A myocontrolled neuroprosthesis integrated with a passive exoskeleton to support upper limb activities

Emilia Ambrosini [a,b,*], Simona Ferrante [a], Thomas Schauer [c], Christian Klauer [c], Marina Gaffuri [d], Giancarlo Ferrigno [a], Alessandra Pedrocchi [a]

[a] NeuroEngineering And Medical Robotics Laboratory, NearLab, Department of Electronics, Information, and Bioengineering, Politecnico di Milano, Italy
[b] Physical Medicine and Rehabilitation Unit, Scientific Institute of Lissone, Institute of Care and Research, Salvatore Maugeri Foundation IRCCS, Lissone, Italy
[c] Control Systems Group, Technische Universität Berlin, Germany
[d] Valduce Hospital, Villa Beretta, Rehabilitation Center, Costa Masnaga, Lecco, Italy

Received 15 April 2013
Received in revised form 13 December 2013
Accepted 17 January 2014

1. Introduction

Neuromuscular Electrical Stimulation (NMES) has been widely used to restore or replace impaired motor functions in people affected by neurological disorders, such as Spinal Cord Injury (SCI) (Gater et al., 2011), stroke (Ambrosini et al., 2011, 2012; Popović et al., 2009), or multiple sclerosis (Barrett et al., 2009).

When muscles are not completely paralyzed it is possible to use the neural information extracted from the EMG signals of the paretic limb to control the timing and the intensity of the stimulation, offering a promising solution for both assistive and therapeutic purposes (Jiang et al., 2010). Myocontrolled neuroprostheses might be used to augment the force produced by the paretic muscles so as to support the users during daily life activities but letting them directly control the execution of the movement (Pedrocchi et al., 2013). Furthermore, the therapeutic effects of NMES seem to be enhanced when NMES is applied co-incidentally with the voluntary drive (Fujiwara et al., 2009; de Kroon et al., 2005; Shindo et al., 2011). To explain these improved therapeutic effects, different hypotheses have been formulated, such as restorative synaptic modifications at the anterior horn cell level (Rushton, 2003), an enhanced cortical excitability (Barsi et al., 2008), and a better prediction of the sensory consequences of motor commands (Iftime-Nielsen et al., 2012).

During hybrid muscle activations, i.e. muscle contractions both volitional and electrically induced (Langzam et al., 2006), the overall EMG signal is due to the combination of these two components. A typical muscle response to electrical stimulation includes the stimulation artifact, a spike lasting few milliseconds after the electrical stimulus, and the M-wave, the compound action potential due to synchronous firing of the excited muscle fibers that can be more than one magnitude order larger than the volitional EMG (Langzam et al., 2006). To detect the EMG signal in the presence of electrical stimulation, blanking or resistor-diode circuits

* Corresponding author. Address: Piazza Leonardo Da Vinci 32, 20133 Milano, Italy. Tel.: +39 0223999509; fax: +39 0223999003.
E-mail address: emilia.ambrosini@polimi.it (E. Ambrosini).

must protect the amplifier inputs, and fast recovery from stimulation artifacts needs to be achieved (Merletti et al., 1992; Thorsen, 1999). Then, to estimate the volitional component a blocking window lasting half of the stimulation period is usually applied on the measured EMG (Langzam et al., 2006). However, since the M-wave spreads over the most of the stimulation period, the blocking window does not remove completely the electrically-induced components. For a more accurate estimate of the volitional EMG, different methods have been proposed. These methods can be classified in two categories: time-domain methods (comb filter (Frigo et al., 2000; Zhang and Ang, 2007), adaptive linear prediction filter (Sennels et al., 1997), optimum eigen filter (Yeom et al., 2007), singular value decomposition (Tabernig and Acevedo, 2008)), and frequency-domain methods (high-pass filters with a cut-off frequency of 200 Hz (Schauer et al., 2004) or 330 Hz (Muraoka, 2002)).

Two different approaches to control NMES based on the residual EMG of the stimulated muscle have been proposed in literature: EMG-triggered (Cauraugh et al., 2000; Saxena et al., 1995) and EMG-proportional (Fujiwara et al., 2009; Shindo et al., 2011; Thorsen et al., 2001; Yeom and Chang, 2010) controllers. In the first approach, the volitional EMG is used to trigger the onset of a predetermined stimulation sequence applied in an open-loop modality. This approach is robust and does not require special hardware and software solutions, but does not allow the subjects to switch off or modulate the stimulation intensity with their own volitional contractions. In the second approach, the stimulation intensity is modulated proportionally to the volitional EMG, thus assuring the synchronization between NMES and voluntary contractions. However, since the volitional EMG is usually low-pass filtered to avoid undesired jumps in the stimulation intensity, an additional time-delay is introduced in a loop with a human acting as feedback controller, potentially causing closed-loop instability. Furthermore, this approach requires smooth muscle contractions to avoid the risk of oscillations. For weak muscles, Sennels et al. (1997) suggested to use an on/off-control or a simple finite state control.

This work aimed at designing and testing a myocontrolled neuroprosthesis to support elbow flexion that could be exploited both as an assistive and a therapeutic system. The proposed system is a solution in between EMG-triggered and EMG-proportional controllers that allows the subject to autonomously activate and deactivate the stimulation support even in case of reduced residual muscle contractions. This neuroprosthesis was integrated with a passive exoskeleton for weight relief to further support the subject in case of severe muscle weakness. A reliable estimate of the volitional EMG in the presence of electrical stimulation is an essential requirement for the proper working of a myocontrolled neuroprosthesis. Since an agreement about the best filtering method for volitional EMG estimate was still missing, the performance of a time-domain (linear prediction adaptive filter (Sennels et al., 1997)) and a frequency-domain method (high-pass filter (Schauer et al., 2004)) were compared. Once identified the best filtering method, the control system was developed and its feasibility was assessed on healthy subjects and people with SCI.

2. Material and methods

2.1. Filters for the estimate of the volitional EMG – Stage A

2.1.1. Data collection

EMG signals were acquired on 10 healthy subjects with no history of muscle weakness or neurological disease (4 males and 6 females, mean age of 26.2 ± 2.9 years) and on 8 neurological patients. Table 1 reports the details of the patients (A1–A8). All recruited patients had a low to mild spasticity on the biceps and triceps muscles (Modified Ashworth Scale $\leqslant 2$). The protocol was approved by the Ethical Committee of the Valduce Hospital and all subjects signed a written informed consent.

