POLITECNICO DI MILANO
Department Of Electronics, Information and Bioengineering
Master of Science in Biomedical Engineering

Neuroengineering Compendium - Neuroprostheses

Professor: Alessandra PEDROCCHI
Tutors: Eng. Alessandra TRAPANI

Academic Year 2021-2022

Chapter 1

Compendium organization

This part of the course compendium is composed by three published documents which have been all put together and made available to students, being only single chapters of the published books or open access.

Here are the full references of the sources.

Peri E., Guanziroli E., Ferrante S., Pedrocchi A., Molteni F. (2018) "Functional Electrical Stimulation and Its Use During Cycling for the Rehabilitation of Individuals with Stroke". In: Sandrini G., Homberg V., Saltuari L., Smania N., Pedrocchi A. (eds) Advanced Technologies for the Rehabilitation of Gait and Balance Disorders. Biosystems Biorobotics, vol 19. Springer, Cham. https://doi.org/10.1007/978-3-319-72736-3-21

Ambrosini, Emilia and Noelia Chia Bejarano, and Alessandra Pedrocchi. "Sensors for Motor Neuroprosthetics: Current Applications and Future Directions." In Emerging Theory and Practice in Neuroprosthetics. edited by Ganesh R. Naik , and Yina Guo, 38-64. Hershey, PA: IGI Global, 2014. http://doi:10.4018/978-1-4666-6094-6.ch003

Pedrocchi A.; S. Ferrante; E. De Momi; G. Ferrigno Error mapping controller: a closed loop neuroprosthesis controlled by artificial neural network 2006 JOURNAL OF NEUROENGINEERING AND REHABILITATION 3 1-13

https://jneuroengrehab.biomedcentral.com/articles/10.1186/1743-0003-3-25

Giorgio Sandrini · Volker Homberg
Leopold Saltuari · Nicola Smania
Alessandra Pedrocchi
Editors

Advanced Technologies for the Rehabilitation of Gait and Balance Disorders

Springer

Editors
Giorgio Sandrini
Department of Brain and Behavioural Sciences, University of Pavia
C. Mondino National Neurological Institute
Pavia
Italy

Volker Homberg
SRH Gesundheitszentrum
Bad Wimpfen
Germany

Leopold Saltuari
Department of Neurology
Hospital Hochzirl
Zirl
Austria

Nicola Smania
Department of Neurological, Biomedical and Movement Sciences
Verona University
Verona
Italy

Alessandra Pedrocchi
Department of Electronics, Information and Bioengineering
Politecnico di Milano
Milan
Italy

ISSN 2195-3562 ISSN 2195-3570 (electronic)
Biosystems & Biorobotics
ISBN 978-3-319-72735-6 ISBN 978-3-319-72736-3 (eBook)
https://doi.org/10.1007/978-3-319-72736-3

Library of Congress Control Number: 2017962982

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer International Publishing AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Functional Electrical Stimulation and Its Use During Cycling for the Rehabilitation of Individuals with Stroke

Elisabetta Peri, Eleonora Guanziroli, Simona Ferrante, Alessandra Pedrocchi and Franco Molteni

1 Introduction

Stroke is a neurological deficit due to an acute injury of the central nervous system with a vascular cause [1]. According to WHO data, it is one of the major causes of long-term disability, affecting 15 million people worldwide [2], of whom a third remains permanently disabled. Stroke therefore has a high social and economic impact on society [3]. Despite considerable efforts to reduce the most important risk factors (high blood pressure and smoking), the incidence of stroke is continuously increasing due to the aging of the population [2]. Most (77%) stroke survivors experience a reduction of motor function resulting in locomotion impairment and thus a reduced quality of life [4].

Some spontaneous recovery of motor activity occurs in the first weeks after stroke as adaptive mechanisms intervene to reinforce the existing pathways and bring about structural and functional changes [5]. In particular, a reorganization of the neural tissues (neuroplasticity) results in a new functional architecture that is different for each patient and crucial to the long-term success of any rehabilitation intervention [6]. Therefore, novel therapeutic strategies in stroke should be aimed primarily at interacting with the phenomenon of neuroplasticity to promote motor recovery.

E. Peri (✉) · S. Ferrante · A. Pedrocchi
NEARLab, Department of Electronic, Information and Bioengineering,
Politecnico di Milano, Milan, Italy
e-mail: elisabetta.peri@polimi.it

E. Guanziroli · F. Molteni
Valduce Hospital, Villa Beretta Rehabilitation Center, Como, Italy

G. Sandrini et al. (eds.), *Advanced Technologies for the Rehabilitation of Gait and Balance Disorders*, Biosystems & Biorobotics 19,
https://doi.org/10.1007/978-3-319-72736-3_21

The use of technologically advanced tools to provide rehabilitation could be helpful to promote motor relearning and neuroplasticity. Functional electrical stimulation (FES), for example, is a technique that uses an electrical stimulus to induce a functional movement. The electrical pulse activates the axons of the intact lower motor neuron, producing an artificial muscular contraction. This system is used temporarily to facilitate recovery of muscle function and of voluntary control [7] in a large number of neurological diseases in which the lower motor neuron is intact, such as stroke [8–11], spinal cord injury (SCI) [12], multiple sclerosis [13] and cerebral palsy [14, 15]. Traditionally, it has been used to treat gait dysfunction in hemiplegic patients. This is because upper extremity FES systems have proven more difficult to employ than lower extremity systems designed to improve walking, which is a rhythmic activity with a standardized motor plan, largely controlled at spinal level [16]. Nevertheless, effective interventions on locomotion require extensive assistance during training because of the reduced balance, muscular strength and coordination of neurologically impaired patients.

A safe, inexpensive and easily controlled way to overcome these issues is to combine FES with the use of a cycle ergometer (FES-cycling). In this design, the stimulus is synchronized with the crank angle and the subject's residual voluntary effort can also be exploited.

FES-cycling is a means of obtaining intensive, goal-oriented, active and repetitive movement in the training of the paretic limb—all these features of the movement are recognized as key factors in facilitating motor relearning through neural reorganization and rewiring in the central nervous system [17].

Studies in post-stroke patients suggest that locomotion improvements can be achieved by means of cycling training [18, 19]. In fact, cycling and walking share certain peculiarities: both involve repetitive movements with coordinated activation of the lower limb muscles that alternate flexion and extension of the hip, knee and ankle in a predetermined way [20].

This chapter focuses on FES and FES-cycling systems used to promote motor recovery in post-stroke patients. It is divided into five sections: in the first, the neurophysiological principles of FES are described. The second focuses on the neuroplasticity changes occurring after a FES treatment; the third looks at cycling training as a means of regaining locomotion ability, and the fourth deals with the therapeutic effects that can be observed in the stroke population. The final section considers future directions in this field.

2 The Neurophysiological Basis of FES

FES is based on the delivery of an electrical volley to excitable tissue, which produces an artificial contraction of the corresponding motor unit [21]. The peculiarity of FES within the field of electrical stimulation techniques is the fact that the alternating sequences of artificial contractions serve to produce a functional movement [7].

Electrical stimulation is generally used to activate nerves rather than muscles, because the activation threshold of intact lower motor neuron axons is lower than that needed to directly activate muscle fibers [22]. Thus, FES can only be used to rehabilitate subjects whose lower motor neurons are intact from the anterior horns of the spinal cord to the neuromuscular junctions in the muscles that are to be activated. Thus, not all pathologies can be targeted with FES. Moreover, FES is effective when the lower motor neurons are excitable and the neuromuscular junction and muscle are healthy. Stroke, head injuries, SCI, cerebral palsy and multiple sclerosis usually meet these conditions [7].

When a current is delivered to a volume of tissue between two stimulation electrodes (an anode and a cathode), a localized electric field creates an ionic flux. In the vicinity of the cathode, a depolarization can be observed and, if its values are higher than a critical threshold, the migration of sodium ions from the extracellular space to the intracellular space generates an action potential that propagates in both directions from the stimulation site [7], as schematically shown in Fig. 1.

Since the majority of the axons are organized into sensory and motor fibers, the action potentials travel in both orthodromic and antidromic directions along the two types of fiber, as shown in Fig. 2. This means that there is an afferent volley that

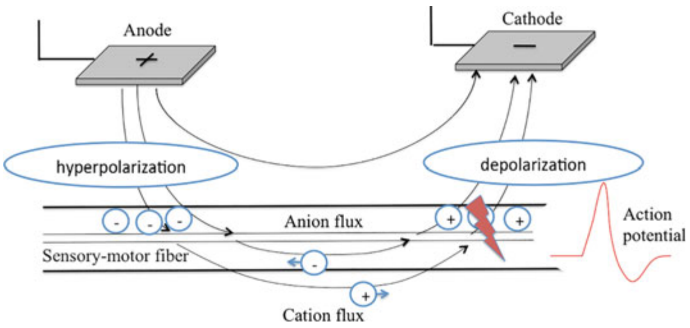


Fig. 1 Neurophysiological principles of FES

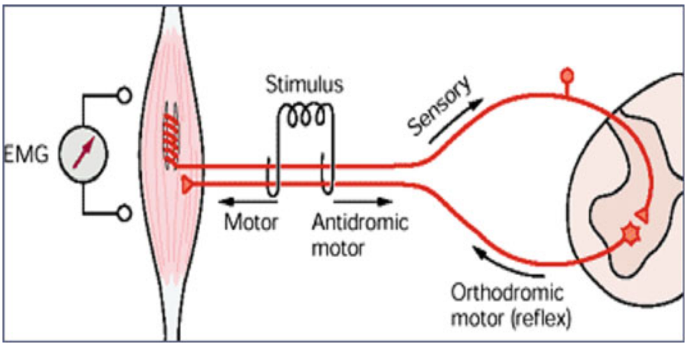


Fig. 2 Afferent and efferent stimuli induced by peripheral stimulation. Adapted from Kandel et al. [23]

reaches the spinal cord and the brain in parallel with an efferent volley that reaches the muscles. This effect is the basis of neuroplasticity facilitation, which is better described in the next paragraph.

When the current is delivered to the tissue, the order of recruitment of motor units is different from that occurring in physiological conditions. First of all, the orientation of the nerve fibers and their distance from the stimulation electrodes plays a major role: the sequence of activation seems to be from superficial to deep muscle layers, and this has the effect of reducing the physiological turnover of the motor units [24, 25]. This mechanism is called spatial summation. Second, the large-diameter axons (strong but not fatigue-resistant fibers), responsible for the larger motor units, are activated before the others at the same distance from the stimulation site, since they have a lower activation threshold than small axons (fine movement, fatigue-resistant fibers). This is due to the larger distance between nodes of Ranvier in large axons, which results in larger induced transmembrane voltage changes [7, 21]. This recruitment mechanism is the opposite of the physiological mechanism that, in accordance with the Henneman principle, ensures less muscle fatigue and a more accurate modulation of force [26]. Another difference compared with physiological contraction is due to the occurrence, at a certain stimulation frequency, of synchronous activation of the motor units which intervenes in the movement (temporal summation), limiting the natural turnover of the fibers. The results of these recruitment mechanisms is a the rapid onset of muscular fatigue, and this is one of the main limitations of FES [21, 27].

To reduce this effect, the waveform of the stimulus can play a role. In fact the FES is delivered with a train of pulses that can be defined through three parameters, as summarized in Fig. 3: the frequency (f), the amplitude (I), and the pulse width (PW). High stimulation frequency increases the rate of muscle fatigue because of the cumulative effect of the twitches occurring within a short period of time (temporal summation). This parameter should, in any case, be higher than the fusion frequency (typically 12.5 Hz) in order to obtain a smooth muscular contraction.

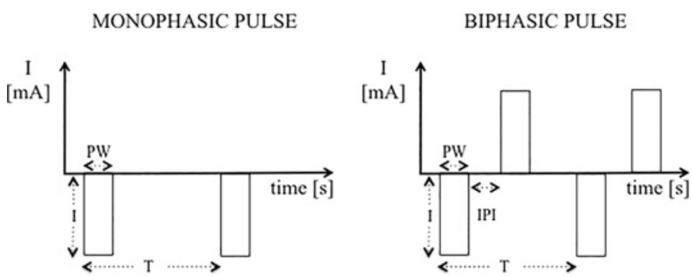


Fig. 3 Electrical stimulus waveform. Monophasic and biphasic pulses are reported in the left and right panel, respectively. The intensity (I), the inter-pulse interval (IPI), the pulse width and the period (T) (i.e. the inverse of the frequency f) are represented

Therefore, the strength of the muscular contraction is generally modulated via the PW and/or the I of the stimuli which act on the electric charge injected determining the spatial summation mechanism [7]. Typical working values are a frequency (f) of between 20 and 30 Hz, a current pulse width (PW) of between 100 and 500 μs, and an amplitude (I) of between 10 and 125 mA.

