torque level) in the human SOL during isometric contractions [16]–[17]. Still, another study has shown no change in SOL H-reflex amplitude up to 10% of MVC [18].

Besides the factors influencing the H-reflex, the SLR is also affected by the MS dynamics, which is dependent on the muscle behavior and on the fusimotor activation. Since the muscle stiffness is dependent on the muscle force (or activation) level [2], it has been proposed that the Ia afferent responses to muscle stretch also varies with muscle force level. This would mainly be due to the MS’s dependence on stretch velocity, which in turn varies with muscle activation [3]–[4]. This is evidenced here by comparing the bottom graph of Fig. 5 with Fig. 3b and Fig. 3c. Ia afferent response as function of muscle force had an ascendant-descendant behavior akin to the behavior of muscle stretch amplitudes and velocities (as functions of activation level). This Ia response modulation by the muscle activation level corroborates the hypothesis raised by [3] to explain the SLR modulation. However, this is not the only mechanism by which SLR is modulated.

Some studies have shown an increase in the SLR of the SOL muscle with torque level up to about 50% [19]–[20]. In contrast, the simulation results showed an increase which leveled at ~20% of $F_{\text{max}}$. This difference is partly explained by the fact that, for the chosen simulation scenario, the MN pool excitability acted as a limiting factor for the SLR (see ahead). In addition, the comparison of the results presented here for the H-reflex and SLR at different levels of muscle force with experimental data is not straightforward since the latter usually refer to the joint torque and not the muscle force. As the muscle force is not necessarily linearly related with joint torque for the full range of movement [22], this comparison should be taken carefully.
Regarding the MN pool excitability, the simulations indicated that the MN refractory period is a limiting factor for the amplitude of any type of reflex. As the MN pool excitability increases, more MNs are in their absolute and/or relative refractory periods at a given time, impeding them from participating in the reflex generation. Another limiting factor is the finite number of MNs in the pool, which causes a decrease in the number of “inactive” neurons (i.e., ready to respond and contribute to the reflex) as the pool excitability increases. These results were very similar to those presented in [21]. In our simulations, these saturation effects are fully responsible for the decline of H-reflex seen in Fig. 4 and partly responsible for the decline of SLR shown in Fig. 5a, since the SLR is also influenced by the variation of Ia response shown in Fig. 5b.

In the scenario chosen for the simulation of the SLR, the fusimotor activations and $g_{Ia-MN_{max}}$ were kept constant. This is probably not the case in many conditions of human behavior. However, the main objective of this study was not to reproduce the exact form of muscle force vs SLR curve, but to evaluate how this relation may be changed by the mechanical characteristics of the MT and by modulating factors such as fusimotor activation and $g_{Ia-MN_{max}}$, the latter being related to the presynaptic inhibition of Ia afferents. The results shown in Fig. 6 evidenced the modulation effect that the dynamic fusimotor activation and $g_{Ia-MN_{max}}$ may exert on the SLR. However, the SLR was insensitive to the static fusimotor activation. It has been proposed that a decrease in presynaptic inhibition may counterbalance the reduction in Ia afferent responses as muscle force increases [4]. As inferred from the result shown in Fig. 6b, it is plausible that, an increase in the Ia-to-MN post-synaptic potentials (by reducing presynaptic inhibition) results in a shift of the SLR to higher levels. Therefore, the modulation of the presynaptic inhibition may indeed represent a mechanism to maintain reflexes functionally active even at high force levels, counterbalancing the decrease seen in Fig. 5a. The same holds for dynamic fusimotor activation, although this activation is expected to reach a maximum value at about 25% of $F_{max}$ [3].

It is worth noting that in this preliminary study not much attention was given to the MN firing rates, which are closely related to the MN pool excitability and could be outside the normal range of human physiology. It seems that, in the chosen scenarios, the excitability of MNs were high at intermediate forces, which caused a premature saturation of the evoked reflexes seen in Fig. 4 and Fig. 5a. Thus, in order to improve the present simulations and allow more direct comparisons with experimental data, the MN pool excitation level should be better controlled and an additional model of the angle joint mechanics should be incorporated. However, in this study, only qualitative and comparative assessments were intended, and it was possible to evaluate important mechanisms and their influence on the feedback activity and reflex generation.

REFERENCES