A 25-Hz biphasic electrical stimulation was applied to the biceps brachii muscle through surface self-adhesive 50×50 mm electrodes (PALS® Platinum, Axelgaard Manufacturing Ltd.) using a current-controlled stimulator (Rehastim™, HASOMED). The elbow angle was measured with a goniometer (Biometrics Ltd.). EMG signals were recorded using Ag/AgCl pre-gelled self-adhesive electrodes (contact size of 30×22 mm) with an inter-electrode distance of 3 cm. The recording electrodes were placed between the stimulation electrodes perpendicular to the muscle fibers direction. This placement was preferred to the one proposed by SENIAM (Hermens et al., 2000) since it reduces the electrically elicited components (Frigo et al., 2000). The ground electrode was placed on the muscle belly. Before attaching the electrodes, the skin was cleaned and abraded until an impedance lower than 10 kΩ was achieved. Data were acquired with a multi-channel signal amplifier (Porti 32™, TMS International) and sampled at 2048 Hz.

Table 1
Clinical and demographical details of the neurological patients recruited for both stage A (analysis of the filters performance) and stage B (testing of the myocontrolled neuroprosthesis).

Subject	Age (years)	Sex	Pathology	Time since injury	Motricity index[a]			
					Pinch grip (0–33)	Elbow flex. (0–33)	Shoulder abd. (0–33)	Total (0–100)
Stage A								
A1	27	M	Incomplete SCI (C2–C3), ASIA C	1 years, 1 month	33	33	33	100
A2	48	F	Hemorrhagic stroke, left-side hemiparesis	1 years, 6 months	19	19	19	58
A3	57	M	Incomplete SCI (C5–C7), ASIA A	2 years, 10 months	19	19	19	58
A4	44	M	Incomplete SCI (C3–C4), ASIA C	2 years, 10 months	19	19	19	58
A5	47	M	Tetraparesis due to syringomyelia secondary to Arnold Chiari malformation	15 years	22	25	25	73
A6	50	M	Incomplete SCI (C2–C3), ASIA A	20 years	11	9	9	30
A7	42	M	Hemorrhagic stroke, right-side hemiparesis	2 months	11	25	25	62
A8	45	M	Ischemic stroke, right-side hemiparesis	2 years, 1 months	11	25	25	62
Stage B								
B1	33	M	Incomplete SCI (C7–T1), ASIA A	1 years, 7 months	11	14	14	40
B2	50	M	Incomplete SCI (C2–C3), ASIA A	20 years	11	9	9	30
B3	71	M	Incomplete SCI (C3–C4), ASIA C	1 years, 3 months	22	19	19	61

[a] The Motricity Index score was assessed for the arm involved in the experimental trials.

A preliminary trial on one healthy volunteer was carried out. The subject received an ON/OFF pattern of stimulation to the biceps muscle (current amplitude of 15 mA; pulse width, PW, of 300 μs) and was instructed to add the volitional effort required to execute an anti-gravity elbow flexion when the stimulation was ON. Three repetitions were performed in three different conditions: free arm; holding a weight of 1 kg; holding a weight of 2 kg.

Then, both healthy volunteers ($N = 10$) and patients ($N = 8$) were involved in the following experimental procedure (stage A). Each subject seated with the forearm lying on the table and the elbow flexed at 145° ± 5°, as shown in Fig. 1a (180° indicates fully extended elbow). The PW was set at 300 μs, while two values of current amplitude, C1 and C2, were identified on each subject, as the values needed to induce an elbow flexion of 60° and 20°, respectively. Each trial consisted of five consecutive phases (Fig. 1b):

(0) 10 s of rest (stimulation off and no volitional contractions);
(1) an electrically-induced elbow flexion of 60° maintained for 5 s (stimulation current C1 and no volitional contractions);
(2) an electrically-induced elbow flexion of 20° maintained for 5 s (stimulation current C2 and no volitional contractions);
(3) a volitional and electrically-induced elbow flexion of 60° maintained for 5 s (stimulation current C2 plus volitional contractions);
(4) a dynamic elbow flexion induced by 5 triangular stimulation profiles (maximal stimulation current C1 and no volitional contractions).

Each subject repeated the trial 5 times. At the beginning of each trial, the subject was asked to perform a maximal isometric voluntary contraction (MVC).

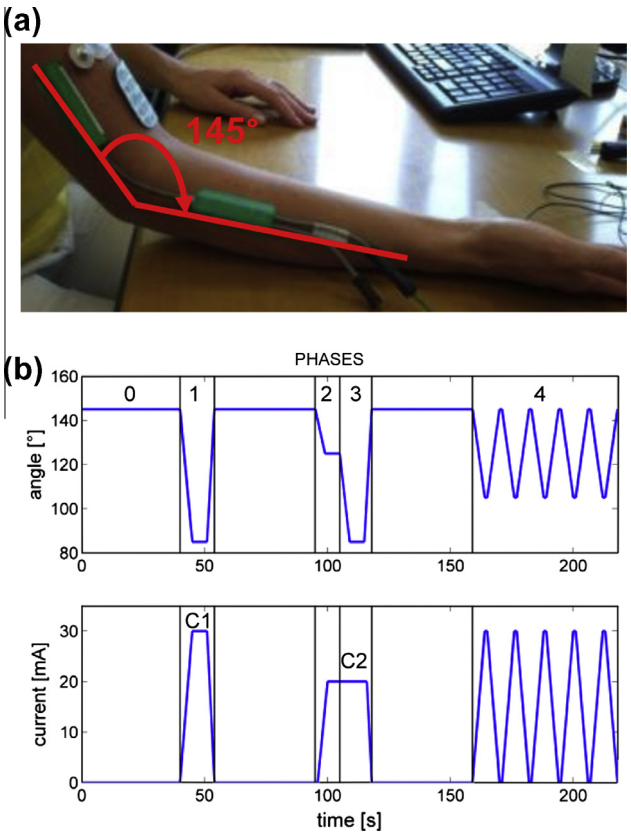

Fig. 1. Panel (a) shows a healthy subject during data collection. Panel (b) shows an example of elbow angle and stimulation current during the five phases of the experimental procedure (stage A).

2.1.2. EMG signal processing

Fig. 2 shows the processing scheme applied on the measured EMG signal at each stimulation period to estimate the volitional component. A blocking window lasting 20 ms and 27 ms for the adaptive and the high-pass filter, respectively, was applied. Then, either the adaptive filter or the high-pass filter was used. The estimated volitional EMG was fully-rectified and the mean value was computed.

2.1.2.1. Adaptive filter. Based on the assumptions that the M-wave is a time-variant signal and the volitional EMG is a band-limited signal with a Gaussian distribution, an adaptive linear prediction filter was proposed (Sennels et al., 1997). The filtering idea is to predict the current stimulation period ($M + 1$) from a linear combination of M foregoing stimulation periods. The output of the filter was computed as:

$$EMG_v(n) = EMG_f(n) - \sum_{j=1}^{M} b_j EMG_f(n - jN) \quad (1)$$

where EMG_v is the voluntary EMG estimated by the filter, EMG_f is the measured EMG after windowing and high-pass filtering (see Fig. 2), M is the number of previous stimulation periods ($M = 6$) used for prediction, and N is the number of samples of each stimulation period.

