Excitation of natural spinal reflex loops in the sensory-motor control of hand prostheses

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One Sentence Summary: Elicitation of afferents is integrated with myocontrol

Abstract: Sensory feedback for prosthesis control is typically based on encoding sensory information in specific types of sensory stimuli that the users interpret to adjust the control of the prosthesis. However, in physiological conditions, the afferent feedback received from peripheral nerves is not only processed consciously, but it also modulates spinal reflex loops which contribute to the neural information driving muscles. Spinal pathways are relevant for sensory-motor integration, but they are commonly not leveraged for prosthesis control. We propose an approach to improve sensory-motor integration for prosthesis control based on modulating the excitability of spinal circuits through the vibration of tendons in closed-loop with muscle activity. We measured muscle signals in healthy participants (N=9) and amputees (N=7) during different motor tasks, and we closed the loop by applying vibration on tendons connected to the muscles, which modulated the excitability of motor neurons. The control signals to the prosthesis were thus the combination of voluntary control and the additional spinal reflex inputs induced by tendon vibration. Results showed that closed-loop tendon vibration was able to modulate the neural drive to the muscles. When closed-loop tendon vibration was used, participants could achieve similar or better control performance in interfaces using muscle activation than without stimulation. Stimulation could even improve prosthetic grasping in amputees. Overall, our results indicate that closed-loop tendon vibration can integrate spinal reflex pathways in the myocontrol system and opens the possibility of incorporating natural feedback loops in prosthesis control.

Main Text:

INTRODUCTION

The loss of a limb directly affects both efferent and afferent pathways. Modern prosthetic devices for amputees aim to establish reliable bidirectional man-machine interfaces for restoring sensory-motor control. The decoding of the neural inputs to limbs [1] and muscles has improved significantly during the past years, boosting the control and functionality of prostheses [2], [3]. However, to further improve prosthetic control, it is necessary to also restore afferent pathways sending sensed information in the periphery back to the central nervous system [4]–[6]. Restoring these natural sensory inputs is a major challenge, with important current limitations [7], [8].

Recent advances in upper limb prostheses have led to promising developments in non-invasive sensory feedback techniques, enhancing functionality and user experience [9]–[13]. These techniques, such as sensory substitution or remapping [10]–[19], involve encoding prosthetic device parameters through different stimulation patterns of the stump [12], [25]. The aim is to convey information about the prosthesis state to the user through preserved sensory pathways that would send different information in an unaffected limb [12], [20]. There are different types of sensory information that can be transmitted to the prosthesis user in this way. For instance, force feedback, achieved through sensor-detected prosthesis force, grants users tactile and pressure sensations [4]. Similarly, mechanotactile feedback, utilizing pressure sensors [21], mimics natural limb sensations by applying pressure to specific areas of the stump. Bone conduction harnesses skull bone vibrations to provide sound and vibration feedback [22] about the prosthesis. These non-invasive and invasive sensory feedback techniques can collectively enhance upper limb prosthetic functionality, offering touch, pressure, and sound sensations that significantly improve control and object manipulation [11], [12], [23]–[25]. Such improvement suggests potential enhancements through task-specific information utilization [9], [23]. However, achieving these improvements poses challenges. Sensory substitution, relies on the subject's ability to process and interpret the perceived feedback information while in motion, and to adapt the motor commands sent to the prosthesis according to the received information [20], [26], [27]. This makes the control of the prosthesis a complex task that can be cognitively demanding. Emerging modalities are exploring sensory fusion to maximise information transmission to the nervous system [9], [28], combining kinaesthesia, touch, and motor intent for comprehensive sensory-motor restoration [29]. Alternatively, achieving natural feedback, in terms of sensations perceived by the user, may be partly achieved by direct nerve stimulation [27], [30]–[33], requiring invasive electrode implants. However, while invasive technologies offer an homologous natural sensation to convey information about the prosthesis and its interaction with the environment, their main working principle still involves cognitive processing of sensory inputs [27], [29], [33].

While providing interpretable sensations is of great importance for sensory-motor control [34], [35], sensory feedback in natural movements does not only have the role of informing the somatosensory cortex, but it is also projected, mono- or poly-synaptically, to spinal motor neurons and spinal interneurons, influencing their activity [36]–[38]. These projections play a fundamental role in motor control by contributing to the modulation of the excitability of pools of motor neurons [39]–[41]. Moreover, sensory processing in spinal pathways is beneficial in promptly compensating for disturbances in motor control by automatically generating correcting responses to the muscles in the presence of external perturbations (e.g., mechanisms for posture stabilisation during grasping control [42]–[44] or prevention of excessive stretch [45]). Importantly, these pathways are commonly preserved in amputees [4]. Their stimulation could potentially be used to further enhance or modulate the motor commands used for prosthesis control in a similar way as sensory reflexes do in natural motor control [46], [47]. In this work, we design artificial mechanical stimulation patterns that do not necessarily maximize the capacity of prosthetic users to cognitively interpret and discriminate different stimuli; rather, we propose patterns of stimulation that maximize the stimulation effect on the activity of spinal motor neurons, i.e. stimuli that target the natural sensory-motor spinal loops. This new view in providing feedback focuses on spinal integration of the feedback and on the involuntary (rather than voluntary) adjustments in motor neuron output (that is the control signal of the prosthesis) as a consequence of the provided feedback. This key difference with respect to classic sensory substitution provides a new paradigm for feedback integration into prosthesis use that may restore or enhance natural sensory-motor pathways.

Mechanical vibration over the muscle tendon has been previously explored to provide illusory kinesthetic perception [37], [48] by excitation of muscle spindles. This technique has been exploited to convey proprioceptive information related to grip movements during prosthetic control [4], [29], [47]. In addition, the tendon vibration induces a secondary mechanism that actively modulates the excitability of the motor neurons innervating the stimulated muscle [40]; this effect is known as the tonic vibration reflex (TVR). The vibratory stimulation activates type Ia and type II sensory afferents [49]–[51] that generate excitatory inputs to the motor neurons controlling the stimulated muscles [41], [52]. The firing impulses are interpreted at the spinal level as if the muscle was stretched, producing further increase in the muscle activation [53]. Concurrently, this process tends to induce a reciprocal relaxation response in the antagonist muscle that opposes the one undergoing vibration [49]. Enhancement of this reflex effect has not been investigated in the context of prosthetic applications, maybe due to concerns of a possible negative influence of stimulation on the volitional modulation of motor outputs [4]. Nonetheless, modulation of motor output by spinal loop pathways is the physiological working conditions for the central nervous system that adjusts the supraspinal drive to motor neurons according to the integration of sensory feedback [42]. The motor neuron output is then the combination of voluntary and sensory drive to the motor neurons [54]. Because the motor neuron output is the drive to the muscles that is then used for the prosthetic control, the sensory-motor loop is closed by the activated prosthesis in the same way as during natural muscle control.

In this study, we investigate the integration of the TVR to modulate muscle activity and its integration with myoelectric control, creating a comprehensive sensory-motor closed-loop system. The aim is to interface reflex sensory-motor loops by modulating the afferent input to motor neurons during concomitant voluntary control in a myocontrol task. This modulation integrates natural mechanisms, such as corrective responses or afferent support for muscle activation [42], into prosthesis control. Some of these types of disturbance corrections can be achieved by endowing the prosthesis with greater intelligence and autonomy [55], [56], including the implementation of mechanisms such as anti-slip features [57], [58], adjusting thresholds and gains at the software level [59]. However, enhancing prosthesis autonomy to handle disturbances comes with the potential drawback of diminishing overall embodiment and reducing the user's perception of prosthetic control [60]. In our present study, we aim to establish an interaction that targets task-related neural activity and that aligns with voluntary control, thus alleviating potential concerns inherent in automatic software implementation regarding lack of embodiment and ownership and preserving the user sense of control throughout the integration process.

Our hypothesis is that adding reflex loops to the closed-loop control of a prosthesis would positively impact prosthetic control by mimicking natural sensory-motor interaction at the spinal level. As a representative approach that modulates the afferent input to motor neurons, we explored the best conditions to evoke and control the TVR by fine-tuning the stimulation parameters. We proposed two closed-loop modalities to integrate this reflex mechanism in sensory-motor control for able-bodied participants (AB) and trans-radial amputees (TA). For amputees, the system was fully integrated into real prosthesis control during activities of daily living.

RESULTS

In our studies, we focused on stimulating the flexor muscles of the forearm, specifically targeting the muscle-tendon ends. The aim was to elicit activity in the muscle spindles and to evaluate the concept of artificially triggering the spinal reflex loops in closed-loop with muscle activity. A band-strap tactor (see Methods) was placed on the flexor common tendon of the participants to target the flexor muscle spindles. The vibration of the muscle-tendon induces activity in Ia fibers innervating the stimulated muscles and projecting to the spinal cord (Fig. 1) [61], [62]. The induced activity in the afferent projections has an excitatory effect on the motor neurons of the stimulated muscle via a monosynaptic reflex pathway. It is worth noting that the tendon vibration also typically induces a reciprocal relaxation response in the antagonist muscle opposing the one undergoing vibration. However, for the purpose of this study, our focus here will be on the excitatory effects of the stimulation. The afferent input, resulting from the muscle stimulation, is combined with other spinal and supraspinal inputs to motor neurons, which integrate these received synaptic inputs and discharge action potentials that reach the muscle, ultimately determining its level of contraction. The overall myoelectric activity generated by the muscle (flexor carpi radialis) of the participants is the result of the combination of voluntary commands generated by the user and the afferent feedback, which includes the modulatory effects of the tendon vibration. This physiological integration of voluntary and sensory inputs is expected to mimic natural reflex mechanisms, adapting muscle activity for specific tasks and forming a reinforcing positive loop to enhance muscle activation, similar to natural sensory-motor closed-loops [35], thus promoting improvements in control and embodiment.