The pulses can be controlled in either voltage or current. The advantage of the voltage-controlled stimulator is that the current density is maintained below dangerous values in case of partial detachment of the electrodes. Instead, current-controlled stimulators are not affected by impedance variation due to the skin-electrode interface, thus they induce more reliable motor unit recruitment and are usually preferred in clinical applications [28].

Moreover, each waveform can have a biphasic or monophasic shape [7, 29], as shown in Fig. 3. Monophasic waveforms consist of repeated unidirectional pulses (usually cathodic), while biphasic waveforms comprise a cathodic pulse briefly followed by an anodic pulse. In this second configuration, the primary phase elicits axons located nearby, while the secondary positive pulse balances the charge injection of the primary pulse, preventing potential damage at the electrode-tissue interface. For this reason the biphasic configuration is usually preferred [7].

Surface, percutaneous and implanted electrodes can be used to deliver the electrical stimulus. Although surface electrodes have low selectivity for deep muscles [11], in rehabilitation applications they are commonly preferred thanks to their minimal invasiveness and the ease of donning and doffing [28]. For this reason, this chapter hereafter refers only to surface electrodes used for FES.

3 Neurological Changes Induced by FES for Rehabilitation Purposes

A core element of neurorehabilitation interventions is facilitation of cortical plasticity processes aimed at obtaining long-term potentiation of the motor cortex and motor recovery.

FES induces afferent and efferent pathway activation together with augmented proprioceptive and cutaneous inputs leading to augmented cortical and spinal activity. Combining these sensorimotor integration effects with goal-oriented, repetitive training could stimulate neural plasticity thus facilitating motor relearning [29].

Recent studies have looked at whether the motor recovery after FES-based rehabilitation could be, at least partially, ascribed to changes in cortical excitation and to brain reorganization mechanisms. A study in 10 healthy subjects showed a dose-response relationship between the stimulation intensity of FES delivered to the dominant quadriceps femoris muscle and the responses in sensorimotor brain regions contralateral to the stimulation [30]. Similar findings were obtained in a functional magnetic resonance imaging (fMRI)-based study in 12 healthy subjects in whom ankle dorsiflexion was induced by an active movement or by FES. During active dorsiflexion, greater activation in brain areas responsible for motor planning, execution and visual-motor coordination was shown, whereas the FES-induced movement produced greater activation in bilateral secondary somatosensory areas and in the insula. This finding is probably attributable both to increased sensory integration and to a nociceptive component due to the electrical stimulation [31].

The role, in motor relearning, of volitional effort concurrent with the movement induced by FES has also been widely investigated [29, 32]. These studies showed that volitional effort synchronized with an afferent volley produced by FES may produce some effects both at spinal [33] and cortical level [29, 32].

The spinal level was investigated by Rushton who hypothesized that the spinal cord anterior horn cells are Hebb-type cells, meaning that they are characterized by an increased firing rate if presynaptic and post-synaptic activities are coincident. Rushton suggested that the activity of Hebb-type synapses is significantly reduced after a brain injury because of the reduced descendent volley. Instead, when a neuromotor electrical stimulus is synchronized with the voluntary descendant volley, the antidromic pulses provide an artificial means of synchronizing presynaptic and post-synaptic activity, restoring the physiological synaptic condition [33] and providing a promising means of stimulating neuroplasticity.

At cortical level, Barsi and colleagues studied corticospinal excitability with transcranial magnetic stimulation (TMS) in a group of 25 healthy subjects who underwent three paradigms involving hand grasping: the first consisted of voluntary movement (VOL), the second exploited FES alone to accomplish the movement, while the third combined FES and voluntary movement (FES + VOL). Their findings showed that cortical excitability was increased by the FES + VOL paradigms much more than by FES or VOL alone, suggesting that the combination of voluntary effort and FES might have a greater potential to induce neuroplasticity [34]. Similarly, in a more recent study using fMRI during the same three paradigms in 17 healthy subjects, Iftime-Nielsen et al. showed that the cerebellum is better able to predict the sensory consequences of movement, reducing the subsequent activation in secondary somatosensory areas. This may reflect a better match between actual sensory feedback and an internal model [35]. With regard to the lower limb, ankle dorsiflexion was studied in four combinations: with and without volitional control and with or without FES. Both the primary motor cortex and primary somatosensory cortex showed a higher activation when the volitional control was combined with augmented proprioception due to FES, suggesting that this paradigm could promote the neuroplasticity changes at cortical level [36]. However, not all patients show carry-over effects. In a recent study on the neural correlates of FES, Gandolla et al. (2016) showed that only patients able to predict the movement and to perceive the stimulation as self-generated (sense of agency/body ownership) show carry-over effects, laying the basis for a prediction of carry-over effect in clinical settings [37].

4 Clinical Applications of FES and FES-Cycling

FES has consistently been shown to be beneficial for the rehabilitation of neuromotor-impaired subjects although no definite conclusions can be drawn concerning its superiority over other treatments [11, 38]. Patients seems to prefer it [11, 39].

A Cochrane review on the use of electrical stimulation for post-stroke rehabilitation which included 24 randomized controlled trials concluded that FES is an effective intervention to improve some aspects of functional motor ability and motor impairment and for promoting normality of movement. According to this review, FES was superior to conventional physical therapy only for the recovery of a few aspects of motor impairment. However, the authors underlined that no conclusion could be drawn due to the heterogeneity (in terms of type of electrical stimulation, dose of training and time since stroke) of the studies analyzed [38].

The main applications of FES for motor relearning in clinical practice can be divided into: FES during gait, electromyography-/biofeedback-mediated electrical stimulation and FES-cycling [29].

The very first use of FES for neuromotor impairment was in the form of a drop foot stimulator developed by Liberson and colleagues [40]. This application used single-channel stimulation of the peroneal nerve and a pressure sensor to detect the initial contact of the foot with the ground. In this context, repetitive movement training is carried out to accomplish a functional task that has a theoretical advantage with respect to conventional therapy. Nevertheless, it should be considered that in these applications the early onset of fatigue could dramatically reduce the dose of training and, consequently, the possibility of motor recovery. Bogataj and colleagues performed a 3-week controlled trial comparing the effects of a multichannel transcutaneous neuroprosthesis system (stimulation delivered to the soleus, hamstring, quadriceps femoris, gluteus maximus muscles) with respect to 3 weeks of conventional therapy. Significantly greater improvements in gait performance and motor functions were obtained by the FES group [41]. A more recent study (a multicenter, randomized, single-blinded trial) conducted in 197 post-stroke subjects compared the effect of 30 weeks' use of a foot drop stimulator or ankle-foot orthosis. The authors reported a significant improvement in gait speed in both groups, with no difference emerging from the between-group analysis [39].

Electromyography-/biofeedback-mediated electrical stimulation is based on the principle that combining afferent feedback with electrical stimulation-mediated repetitive training may stimulate corticospinal changes. EMG-triggered stimulation of the lower limb was delivered to 69 post-stroke patients who showed increases in voluntary EMG activity and mobility [42]. FES combined with biofeedback training was studied by Cozean and colleagues in 36 stroke patients who received 6 weeks of either control, FES, biofeedback or FES + biofeedback training. The authors reported that FES + biofeedback training was associated with improvements in knee and ankle joint angles during locomotion, velocity, and symmetry in stance [43]. It should be considered that these applications exploit patients' residual motor and cognitive ability. They may be not suitable for the most impaired subjects, especially during the post-acute phase of stroke when rehabilitation intervention is particularly important to trigger motor recovery.

FES-cycling is a safe, economical and widely accessible training method that combines a repetitive, goal-oriented task with sensorimotor information provided by FES, which thus facilitates neuroplasticity.

Motor impairments following a stroke often leave patients unable to walk. This is particularly true during the post-acute phase, when intensive intervention is recognized to be crucial to the subsequent motor outcomes. Functional training of patients with severe ambulatory limitations is often time consuming and costly, as extensive assistance is required during gait-related activities.

Studies suggest that pedaling could be a supplementary method for the recovery of walking. Indeed, it is safe, goal oriented and may avoid collateral risks due to the reduced motor activity (e.g. reduced cardiovascular performance and bone density). The pedaling motion in humans has been shown to activate some of the sensorimotor control mechanisms employed during locomotion [44] whose recovery is one of the main goals of post-stroke rehabilitation [8]. Moreover, as mentioned, cycling and walking share certain characteristics: both are rhythmic patterns that involve reciprocal flexion and extension of the hip, knee and ankles, with correct synchronization of agonist and antagonist muscles.

Studies in healthy subjects have shown that cycling training induces both short- and long-lasting changes in the spinal circuitry contributing to locomotion activity [44]. Similarly, it can be used to act on functional and motor abnormalities [44, 45], and to obtain improvements in aerobic fitness, balance and motor ability [46].

In this context, FES-cycling could be an effective intervention in post-stroke rehabilitation training. Severely impaired patients with no possibility of autonomous locomotion are eligible for a FES-cycling training, as it does not require residual motor activity and balance.

As described in Fig. 4, FES-cycling training can be delivered by means of a motorized cycle ergometer that imparts a smooth and safe pedaling motion to the patient' legs. The crank angle is used to deliver the stimulation synchronized with the pedaling phase in order to activate each muscle according to its physiological purpose (biomimetic stimulation strategy, Fig. 5), thereby promoting the motor relearning [9, 10]. Different stimulation paradigms can be used: FES during passive pedaling (during which the motorized cycle ergometer generates the movement) is widely used for the most impaired patients. FES-cycling can also be synchronized with a volitional effort that triggers the neuroplasticity facilitation mechanisms described above. Finally, patients can also be provided with visual biofeedback of the work produced by the two legs during volitional cycling augmented by FES. From a theoretical point of view, this should further enhance the neuroplasticity.

As can be seen in Fig. 4, the multichannel stimulation paradigms usually target different muscle groups that are massively involved both in walking and in cycling movements: the quadriceps femoris, the hamstrings, the gluteus maximus, the tibialis anterior and the gastrocnemius medialis or lateralis. The size of the stimulation electrodes placed over the muscle belly depends on the individual patient's

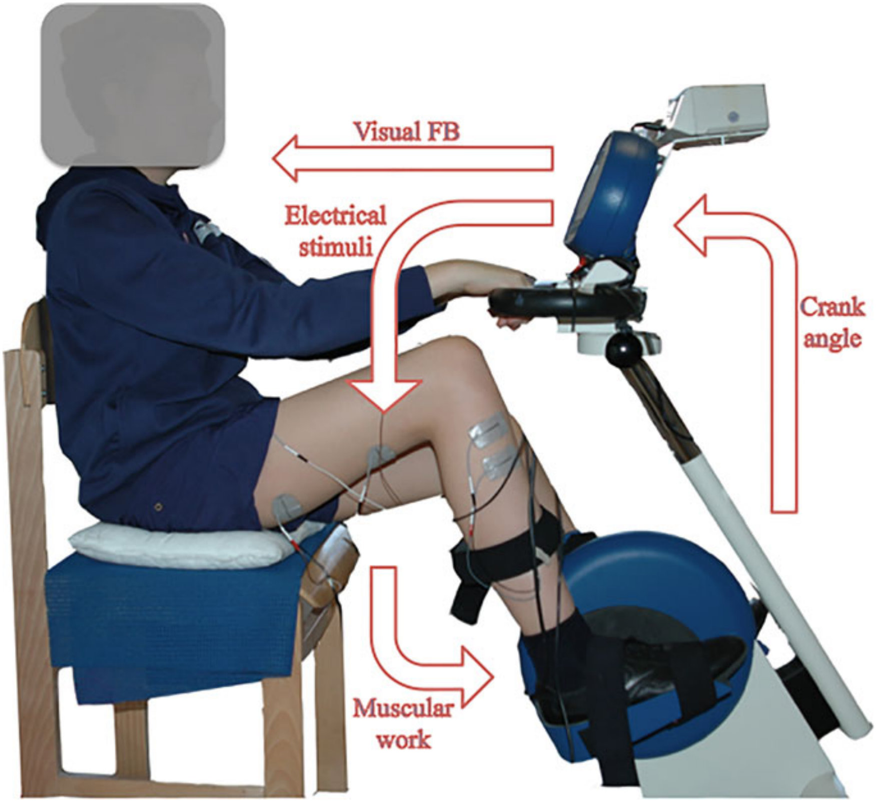
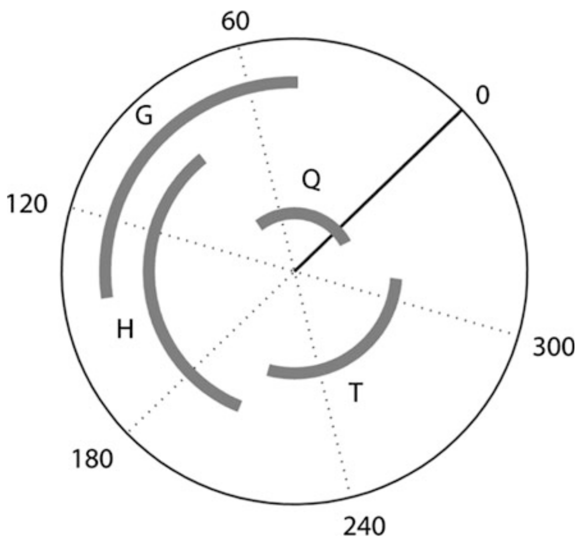


Fig. 4 A schematic representation of the FES-cycling, showing the cycle ergometer, the stimulator and the patient. The interactions between each block are also shown

Fig. 5 Stimulation ranges in a biomimetic strategy. 0: Corresponds to the maximal flexion of the hip. Q: Quadriceps. H: Hamstrings. T: Tibialis anterior. G: Gluteus maximus. Adapted from Ambrosini and colleagues [8]



anthropological dimensions. They are typically between 2″ × 2″ and 2″ × 5″ for adult patients.