The optimal filter coefficients (b_j) were updated after each stimulation period (i.e., at a rate equal to the stimulation frequency) by solving a least square algorithm, where the output energy of the current stimulation period was minimized with respect to the filter coefficients. To solve the least square algorithm the Cholesky decomposition was used.

2.1.2.2. High-pass filter. About 20 to 30 ms after the stimulation pulse, only low frequency electrically-induced components affect the measured EMG signal. These components were eliminated by applying a non-causal digital high-pass filter with a cut-off frequency of 200 Hz to the windowed EMG (EMG_{w2} in Fig. 2) of each stimulation period (Schauer et al., 2004). An infinite impulse response Butterworth filter (2nd order) was used. It should be noticed that the most of the spectral energy of the volitional EMG signal is located between 30 and 300 Hz with a peak around 120 Hz. Thus, using this filter, only higher frequency components were considered.

2.1.3. Statistical analysis

The output of the two filters ($eEMG_v$ in Fig. 2) was normalized to MVC. A two-factors repeated measures ANOVA (the filter as between-factor and the phase as within-factor) was performed to compare the performance of the two filters across the five different phases of the experimental procedure. The statistical analysis was performed separately on the two groups of subjects.

2.2. Design of the myocontrolled neuroprosthesis – Stage B

2.2.1. Control system

The control system was designed to allow the patients to activate and de-activate the stimulation support provided to the biceps exploiting their own residual muscle activation. To estimate the volitional EMG the best filter identified from stage A was used. When the volitional EMG exceeded a threshold, $eEMG_v^{ON}$, the controller linearly increased the pulse width with a slope of K (0.001) till the maximal value (400 μs), and then kept it constant. As soon as the volitional EMG dropped below a lower threshold, $eEMG_v^{OFF}$, the pulse width was gradually reduced (Fig. 3). The smooth increase and decrease of PW avoided jerky muscle contractions. The stimulation frequency was fixed at 25 Hz, while the

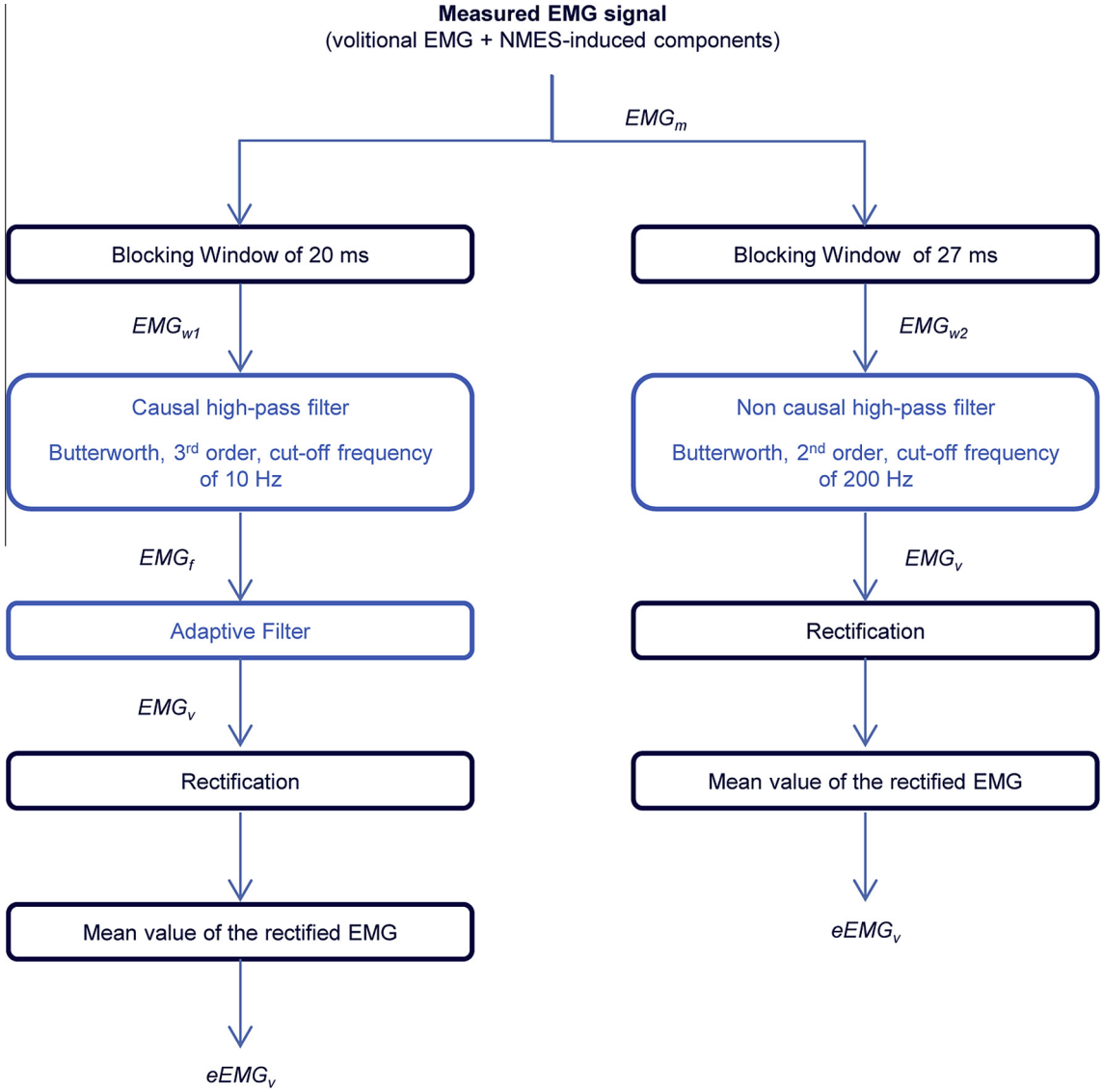

Fig. 2. Signal processing scheme of the EMG signal.

thresholds and the current amplitude were subject-specific and identified through a fast calibration procedure. First, the maximal volitional EMG without NMES support was measured, and $eEMG_v^{ON}$ was set to 20% and 80% of this value, for healthy and patients respectively. Then, the current amplitude was fixed at a value producing a visible movement within the patient's tolerance constraint with a pulse width of 400 μs. Using these stimulation parameters and asking the subject to be relaxed, $eEMG_v^{OFF}$ was set to 120% of the estimated volitional EMG. The identified thresholds were checked for feasibility and robustness: $eEMG_v^{ON} \geq 2\ eEMG_v^{OFF}$. Using the proposed control system, the subject could adjust his/her volitional effort during stimulation in order to achieve the desired joint angle.

2.2.2. Experimental setup

The experimental setup (Fig. 3) consisted of the stimulator (Rehastim™, HASOMED), the signal amplifier (Porti 32™, TMS International), a lightweight passive exoskeleton for weight compensation, and a PC running Scilab/Scicos under RTAI-Linux. The exoskeleton provided 3 degrees of freedom: shoulder elevation in the sagittal plane, shoulder rotation in the horizontal plane, and elbow flexion–extension (Reichenfelser et al., 2012). The electrodes and their placement were identically to the ones described in Section 2.1.1.