Fig. 1 (TVR evaluation framework) schematically shows the experiments conducted, from basic physiological investigations of the TVR to functional tests with prostheses. The experiments aimed to evaluate the viability of incorporating the TVR in sensory-motor control with the goal of improving and refining muscle contractions during prosthetic operation. For this purpose, we first conducted three physiological experiments and then explored the potential functional benefits of our proposed approach in two additional tests involving the control of a prosthetic hand. The first physiological test aimed to characterise the impact of the stimulation frequency on the elicited TVR response (Experiment I). This allowed us to identify subject-specific optimal stimulation frequencies to induce significant TVR effects. Then, we investigated the feasibility of controlling the TVR effect in closed-loop by intermittently enabling and disabling it based on the recorded muscle activity (Experiment IIA). Demonstrating the controllability of these effects allowed us to adjust in closed-loop the motor output activity to reach specific reference levels. Lastly, we assessed the integration of the TVR effect into voluntary control (Experiment IIIA). This evaluation involved stimulating through a proportional closed-loop approach, where the level of stimulation (i.e., the amplitude of the vibration) was proportionally controlled based on the recorded muscle activity. This was the first test of the closed-loop stimulation (acting as a positive feedback loop with muscle activation) combined with the volitional adaptation of muscle activity by the subjects, and it allowed us to test if the closed-loop stimulation could be successfully integrated by the subjects to perform a target tracking task with the level of muscle activity. By showing that this stimulation condition did not disrupt performance, we were able to show that closed-loop TVR could be integrated into the voluntary control. Having established the feasibility of controlling and integrating TVR into sensory-motor control, the last two experiments (Exp. IIB and IIIB) were done to determine whether the tested closed-loop TVR framework could lead to functional benefits in the control of a prosthetic device.

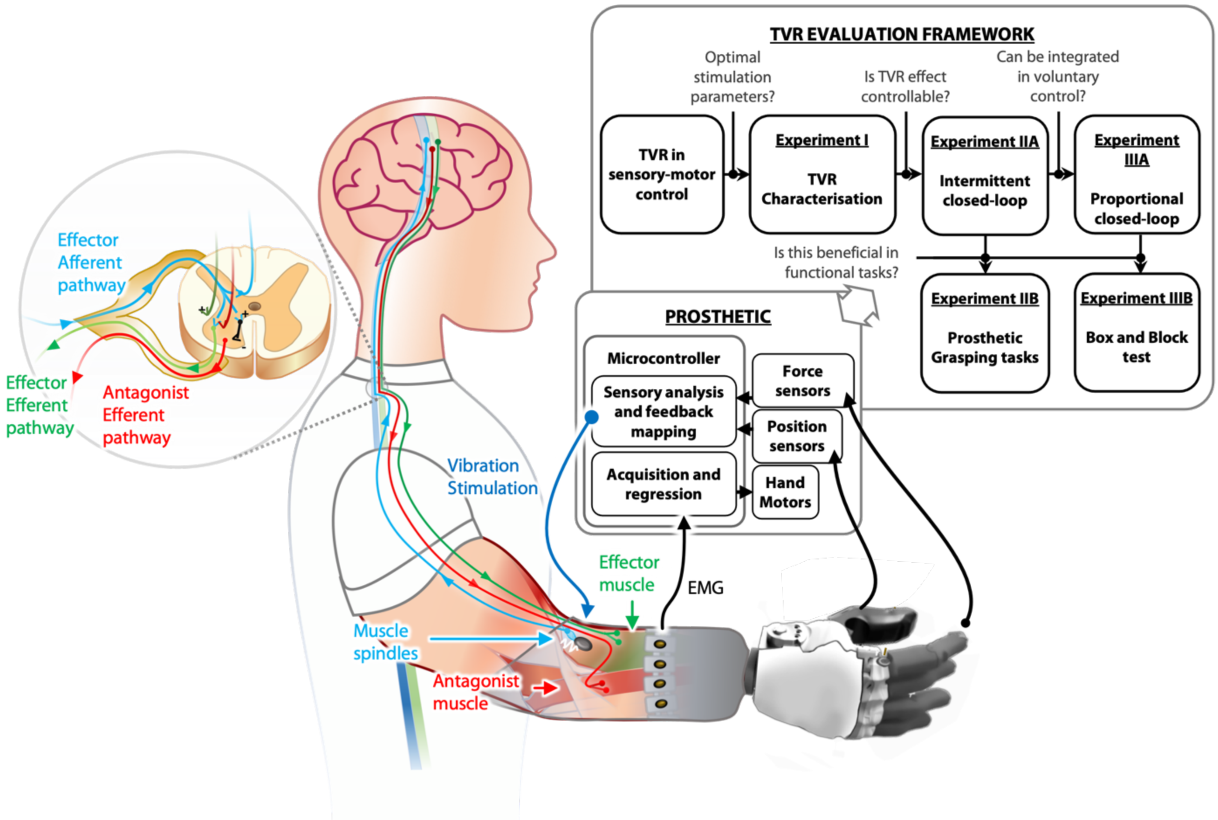

Fig. 1. Concept for the afferent spinal closed-loops integration for sensory-motor control and evaluation framework. Muscle-tendon stimulation (dark blue arrow) elicits activity in muscle spindles modulating afferent inputs to motor neurons via a spinal reflex arc (light blue arrow). The integrated set of neural inputs to motor neurons (including the evoked afferent activity) determine muscle contraction by modulating the level of activity in the agonistic efferent input green arrow). This scheme allows direct modulation of motor outputs (muscle activity) for prosthesis control via a spinal cord-mediated artificial loop. The top-right box summarizes the experiments performed to test the proposed closed-loop scheme for prosthetic control. Three physiological experiments (I, IIA & IIIA) evaluated the TVR effects during contractions periods and subjects' ability to integrate the TVR effects in their volitional control of muscle activation. Two functional experiments (IIB & IIIB) assessed potential benefits in real-life scenarios in amputees.

Experiment I: Physiological characterization to optimally induce TVR effects

We first evaluated the relevance of the stimulation frequency on the elicited TVR responses. In this initial part, we aimed to identify, on a participant-by-participant basis, the stimulation frequencies that elicited the highest TVR effects and tested whether the induced force modulation (or EMG amplitude modulation) changed with the stimulation amplitude. Previous studies have reported maximum TVR effects at vibration frequencies from 80 to 160 Hz and stimulation amplitudes close to 1 mm [49]–[51], [63]. However, the reported frequencies and amplitudes that evoke the highest EMG responses vary largely across participants and studies. This is due to the different setup strategies or stimulation conditions tested and to the complexity of measuring the actual force exerted on the tendon.

Participants were asked to perform isometric wrist flexions with application of force with the palm of the hand to an isometric force measurement platform. The force and EMG exerted by the palm was recorded to track changes in the generated force output. The RMS of the EMG signal was calculated and then normalized using resting and maximum voluntary contraction EMG levels. These normalized RMS EMG values, representing the contraction level, are simply denoted as NormEMG in the following. Participants received visual feedback in the form of NormEMG to inform them about their muscle contraction level. Initially, participants were instructed to attain a 10% NormEMG level during an isometric wrist flexion task while receiving visual feedback. After the participant reached the requested level of contraction, the visual feedback was disabled and the participant was instructed to keep the same level of contraction for 20 s without visual feedback. After 5 s, the stimulation was enabled for 10 s at 80, 100, 120, or 140 Hz. A control condition with an identical task without the stimulation was also added. The difference in the average NormEMG measured from the flexor carpi radialis at the beginning and end of the stimulation period (ΔEMG) was used to quantify the TVR effect on the motor output of the participants.

The changes in force (ΔF) and ΔEMG during the stimulation phase are displayed in Fig. 2A for all the able-bodied (AB) participants. In both measurements, an initial transitory phase followed by a steady-state phase could be observed, suggesting a cumulative effect of the TVR over time. For all frequencies tested, the steady state was reached within the first second after stimulation. Overall, there was an increase in the force produced and in the NormEMG for all participants (both able-bodied and amputees) for most stimulation frequencies. There was a significant increase in the ΔEMG level at the end of the blocks (relative to the NormEMG level before the stimulation started) for the cases in which stimuli were given at 100 (2.66 ± 2.41%), 120 (2.35 ± 3.40%) and 140 Hz (2.97 ± 4.02%), compared to the no stimulation condition (0.78 ± 2.14%) (Fig. 2B) [Turkeys' honestly significant difference procedure $p < 0.001$, $p < 0.01$ and $p < 0.001$, respectively]. In accordance with previous studies [64]–[66], there was a positive correlation between the frequency of stimulation and the TVR effect. The frequencies leading to the highest effect on force were 120 and 140 Hz for both able-bodied and amputee participants. However, there was no significant difference in the effect produced by these two frequencies ($p = 0.311$). Fig. 2C shows the maximum ΔEMG elicited during stimulation for each able-bodied participant for the optimal stimulation frequency. The frequency that elicited the maximum ΔEMG was selected as the optimal individual frequency for each participant.