Some commercial devices are currently available to provide FES-cycling training in clinical practice. Among others, the RehaStim stimulator (Hasomed GmbH) together with the MOTOmed cycle ergometer (Reck GmbH) and the RT300 (Restorative Therapies, Inc.) are widely used.

In recent years, FES-cycling has increasingly been used for lower limb rehabilitation of hemiparetic subjects.

Ferrante and colleagues studied the effect of FES-cycling training compared with standard physiotherapy in a group of 20 post-acute stroke patients. Both groups received a dose of training equal to 3 h per day for 4 weeks. The FES-cycling was applied daily for 35 min and the stimulation was delivered to the quadriceps, hamstring, gluteus maximus and tibialis anterior muscles bilaterally. After the treatment the FES-cycling group produced a significantly increased maximum isometric voluntary contraction of the quadriceps, with respect to the control group. Long-term effects were not investigated [10].

A subsequent work by Ambrosini and colleagues assessed the effectiveness of FES-induced cycling with respect to passive cycling in lower limb rehabilitation through a randomized controlled trial conducted in 35 post-acute hemiparetic subjects. Patients were randomly allocated to receive FES-cycling training (experimental group) or an equal dose of passive cycling training with FES placebo, i.e. the stimulation electrodes were placed over the lower limb but no stimulation was delivered (placebo group). The stimulation was delivered to the quadriceps, hamstrings, gluteus maximus and tibialis anterior of each leg via surface electrodes. The 4-week intervention consisted of 20 sessions, each lasting 25 min, with 5 min of passing pedaling, 15 min of FES-cycling or placebo FES-cycling, and 5 min of passive pedaling.

The experimental group showed significant improvements in terms of the Motricity Index, Trunk Control Test, and the Upright Motor Control Test, as well as gait speed, mean work of the paretic leg and unbalance of mechanical work between healthy and paretic legs, both after training and at a 6-month follow-up assessment. Instead, none of the outcome measures demonstrated significant improvements after training in the placebo group, strongly suggesting that a four-week FES-cycling training intervention, more than cycling training alone, improves symmetry, mechanical work and motor coordination in post-acute hemiparetic patients [8, 9].

Although the volitional volley is recognized to play a role in enhancing neuroplasticity, producing long-term potentiation of the recovery, residual voluntary effort was not exploited in the two studies mentioned above. Differently, Alon and colleagues performed a study in 10 stroke subjects who were trained 3 times a week for 8 weeks with 30 min of FES-cycling training with voluntary effort. The quadriceps, hamstring and dorsal and plantar flexors were involved in the stimulation. The results showed an improved locomotor capability in terms of gait velocity and time to stand up, proceed to walk 3 m, turn around, walk back and sit down. Moreover the peak pedaling power increased during the intervention [47].

An attempt to exploit both biofeedback and cycling paradigms coupled with FES was made by Ferrante and colleagues. Patients were provided with information about their performance (i.e. the symmetry of work produced by the two legs during pedaling) in the form of online visual biofeedback. A case-series study in 3 post-stroke patients showed that this training paradigm could be promising, especially for patients with a strongly asymmetrical locomotion pattern and slow gait velocity. However, further studies should be performed to confirm these findings in a larger sample [19].

5 Conclusion and Future Perspectives

Evolving studies on central motor neuroplasticity support the role of goal-oriented, repetitive, voluntary training to obtain long-term potentiation in post-stroke rehabilitation.

Combining this kind of training with the augmented proprioceptive and cutaneous afferents mediated by FES, the motor relearning effect could be potentiated via both cortical and spinal mechanisms.

For the most impaired subjects, who are not able to walk autonomously, a safe and widely accessible means of providing FES training is to synchronize the stimulation with a cyclic movement imparted by a cycle ergometer.

Although some studies have already shown valuable short- and long-term results after exploiting FES in post-stroke patients, a definitive conclusion cannot yet be drawn. Furthermore, given the substantial lack of shared guidelines that might lead to the choice of intervention protocols customized to the single subject and/or pathology, the results of different studies are often not comparable. Establishing an evidence-based protocol could be a key factor in extending the use of FES in clinical practice.

Future investigations should take the form of large, multicenter, randomized clinical trials to evaluate long-term outcomes, maybe also including direct assessment of cortical changes (i.e. fMRI or TMS).

Furthermore, new technological advances should be sought in order to maximally exploit the benefits of FES. One of the most promising approaches is the use of the volitional residual muscle activation to trigger the FES-induced contraction (neuroprosthesis based on myocontrolled FES), for both rehabilitation and assistive purposes [28]. This paradigm ensures that the voluntary contribution is exploited, and it is thus particularly interesting from the perspective of long-term potentiation. However, its use is still limited because it is technologically challenging and also requires residual voluntary control, which makes it unsuitable for the most impaired patients. Another possible future research direction is the use of a robotic exoskeleton to assist and complete the movement where the patient is not able to achieve this. At present, however, this hybrid approach is still limited, partly because the technology is not yet sufficiently developed to guarantee optimal physical and cognitive interaction with patients, and partly because of portability and energy management issues [48].

References

1. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, Elkind MSV, George MG, Hamdan AD, Higashida RT, Hoh BL, Janis LS, Kase CS, Kleindorfer DO, Lee JM, Moseley ME, Peterson ED, Turan TN, Valderrama AL, Vinters HV. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American heart association/American stroke association. Stroke. 2013;44(7):2064–89.
2. WHO. The atlas of heart disease and stroke. 2004.
3. Fattore G, Torbica A, Susi A, Giovanni A, Benelli G, Gozzo M, Toso V. The social and economic burden of stroke survivors in Italy: a prospective, incidence-based, multi-centre cost of illness study. BMC Neurol. 2012;12(1):137.
4. Bonita R, Beaglehole R, Bonita R, Beaglehole R. Recovery of motor function after stroke. Stroke. 1988;19:1497–500.
5. Brown JA. Recovery of motor function after stroke. Prog Brain Res. 2006;157:223–8.
6. Ward NS. Neural plasticity and recovery of function. Prog Brain Res. 2005;150:527–35.
7. Peckham PH, Knutson JS. Functional electrical stimulation for neuromuscular applications. Annu Rev Biomed Eng. 2005;7:327–60.
8. 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(3):320–30.
9. 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(4):1068–73.
10. Ferrante S, Pedrocchi A, Ferrigno G, Molteni F. Cycling induced by functional electrical stimulation improves the muscular strength and the motor control of individuals with post-acute stroke. Europa Medicophysica-SIMFER 2007 Award Winner. Eur J Phys Rehabil Med. 2008;44(2):159–67.
11. Kafri M, Laufer Y. Therapeutic effects of functional electrical stimulation on gait in individuals post-stroke. Ann Biomed Eng. 2015;43(2):451–66.
12. Gater DR, Dolbow D, Tsui B, Gorgey AS. Functional electrical stimulation therapies after spinal cord injury. NeuroRehabilitation. 2011;28(3):231–48.
13. 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. Multiple Sclerosis J. 2009;15(4):493–504.
14. Peri E, Ambrosini E, Pedrocchi A, Pagliano E, Riva D, Baranello G, Arnoldi MT, Foscan M, Corlatti A, Marchi A, Ferrigno G, Ferrante S. Volitional cycling augmented by functional electrical stimulation in hemiparetic adolescents: a case series study. J Autom Control. 2013;21(1):37–42.
15. Trevisi E, Gualdi S, De Conti C, Salghetti A, Martinuzzi A, Pedrocchi A, Ferrante S. Cycling induced by functional electrical stimulation in children affected by cerebral palsy: case report. Eur J Phys Rehabil Med. 2012;48(1):135–45.
16. Singer B. Functional electrical stimulation of the extremities in the neurological patient: a review. Aust J Physiotherapy. 1987;33(1):33–42.
17. Harvey RL. Improving poststroke recovery: Neuroplasticity and task-oriented training. Curr Treat Options Cardiovasc Med. 2009;11(3):251–9.
18. Brown DA, Nagpal S, Chi S. Limb-loaded cycling program for locomotor intervention following stroke. Phys Ther. 2005;85(2):159–68.

19. Ferrante S, Ambrosini E, Ravelli P, Guanziroli E, Molteni F, Ferrigno G, Pedrocchi A. A biofeedback cycling training to improve locomotion: a case series study based on gait pattern classification of 153 chronic stroke patients. J Neuroeng Rehabil. 2011;8(1):47.
20. Burnfield JM, Shu Y, Buster T, Taylor A. Similarity of joint kinematics and muscle demands between elliptical training and walking: implications for practice. Phys Ther. 2010;90 (2):289–305.
21. Grill WM, Mortimer JT. Stimulus waveforms for selective neural stimulation. IEEE Eng Med Biol Mag. 1995;14(4):375–85.
22. McNeal DR. Analysis of a model for excitation of myelinated nerve. IEEE Trans Biomed Eng. 1976;BME-23(4):329–337.
23. Kandel ER, Schwartz JH, Jessell TM. Principles of neural science 4th ed. New York: McGraw-Hill, Health Professions Division. 2000.
24. Knaflitz M, Merletti R, De Luca CJ. Inference of motor unit recruitment order in voluntary and electrically elicited contractions. J Appl Physiol. 1990;68(4):1657–67.
25. Farina D, Blanchietti A, Pozzo M, Merletti R. M-wave properties during progressive motor unit activation by transcutaneous stimulation. J Appl Physiol. 2004;97(2):545–55.
26. Mortimer JT. Comprehensive physiology. Hoboken, NJ, USA: Wiley; 2011.
27. Bickel CS, Gregory CM, Dean JC. Motor unit recruitment during neuromuscular electrical stimulation: a critical appraisal. Eur J Appl Physiol. 2011;111(10):2399–407.
28. Ambrosini E, Ferrante S, Pedrocchi A. Design of myocontrolled neuroprosthesis: tricks and pitfalls. Appl Challenges Adv Electromyogr Signal Process. IGI Global, 2014;275–303.
29. Sheffler LR, Chae J. Neuromuscular electrical stimulation in neurorehabilitation. Muscle Nerve. 2007;35(5):562–90.
30. Smith GV, Alon G, Roys SR, Gullapalli RP. Functional MRI determination of a dose-response relationship to lower extremity neuromuscular electrical stimulation in healthy subjects. Exp Brain Res. 2003;150(1):33–9.
31. Francis S, Lin X, Aboushoushah S, White TP, Phillips M, Bowtell R, Constantinescu CS. fMRI analysis of active, passive and electrically stimulated ankle dorsiflexion. Neuroimage. 2009;44(2):469–79.
32. Krakauer JW. Motor learning: its relevance to stroke recovery and neurorehabilitation. Curr Opin Neurol. 2006;19(1):84–90.
33. Rushton DN. Functional electrical Stimulation and rehabilitation—an hypothesis. Med Eng Phys. 2003;25:75–8.
34. Barsi GI, Popovic DB, Tarkka IM, Sinkjær T, Grey MJ. Cortical excitability changes following grasping exercise augmented with electrical stimulation. Exp Brain Res. 2008;191 (1):57–66.
35. Iftime-Nielsen SD, Christensen MS, Vingborg RJ, Sinkjær 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(1):40–9.
36. Gandolla M, Ferrante S, Molteni F, Guanziroli E, Frattini T, Martegani A, Ferrigno G, Friston K, Pedrocchi A, Ward NS. Re-thinking the role of motor cortex: context-sensitive motor outputs? Neuroimage. 2014;91:366–74.
37. Gandolla M, Ward NS, Molteni F, Guanziroli E, Ferrigno G, Pedrocchi A. The neural correlates of long-term carryover following functional electrical stimulation for stroke. 2016; (2016).
38. Pomeroy VM, King L, Pollock A, Baily-Hallam A, Langhorne P. Electrostimulation for promoting recovery of movement or functional ability after stroke. Cochrane Database Syst Rev. 2006; (2).
39. Kluding PM, Dunning K, O'Dell MW, Wu SS, Ginosian J, Feld J, McBride K. Foot drop stimulation versus ankle foot orthosis after stroke: 30-week outcomes. Stroke. 2013;44 (6):1660–9.