2.3.3. Subjects

Two healthy subjects (both females, 29 and 34 years old) and three people with incomplete SCI were recruited. Table 1 reports the patients details (B1–B3). The protocol was approved by the Ethical Committee of the Valduce Hospital and all subjects signed a written informed consent.

2.2.4. Experimental protocol

Subjects were asked to perform 8 repetitions of elbow flexion–extension with and without myocontrolled-NMES support, while tracking a trapezoidal target (increasing for 2 s, maintaining the flexed position for 6 s, and decreasing for 1 s). A trapezoidal target was chosen to measure the controllability of a dynamic movement and the ability to maintain a constant angle (Thorsen et al., 2001). The maximal level of the target was chosen at 90% of the maximal value of flexion the subject could reach with the myocontrolled-NMES support, so as to encourage him to commit to the trial. The starting value was identified for each subject as the most comfortable position.

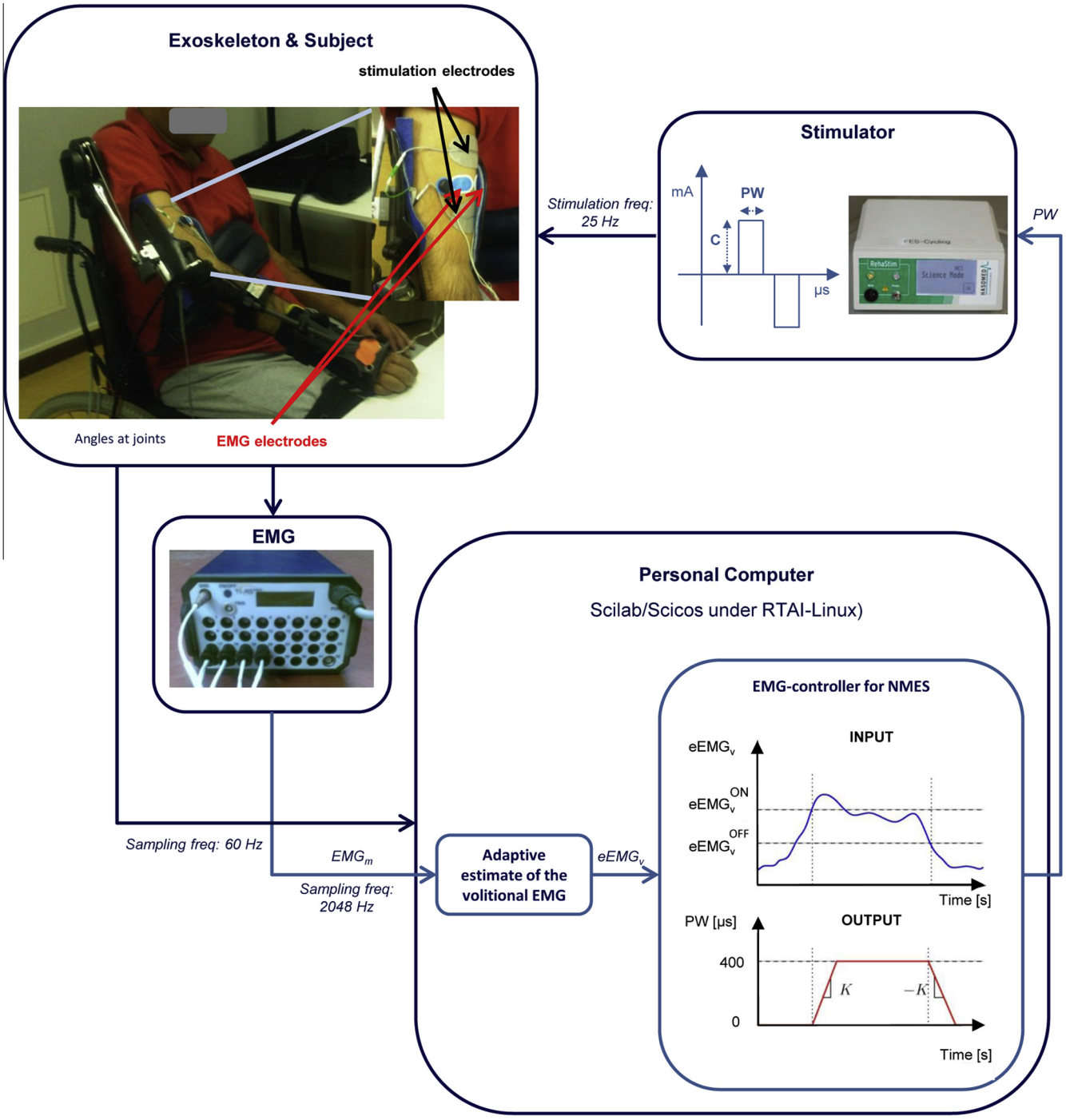

Fig. 3. Experimental setup (EMG_m: measured EMG; $eEMG_v$: volitional EMG; PW: pulse width; C: current amplitude).

2.2.5. Data analysis

To evaluate the tracking performance, the following parameters were computed for each repetition:

- the Root Mean Square Error (RMSE) between the actual and the target angle during the constant level of the target (*flat RMSE*);
- the integral of the volitional EMG (*int* $eEMG_v$).

A non-parametric Kruskal–Wallis test (p-value < 0.05) was performed to evaluate the effect of the myocontrolled-NMES support on the tracking performance for each subject.

3. Results

3.1. Estimate of the volitional EMG – stage A

Figs. 4 and 5 provide a qualitative comparison between the output of the two filters. In both figures, the upper panels represent the EMG signals measured during 20 consecutive stimulation periods (the stimulation artifact was removed), while the middle and the lower panels depict the volitional EMG estimated by the adaptive and the high-pass filter, respectively. Fig. 4 shows the results of a healthy subject during an anti-gravity elbow flexion without any