For the trans-radial amputee (TA) participants (Fig. 2D), all the frequencies evoked a significant positive drift. The frequency that led to the largest effect compared to non-stimulation (-0.57 ± 3.59%) was 120 Hz (3.23 ± 7.48%) [$p < 0.001$], followed by 140 Hz (2.51 ± 6.73%) [$p < 0.05$]. The stimulation frequency with the smallest effect was 100 Hz (1.63 ± 7.89%) [$p < 0.01$]. Similar to able-bodied individuals, the higher the stimulation frequency, the higher the TVR effect. However, in this case, the plateau frequency was observed at 120 Hz (the optimal frequency was 140 Hz in one case, 120 Hz in three cases, and 100 Hz in two cases). These participant-specific optimal frequencies were used in the subsequent experiments to implement the sensory-motor integration (Fig. 2E).

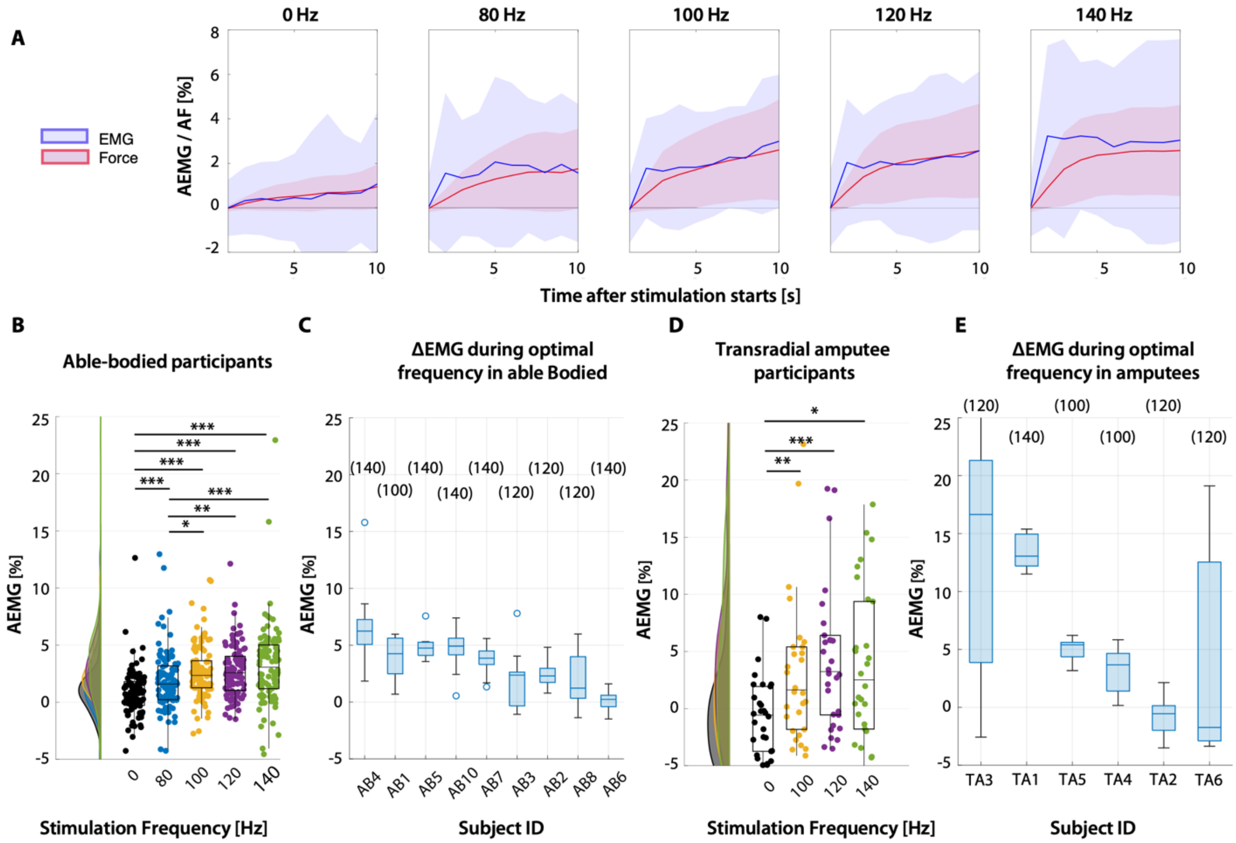

Fig. 2. Motor output drifts during stimulation and disabled tracking visual feedback. (**A**) Evolution of TVR effects on Forces and EMG over time in Able-Bodied participants (n = 9, trials = 90). The NormEMG is in blue and and the force in red (traces and shades show the average and standard deviation respectively across subjects; n = 9; participants performed 10 trials per condition). (**B**) Density plots and individual measurements of the ΔEMG motor output across able-bodied participants (AB) (n = 9; participants performed 10 trials per condition). Each sample (point) represents a single trial of the ΔEMG over 10 s between the beginning and the end of the stimulation period. (**C**) Overall optimal stimulation effects for each able-bodied participants (10 trials performed per participant). The optimal stimulation frequency is noted in parenthesis on top of each boxplot. Each sample represents the average ΔEMG during the stimulation time per trial. For this plot, the order in which participants are arranged on the x-axis was based on the level of ΔEMG observed. (**D**) Density plots of the ΔEMG motor output in trans-radial amputee participants (TR) (n = 6; participants performed 5 trials per condition). Each sample (point) represents a single trial of the ΔEMG over 10 s between the beginning and the end of the stimulation period. (**E**) Overall optimal stimulation effects for each amputee participant (5 trials performed per participant). The optimal stimulation frequency is noted in parenthesis on top of each boxplot. The order in which participants are arranged on the x-axis was based on the level of ΔEMG observed.

Experiment IIA: Control of TVR effect through intermittent stimulation

In the first experiment, we observed that the TVR effect increased the motor output over time (Fig. 2A). To assess its applicability in sensory-motor control, we examined the potential to regulate the magnitude of the TVR effect online using a closed-loop framework. For this purpose, we integrated the TVR into the participant's sensory-motor control using an *optimal intermittent* closed-loop stimulation controller capable of activating and deactivating the TVR on the basis of the observed NormEMG level. We assessed the capacity of this *intermittent* closed-loop approach to drive the TVR effect by modulating the initial motor output activity of a participant to a desired level. Through this implementation, our aim was to harness spinal reflex circuits in real-world scenarios, to fine-tune limb contractions without the participants' involvement for specific tasks and compensate the effect of external perturbations [42], [67].

The *optimal intermittent* closed-loop was implemented by minimizing the error between the exerted output NormEMG level produced by the participant and a given reference EMG amplitude level (Fig. 3A). Based on the error, the stimulation to elicit the TVR was controlled in an on-off fashion: it was activated when the measured NormEMG level was below the target and disabled when the measured level was above the target level. This design aimed to stabilize the participants' output NormEMG level at the reference level used as target in the task. The stimulation frequency used to implement the *optimal intermittent* closed-loop was the optimal frequency obtained from Experiment I.

To assess the controllability of the TVR, we isolated its contribution from the participants' voluntary muscle control by deactivating visual feedback during the *optimal intermittent* closed-loop activation. Participants were instructed to maintain a sustained isometric wrist flexion at an initial baseline target. Subsequently, we removed the visual feedback and initiated the *optimal intermittent* closed-loop to adjust the motor output. It is important to note that while we attempted to isolate the TVR effect from the voluntary control, the overall EMG output still included the drive generated by the participants to hold the contraction at a constant level (Fig. 3A). TVR controllability was evaluated by calculating the success rate (evaluated by the ratio of the root-mean-square values between the current NormEMG and the target level) of the *intermittent* closed-loop stimulation in making the NormEMG activity track a certain target level.

We included a *baseline* condition to ascertain participants' peak performance potential within the experimental task. This condition and the target during the task were adjusted considering the participants' physical differences between able-bodied and amputee individuals. We set a step target (0% to 10% NormEMG) and enabled visual feedback during the baseline for able-bodied individuals. This provided insight into how they adapted their control to minimize errors between the signal and the target level. In contrast, amputee participants encountered a constant target with visual feedback disabled. This choice accounted for physiological differences: amputees rely on distinct neuromuscular control and sensory cues, making rapid muscle activity changes challenging. A constant target (10% NormEMG) aligns with their control strategy, emphasizing proprioception due to limb absence and mimicking how they naturally stabilize limb position without continuous visual input. Additionally, to ensure that the observed effects with the optimal intermittent condition were attributable to TVR, we included a suboptimal intermittent closed-loop condition. In this condition, the stimulus frequency was set at 40 Hz, a frequency not expected to induce a TVR effect [65], [66]. This condition allowed us to disentangle the effects induced by the TVR from the possible modulation of muscle contraction done by the participants when receiving intermittent stimulation.

For able-bodied participants, the reference target used in the tasks in this experiment consisted of maintaining a stable level of muscle activation and then producing a step increase (from 10% to 15% NormEMG) in the muscle activation (purple dotted line in Fig. 3B). We observed that the optimal *intermittent* closed-loop could modulate the control variable to track the target level. An example of the measured NormEMG traces in one able-bodied participant, AB6, is shown in Fig. 3B. The success rate in the *baseline* condition was 93.72 ± 22.57% across participants. This was significantly higher than the success rates with the optimal *intermittent* closed-loop (87.84 ± 22.57%) [$p < 0.01$] and the *suboptimal intermittent* closed-loop (65.58 ± 16.64%) [$p < 0.001$] (Fig. 3C). The relatively small difference in success rate between the baseline condition and the *optimal intermittent* one demonstrates that the *optimal intermittent* condition was able to partly compensate for the drop in performance due to the removal of the visual feedback by increasing the level of NormEMG activation via the TVR. Importantly, the *optimal intermittent* closed-loop led to significantly higher success rates than the *suboptimal* closed-loop [$p < 0.001$], emphasizing the importance of using an adequate stimulation frequency for the tendon vibration. This result also implies that the outcomes achieved through the optimal frequency were a result of modulating the afferent feedback affecting motor neurons activity, rather than just acting as an interpretable sensory cue for participants.