40. Liberson WT, Holmquest HJ, Scot D, Dow M. Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. Arch Phys Med Rehabil. 1961;42:101–5.
41. Bogataj U, Gros N, Kljajic M, Acimovic R, Malezic M. The rehabilitation of gait in patients with hemiplegia: a comparison between conventional therapy and multichannel functional electrical stimulation therapy. Phys Ther. 1995;75(6):490–502.
42. Fields RW. Electromyographically triggered electric muscle stimulation for chronic hemiplegia. Arch Phys Med Rehabil. 1987;68(7):407–14.
43. Cozean CD, Pease WS, Hubbell SL. Biofeedback and functional electric stimulation in stroke rehabilitation. Arch Phys Med Rehabil. 1988;69(6):401–5.
44. Mazzocchio R, Meunier S, Ferrante S, Molteni F, Cohen LG. Cycling, a tool for locomotor recovery after motor lesions? NeuroRehabilitation. 2008;23(1):67–80.
45. Meunier S, Kwon J, Russmann H, Ravindran S, Mazzocchio R, Cohen L. Spinal use-dependent plasticity of synaptic transmission in humans after a single cycling session. J Physiol. 2007;579(Pt 2):375–88.
46. Katz-Leurer M, Sender I, Keren O, Dvir Z. The influence of early cycling training on balance in stroke patients at the subacute stage. Results of a preliminary trial. Clin Rehabil. 2006;20 (5):398–405.
47. Alon G, Conroy VM, Donner TW. Intensive training of subjects with chronic hemiparesis on a motorized cycle combined with functional electrical stimulation (FES): a feasibility and safety study. Physiother. Res. Int. 2011;16(2):81–91.
48. del-Ama AJ, Koutsou AD, Moreno JC, delos-Reyes A, Gil-Agudo N, Pons JL. Review of hybrid exoskeletons to restore gait following spinal cord injury. J Rehabil Res Dev. 2012;49 (4):497.

Emerging Theory and Practice in Neuroprosthetics

Ganesh R. Naik
University of Technology Sydney (UTS), Australia

Yina Guo
Taiyuan University of Science and Technology, China

A volume in the Advances in Bioinformatics and Biomedical Engineering (ABBE) Book Series

Medical Information Science Reference
An Imprint of IGI Global

Managing Director: Lindsay Johnston
Production Editor: Jennifer Yoder
Development Editor: Allison McGinniss
Acquisitions Editor: Kayla Wolfe
Typesetter: Kaitlyn Kulp
Cover Design: Jason Mull

Published in the United States of America by
Medical Information Science Reference (an imprint of IGI Global)
701 E. Chocolate Avenue
Hershey PA 17033
Tel: 717-533-8845
Fax: 717-533-8661
E-mail: cust@igi-global.com
Web site: http://www.igi-global.com

Library of Congress Cataloging-in-Publication Data

Emerging theory and practice in neuroprosthetics / Ganesh R. Naik and Yina Guo, editors.
p. ; cm.
Includes bibliographical references and index.
Summary: “This book brings together the most up-to-date research surrounding neuroprosthetics advances and applications, presenting several new results, concepts, and further developments in the area of neuroprosthetics”--Provided by publisher.
ISBN 978-1-4666-6094-6 (hardcover) -- ISBN 978-1-4666-6095-3 (ebook) -- ISBN 978-1-4666-6097-7 (print & perpetual access)
I. Naik, Ganesh R., editor. II. Guo, Yina, 1981- editor.
[DNLM: 1. Neural Prostheses. 2. Biomedical Engineering--methods. 3. Brain-Computer Interfaces. WE 172]
R856
610.28--dc23
2014008005

This book is published in the IGI Global book series Advances in Bioinformatics and Biomedical Engineering (ABBE) Book Series (ISSN: 2327-7033; eISSN: 2327-7041)

British Cataloguing in Publication Data
A Cataloguing in Publication record for this book is available from the British Library.

Chapter 3
Sensors for Motor Neuroprosthetics:
Current Applications and Future Directions

Emilia Ambrosini
Politecnico di Milano, Italy & Salvatore Maugeri Foundation, Scientific Institute of Lissone, Italy

Noelia Chia Bejarano
Politecnico di Milano, Italy

Alessandra Pedrocchi
Politecnico di Milano, Italy

ABSTRACT

Clinical applications of Functional Electrical Stimulation (FES) provide both functional and therapeutic benefits. To enhance the functionality of FES systems and to improve the control of the activated muscles through open-loop or feedback controllers, solutions to gather information about the status of the system in real time and to easily detect the intention of the subject have to be optimized. This chapter summarizes the state of art of sensors used in motor neuroprostheses. These sensors can be classified in two categories: sensors of biological signals, such as electromyogram, electroencephalogram, electroneurogram, eye tracking, and voice control, and sensors of non-biological signals, such as sensors of force/pressure (e.g. force sensitive resistors and strain gauges) and sensors of movement (e.g. accelerometers, electrogoniometers, inertial measurement units, and motion capture systems). Definitions, advantages and disadvantages, and some example of applications are reported for each sensor. Finally, guidelines to compare sensors for the design of motor neuroprostheses are drawn.

INTRODUCTION

A neuroprosthesis is a device that uses electrical stimulation to activate the neuromuscular system in order to improve or substitute motor or sensory functions of an impaired central nervous system. This chapter is focused on motor neuroprostheses.

NeuroMuscular Electrical Stimulation (NMES) has been used for 50 years and has been well acknowledged to improve motor recovery and independence of people affected by neurological diseases. However, despite the significant technological progress of the last 20 years, many challenges remain to be resolved to provide a more

DOI: 10.4018/978-1-4666-6094-6.ch003

efficient functionality of NMES systems. Current commercial NMES systems still operate in an open-loop modality. This means that the stimulator's controller does not adapt the stimulation patterns based on a direct feedback of the actual state of the system (i.e., the spatiotemporal position of the limbs). In addition, a natural interaction with the system is not always made available to the subject. To improve the control of the stimulated muscles and the usability of these systems, solutions to gather information about the status of the system in real time and to easily detect the intention of the subject have to be optimized.

To promote the development of motor neuroprostheses and to favor their application outside the research environment, this chapter reviews the state of art of sensors used in FES systems to detect the intention of the user and/or to feed back information so as to develop closed-loop control systems. Some examples of sensors used to provide a quantitative assessment of the FES-induced movements are also reported.

The chapter is organized in three sections. The Background section provides an overall definition of NMES, sensors, and categories of sensors used in motor neuroprostheses. The central section lists the main sensors that have been used in literature to control NMES systems. This section is divided in two parts, one describing the biological sensors (such as electromyogram, electroencephalogram, eye tracking, etc) and one describing the non-biological sensors (force sensitive resistors, accelerometers, inertial measurements units, etc.). For each sensor, a brief description, advantages and disadvantages, and some examples of applications are provided. In the last section, future and emerging research directions are presented.

BACKGROUND

NMES refers to the electrical stimulation of an intact lower motor neuron to activate paralyzed or paretic muscles. Clinical applications of NMES provide either functional or therapeutic benefits. Moe and Post (Moe & Post, 1962) introduced the term functional electrical stimulation (FES) to describe the use of NMES to activate paralyzed muscles in precise sequence and magnitude so as to directly accomplish functional tasks. FES was started with the simple and ingenious idea of Liberson et al. (1961) of lifting the drop-foot of a hemiplegic patient with a portable electronic stimulator (Liberson, 1961).

Restoration of motor functions based on FES has been widely studied since the first developments by Vodovnik and Grobelnik (Vodovnik & Grobelnik, 1977). Clinical application provides both therapeutic and functional benefits by re-training atrophied muscles. Once trained, the muscles can be used again to generate functional movements. NMES is also used for therapeutic purposes. NMES may lead to a specific effect that enhances function but does not directly provide function. One therapeutic effect is motor relearning, which is defined as "the recovery of previously learned motor skills that have been lost following localized damage to the central nervous system" (Lee & van Donkelaar, 1995). Indeed, in addition to the well-known peripheral effects on muscles themselves, FES is considered to have some central therapeutic effects. Some hemiplegic patients treated with FES for foot-drop correction during walking have shown a relearning effect that outlasts the period of stimulation. This was firstly observed by Liberson and colleagues (Liberson, 1961) and it is currently known in literature as "carryover effect" (Ambrosini, 2012; Ambrosini, 2011; Burridge, 2001). However, we know from literature (Burridge, 2001; Merletti, 1979) and from clinical practice that it is not possible to infer which patient will get the carryover effect from a peripheral evaluation. This further supports the hypothesis that FES induces some plasticity mechanisms in the reorganization of the central nervous system that allows maintaining recovery of motor control, whose mechanisms of action are still under investigation, although some possibilities have been hypothesized (Bergquist, 2011; Gandolla, 2014; Rushton, 2003).

Sheffler and Chae in 2007 reviewed the use of FES in the clinical literature and offered a very clear statement: "evolving basic and clinical studies on central motor neuroplasticity supports the role of goal-oriented, active repetitive movement training of a paretic limb to enhance motor relearning" (Sheffler & Chae, 2007).

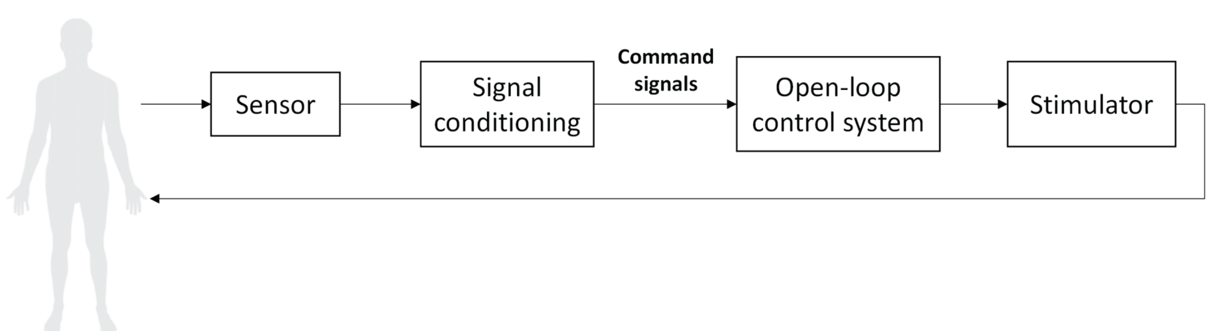
We want here to focus on what from a technological point of view is essential to assure a goal-oriented, active, repetitive movement training, and specifically we want to focus on the sensors. Indeed, we all know that FES needs a stimulator and the intact nerve of the subject, with proper electrodes, for the actuation part. However, an essential contribution to the design of a neuroprosthesis for motor relearning are the sensors, which provide command and/or feedback signals to the control system.

A 'sensor' is a device that detects a change in a physical stimulus and turns it into a signal which can be measured or recorded. Often, the word 'transducer' is used as a synonymous of the word 'sensor'. A sensible distinction is to use 'sensor' for the sensing element itself and 'transducer' for the sensing element plus any associated circuitry. All transducers would thus contain a sensor and most (though not all) sensors would also be transducers.