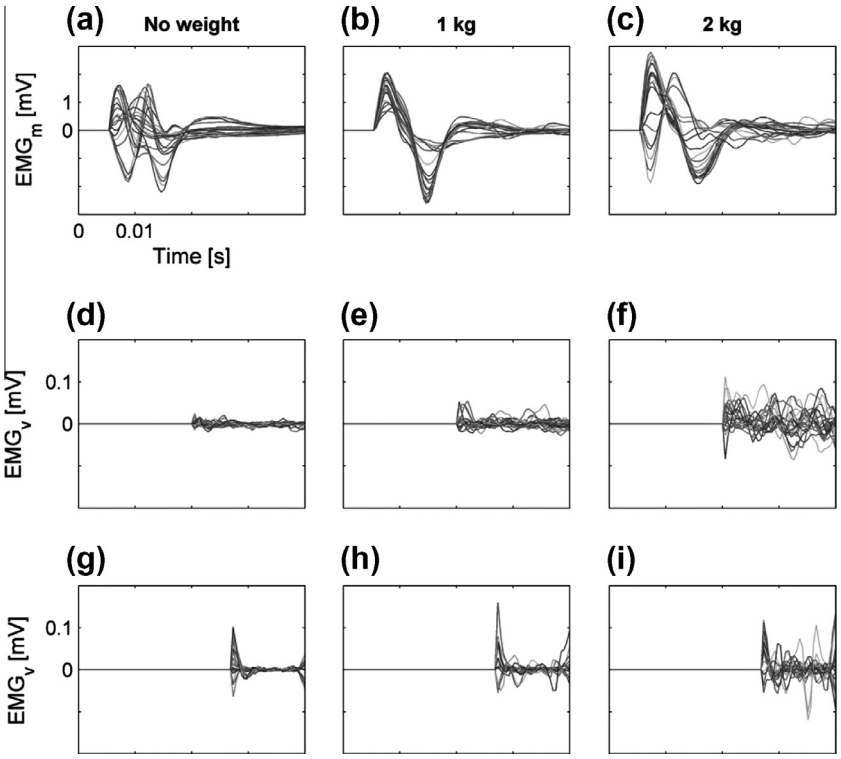

Fig. 4. Results of a healthy subject during dynamic hybrid biceps contractions, without any load, holding a 1 kg- and a 2 kg-weight. Panels (a–c) report the measured EMG. The volitional EMG estimated by the adaptive and the high-pass filter are shown in panels (d–f) and (g–i), respectively.

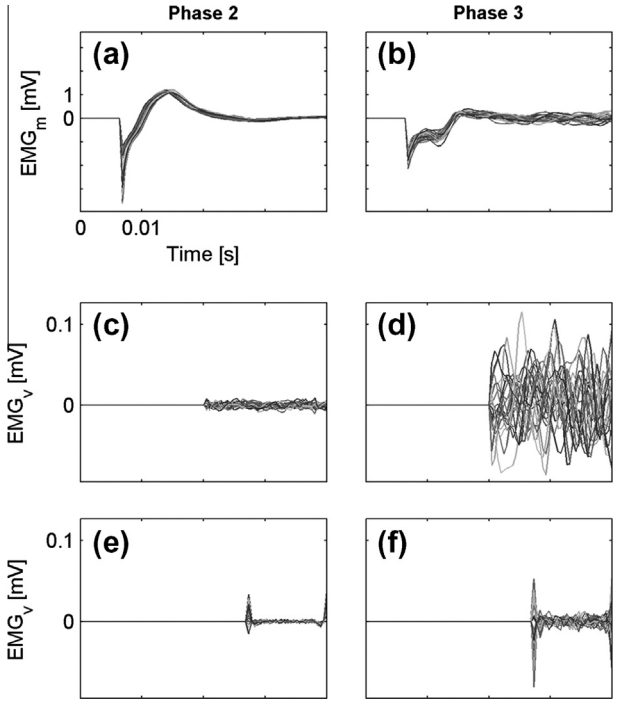

Fig. 5. Example of data collected on a patient (A4) during two phases of the stage A – experimental procedure (phase 2: stimulation C2, no volitional; phase 3: stimulation C2 plus volitional). Panels (a and b) report the measured EMG. The volitional EMG estimated by the adaptive and the high-pass filter are shown in panels (c and d) and (e and f), respectively.

load, holding a 1 kg- and a 2 kg-weight. The amplitude of the volitional EMG increased among the three experimental conditions, as expected: the value of $eEMG_v$ increased from 3.5 ± 1.5 μV (no weight), to 6.9 ± 4.0 μV (1 kg), and 19.5 ± 11.1 μV (2 kg) and from 12.1 ± 7.8 μV (no weight), to 18.7 ± 10.1 μV (1 kg), and 35.6 ± 17.0 μV (2 kg) for the adaptive and the high-pass filter, respectively, suggesting a better ability of the adaptive filter in discriminating between different levels of volitional effort. Fig. 5 reports an example of data acquired on a patient (A4) during two phases (phase 2, stimulation with no volitional contribution, and phase 3, stimulation plus volitional contribution) of the stage A – experimental procedure. The adaptive filter was better capable of estimating the volitional contribution during phase 3 (panel d), whereas both filters estimated only a small baseline activity during phase 2 (panels c and e). Furthermore, in both Figs. 4 and 5, it can be noticed that, besides using a longer blocking window, the high-pass filter was characterized by a distortion of the output especially around the edges.

Fig. 6 shows the results of the statistical comparison between the two filters: the normalized volitional EMG during the five phases of the experimental procedure obtained for both the healthy subjects (panels a and b) and the neurological patients (panels c and d) are represented. For both groups, significant effects of filter ($p = 0.017$ for healthy subjects; $p < 0.001$ for patients), phase ($p < 0.001$ for healthy subjects; $p < 0.001$ for patients) and filter by phase interaction ($p = 0.001$ for healthy subjects; $p < 0.001$ for patients) were found. Regarding the healthy subjects group, the post hoc analysis (Scheffè test) indicated significant differences ($p < 0.05$) between phase 0 (rest) and all the other phases as well as between phase 3 (stimulation plus volitional contraction) and all the other phases for the adaptive filter; for the high-pass filter a significant difference between phase 0 and all the other phases and between phase 3 and phase 4 was found. Regarding the patients group, a significant difference between phase 3 and all the other phases was found for the adaptive filter, while phase 0 was significantly different from all the other phases for the high-pass filter.

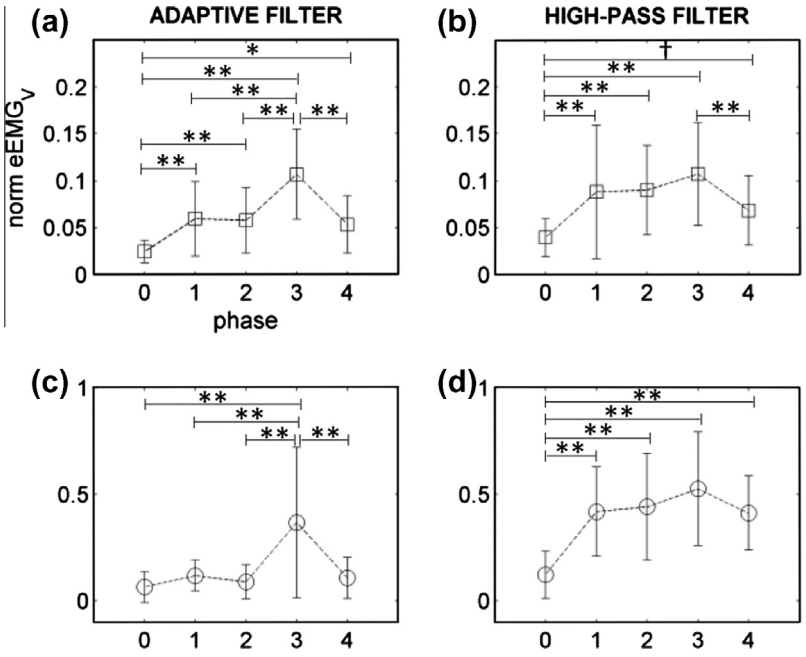

Fig. 6. Results of stage A: normalized volitional EMG estimated by the two filters (phase 0: rest; phase 1: stimulation C1, no volitional; phase 2: stimulation C2, no volitional; phase 3: stimulation C2 plus volitional; phase 4: variable stimulation, no volitional). Mean values and standard deviation (vertical bar) computed for both the healthy subjects ($N = 10$) and the neurological patients ($N = 8$) are shown in panels (a and b) and (c and d), respectively. *Indicates $p = 0.002$; †Indicates $p = 0.015$; **Indicates $p < 0.001$.