In the case of the amputee participants, overall (Fig. 3D), the success rate in maintaining the reference target with the *optimal intermittent* closed-loop (63.70 ± 15.01%) was significantly higher than the *baseline* condition (49.52 ± 16.78%) [$p < 0.01$]. The success rate to follow the target using the *optimal intermittent* closed-loop condition was also significantly higher than the success rate obtained using the *suboptimal intermittent* closed-loop condition (58.77 ± 21.12%) [$p<0.05$]. The suboptimal intermittent closed-loop was able to improve the baseline results; however, these improvements were not significantly different. The individual trials for TA1 during this task are depicted in Fig. 3E as an example. For the *baseline* and *suboptimal intermittent* closed-loop conditions, the NormEMG tended to decrease after the visual feedback was disabled in all cases, leading to a reduction of the control success rates. The *optimal* closed-loop stimulation, on the contrary, was able to maintain a relatively stable output level during the whole trial. The individual patterns of activations for two participants (TA1 and TA2) are shown in Fig. 3F; the *optimal* closed-loop stimulation was able to modulate the NormEMG level without generating overshoots. Overall, the result from amputees indicates that the TVR reflex is also controllable in this population. Moreover, it suggests that even in scenarios with a low voluntary baseline, the optimally induced afferent spinal pathways can be used to actively modulate muscle activation in amputees.

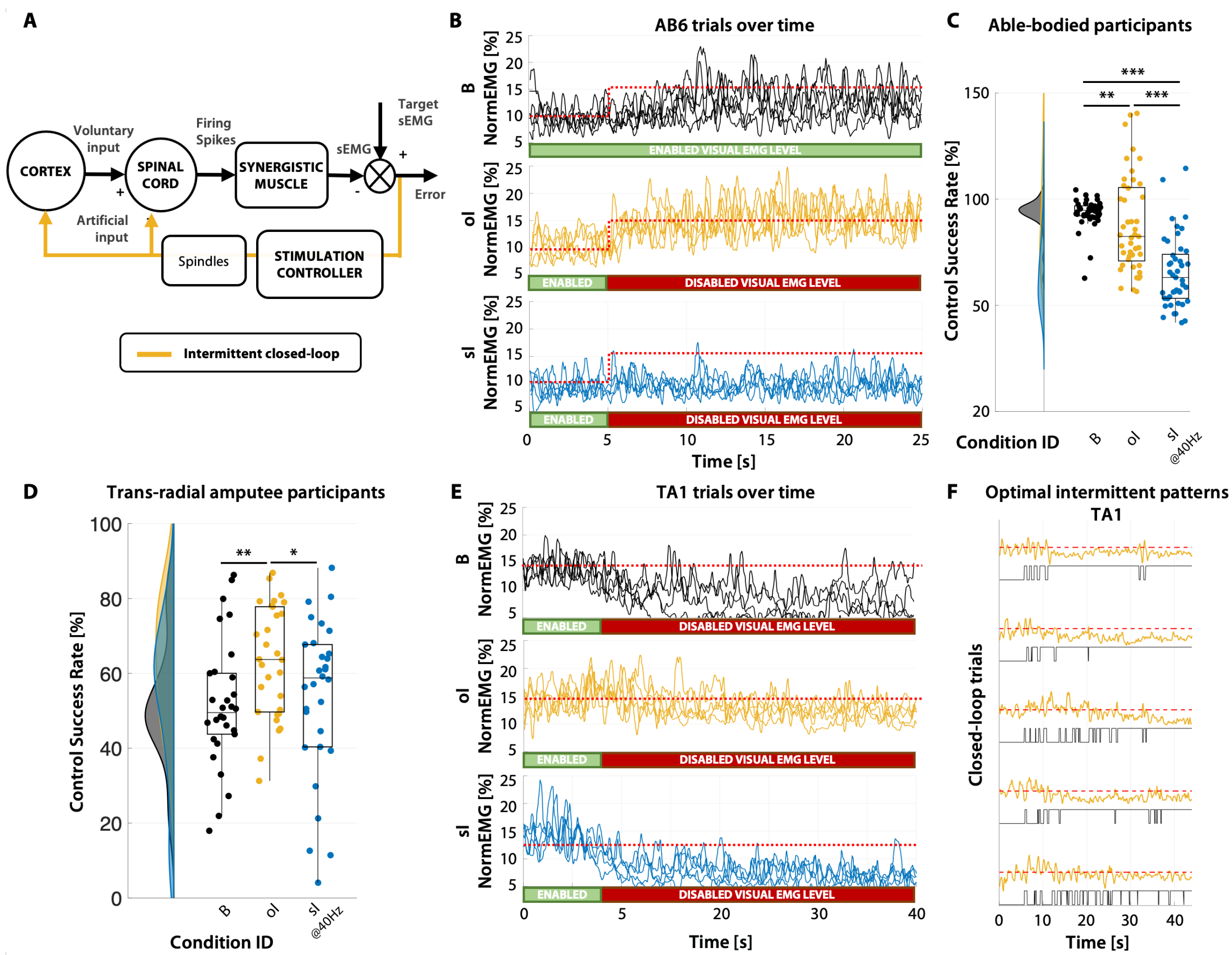

Fig. 3. Intermittent afferent closed-loop performance. (**A**) Concept of this reflex closed-loop. The difference between a given EMG target and the actual EMG output of the participant is used to activate the stimulator and create a positive loop on the targeted muscle to reach the desired target. (**B**) Individual trials of a representative able-bodied participant (AB6) in the *baseline* (B), *optimal intermittent* (oI) and *suboptimal intermittent* (sI) closed-loop stimulation conditions. Each subplot displays five trials conducted by the participant. The horizontal red dotted line represents the EMG target level that participants should generate. (**C**) Success rate for the control conditions across all able-bodied participants (n = 9; each dot represents a single trial, participants performed 5 trials per condition). (**D**) Success rate for the control conditions across all amputee participants (n = 6; dots represent individual trials, participants performed 5 trials per condition). (**E**) Individual trials of a representative participant (TA1) for the *baseline*, *optimal intermittent* and *suboptimal intermittent* closed-loop stimulation conditions. Each subplot includes the traces of the 5 trials conducted by the participant. The horizontal red dotted line represents the EMG target that participants were instructed to maintain throughout the trials. (**F**) Individual trials of a representative participant (TA1) for the *optimal intermittent* closed-loop stimulation condition. The plots combine information about the EMG output (yellow traces) and the intervals of stimulation (black traces; low level – deactivated, high level – activated).

Experiment IIB: Biomimetic object anti-slippage via intermittent closed-loop in amputees

To further assess the potential functional benefits of the *intermittent* closed-loop stimulation strategy tested in Experiment IIA, we integrated this closed-loop method in the control of a prosthetic hand (Taska Prosthetics, New Zealand). It is important to note that the *intermittent* closed-loop stimulation strategy cannot be directly implemented in prosthesis control due to the absence of a predefined reference EMG trajectory. Nonetheless, a fundamental initial step in establishing the feasibility of integrating the TVR into sensory-motor control involved demonstrating its capability to modulate motor output effectively in tasks aimed at improving grasping. Moreover, simple processing methods can be devised to estimate a reference EMG level, e.g., the EMG level shortly after contact.

Following the preliminary study on force tracking, we conducted a grasping experiment. The object to grasp included a force sensor that allowed us to track the amount of force that the prosthesis was exerting. In these grasping tasks, we evaluated whether intermittent closed-loop control could improve the grasping stability, enabling the prolonged and controlled retention of an object with a consistent level of force. In this type of scenario, the participant should ideally exert a minimal range of force to avoid breaking the grasped object. To simulate this scenario, we displayed in the monitor a red visual sign when the grasping force exceeded a certain threshold to indicate rupture of the object. This red sign and the visual inspection of the object was the only information given to the participant to hold it. The number of times that the object was dropped during the task was counted and used as a slipping indicator. To evaluate the effect of the *intermittent* closed-loop stimulation condition in this task, participants were requested to maintain a constant force on the object that was 20% of the maximum force that the prosthetic hand could exert. This percentage was determined through experimental pilot trials to ensure a stable grip. From the initial group of TA participants, only TA4, TA5 and TA7 were able to take part in this experiment due to time constrains in the conducted experimental sessions. The performance of the closed-loop conditions in assisting the participants to hold the object for prolonged periods was assessed by counting the number of drops and by measuring the average and standard deviation of the exerted gripping force during the trial.

An example of the exerted force traces during the trials is shown in Fig. 4A. In these three participants there was a decrease in the average gripping force exerted between the suboptimal condition (54.04 ± 12.90%) and the optimal condition (42.05 ± 5.71%), which indicates that the stimulation parameters have a relevant role in the assistance achieved with the stimulation (Fig. 4B). The differences in the exerted force between optimal and the baseline conditions followed a similar trend, with the baseline condition resulting in a higher force level applied to the object (46.52 ± 13.99%). The standard deviation of the exerted force (Fig. 4C) was also lower in the optimal condition (27.31 ± 5.01%), than in the suboptimal (29.72 ± 5.13%) and baseline conditions (31.73 ± 6.34%). We could observe a decrease in the number of drops per trial, from 1.33 ± 0.98 drops/block to 0.50 ± 0.67 drops/block when the optimal intermittent closed-loop was enabled (Fig. 4D). The suboptimal condition exhibited an intermediate performance level between the optimal and baseline conditions (1.08 ± 1.08 drops/block). These results reveal a reduction in the net exerted force alongside a decrease in its standard deviation with the optimal stimulation condition. Importantly, this was achieved while participants produced fewer drops in this condition than in the other two. These results suggest an improved performance in exerting lower-amplitude forces during the task during this optimal closed-loop condition. This improvement could potentially offer functional benefits by automatically adjusting the generated EMG command of the participant during tasks such as grasping.