To make an overview of the sensors adopted so far in neuroprostheses for motor relearning, we want first to highlight what information sensors are required to collect and provide. There are two basic categories of input information that are essential to control a neuroprosthesis:

1. Where and when to go, i.e. the intention of the subject. A simple triggering input is necessary also in the case of an open-loop control. Figure 1 shows a simplified flowchart in which the sensors are used to send the command signals to the neuroprosthesis. Beyond the simple triggering, the real challenge to be tackled here to get an active, goal-oriented exercise concerns the capability to integrate the control of the artificial movement induced by NMES with the subject's intention and, when possible, with the subject's residual movement capacity. This challenge has recently played the major role in the research on neuroprostheses.
2. Where we are, i.e. the status. The status of the system has to be controlled in real time in case of closed-loop neuroprostheses, and many different sensors solutions have been adopted to reach this purpose. Figure 2 shows an example of a closed-loop neuroprosthesis, where the sensors are used to provide the feedback signal.

Figure1. Flowchart of an open-loop control of a neuroprosthesis. The sensor provides the command signals.



There is a growing evidence that FES can enhance functional movements, such as gait, grasping, and reaching. When it comes to control multiple articulations by stimulating a consistent number of muscles, the control system becomes more complex. The number of degrees of freedom (DoF) and the absence of reliable models for FES-generated muscle force make the control problem extremely complex. The crucial functional goals that sensors have to achieve into a neuroprosthesis control can be summarized as follows:

- To implement more complex control algorithms to simulate real movements with many DoFs.
- To generate adaptive stimulation patterns, that compensate for muscle fatigue and other time-variant disturbances.

In addition, it is worth mentioning that sensors used for controlling FES systems can be also exploited to provide a quantitative evaluation of the achieved movements and the changing performances of the patient.

Two categories of sensors have been used so far in the development of motor neuroprostheses:

- The biological sensors, i.e. those measuring biological parameters capable to provide inputs mainly on the intention of the users; and
- The non-biological sensors, which measure the kinematic and kinetic of the joints so to be able to continuously get a reliable description of the status of the system to be controlled.

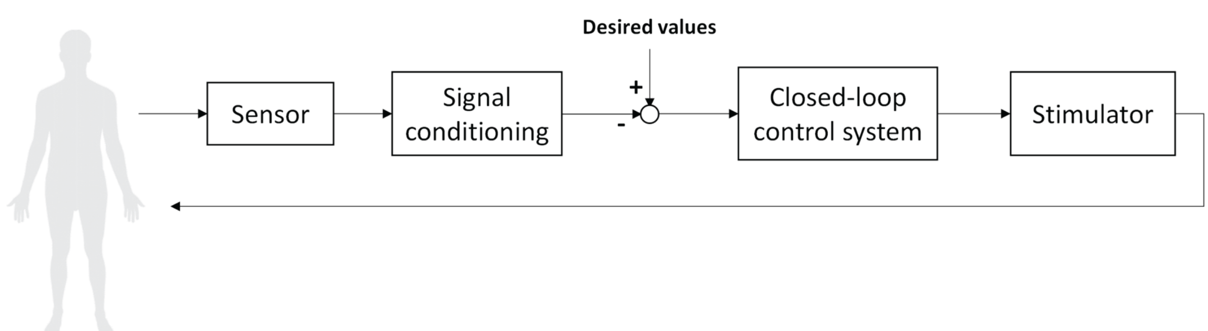
Most applications in the literature use multiple sensors, and the final goal of this chapter is not to choose which sensor should be used for all the different scenarios, but to examine the solutions. Different advantages and disadvantages for each choice are discussed, and often the best configuration exploits more than one sensor modality, to gather information from different sources, and have redundant configurations, also for safety reasons.

SENSORS: TYPES AND CHARACTERISTICS

Measurement of Biological Signals

For more than 30 years, recordings of biological signals have been used to improve the control of FES systems and to provide them a more efficient functionality (Braz, 2009). Biopotentials can be measured from muscle activity (electromyogram, EMG), brain activity (electroencephalogram, EEG), and nerve activity (electroneurogram, ENG). The detection of eye/gaze movements and methods for speech recognition are other examples

Figure 2. Flowchart of a closed-loop control of a neuroprosthesis. The sensor provides a feedback signal that allows a real-time control.



of solutions to control motor neuroprostheses based on biological commands.

The possibility to control FES systems starting from biological signals is an attractive feature both from the assistive and the rehabilitative point of view. Indeed, the measurement of biological signals can be used to detect the user's intention in a natural manner, which is a crucial characteristic of any well-accepted assistive device. On the other side, the recordings of biopotentials can be used to assure the synchronization of the artificial command with the users' intention, and to maximize the involvement of the subject in the training, so as to enhance motor re-learning.

In clinical applications, biological signals have been mainly used to provide command signals since they are characterized by a low information transfer rate. In some cases, biopotientials have been exploited also as feedback signals for real-time control (Sinkjaer, 2003). As a drawback, EMG, ENG and EEG are signals that strongly vary between subjects and even on the same subject between sessions, thus requiring a single-session calibration procedure that can be time-consuming and require skilled personnel.

Electromyogram

The EMG signal is the summation of the action potentials discharged by the active muscle fibers in the proximity of the recording electrodes, which can be placed over the skin surface or inside the muscle. The electrodes should be connected to a low noise, high impedance, high common mode rejection ratio amplifier. When surface electrodes are used, the relevant frequency range is from 10 Hz to 450 Hz (De Luca, 1997).

By applying appropriate processing methods, information about the executed task can be extracted from the EMG signals. Muscle activities can also be used to predict movements, even in weak patients that cannot fully perform the task. Naturally, to be able to measure an EMG signal, muscles cannot be completely paralyzed: they must have some residual natural contraction. Because of its easy accessibility and relatively high signal-to-noise ratio, the EMG has been applied as a control signal in several neurorehabilitation systems, such as prostheses and orthoses, rehabilitation robots, and FES systems (Jiang, 2010).

Focusing on EMG-controlled FES systems, three different approaches have been proposed in the literature:

- EMG signals can be used to trigger the onset of a predetermined stimulation sequence applied in an open-loop modality to muscles different from the ones used for FES control (Graupe, 1989; Scott, Peckham, & Kilgore, 1996).
- EMG signals of paretic muscles can be used to trigger the onset of a predetermined stimulation sequence applied in an open-loop modality to the same muscles used for FES control (Caurаugh, 2000; Kimberley, 2004; Saxena, 1995).
- EMG signals of paretic muscles can be used to continuously control the FES applied in a closed-loop modality to the same muscles used for control. Stimulation parameters, such as current amplitude and pulse width, are usually modulated based on the amplitude of the volitional EMG (Ambrosini, 2014; Shalaby, 2011; Thorsen, 2001).

In the first two approaches, the EMG signals are used to extract command signals, whereas in the third approach the EMG signals can be exploited also as feedback signals for real-time control. However, the third approach requires the most technologically advanced solution both from a hardware and a software point of view. Indeed, due to the presence of the stimulation artifact, special amplification units are needed for EMG recordings during FES (Merletti, 1992). Furthermore, appropriate filtering solutions are required to remove the electrically-induced component

(M-wave) so as to estimate the volitional part of a hybrid muscle contraction (Ambrosini, 2014).

An example of the first approach is the system developed by Graupe (1989). In his system, above-lesion surface EMG signals were used to trigger stimulation sequences for the restoration of standing and walking functions in paraplegic subjects. The approach was based on the observation that when a paraplegic patient attempts to stand up from a chair (via FES), his above-lesion upper-trunk muscles (pectoralis major, trapezius, and deltoid muscles) undergo a pattern of contraction that is unlike any pattern produced otherwise while sitting and that can be clearly identifiable and used for triggering FES.

EMG recordings from unimpaired muscles have also been used for controlling hand neuroprostheses. For example, Scott and colleagues (1996) used the EMG recordings from sternocleidomastoid (SCM) muscles to control a FES system for restoration of hand functions in tetraplegic individuals. The control could be described as a three-state machine: 1) strong flexion of the ipsilateral SCM opens the hand, 2) weaker flexion closes the hand, and 3) no flexion (below a selected threshold) locks the grasp.

In general, this approach is simple and reliable but requires the contractions of muscles otherwise not involved in the task execution, thus compromising the naturalness of the interaction.

To overcome this shortcoming, others systems use the EMG signal of the stimulated muscle to trigger the FES. This research has grown for the last 20 years, and the different systems that have been developed show promising results. EMG-triggered FES has been reported to improve wrist and finger extension movements in chronic post-stroke patients (Cauraugh, 2000). A 3-week home treatment of EMG-triggered FES applied on the extensors muscles of the impaired forearm significantly improved hand functions in chronic stroke patients (Kimberley, 2004). A review investigating the variety of ways that can be used to apply FES to the hemiparetic upper extremity after stroke concluded that EMG-triggered FES may be more effective than non-triggered FES solutions (de Kroon, 2005). Applications for the lower limbs have also been proposed (Dutta, 2009). An EMG-triggered FES-assisted gait initiation system was developed and tested on two individuals with incomplete spinal cord injury (SCI). This solution was found to be more coordinated and dynamically more stable than autotriggered and switch-triggered cases. Commercial solutions based on EMG-triggered FES are also available. For example, the Saebo MyoTrac Infiniti (www.saebo.com/products/saebo-myotrac-infiniti) or the Biomove 3000 (www.biomove.com/stroke-therapy-device.html) are single-channel stimulators: they detect the EMG signals still present in the muscles and trigger the stimulation. They can be used both for foot drop treatment or for the recovery of hand functions.

EMG-triggered FES is a robust method that does not require special software solutions, but it does not allow the subjects to switch off or modulate the stimulation intensity with their own volitional contractions.

The third approach is the only one that allows a real-time control of the stimulation intensity based on the residual EMG activity of the impaired muscles. Control systems for providing a stimulation intensity proportional to the residual volitional EMG have been proposed to support arm/hand functions (Fujiwara, 2009; Shindo, 2011; Thorsen, 2001), and ankle dorsi-flexion (Yeom & Chang, 2010). In nearly all the reported cases, a single stimulation channel was tested. The stimulation intensity was modulated in terms of pulse width, current amplitude, or voltage amplitude. Figure 3 shows the principle of an EMG-based proportional controller for FES. In the example, FES is applied on the wrist extensors. The raw EMG signal is processed to estimate the volitional EMG component. Then, the volitional EMG is low-pass filtered. The cut-off frequency of this filter has to be carefully chosen in order to obtain a good compromise between smooth stimulation and acceptable delay between the patient's muscular activation and the stimulation response. The gain of the proportional controller is defined by the saturation function shown in the figure, where EMG_{vfmax} is the maximal residual filtered volitional EMG that the patient is able to generate and EMG_{vfmin} is the baseline level of the filtered volitional EMG when the muscle is at rest.

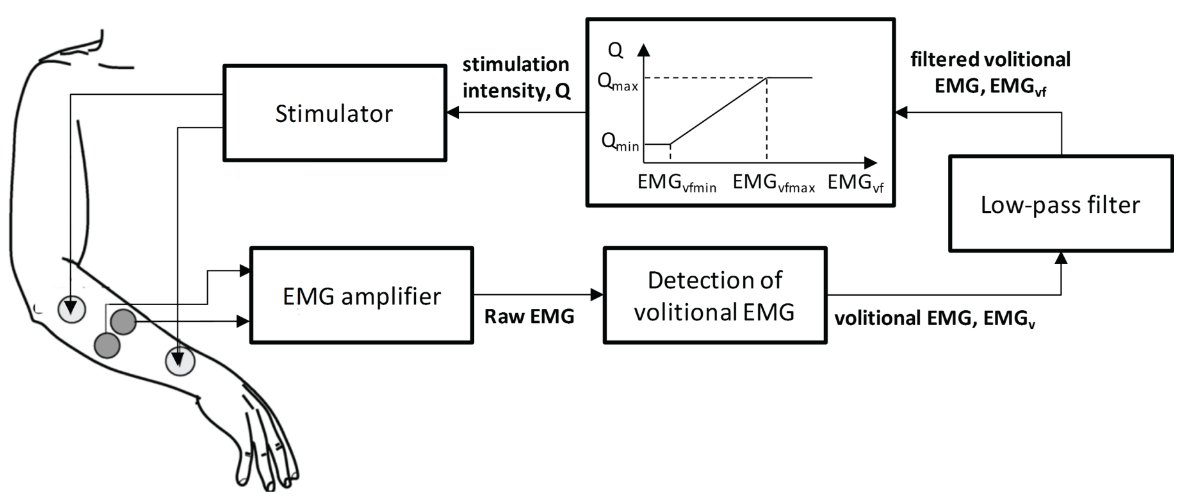
Proportional controllers require smooth muscle contractions to avoid the risk of oscillations. To increase the number of subjects who could benefit from such a system, an on/off non-linear control system has been proposed in a recent work of our group (Ambrosini, 2014). The controller, which was integrated with a passive robotic exoskeleton arm for weight relief, allowed the patient to activate/deactivate the stimulation intensity delivered to the biceps brachii muscle based on the residual EMG of the same muscle. Three people with SCI were asked to flex the elbow while tracking a trapezoidal target with and without myocontrolled-FES support. All patients easily understood how to use the controller in a single session and two patients reduced their tracking error by more than 60% with FES support.