The high-pass filter estimated higher values of normalized volitional EMG than the adaptive filter when stimulation was provided and no volitional effort was required (phases 1, 2, and 4), indicating that it was not able to totally remove the electrically induced components. The adaptive filter better rejected these components, thus being able to distinguish even low levels of volitional EMG in the presence of NMES. Therefore, the adaptive filter was preferred to the high-pass filter and was used for estimating the volitional EMG at the input of the NMES controller.

3.2. Myocontrolled neuroprosthesis – stage B

Some representative repetitions of the tracking trials are shown in Figs. 7 and 8 for B1 and B2, respectively. In both figures, panels (a and b) show the actual (solid line) and the target angle (dashed line), while panels (c and d) depict the volitional EMG (solid line) computed by the adaptive filter. In panel (d), the corresponding value of PW delivered to the biceps (dashed line) is also reported. It can be noticed that for both patients the value of PW increased

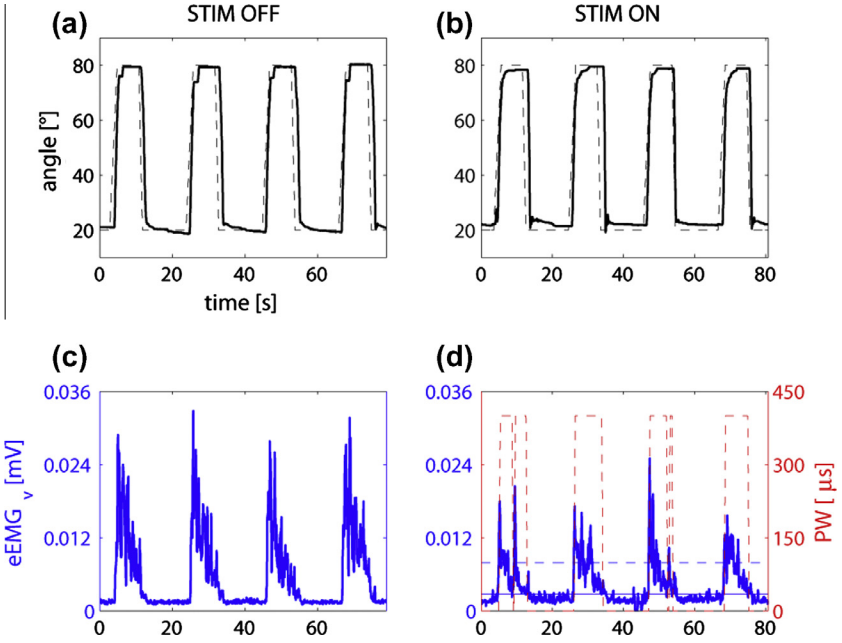

Fig. 7. Tracking performance of B1 during elbow flexion without and with myocontrolled-NMES support (stage B). The actual (solid line) and the target angle (dashed line) are shown in panels (a and b), while panels (c and d) represent the volitional EMG estimated by the adaptive filter. Panel (d) depicts the PW (dashed line) and the activation and de-activation thresholds (horizontal lines).

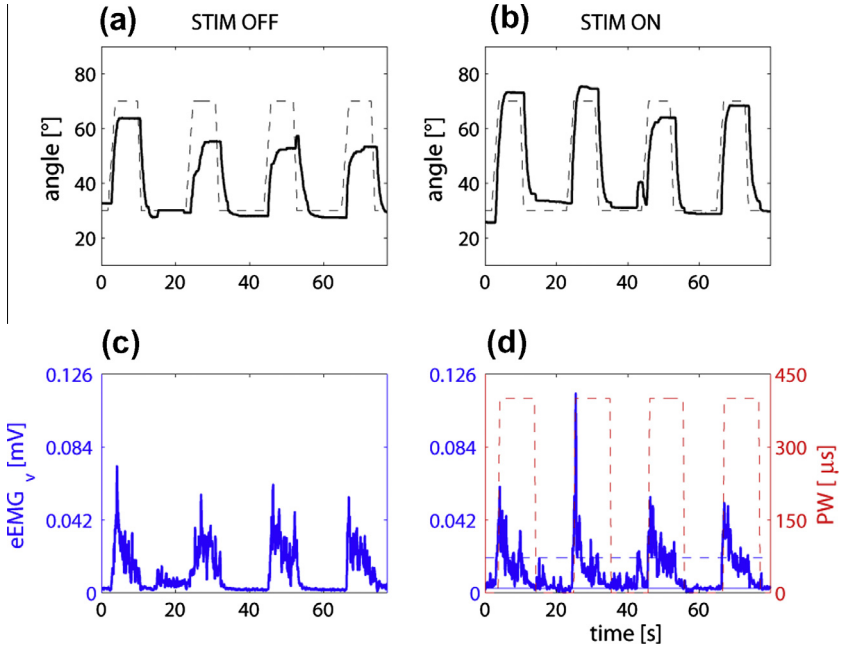

Fig. 8. Tracking performance of B2 during elbow flexion without and with myocontrolled-NMES support (stage B). The actual (solid line) and the target angle (dashed line) are shown in panels (a and b), while panels (c and d) represent the volitional EMG estimated by the adaptive filter. Panel (d) depicts the PW (dashed line) and the activation and de-activation thresholds (horizontal lines).

Table 2
Performance of the healthy subjects (H1 and H2) and the neurological patients (B1–B3) during the tracking trials with and without myocontrolled-NMES support (stage B).