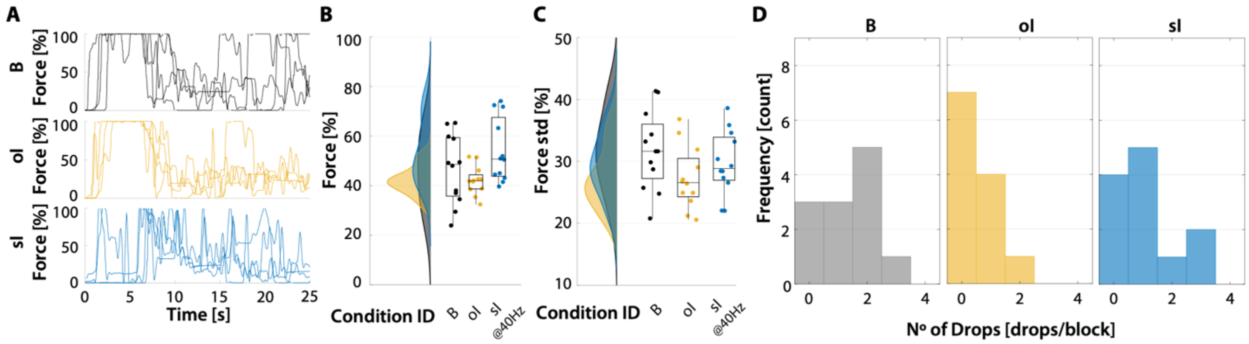

Fig. 4. Intermittent afferent closed-loop performance during prolonged object holding. (A) Individual trials of the exerted force by a representative participant (TA7) in the *baseline* **(B)**, *optimal intermittent* (oI) and *suboptimal intermittent* (sI) closed-loop stimulation conditions. Each subplot displays 4 trials conducted by the participant **(B)** Mean and standard deviation **(C)** of the gripping force exerted per trial for each stimulation condition across trans-radial amputees participants (n = 3; 4 trials performed per participant and condition). Dots represent individual trials. **(D)** Number of drops during prolonged object holding for all control conditions across trans-radial participants, n = 3.

Experiment IIIA: TVR afferent integration via *proportional* stimulation in voluntary control

The previous tests focused on controlling the tendon vibration stimulation using an *intermittent* closed-loop stimulation, regulating the on/off periods of stimulation. This strategy may be implemented during grasping, as exemplified in Experiment II. However, for prosthetic myocontrol implementation, it is important to examine how the afferent input integrates into a control loop in a continuous way, as in natural conditions. In this experiment, we evaluated whether the added afferent input disrupts the participant's overall voluntary control. For this purpose, we implemented a *proportional* closed-loop approach that superimposes the TVR afferent input onto voluntary activity.

The *proportional* closed-loop stimulation framework tested here adjusted the amplitude of the vibrators stimulating the tendon proportionally to the NormEMG (Fig. 5A). The stimulation frequency was fixed at the optimal value obtained in Experiment I. The effects of the stimulation on motor neurons were superimposed to the voluntary drive to the muscles generated by the participants to determine the overall level of muscle activation. This proportional control of the stimulation was meant to mimic natural sensory-motor closed-loops, in which the input from primary and secondary afferents depends on the level of muscle activity (i.e., on the control variable) and acts as positive feedback to support muscle activation [66][38].

Participants were asked to follow a reference EMG ramp trajectory to evaluate the impact of the stimulation on the produced EMG. The evaluation tasks involved tracking a ramp target at 0.75%/s for 20 seconds, starting at 10% NormEMG, mirroring the average EMG increase gradient seen in pilot experiments. Following the slope, there was a 5-s plateau at 25% NormEMG (Fig. 5B). The performance in tracking the ramp while receiving the stimulation was compared to the performance achieved by the participants when they did the same task without receiving the stimulation (baseline condition). In both conditions, participants received visual feedback about their exerted NormEMG output to follow the ramp trajectory. The performance to follow the trajectory was assessed by the root-mean-square error (RMSE) between the reference ramp trajectory and the exerted NormEMG activity. Given the paradigm shift in this closed-loop stimulation, we conducted an additional evaluation (only reported in supplementary materials) to verify the effectiveness of the *proportional* closed-loop to induce TVR. This evaluation confirmed that the isolated contribution of this *proportional* closed-loop condition can indeed elicit positive drifts in the motor output. These results are included in the supplementary material (see text S1).

The inclusion of proportional stimulation did not significantly affect the overall error made by the able-bodied participants, and it remained comparable to the condition in which the stimulation was disabled [$p = 0.65$] (Fig. 5C). An increase in error would have been anticipated if the stimulation disrupted voluntary control. However, no increase or decrease was observed; the error remained at baseline levels. These findings indicate that the modulatory effects of the *proportional* closed-loop stimulation were successfully integrated by the able-bodied participants. Having established the integration of sensory-motor control of able-bodied individuals, our subsequent objective was to evaluate whether it could also be effectively integrated by amputees or even result in beneficial effects in their cases.

The average error (ramp + hold) across the 6 amputee participants was not significantly different ($1.41 \pm 0.95\%$ to $0.95 \pm 0.99\%$; $p = 0.24$) when the *proportional* closed-loop was enabled (Fig. 5D). However, in two amputee participants (TA1 and TA5; Fig. 5E), the *proportional* closed-loop stimulation significantly decreased the overall error (ramp + hold) to follow the trajectory from $1.02 \pm 0.48\%$ to $0.27 \pm 0.41\%$ [$p < 0.05$] and from $1.02 \pm 0.33\%$ to $0.55 \pm 0.22\%$ [$p < 0.05$], respectively. These findings indicate that the amputee participants integrated the modulatory effects of the *proportional* closed-loop without any major perturbation in their voluntary control.