Recent studies suggest that the therapeutic effects of FES are maximized when the stimulation is delivered in close synchrony with the attempted voluntary movement (Barsi, 2008; Gandolla, 2014). Only when FES is continuously controlled based on the residual volitional activity of the same stimulated muscle this combination is assured. For this reason, the third approach can be considered the most promising one from a rehabilitative point of view. However, in order to be used in clinical settings, some steps further need to be performed. A compact system able to both stimulate and record EMG signals is needed. Multi-site electrodes can be used both for stimulation and EMG recordings in order to optimize electrode placements, and self-calibration algorithms should be defined to reduce the set-up time.

Electroencephalogram

EEG signals in brain computer interfaces (BCIs) are typically recorded through surface scalp electrodes in order to record activity at several sites

Figure 3. Scheme of an EMG-based proportional controller for FES systems



within the relevant brain regions. The electrodes are typically mounted according to the international 10–20 system and the relevant frequency range is from DC to 100 Hz.

The use of the cortical signal for the operation of FES systems has received much interest in the literature, since it provides a mean to restore the interrupted link between thought and movement in the most natural way. BCI systems based on difference principles have been developed, and they have been integrated into motor neuroprostheses. Some systems exploit the natural rhythms or spontaneous EEG, i.e. activity not tied to a specific evoking stimulus (Lauer, Peckham, & Kilgore, 1999); others are based on movement-related potentials (MRPs), event related synchronization and desynchronization (Looned, 2014; Müller-Putz, 2005; Tavella, 2010) or on event related potentials (e.g. P300 that is an event related potential of the brain in response to oddball events) (Pedrocchi et al., 2013). The central element in each BCI system is the translation algorithm that converts EEG biopotentials from the user into an output signal that controls an external device.

The feasibility of using the EEG signals to operate a hand grasp FES system was investigated (Lauer, 1999). One FES user and two able-bodied subjects were trained to control the amplitude of the β rhythm recorded over the frontal areas. After six months, the users exhibited a high level of control, being able to use the processed EEG signal to move a cursor to targets on a computer screen with a high accuracy (>90%). To provide a proof of concept of the system, the FES user operated the stimulator by using his cortical signals, and he was able to effectively manipulate several objects.

A decrease in the amplitude of the μ and/or β rhythm wave, known as event related desyncronization, occurs upon both motor movement and imagined motor movement. The detection of this change has been recently used to command a hybrid assistive system (Looned, 2014). The authors developed a BCI-controlled wearable robot integrated with electrical stimulation to support drinking. The drinking task was split into eleven phases of which seven were executed by detecting EEG-based signals through the BCI. The user was asked to imagine the upper limb motion related to the specific phase of the task to be assisted. Once detected by the BCI, the phase was initiated. Each phase was concluded when the BCI detected the volunteers clenching their teeth. The system, which was tested on five healthy volunteers, seems to be promising, but tests on people affected by neurologic diseases are needed to confirm the results.

In another study (Tavella, 2010), the authors showed that healthy subjects can effectively operate a non-invasive asynchronous BCI for controlling a FES neuroprosthesis and manipulate objects. Their neuroprosthetic approach relies on a natural interaction paradigm, where subjects delivers congruent motor-imagery commands (i.e., they imagine a movement of the same hand they control through FES). However, tests on disable people are still missing.

EEG-based BCI systems have also been used to control an implanted neuroprosthesis (Freehand system) (Müller-Putz, 2005). Their goal was to demonstrate the possibility of a patient with SCI to gain control over the motor imagery-based BCI system within a 3-day training. The patient was able to generate distinctive EEG-patterns by the imagination of movements of his paralyzed left hand. These patterns consisted of power decreases in specific frequency bands that could be classified by the BCI. The output signal of the BCI emulated the shoulder joystick usually used, and by consecutive imaginations, the patient was able to switch between different grasp phases of the lateral grasp that the Freehand system provided. These results showed that BCIs are an option for the control of neuroprostheses in patients with high spinal cord lesions.

One of the most important applications of BCIs is a spelling device to aid severely disabled individuals with communication, for example people disabled by amyotrophic lateral sclerosis. P300-based BCI systems consist of a paradigm that displays flashing characters and a classification scheme which identifies target characters. They are optimal for spelling characters with high speed and accuracy, as compared to other BCI paradigms such as motor imagery. In a recent study involving 100 healthy volunteers (Guger, 2009), it has been shown that high spelling accuracy can be achieved with the P300 BCI system using approximately 5 min of training. P300-based BCI systems have been recently used also to control upper limb neuroprostheses. An example of this application is the one proposed in the European project MUNDUS (www.mundus-project.eu). MUNDUS aimed at designing an assistive framework for recovering direct interaction capability of severely motor impaired people based on arm reaching and hand functions (Pedrocchi et al., 2013). It consisted of an antigravity lightweight and non-cumbersome passive exoskeleton integrated with a closed-loop controlled FES system for the restoration of arm and hand functions. A P300-based BCI system was used to detect the user's intention when the subject does not preserve any residual motor functions (muscle activity and eye movement were lost). By paying attention to a rare event between a sequence of frequent ones, a time and phase locked positive polarity is evoked in the EEG. To infer which action/object the user tries to select, spatio-temporal features of the event-related potentials were extracted with machine learning techniques and used to feed a Linear Discriminant Classifier. Once the task was selected, the appropriate muscle stimulation patterns were delivered to drive the hand to the target. The BCI system was also used to trigger the sub-actions, such as to grasp the glass, to reach the mouth, etc. Specific questions were displayed on the screen and the user could reply by selecting a GO or a STOP icon. Figure 4 shows a potential user (33 years old male with an incomplete C7 lesion) while using the BCI system to select the desired task.

The use of EEG signals to control FES systems is particularly promising since it maximizes the naturalness of the interaction. However, there is still much that needs to be explored, not only with the technology, but also with the conversion of the signal into neuroprosthetic control. A limitation of EEG-based FES command signals is the low information transfer rate that does not allow a real-time control. Many electrodes need to be placed on the scalp, and long calibration procedures (about 30 minutes) as well as a training phase (up to several days, in case of motor imagery) are required to increase the accuracy. Furthermore, not all the subjects are able to achieve a high level of accuracy. This is particularly true for motor imagery BCI, which represents the most natural approach of interaction. For all these reasons, only tests on healthy subjects or on a limited number of patients have been performed so far. Further investigations are needed to foster the use of cortical signals in the control of motor neuroprostheses.

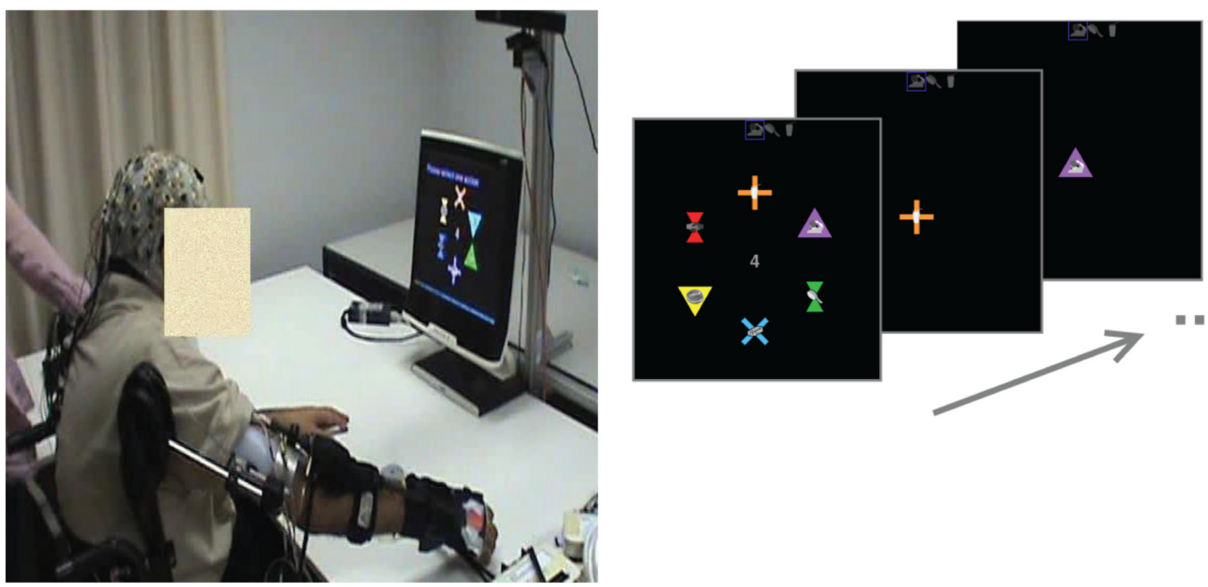
Electroneurogram

The ENG is a signal generated by the electrical activity of peripheral nerves. Despite the limitation of selectivity, implanted nerve cuff electrodes are usually used for ENG recordings. Measuring the activity of nerves innervating naturals sensors, such as those found in the skin, muscles, tendons and joints, seems to be a more natural alternative to artificial sensors for the control of FES systems (Sinkjaer, 2003).

Sensory nerve cuff recordings have been used to correct foot drop in hemiplegic patients (Upshaw & Sinkjaer, 1998). Stimulation of the peroneal nerve has been effectively applied to induce dorsiflexion during the swing phase of walking, usually triggered by an external heel-switch (Lyons, 2002). Instead of using the external heel-switch, a cuff electrode on a cutaneous nerve innervating the foot was implanted, and an algorithm to detect the differences in ENG recordings

Figure 4. A potential user while testing the MUNDUS system. On the right, the P300-based interface for user's intention detection is shown.

(a) (b)



between swing and stance phases was developed. The system proved to be reliable on a chronic stroke patient, but more subjects are needed to investigate intersubject performance (Upshaw & Sinkjaer, 1998).

Sensory nerve cuff recordings have also been used to control hand neuroprosthesis in tetraplegic individuals (Inmann, 2001; Inmann & Haugland, 2004). A nerve cuff electrode was implanted to record activity from the cutaneous mechanoreceptors at the radial aspect of the index finger. The signal recorded from the cuff electrode was processed and fed back into the controller of the muscle stimulation. The system was tested on a volunteer with tetraplegia, both in a laboratory setting and in a home environment.

The use of ENG is an attractive alternative to external sensors, since it maximizes the naturalness of the interaction. However, since it requires an implantation procedure, it is suitable only as an assistive system and not as part of a rehabilitation treatment. In addition, tests on a limited number of subjects are usually performed, thus preventing a full demonstration of its applicability. Efforts are being made to simplify the implantation procedure (Chu, 2013), but further investigation is still needed.

Recently, the number and type of detectable sensory events that can be differentiated from the whole nerve recordings have been investigated (Raspopovic, 2010). This work showed that single-channel cuff electrodes are able to provide information on two to three different afferent (proprioceptive, mechanical and nociceptive) stimuli, with reasonably good discrimination ability. These results suggested that it might be possible to develop robust closed-loop control algorithms for neuroprostheses, by means of the sensory information extracted with single-channel cuff electrodes from the peripheral nerve.

Thanks to the current trend towards minimally invasive surgical procedures and the design of advanced signal processing algorithms, ENG recordings might represent an interesting solution for FES systems in the near future.

Eye Tracking

Since eye movements are rarely paralyzed, different gaze- and eye-tracking solutions using high-speed cameras are being developed (e.g., eye-tracking glasses, head-mounted or desk-mounted systems) to help people with high level of disability to communicate and gain more independence (Mele & Federici, 2012). Eye-tracking communication devices have been shown to reduce communication disability and improve quality of life in people with late-stage amyotrophic lateral sclerosis (Armstrong & Olatunji, 2012). Nowadays, commercial systems that convert text and symbols into clear speech are available (e.g. Tobii Technology; www.tobii.com).

The recent development of lighter and cheaper eye tracking systems that can produce 3-D estimates of the point of regard has led to some interest for neuroprosthetics interfaces (Abbott & Faisal, 2012). Indeed, these systems can communicate to the neuroprosthesis the target the subject would like to reach so as to trigger a proper stimulation strategy. The main advantages are that no electrodes or sensors have to be placed on the user and that they can be easily used after a fast calibration procedure. However, they can provide only command signals, whereas other sensors are needed to control the movement in real time.