Subject		Target (°)	Current	Flat RMSE (°)		*Int eEMG$_v$*	
H1	Without NMES	20–80		2.81 (1.92)[a]	0.683[b]	0.062 (0.014)[a]	<0.001[b]
	With NMES		8 mA	2.90 (2.92)[a]		0.051 (0.005)[a]	
H2	Without NMES	10–70		4.28 (2.33)[a]	0.552[b]	0.086 (0.003)[a]	0.012[b]
	With NMES		10 mA	4.01 (1.75)[a]		0.078 (0.008)[a]	
B1	Without NMES	20–80		2.8 (1.3)[a]	0.130[b]	0.100 (0.019)[a]	<0.001[b]
	With NMES		92 mA	3.6 (1.6)[a]		0.064 (0.007)[a]	
B2	Without NMES	30–70		18.7 (3.4)[a]	0.038[b]	0.191 (0.021)[a]	0.345[b]
	With NMES		10 mA	6.3 (2.9)[a]		0.201 (0.032)[a]	
B3	Without NMES	20–80		10.4 (15.9)[a]	0.016[b]	0.053 (0.009)[a]	0.002[b]
	With NMES		36 mA	3.2 (4.5)[a]		0.038 (0.009)[a]	

[a] Median (Interquartile range).
[b] *p*-Value, Kruskal Wallis test.

when the elbow flexion started while it was equal to zero in the resting phase between two consecutive repetitions. This suggests that the subjects were supported by NMES when desired and they were able to relax the biceps, although stimulated, to switch off the stimulation.

Table 2 outlines the subject-specific parameters and the tracking performances with and without myocontrolled-NMES support for the two healthy subjects and the three patients involved in stage B. For both the healthy subjects, no difference was found in the *flat RMSE* while a slight but significant decrease was obtained in terms of amplitude of the volitional EMG when NMES support was provided ($p < 0.001$ and $p = 0.012$ for H1 and H2, respectively). Two out of three patients (B2 and B3) significantly improved their tracking performance thanks to the NMES support (reduction of the *flat RMSE* of 66% for B2 and 69% for B3). The volitional EMG needed to execute the movement was significantly reduced when NMES was applied for B1 (reduction of about 40%) and B3 (reduction of about 30%), while no difference was highlighted for B2.

4. Discussions

Recent neurophysiological studies (Barsi et al., 2008; Iftime-Nielsen et al., 2012) advocated the use of NMES co-incidentally with the voluntary drive. Controlling the stimulation through the residual volitional EMG assures the association between the intended movement and the application of the stimulation. A reliable estimate of the volitional EMG able to detect even small muscle activations is an essential requirement for the development of such a control system. To fulfill this requirement, we compared, for the first time, the performance of a linear prediction adaptive filter and a high-pass filter in estimating the volitional EMG during dynamic hybrid muscle contractions of both healthy volunteers and neurological patients. On healthy subjects, both filters estimated higher amplitudes of volitional EMG when stimulation was provided without any additional voluntary activity than those estimated during the resting phase (EMG baseline). This suggests that either some residual electrically-induced components remained after fil-

tering or that the healthy volunteers were not able to be completely relaxed when NMES was provided. On the contrary, on patients the output of the adaptive filter when only stimulation was provided was comparable to the EMG baseline (phase 0), while for the high-pass filter phase 0 was significantly lower than all the other phases. In both groups, different current amplitudes and dynamic current modulation did not affect the output of the filters, but only the adaptive filter was able to significantly distinguish the phase during which a volitional activation was present from all the other phases. These results demonstrated the superiority of the adaptive filter in estimating the volitional EMG.

The adaptive filter was then included in the myocontrolled neuroprosthesis. An on/off non-linear control system was developed to allow even patients with a reduced muscle activity to continuously control the stimulation intensity. To further enlarge the number of patients who could benefit from the system, the developed neuroprosthesis was integrated with a passive exoskeleton for weight relief. Indeed, for patients affected by severe muscle weakness, NMES support might be not enough to guarantee the completion of antigravity movements. Looking at the Motricity Index, elbow flexion subscale (Table 1), 2 out of 3 patients (B1 and B2) were not able to perform an elbow flexion against gravity. The weight support provided by the exoskeleton allowed B1 to execute an elbow flexion of 60° even without NMES support.

The feasibility of the developed system was tested both on healthy volunteers and on people with SCI during elbow flexion. All subjects easily understood how to control the stimulation in a single session and succeeded in relaxing the biceps in the presence of stimulation. The tracking performance was not altered by NMES support on healthy subjects, suggesting that the myocontrolled neuroprosthesis did not affect the ability to execute the desired movements. In 2 out of 3 patients the myocontrolled-NMES support significantly improved the ability in reaching and maintaining a pre-defined level of elbow flexion. Indeed, the RMSE between the target and the actual angle was reduced for B2 and B3 till reaching values comparable to the ones obtained by the healthy subjects, thanks to an increased range of motion for B2 and a better ability in maintaining the required level of flexion for B3. These results highlighted that the myocontrolled neuroprosthesis effectively amplified the intention of the subjects, supporting them in the execution of the task. No improvements were highlighted for B1, since also without NMES support he achieved a tracking error similar to the one of the healthy subjects.

A reduction of the amplitude of the volitional EMG was observed in healthy subjects and in two patients when NMES support was provided. Different mechanisms might explain this reduction. It might be due to the support provided by NMES that reduced the volitional effort needed to execute the same movement. A reduced volitional effort might result in a reduction of fatigue, so as to prolong the interval the subject could successfully perform the task, especially when natural contractions elicited a reduced numbers of fibers, limiting the possibility of turnover. However, the reduction of the volitional EMG might also be explained by the collision of antidromic and orthodromic motor impulse and the increased recurrent inhibition (H. Yeom and Chang, 2010). B2 was the only subject who did not reduce the volitional EMG in the presence of NMES but he reached a wider range of motion with NMES support.

A limitation of the developed system is the use of different pairs of electrodes for recording and stimulating, that requires to place four electrodes for each target muscle. At the best of our knowledge, few systems to measure the EMG signals from stimulation electrodes have been proposed (Muraoka, 2002; Shalaby et al., 2011), but these systems do not allow to acquire the M-wave. However, the acquisition of the M-wave is required to estimate the volitional EMG using the adaptive filter, that our study demonstrated to be superior.

So far the controller did not include specific measures to compensate for muscle fatigue or any other time-variant disturbances (such as muscle tone), beyond the compensation eventually provided by the subject himself. For further compensations, an adaptation of the controller parameters might be introduced: the values of the EMG-thresholds might be updated when the estimated volitional EMG slowly changes from trial to trial; the current amplitude might be adjusted as well in order to favor the achievement of the desired joint angle.

Another limitation of the proposed neuroprosthesis is the possibility to use it only with patients with low to mild level of spasticity (Modified Ashworth scale $\leqslant 2$). Indeed, strong spasms would deteriorate the controller performance. However, this is a general limitation for the majority of NMES applications. Furthermore, although even patients with reduced muscle activity could benefit from the system, it is necessary that the activation threshold is at least the double of the deactivation threshold to avoid the risk of oscillation of the stimulation intensity.