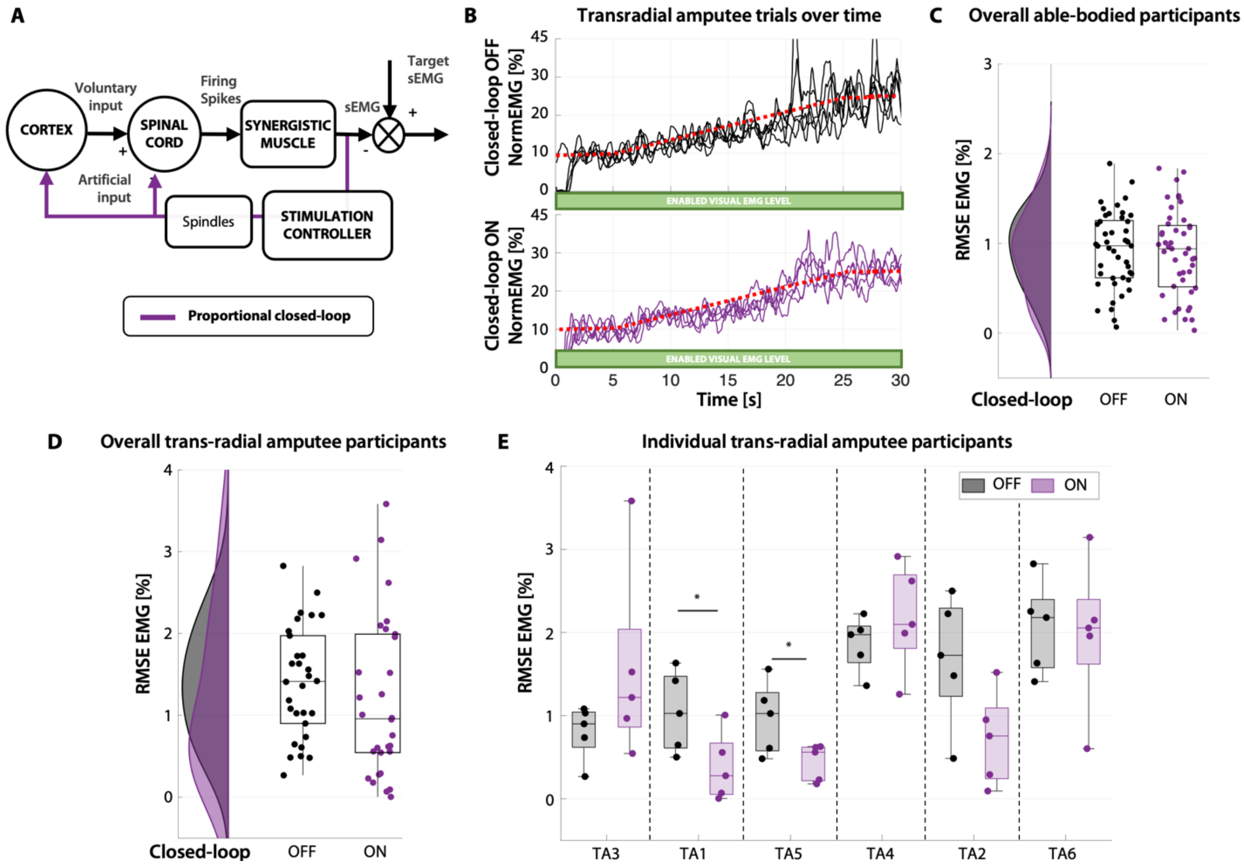

Fig. 5. Proportional closed-loop afferent effects superimposed to voluntary control. (**A**) Concept of the *proportional* closed-loop: the exerted EMG envelope was proportionally mapped into the amplitude of stimulation to create a positive closed-loop to modulate the excitability of the motor neurons innervating the target muscle. (**B**) Individual trials for TA1 following a ramp target with the *proportional* closed-loop disabled (top) and enabled (bottom). The red dotted line indicates the ideal EMG target trajectory that the participant needs to voluntarily follow. Each subplot displays 5 trials conducted by the participant. (**C**) RMSE when following a target EMG trajectory with the *proportional* closed-loop disabled (black) and enabled (purple) across all able-bodied participants (n = 9; dots represent single trials; participants performed 5 trials per condition). (**D**) RMSE in trials performed by trans-radial amputees following a target EMG trajectory with the *proportional* closed-loops disabled (black) and enabled (purple) (n = 6; each dot represents a single trial, participants performed 5 trials per condition). (**E**) RMSE measured from each trans-radial amputee participant with the *proportional* closed-loop disabled (black) and enabled (purple) (participants performed 5 trials per condition).

Experiment IIIB: Proportional afferent feedback during grasping in amputees

Given the results on integration of a proportional stimulation into voluntary control in standardized conditions, we then aimed at adding this feedback strategy in a more natural functional task, where the effects may not only be of effective integration but also of functional benefits. To evaluate the effect of the proportional closed-loop control on grasping dexterity during real-life object manipulation with a prosthetic, we conducted additional assessments using the targeted box and block test (tBBT) [68]. The participants needed to move 9 blocks from one compartment to another separated by a partition. Each block needed to be transported one by one in a specific order to a defined target location. The improvement in the manual dexterity was evaluated by measuring the time needed to successfully transport all 9 blocks from one compartment to the other. The number of times that the blocks fell during the task were also counted and used as slipping indicator of the prosthesis control. Only participants TA2, TA4, TA5 and TA7 participated in this task due to time constraints in the experiments with the other participants. In the tested participants, while not significant different [$p = 0.25$], we observed a decrease in the time needed to transport all the blocks when the *proportional* closed-loop was enabled (Fig. 6A) to 51.08 ± 9.62 s (Movie S1) compared to when it was disabled, 63.83 ± 23.22 s (Movie S2). In addition, the number of total block drops per trial decreased from 0.91 ± 0.90 drops/block to 0.33 ± 0.65 drops/block when the *proportional* closed-loop was enabled (Fig. 6B). The observed reduction in the time required to complete the task and in the number of drops among amputee participants in a functional task suggests the potential assistance provided by *proportional* closed-loop control in developing muscle contractions for transporting the blocks during the task.

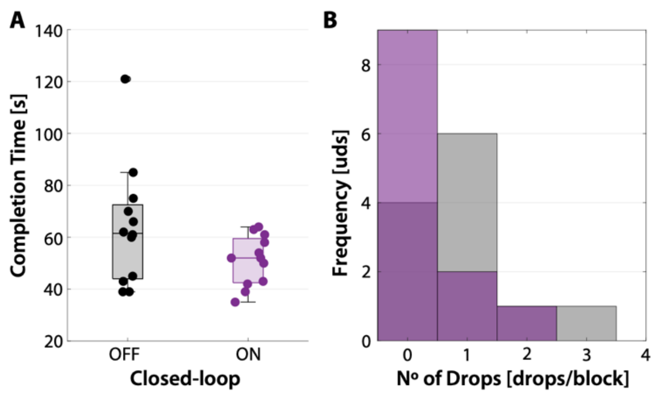

Fig. 6. Prosthesis control manoeuvring with proportional closed-loop. (A) Competition times and **(B)** histogram of number of drops for targeted Box and block test when using Taska hand with the *proportional* closed-loop disabled (black) and enabled (purple) across trans-radial amputee participants ($n = 4$; dots represent individual trials; participants performed 3 trials per condition).

DISCUSSION

Effective sensory-motor control requires the contribution of both supra-spinal and spinal circuits to regulate the input to motor neurons controlling muscle activation. Here, we have proposed a new framework for sensory feedback for prosthesis control based on the use of natural spinal reflex circuits. Our proposed framework aims to actively control the modulation of the afferent inputs to motor neurons. This becomes an additional source of synaptic input to spinal motor neurons modulating the output of the motor neurons. The output of the motor neurons then determines the level of muscle activity, which is used as control signal, thus effectively closing the sensory-motor loop at the spinal level. To validate the concept, we presented results involving both able-bodied and amputee participants who performed various physiological and functional motor tasks. During these tasks, we applied tendon vibration in a closed-loop manner to modulate input to motor neurons, thereby influencing the motor command through muscle activation. Results suggested that this stimulation can guide reflex changes in the motor neuron outputs to muscles and that participants can integrate this sensory input to adapt the motor commands to the muscles in order to ensure a correct motor performance.

We have proposed the control and integration of spinal reflex loops through peripheral sensory feedback to improve sensory-motor control in amputees. This approach facilitates corrective responses by modulating afferent inputs to motor neurons while preserving the users' voluntary input, thus maintaining a sense of control and ownership. This could potentially improve the overall control experience, making it more natural and intuitive compared to prosthesis with automated functions for adjusting the forces produced. The approach has been validated with the TVR, as a means to excite the sensory input to motor neurons. However, the same approach can be implemented with any other type of artificial stimulation of afferents, e.g. by direct nerve stimulation. For the control, we studied the afferent modulation of the motor output to mimic the reflex spinal circuits that fine-tune hand movements. For this purpose, we implemented an *intermittent* closed-loop paradigm that was able to actively modulate continuously the muscle output when the stimulation frequency was optimally selected for each participant. Additionally, we assessed the integration of the reflex loop by proposing an afferent stimulation with an amplitude *proportional* to the voluntary commands, which aimed to establish a positive feedback loop with motor neurons. These different implementations of closed-loop stimulation were integrated into the sensory-motor control of able-bodied and amputees. Additionally, integrating these closed-loop stimulation strategies into a prosthetic hand seemed to contribute to enhanced performance in functional tasks for amputees. The results demonstrated the possibility to control and integrate the TVR effects into sensory-motor closed-loops, which may have positive effects on control performance as well as in prosthesis embodiment.

For the initial physiological characterization, in agreement with the literature, there was a positive correlation between the TVR effects and the frequency of stimulation. For this specific stimulation setup, 80 Hz had the lowest rate to elicit clear TVR effects and the highest effects were observed in the range of 120 and 140 Hz for both able-bodied and amputee participants. In [65], 150 Hz was found to be the upper threshold frequency to elicit TVR responses, which is similar to our upper limit of 140 Hz.

The *intermittent* closed-loop paradigm was able to control the effects of the TVR and actively modulated the EMG level in able-bodied participants and trans-radial amputees in standard laboratory tests. As hypothesized, the functional effect on the able-bodied participants was negligible, presumably because the control in these individuals was already optimal. Conversely, the *intermittent* strategy improved the overall performance of the amputees. More importantly, the inclusion of the *intermittent* closed-loop to the prosthetic system seemed to improve fine object manipulation during the functional tests in amputees. The participants had to maintain the grasp of an object without exceeding a threshold force level and without slippage of the object. This task requires the participant to maintain a steady muscle contraction for prolonged object holding, increasing slippage risk. The inclusion of *intermittent* closed-loop showed promise in maintaining a lower-amplitude force while reducing the number of drops, suggesting potential improvements in the stability and control of the prosthesis during object manipulation.

In a subsequent experiment, we successfully integrated the positive afferent input of the TVR during the *proportional* closed-loop stimulation paradigm. It is important to note that increasing the algorithm gain typically boosts the EMG level while also amplifying its variability. However, in our data analysis, we observed that the integration of afferent feedback from TVR did not lead to an increase in EMG variability. The inclusion of this additional sensory feedback did not substantially impact the baseline voluntary performance of able-bodied participants. Conversely, for trans-radial amputees, the voluntary performance to follow the EMG targets tended to improve when the proportional closed-loop was activated. In addition, the used stimulation strategy showed positive functional effects on the targeted box-and-block test. The positive feedback loop of the proportional sensory input appeared to amplify muscle contractions, resulting in a more stable grip as participants moved the blocks. This enhancement resulted in reduced completion times and lower number of drops when the *proportional* closed-loop was enabled. While we suggest that this afferent input might activate spinal circuits affecting the neural inputs to muscles, potentially contributing to a gradual enhancement in the embodiment and intuitiveness of prosthetic device control, further investigation is warranted. Additional measurements, such as force exertion or control output, should be included in future studies using the box-and-bock test to appropriately assess and determine the functional improvement caused by the stimulation in this type of functional tasks.