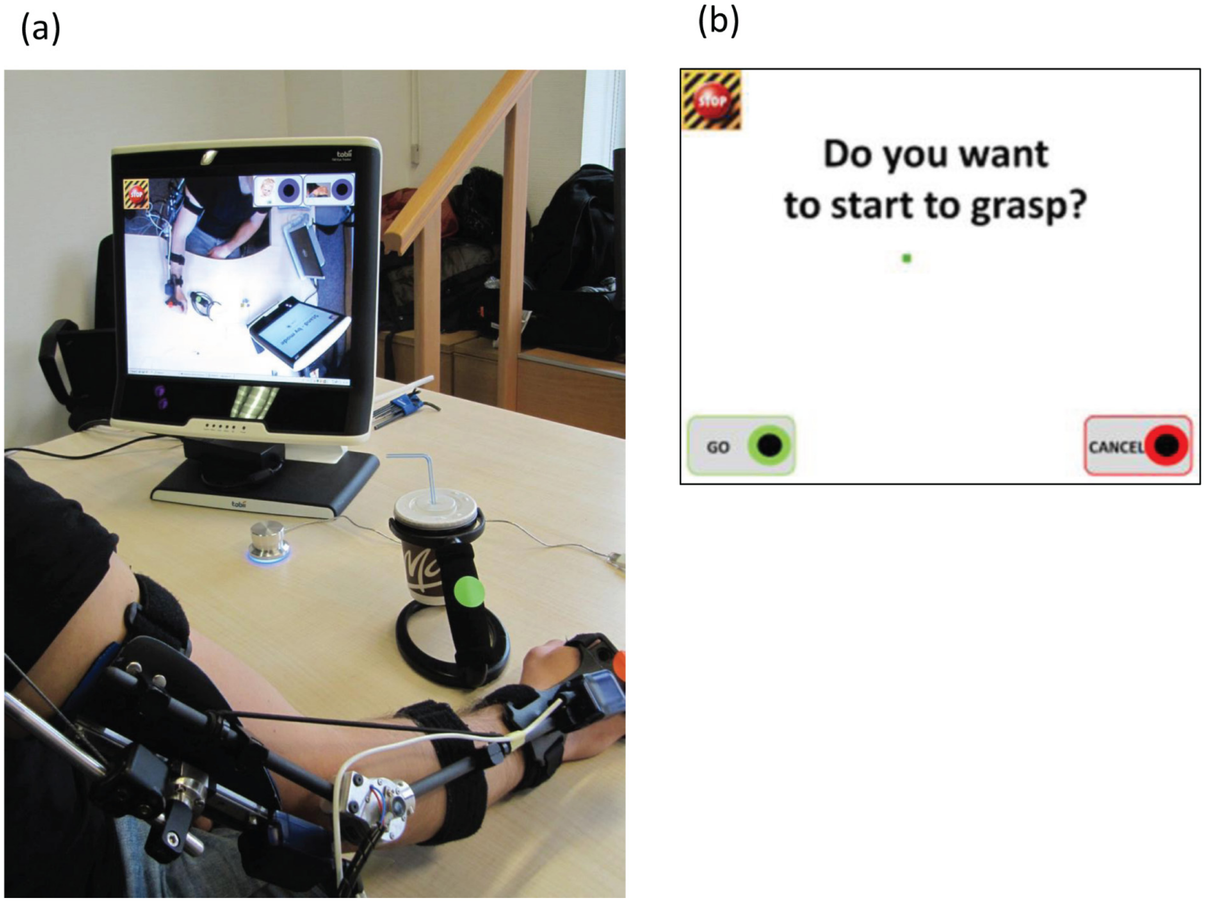
Within the European project MUNDUS, a table-mounted eye tracker integrated into a 17” TFT monitor (Tobii T60W system) was used to detect the user’s intention, in alternative to the BCI solution previously described (Pedrocchi, 2013). During tracking, the Tobii T60 used infrared diodes to generate reflection patterns on the corneas of the user’s eyes. Image processing algorithms were used to identify the gaze point on the screen. One Microsoft Kinect camera was used to show on the screen the live scene of the objects on the table the subject could choose to interact with, while special parts of the screen were dedicated to other available tasks (i.e., emergency button, touching spots of the body). Figure 5a shows an example of the selection interface, which was positively tested on patients, proving its usability. Once the subject selected the object or the task, MUNDUS assisted the execution of the desired task (e.g. a drinking task was performed if a glass was chosen). To trigger the sub-actions, specific questions were displayed on the screen and the user could reply by staring at a GO or a STOP icon (Figure 5b).

A system based on gaze alone might require restrictions on the user’s normal eye and head behavior to avoid eliciting unintended movements. While this might be acceptable during computer-based tasks, a motor neuroprosthesis should not restrict the remaining healthy functions of the user. To overcome this limitation, a solution has been recently proposed, combining shoulder EMGs with target estimates obtained from gaze (Corbett, 2013). The results from this study showed a nearly optimal combination of both physiological signals, making control more intuitive and allowing a natural trajectory that reduced the burden on the user. However, this approach was tested during closed-loop robotic control of the arm on six able-bodied subjects. Its integration with FES systems and tests on potential users are needed to truly evaluate the system.

Voice Control

The use of speech recognition as volitional control command for the electrical stimulation has received little attention in literature. Bohs et al. published in 1988 a method to restore some hand functions in C5-6 quadriplegics that had their hands and wrists paralyzed (Bohs, 1988). The

Figure 5. Examples of the graphical interface of the eye tracker used in the MUNDUS project. Panel (a): example of tasks selection interface; panel (b): example of sub-action triggering interface.



system provided a voice-triggered grasp function that could help the patients gain some of the lost independence. The subjects had to complete an initial three-month phase of electrical stimulation training, in order to increase their muscle strength and fatigue resistance. Then, each subject was fitted with a forearm cover with four to eight electrode pairs, which allowed wrist and digit extension, thumb abduction/flexion, and finger flexion. The software recognized some easy voice commands ('system on', 'off', 'grip', 'open') by matching the recorded signal with previously stored templates. The authors reported that the system increased grip strength for some patients; unfortunately, the accuracy of the voice-command detection was not quantitatively reported.

In another work, a computerized neuromuscular stimulation system was applied to the upper limbs of two patients with complete quadriplegia below the C4 level (Nathan & Ohry, 1990). Simple vocal commands to the computer triggered pre-programmed hand grasps, arm motion, and other functions, giving the patient complete control over the system. In pilot clinical trials of six weeks, eating, and drinking, including picking up and replacing the pen or cup, were achieved. However, tests in a real environment were not performed.

The little attention received in literature by voice-controlled FES systems is probably due to the eagerness of researchers to create a well-accepted system, transparent to the user. The main challenge that speech recognition has to tackle is the parameterization of the background sound captured by the microphones. In order to base the control algorithm on the microphone signals, the environment where the neuroprothesis is used has to be known beforehand, and also to be periodically parameterized. Even in that case, a voice-controlled FES system would be susceptible to unexpected environment noises that could erroneously trigger the stimulation. Nevertheless, technology has made huge processes in natural language processing, speech recognition and human-computer interaction; therefore, the use of voice-controlled FES system is not a remote possibility anymore.

Measurements of Non-Biological Signals

Sensors of Force/Pressure

There are several methods to measure the subject's interaction with the environment and the rehabilitation instrumentation. The most widely used sensors are the force sensitive resistors, which change their resistance in response to a force, and the strain gauges, that change their resistance when strain is applied.

There are other alternative sensors not so widespread in literature, such as capacitive sensors, whose main advantage against resistance-based sensors is the lack of temperature and time drifts, resulting in more stable output signals (Honiger, 2001). The main drawback is the robustness of the technology, which is subdued by choosing strong materials (Honiger, 2001). Honiger et al. have designed an ergonomic, low-cost insole built with capacitive sensors that detects four phases of gait; this detection was integrated with an existent FES system, using the gait events as the trigger of the stimulation. The authors tested the system on a paraplegic user with very high successful rates.

Force Sensitive Resistors

A Force Sensitive Resistor (FSR) is a device that changes its resistance in response to the applied force. Its main advantage is its ease of use and processing. On the other hand, they provide scarce information, have a short-life, are unreliable when worn by patients with shuffling feet, and have also been reported to cause discomfort.

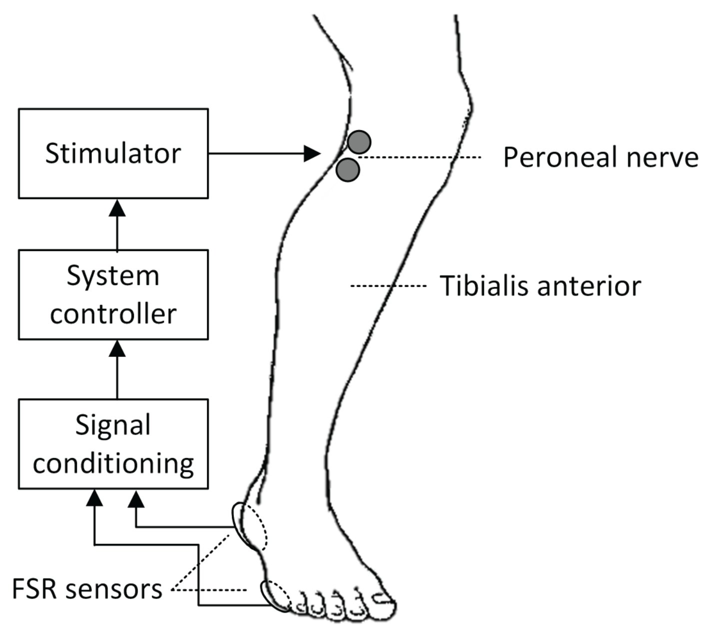
FSR have been widely used in literature to detect gait events, by measuring the force that the foot exerts on the ground. Initially, the sensors were placed under the heel, providing the events ‘heel strike’ and ‘heel off’, which were reported to be insufficient with pathological subjects that do not place the foot sole the way a healthy subject does. Other methods strategically place other FSR sensors on the foot sole under the 1st and 5th metatarsals, or under the big toe, obtaining more detailed information of the contact of the foot with the floor; there are also insoles that completely cover the foot sole with an array of sensors, obtaining high-density information of the foot contact.

FSR sensors have been used since the 1960s as the trigger of the stimulation for the peroneal nerve of stroke survivors during the swing phase of gait. This system is well known as drop-foot stimulator and helps patients that cannot dorsiflex the ankle during the swing phase of gait. Liberson et al. (Liberson, 1961) were the firsts to propose a system to apply electrical stimulation to the paretic leg of patients during the swing phase of gait. The stimulation was synchronized to the gait cycle by means of footswitches. Many have contributed to this research, extended to other pathologies, although real-time control of stimulation intensity has received little attention (Lyons, 2002). The basic diagram of a drop-foot stimulator is shown in Figure 6. Two FSR sensors placed under the heel and fifth metatarsal are acquired an analyzed in real time, to detect the swing phase of gait and stimulate the peroneal nerve. As a result, the stimulation on the tibialis anterior induces the ankle dorsiflexion, allowing toe clearance during the swing phase.

Recently, Postans et al. conducted a study where they used FES during gait in children with cerebral palsy, motivated by possible improvements in the range of movement, muscle strength and spasticity (Postans & Granat, 2005). The onset and cessation of the stimulation was controlled by four FSRs sensors placed under the heel, first metatarsal, fifth metatarsal, and great toe. The other stimulation parameters (amplitude, ramp time and delay with respect to gait phases) were established with a control algorithm. The FES strategy was designed to control the knee flexion/extension and the ankle plantar/dorsiflexion, based on the children's gait deviations, assessed with the VICON motion capture system.

Using a completely different approach, Davoodi et al. proposed in 2002 an indoor rowing machine to improve the cardiovascular fitness of individuals with SCI (Davoodi, 2002). The system used two FSR sensors placed on the handles to measure the thumb pressure and command the manually-triggered FES, in what was reported an intuitive method that can be easily learnt. The stimulation was applied to the quadriceps and hamstrings of both legs, activated by the user commands and the seat position, monitored with encoders. The degrees of freedom of the lower limbs were virtually reduced by physical constraints applied to the feet and trunk of the user, guaranteeing the safety of the system and allowing its use in home environments.