This study provides an intuitive and feasible method to apply NMES co-incidentally with the voluntary drive also in case of weak muscle contractions. Such a method paves the way towards a better understanding of the benefits of combining NMES and voluntary effort. The system is modular and versatile: it can be easily extended to more than one muscles both of the upper and lower limbs. The integration with the exoskeleton agrees with the current trends to combine several means of assistance, robotics and NMES, to take benefits from the strength of each technology, overcoming the limited performance of each single approach. The proposed system might represent an interesting solution both as an assistive and rehabilitative system.

Conflict of interest

There are no conflicts of interest associated with this publication.

Acknowledgments

This work was partially supported by the European Project MUNDUS (FP7 ICT 2009-4; Grant Agreement No.: 248326). We would like to acknowledge Axelgaard Manufacturing Ltd for donating us the stimulation electrodes and all the people who agreed to participate to the study.

References

Ambrosini E, Ferrante S, Pedrocchi A, Ferrigno G, Molteni F. Cycling induced by electrical stimulation improves motor recovery in postacute hemiparetic patients: a randomized controlled trial. Stroke 2011;42:1068–73.

Ambrosini E, Ferrante S, Ferrigno G, Molteni F, Pedrocchi A. Cycling induced by electrical stimulation improves muscle activation and symmetry during pedaling in hemiparetic patients. IEEE Trans Neural Syst Rehabil Eng 2012;20:320–30.

Barrett CL, Mann GE, Taylor PN, Strike P. A randomized trial to investigate the effects of functional electrical stimulation and therapeutic exercise on walking performance for people with multiple sclerosis. Mult Scler 2009;15:493–504.

Barsi GI, Popovic DB, Tarkka IM, Sinkjaer T, Grey MJ. Cortical excitability changes following grasping exercise augmented with electrical stimulation. Exp Brain Res 2008;191:57–66.

Cauraugh J, Light K, Kim S, Thigpen M, Behrman A. Chronic motor dysfunction after stroke: recovering wrist and finger extension by electromyography-triggered neuromuscular stimulation. Stroke 2000;31:1360–4.

De Kroon JR, Ijzerman MJ, Chae J, Lankhorst GJ, Zilvold G. Relation between stimulation characteristics and clinical outcome in studies using electrical

stimulation to improve motor control of the upper extremity in stroke. J Rehabil Med 2005;37:65–74.
Frigo C, Ferrarin M, Frasson W, Pavan E, Thorsen R. EMG signals detection and processing for on-line control of functional electrical stimulation. J Electromyogr Kinesiol 2000;10:351–60.
Fujiwara T, Kasashima Y, Honaga K, Muraoka Y, Tsuji T, Osu R, et al. Motor improvement and corticospinal modulation induced by hybrid assistive neuromuscular dynamic stimulation (HANDS) therapy in patients with chronic stroke. Neurorehabil Neural Repair 2009;23:125–32.
Gater Jr DR, Dolbow D, Tsui B, Gorgey AS. Functional electrical stimulation therapies after spinal cord injury. NeuroRehabilitation 2011;28:231–48.
Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. J Electromyogr Kinesiol 2000;10:361–74.
Iftime-Nielsen SD, Christensen MS, Vingborg RJ, Sinkjaer T, Roepstorff A, Grey MJ. Interaction of electrical stimulation and voluntary hand movement in SII and the cerebellum during simulated therapeutic functional electrical stimulation in healthy adults. Hum Brain Mapp 2012;33:40–9.
Jiang N, Falla D, d' Avella A, Graimann B, Farina D. Myoelectric control in neurorehabilitation. Crit Rev Biomed Eng 2010; 38: 381–91.
Langzam E, Isakov E, Mizrahi J. Evaluation of methods for extraction of the volitional EMG in dynamic hybrid muscle activation. J Neuroeng Rehab 2006;3:27.
Merletti R, Knaflitz M, DeLuca CJ. Electrically evoked myoelectric signals. Crit Rev Biomed Eng 1992;19:293–340.
Muraoka Y. Development of an EMG recording device from stimulation electrodes for functional electrical stimulation. Front Med Biol Eng 2002;11:323–33.
Pedrocchi A, Ferrante S, Ambrosini E, Gandolla M, Casellato C, Schauer T, et al. MUNDUS project: multimodal neuroprosthesis for daily upper limb support. J Neuroeng Rehabil 2013;10:66.
Popović DB, Sinkaer T, Popović MB. Electrical stimulation as a means for achieving recovery of function in stroke patients. NeuroRehabilitation 2009;25:45–58.
Reichenfelser W, Karner J, Gfoehler M. Modular instrumented arm orthosis with weight support for application with NMES. Toledo, Spain: Springer; 2012. p. 1159–1163.
Rushton DN. Functional electrical stimulation and rehabilitation – an hypothesis. Med Eng Phys 2003;25:75–8.
Saxena S, Nikolic S, Popovic D. An EMG-controlled grasping system for tetraplegics. J Rehabil Res Dev 1995;32:17–24.
Schauer T, Salbert R, Negård N-O, Raisch J. Detection and filtering of EMG for assessing voluntary muscle activity during FES. In: 9th annual conference of the international FES society. Bournemouth, UK; 2004. p. 1–3.
Sennels S, Biering-Sørensen F, Andersen OT, Hansen SD. Functional neuromuscular stimulation controlled by surface electromyographic signals produced by volitional activation of the same muscle: adaptive removal of the muscle response from the recorded EMG-signal. IEEE Trans Rehabil Eng 1997;5:195–206.
Shalaby R, Schauer T, Liedecke W, Raisch J. Amplifier design for EMG recording from stimulation electrodes during functional electrical stimulation leg cycling ergometry. Biomed Tech (Berl) 2011;56:23–33.
Shindo K, Fujiwara T, Hara J, Oba H, Hotta F, Tsuji T, et al. Effectiveness of hybrid assistive neuromuscular dynamic stimulation therapy in patients with subacute stroke: a randomized controlled pilot trial. Neurorehabil Neural Repair 2011;25:830–7.
Tabernig CB, Acevedo RC. M-wave elimination from surface electromyogram of electrically stimulated muscles using singular value decomposition: preliminary results. Med Eng Phys 2008;30:800–3.
Thorsen R. An artefact suppressing fast-recovery myoelectric amplifier. IEEE Trans Biomed Eng 1999;46:764–6.
Thorsen R, Spadone R, Ferrarin M. A pilot study of myoelectrically controlled FES of upper extremity. IEEE Trans Neural Syst Rehabil Eng 2001;9:161–8.
Yeom H, Chang YH. Autogenic EMG-controlled functional electrical stimulation for ankle dorsiflexion control. J Neurosci Methods 2010;193:118–25.
Yeom HJ, Park YC, Chang YH. Eigen filter to detect volitional EMG signals in autogenic EMG-controlled FES. Electron Lett 2007;43:1410–1.
Zhang D, Ang WT. Reciprocal EMG controlled FES for pathological tremor suppression of forearm. Conf Proc IEEE Eng Med Biol Soc 2007;2007:4810–3.