Overall, the results demonstrated beneficial functional effects in incorporating spinal loops into closed-loop applications for prosthesis control. Unlike previous claims [4], when these loops are integrated and controlled in a closed-loop, the resulting elicited reflexes can be effectively integrated or beneficial for the user. In optimal scenarios, the proportional addition of the afferent feedback to the voluntary command was able to improve the performance of participants to generate a certain level of muscle contraction. During afferent modulatory experiments, the *intermittent* closed-loop was able to modulate the neural input to the motor neurons and modulate the overall muscle output to reach a certain force target. By fine-tunning this concept, the closed-loop could be incorporated as a mechanism to modulate the grip command of the prosthesis and auto regulate the force to apply to an object. This type of functionality is automatized in some commercial prosthesis using embedded sensors to regulate grip forces applied to an object [69]. However, whenever these automatic functions are active, the user partially loses the ownership of the overall grip as the internal microcontroller takes over the voluntary inputs of the user. This lack of control ownership decreases the user's feeling of embodiment [21]. A similar effect would be felt if the proportional sensory input was added via software to the control signal rather than processed through the physiological integration at the motor neuron level. The potential benefit of the spinal feedback proposed here is that it could incorporate these automatic functions for grasping manipulation while maintaining a regulatory voluntary input from the user and with a natural integration of inputs that does not feel as an artificial change in the prosthesis commands. Moreover, this automatic mechanism engages the remaining muscles of the stump as they are being modulated by the spinal reflex closed-loops. These findings suggest the potential effectiveness of the afferent closed-loop in enhancing maneuverability and grip control during object manipulation, thereby contributing to improved functionality and usability of the prosthesis in real-world scenarios.

A limitation of the current study is the observed variability in the results among participants, which can be due to intrinsic or extrinsic factors of the stimulation interface. There are additional intrinsic stimulation factors than those stated in this study that need to be addressed in order to tailor a stable interface. The stimulation point and area of stimulation are critical points to ensure the excitability of type Ia and type II sensory afferents. Moreover, the direct assessment of the Ia spinal reflex pathways, including tests like the H-reflex, would have been pivotal to confirm their role in eliciting the TVR. These additional measurements could have enhanced our understanding of the underlying mechanisms. Nevertheless, our experimental data complement existing literature, particularly within the selected stimulation frequencies known to induce a one-to-one response of muscle spindles. Importantly, it is worth noting that, in this study, our primary focus was on the excitatory effect of the TVR. However, a comprehensive understanding of the effects of TVR on agonist-antagonist relations could potentially contribute to a further understanding of muscle coordination and interaction. Additionally, an evaluation of the adaptability of these afferents to continuous stimulation needs to be assessed for long-term usage of these mechanisms in daily life for amputees. Ultimately, a direct selective nerve stimulation with electrode implants may result in a more specific activation, with less variability across subjects. The present work demonstrates a concept that can be translated in the future into more complex interfaces.

In conclusion, this study demonstrates the new concept of integrating sensory feedback into natural spinal sensory-motor control closed-loops. This approach naturally adds an involuntary component to the neural drive to the muscles that in turn generates the motor control signals for external devices. The method allows for the first time to restore a continuous sensory contribution to the neural commands to external devices. These results may have an impact in the performance and embodiment of prostheses.

MATERIALS AND METHODS

Study design

The study included two experimental sessions run on separate days for able-bodied participants. Upon analysing the results of the able-bodied participants, the experimental protocol was adapted to the trans-radial amputees also reducing the total experimental duration to one day. The experiments included ten able-bodied participants (four males and six females, age 25.8 ± 4.6 years) who were all right-handed. Additionally, six trans-radial amputees (two females and five males, age 41.28 ± 13.91 years) were recruited. TA1 had actively used a prosthetic for four years but ceased using it in the past two years. The remaining participants were current prosthetic users. Table 1 summarizes the information regarding the year of amputation, amputation level, and prosthetic usage. Due to time constraints, not all trans-radial amputee participants were able to complete the functional tasks. Informed consent was obtained from all participants prior to the experiments. The experimental procedure was approved by the Imperial College Research Ethics Committee (ref number 18IC4685).

Table 1. Clinical data of the recruited amputees in this study

Participant ID	**TA1**	**TA2**	**TA3**	**TA4**	**TA5**	**TA6**	**TA7**
Gender	Female	Female	Male	Male	Male	Male	Male
Age	37	35	21	54	33	47	62
Dominant	right	right	right	Ambidextrous	right	right	right
Amputation level	Trans-radial	Trans-radial	Trans-radial	Trans-carpal	Trans-radial	Trans-carpal	Trans-radial
Surgery type	Congenital	Traumatic	Congenital	Traumatic	Traumatic	Traumatic	Traumatic
Time of amputation	Congenital	6 years	Congenital	8 years	9 years	5 years	1987
Years using prosthetic	4 years	4 years	1 year	8 years	8 years	2 years	1989

Forearm diameter [cm]	22	22	19	25	29	24.5	22.5
Amputation length [cm]	10	21	7	23	12	17	16

Reflex-induced feedback and recording interface

During the experimental sessions, able-bodied participants were seated comfortably in front of a table with a bilateral force platform that restricted the forearm and hand of both arms of the participants. The platform was designed to measure isolated isometric flexion forces with the wrist (Fig. 7A). Both forearms were positioned parallel on a desk with elbows at a 120º angle. The palms of both hands were placed on the centre of hand rests and secured with Velcro belts, with palms perpendicular to the desk (wrists at 90º to the desk).

Tendon vibration was induced using a C2-HDLF tactor (Fig. 7B; Engineering Acoustics Inc., USA). This device allowed independent control of stimulation frequency and displacement amplitude. It could operate at frequencies up to 200 Hz, with amplitudes ranging from 0.6 to 1.3 mm (Fig. S1). To measure perpendicular forces between the stimulator tip and the skin, the tactor was modified to include an internal force sensor (FlexForce A101, Tekscan Inc., USA) (Fig. 7B). The stimulator was placed on the dominant arm's common flexor tendon using a soft strap to prevent vibration from affecting other muscles (Fig. 7-E), with a contact force of approximately 2 N. The tendon location was determined through palpation while the participant performed wrist flexion. In pilot tests, we found that higher effects were found when the stimulation was delivered at the proximal end rather than at the distal end of the muscle. In addition, the proximal end is the only area available for stimulation in amputees. Therefore, stimulation of the proximal end was used in all of our tests.

For able-bodied participants, the surface electromyographic (EMG) activity of their flexor carpi radialis (FCR) was acquired using a table-top amplifier (OT Quattrocento, OT Bioelettronica, Italy). Bipolar electrodes with a 2 cm interelectrode distance along the FCR was used to capture the surface EMG signals. The EMG data were sampled at 2048 Hz and filtered using a 2nd order digital Butterworth band-pass filter (passed band 20-500 Hz). To assess the level of muscle contraction, the root mean square (RMS) of the EMG signal was calculated in sliding windows of 160 ms with 120 ms overlap. The RMS signals were then normalized using the participant's EMG levels at rest and during a maximum voluntary contraction (MVC). The resulting normalized RMS EMG values served as a feedback signal, visually representing the level of contraction. In this manuscript, for simplicity, the normalized RMS EMG values are denoted as NormEMG.

To acquire EMG data from trans-radial amputees, a custom-made multichannel sEMG bracelet was developed (Fig. 7E). This bracelet replaced the commercial table-top amplifier to enable integration with the prosthetic hand in closed-loop experiments. The bracelet featured ten individual channels, each implementing dry active differential amplification to acquire EMG signals and minimize noise before amplification. Prior to placing the bracelet, the FCR was palpated, and a single channel was positioned atop it. The overall amplification gain was set to 812 V/V. Signals were filtered using a 2nd order Sallen Key hardware-based low-pass and high-pass filter with cut-off frequencies of 20 Hz and 500 Hz, respectively. An internal microprocessor within the bracelet converted the analogue EMG signals to digital data at a sampling frequency of 1 kHz with 12-bit precision. The processing of digital EMG signals followed a similar methodology to that used for EMG signals recorded with the commercial device in able-bodied participants.

The EMG signals and stimulation control were processed in Matlab (MathWorks, US) on a central computer with a custom interface. This interface executed real-time control closed-loops and calculated stimulation parameters. It featured a virtual environment displaying a visual representation of a cursor moving along a y-axis, where the limits corresponded to the NormEMG values ranging from 0% to 100%. This visualisation was used to indicate to the participant the level of muscle contraction at any given point in time based on the EMG activity.

A commercial hand prosthesis (Taska Prosthetics, New Zealand) was used to implement the reflex-induced feedback. The custom EMG interface and tactor stimulator were embedded on the Mitt sleeve (Koalaa LTD, UK), a soft socket sleeve which fastens with a BOA system (Fig. 7F). A custom adapter was designed to adapt the quick disconnect wrist system of the Taska Hand to the Mitt sleeve. The hand was configured in a pinch grip mode for object interaction, with the pinch aperture controlled by proportionally mapping the EMG output of the target stimulated muscle to the grip range of motion.

For the functional tasks with the prosthesis, a custom force-sensing object was developed (Fig. 7G). It consisted of a sliding cylindrical structure with a central load cell (FC2231-0000-0010-L, TE CONNECTIVITY, Switzerland). The upper side of the cylinder was adhered to the load cell, concentrating the exerted forces from the hand onto the shaft. The applied forces were perpendicular to the fingertips, with a maximum operating force of 10 lbs. The cylinder had a height of 7 cm to optimize the range of forces that the hand could apply to the object.

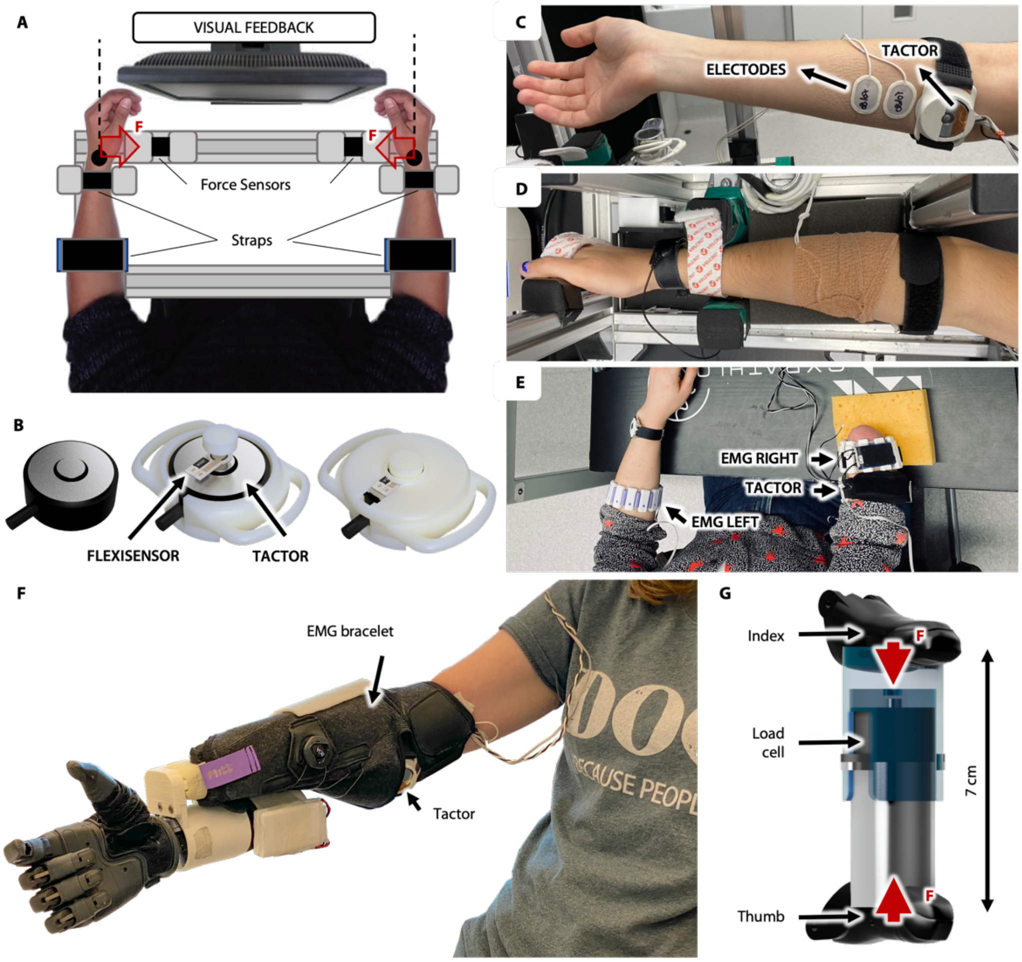

Fig. 7. Experimental setup. (A) Force platform setup, participants sat in front of a monitor with the arms strapped in supports to ensure the development of isometric contractions. Participants needed to exert isometric wrist flexion. A force sensor was embedded in the platform hand supports to record the exerted force by the participant. **(B)** Modified stimulator tactor to induce tendon vibration. A force sensor was embedded on the tactor stimulation contact point to measure the perpendicular force to the skin. **(C)** Electrodes and stimulation site in the experiments with able-bodied participants. **(D)** Forearm arrangement in the force platform to constrain movements and secure isometric wrist flexions. **(E)** Electrodes and stimulation arrangement in the case of trans-radial amputees. **(F)** Taska prosthesis mounted on the Mitt sleeve by a custom wrist adapter. EMG recording armband and stimulator tactors are in contact with the stump of the participant underneath the sleeve. (**G**) Custom force-object for force tracking tasks. The forces exerted by the hand are concentrated over the load cell shaft located in the centre of the cylinder structure.

Physiological evaluation of the TVR

This evaluation took place during the first day for able-bodied participants. The task involved exerting an isometric wrist flexion at 10% of the NormEMG, a level reported in the literature to facilitate TVR effects [21]. Initially, participants had 5 seconds of visual feedback to reach and stabilize the 10% NormEMG target. After this period, the visual feedback was disabled, and participants were instructed to maintain a constant muscle contraction level for 20 seconds. The tendon stimulation started 5 seconds after the trial started and lasted for 10 seconds. The tested stimulus frequencies were 0, 80, 100, 120, and 140 Hz, selected based on previous studies [49]–[51], [63], to determine conditions evoking the largest TVR effects. The stimulation amplitude was set to the maximum of the tactor (1.3 mm). Each frequency was presented randomly in two consecutive blocks of 5 trials (50 trials in total). For amputee participants, we adjusted the physiological evaluation to accommodate their time constrains. Based on results from able-bodied participants, we found that the first block of trials (5 per frequency) was sufficient to determine the optimal frequency and reduce experimental time for the amputee. Furthermore, the frequency of 80 Hz was excluded to the reduce experimental process as it had the least effect in all healthy participants.

Intermittent closed-loop tasks

To evaluate the afferent modulation of the motor output, we implemented an *intermittent* closed-loop. For able-bodied participants, this test took place on the second day, while for amputees, it was conducted within the same day. During the initial phase, all participants had an initial 5-second period with visual feedback enabled to reach an initial 10% NormEMG target. Following this period, the trial commenced.

The *intermittent* closed-loop compared the error between a given EMG target reference and the measured EMG levels. This error served as the feedback signal for the closed-loop in an on-off fashion, activating when the measured EMG level was below the target and deactivating when it was above the target. The performance of the closed-loop system is evaluated by the ratio of the root-mean-square values between the current EMG and the target level, providing insight into how effectively the closed-loop tracks the reference EMG target.

All able-bodied and amputee participants experienced the *intermittent* closed-loop at two stimulation frequencies: *optimal* (determined in the previous section) and *suboptimal*. The suboptimal frequency was set at 40 Hz to include a stimulation condition that should not evoke any TVR effect [65], [66]. The suboptimal implementation aimed to confirm that the results obtained with the optimal frequency were attributable to TVR effects on motor output. The performance of the *optimal* and *suboptimal intermittent* closed-loop conditions was compared to the pure *voluntary* performance, where participants followed the target EMG displayed in the visual interface. Each condition (*voluntary*, *optimal* closed-loop, and *suboptimal* closed-loop) was repeated five times.

Proportional closed-loop evaluation

A *proportional* closed-loop control condition was implemented to evaluate whether the TVR effects could be integrated with the participant voluntary control. This closed-loop was superimposed to the voluntary drive to create positive feedback and that way modulate the overall level of muscle activation. The closed-loop involved setting the stimulation frequency at the optimal value to evoke the TVR effect, while proportionally modulating the stimulation amplitude. This stimulation amplitude was linearly mapped from 0 to 100% based on the range of 0 to 25% NormEMG. This *proportional* range allowed for increasing stimulation amplitude as the exerted EMG increased, encompassing muscle contraction levels at which the TVR is prominent to drive and excite alpha motor neurons [66].

The evaluation tasks included following a ramp target with a slope of 0.75%/s for 20 seconds, starting at a level of 10% NormEMG. This slope was the average EMG increase gradient among participants during stimulation on pilot experiments. After the slope, there was a 5 second plateau at 25% NormEMG. The impact of the *proportional* closed-loop was assessed by the performance to follow the target with and without the closed-loop stimulation. This performance was measured by computing the root-mean-square error (RMSE) between the reference trajectory and the exerted EMG. Each condition was repeated five times.

Functional assessment of afferent closed-loop integration within the prosthesis

A linear regressor was implemented to proportionally control the grip opening and closing of the Taska hand in proportion to the RMS activity of the EMG channel corresponding to the flexor carpi radialis (FCR). This processing was performed internally by the EMG bracelet microcontroller. Both the *intermittent* and *proportional* closed-loops were implemented to operate in real-time with the prosthesis.

The targeted Box and Block Test was conducted as part of the *proportional* closed-loop assessment, following the predefined protocol in [68]. Participants were required to move 9 blocks from one compartment to another separated by a partition (Movie S1). Each block had a specific target location and order for transport. A successful transportation was achieved when the block lay flat in the target space. As the prosthesis passed over the partition, the task became more challenging due to the increased difficulty of maintaining a stable grasp while elevating the arm. The overall manual dexterity was evaluated by measuring the time taken to successfully transport all 9 blocks from one compartment to the other. The number of block slips during transportation served as an indicator of prosthesis control stability.

Statistical analysis

For the physiological experimentation, a repeated measures ANOVA with Tukey's honestly significant difference criterion was used for each participant to compare the ΔEMG elicited by the TVR at the proposed stimulation frequencies. The stimulation frequency that produced the highest ΔEMG was selected as the optimal stimulation frequency. For the *intermittent* closed-loop experimentation, the success rate was calculated and defined as the root-mean-square of the ratio between current RMS EMG and RMS target level. A repeated measures ANOVA was used to compare the success rate between the different closed-loop conditions: voluntary, optimal intermittent, and suboptimal intermittent. In the *proportional* closed-loop experimentation, the RMSE between the actual EMG level and the target EMG was calculated. A repeated measures ANOVA was used to compare the success rate when the closed-loop was enabled or disabled.

List of Supplementary Materials

- Movie S1: Box and block test with proportional closed-loop enabled.
- Movie S2: Box and block test with proportional closed-loop disabled.
- Figure S1: CD-HDLF amplitude displacements over frequency
- Text S1: Isolated motor output contributions by proportional stimulation

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