Figure 6. Drop-foot stimulator, a FES system designed to correct the lack of ankle dorsiflexion in stroke subjects



Strain Gauges

A strain gauge is a device used to measure a strain applied on an object. The most widely used is the metallic strain gauge, that consists of a very fine wire or, more commonly, a metallic foil arranged in a grid pattern. The grid is bonded to a thin backing, called the carrier, which is attached directly to the object. As the object is deformed, the foil is deformed, causing its electrical resistance to change. This resistance change, usually measured using a Wheatstone bridge, is related to the strain by the quantity known as the gauge factor.

Few examples of strain gauges used for controlling FES systems can be found in the literature. In a study from our group (Comolli, 2010), a commercial cycle-ergometer was equipped with resistive strain gauges in order to provide the torque produced at the right and left crank arm, independently. In a later work, this information was used to develop a control system for FES-induced cycling training (Ambrosini, 2010). The controller modulated the stimulation intensity delivered to the lower limb muscles of the two legs in order to nullify the unbalance between the torques produced at the two crank arms. Trials on healthy subjects and stroke patients showed that the controller was able to reach and maintain a symmetrical pedaling.

In another study, strain gauges were used to develop an instrumented object for quantitatively evaluating functional tasks performed with lateral hand grasp (Inmann, 2001). The strain gauges allowed the simultaneous monitoring of the grasp force, the perpendicular force at the tip, and the force in the long axis of the instrumented object. The device was used to evaluate a simulated eating task performed by able-bodied subjects and a tetraplegic subject supported by an FES hand grasp system.

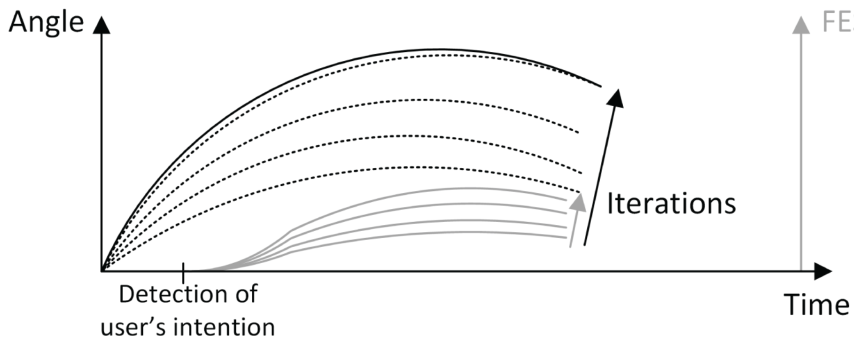
Measurements of Movement

As an alternative to or in combination with biological signals, many researchers have used the movement of the body to control neuroprostheses, in both open and closed-loop approaches. Body kinematics have been widely exploited to trigger the stimulation based on the user's intention (Kotiadis, 2010; Tong, 2003), sometimes combined with the tracking of the induced movement to adapt accordingly the stimulation parameters (Miura, 2011; Seel, 2013). Indeed, the response of the musculoskeletal system to electrical stimulation is neither linear nor immediate; therefore, the use of the joint angles to control the stimulation profile guarantees low errors in the desired motion, even when muscles start to fatigue.

Figure 7 shows how the joint angle can be used for the iterative learning of the electrical stimulation parameters. The FES controller needs to create an angle trajectory that mimics a predefined angle template (black solid line). When the real-time control algorithm detects the user's intentions, it triggers the FES using a first set of stimulation parameters. Iteration after iteration, the system adapts the stimulation parameters to minimize the error of the angle trajectory. After a series of iterations, the error is minimized, and it is maintained low even when muscles start to fatigue.

The motion sensors that have been most widely used are inclinometers, accelerometers, electrogoniometers, gyroscopes, and other derivatives created with sensor fusion. The main advantages of motion sensors are low cost, size, weight, and donning/doffing times, allowing their use in clinical settings and home applications. The extracted kinematic signals have an intrinsic between-subject variability, which increases when

Figure 7. Angle-based control for FES system. The desired angle trajectory (black solid line), and the real angles obtained at each iteration (black dotted lines) are shown, along with the electrical stimulation that was applied after detecting the user's intention (grey lines).



comparing groups with different pathologies or levels of impairment; nevertheless, similar waveforms can be found across them to accurately control the stimulation (Tong, 2003). The most challenging use of motion-sensor control are upper-limb neuroprostheses, due to the high number of degrees of freedom and the intrinsic redundancy of the trajectory profile.

FES-induced cycling training is an example of neuroprosthesis quite used in clinics whose functionality is based on a motion sensor. Indeed, the system is made of a stimulator connected with a cycle-ergometer. The stimulation strategy consists of delivering current pulses to several muscles of the lower limb (usually, the quadriceps, the hamstrings, the tibialis anterior, and the gluteus) based on the crank angle measurement. The objective is to stimulate each muscle in the proper phase of the movement. The crank angle is usually measured through optical encoders. An optical rotary encoder consists of a disk with transparent and opaque areas distributed along the polar angle, that are the coded symbols of the angle they represent. The disk rotates with the main axis of movement, which allows the recollection of the current angle by illuminating the disk and reading the output with a photodetector array. Cycle-ergometers equipped with optical encoders are commercially available, such as Thera-Live (Medica Medizintechnick GmbH, Germany) or Motomed (Reck GmbH, Germany). These systems are used in clinics to deliver FES-cycling training, which has been proven to be an effective treatment for the lower-limb rehabilitation of post-acute stroke patients (Ambrosini, 2012).

Accelerometers

Accelerometers are a type of inertial sensors that measure rotational or translational accelerations along two or three directions. They are a low-consumption choice to monitor kinematics, but they are affected by high-frequency peaks due to soft tissue artifacts, and by gait-event vibrations when they are placed on the lower limbs. Joint angles can be extracted from rotational accelerometers by integrating twice their signals; nevertheless, special attention must be paid to correctly preprocess the accelerations, removing the noise and the influence of gravity. Luinge et al. proposed a method to measure inclination based on an accelerometer, using a Kalman filter to correct the fluctuating offset that depends on temperature and changes in the structure (Luinge & Veltink, 2004). They reported low errors, but the system requires the measured acceleration to be smaller than gravity.

When placed on a limb that rotates around an axis, the output of the accelerometer depends on the distance between the sensor and the center of rotation, which could lead to high inter-session variability due to modifications in sensor placement. The imprecisions could also increase by differences in the orientation of the sensors with respect to the body segment. Furthermore, due to their working principle, they are unable to measure the rotational angle around the gravity axis. To overcome these disadvantages, accelerometers are often combined with gyroscopes to create an Inertial Measurement Unit (IMU) that uses sensor fusion to create new measurements that improve the deficiencies of the individual sensors.

Accelerometers have been placed numerous times on the lower limbs to detect the swing phase of gait and trigger the electrical stimulation that could support or rehabilitate the movement of an impaired leg. Shimada et al. used a two-axis accelerometer placed on the thigh to detect the swing phase of the paretic leg of stroke subjects, and control the electrical stimulation that would correct drop foot (Shimada, 2005). A neural network was trained with the accelerometer signals and a footswitch placed on the heel, and the system was tested on healthy (N=5) and stroke patients (N=3), providing acceptable results.

Kojović et al. developed a multichannel FES rehabilitation system for gait, tested on 13 stroke subjects for four weeks with successful outcomes (Kojović, 2009). The system combined two accelerometers placed on the paretic shank and one FSR under the heel, to create a rule-based control for the stimulation of quadriceps, tibialis anterior, soleus, and hamstrings. The accelerometer and FSR signals were transformed into ON/OFF signals, applying a threshold method. Then, they applied inductive learning to linearly map the sensors data to the muscle activation patterns, resulting in IF-THEN rules that controlled the timing of the stimulation. The amplitude of the stimulation was individually adjusted to comfortable levels in the initial calibration procedure, and kept constant.

Electrogoniometers

Electrogoniometer are an instrument to measure angles in one or two planes of movement, consisting of two ends connected by a transducer, usually a strain gauge. To place it, the two ends of the sensor have to be attached to the two body segments connected by the joint; this setting sometimes limits the range of the motion, or leaves the flexible transducer susceptible to over bending and stretching. However, they are commercialized in different sizes and number of channels (one or two); the choice depends on the joint where they are placed. Their main advantage is their ease of use, since an initial calibration and little processing are the only things needed to map linearly their output to the real angle.

Miura et al. developed in 2011 a fuzzy algorithm to control the electrical stimulation on the vastus and hamstring muscles, in order to perform repetitive movements of flexion/extension of the knee (Miura, 2011). The knee-joint control algorithm analyzed the angles acquired with an electrogoniometer, and adapted cycle-by-cycle the duration of the stimulation pulses, compensating the intrinsic differences in the muscles properties of healthy and hemiplegic subjects.

Pedrocchi et al. used an electrogoniometer to control the stimulation of the quadriceps, based on a feedforward and feedback controller, using neural networks aimed at compensating time variant and non-linear disturbances typical of FES, such as muscle fatigue, electrode positions or spasms (Pedrocchi, 2006).

For applications with multiple degrees of freedom, such as upper-limb tracking, the use of electrogoniometers is limited by the complexity of using a multiple set of them, in terms of wearability and calibration procedures. Exell et al. used an electrogoniometer to track the wrist movements during reaching tasks on upper-limb stroke rehabilitation (Exell, 2013). Combining a Kinect motion capture device and an electrogoniometer, the authors controlled the stimulation on deltoids and triceps, using an iterative learning approach based on the resultant arm and hand movements. A de-weighting spring support allowed the control system to apply lower stimulation amplitudes and still obtain the complete range of movement, diminishing muscle fatigue. Optionally, a 40-electrode array on the wrist and a data glove for collection of finger movement, could be integrated into the system; in this case, the iterative learning control would not only adapt the duration of the stimulation pulses, but also select the optimal array electrodes that need to be active to perform a specific movement.

Inertial Measurement Units

Gyroscopes are sensors that provide the angular velocities of the body segment where they are attached, around one, two or three axes. They provide nearly similar signals when placed on the same body plane, reducing inter-session errors. Vibrations or gravity does not affect them, but like accelerometers, some processing is needed before obtaining the angle by numerical integration.

Gyroscopes are usually combined with accelerometers to form the Inertial Measurement Unit (IMU), a device that uses sensor fusion to overcome some of the deficiencies of the individual sensors, and provides the real-time orientation of the IMU with respect to a global reference frame. The errors caused by sensor drifts are generally reduced with a Kalman filter, assuming that the timing average of the measured acceleration corresponds to the gravity. However, IMUs often include magnetometers to correct heading errors, and the term Inertial/Magnetic Measurement Unit (IMMU) is then used. IMMUs are more expensive and are not always better, since the magnetometer can lead to errors when they are affected by magnetic disturbances, which is common indoors or near a treadmill.

This type of sensors has been recently proposed as a real-time, ambulatory method to assess body kinematics during gait, as an alternative to laboratory-based methods with limited workspace. There are many studies that compare the angles obtained with inertial sensors, to optical tracking systems (Cutti, 2010; Lee & Park, 2009). This is still an ongoing research, but the minimum errors that have been already obtained show the potential of this option in future neuroprostheses applications.

Kotiadis et al. tested four algorithms based on an IMU placed on the shank, to detect the heel-strike and heel-down events (Kotiadis, 2010). The best results were obtained when the algorithm was based on the gyroscopes. The aim of this study was to assess the possibility of replacing the footswitches of drop foot stimulators, introducing inertial sensors that could simultaneously assess body kinematics. The main complexity that these systems have to face is the necessity of establishing detection rules that can be accurately used with a wide variety of subjects, and doing so in real time, in order to synchronously trigger the stimulation. Seel et al. have proposed a system to detect four gait phases with an inertial sensor placed on the foot or the shoe, and apply electrical stimulation to correct the drop foot (Seel, 2013) . The interesting upgrade of their approach is the use of the foot-to-ground angle (or the ankle dorsiflexion, in case a second inertial sensor is placed on the shank) to control the stimulation intensity by means of an iterative learning control. This way, muscular fatigue is compensated automatically, and the error between the desired and the real foot trajectory is minimized.

Tong et al. have developed an IMU-based control system to capture the intentions of the user, and electrically stimulate the hand grasp (Tong, 2003). The IMU was tested on four different locations: shoulder, upper arm, wrist, and hand. Healthy and spinal cord injured subjects were instructed to do a quick forward-backward movement that produced a distinctive waveform, used to trigger the stimulation aimed at controlling different FES hand grasp patterns. The waveform was detected with very high accuracy, especially after the subjects tried a few times and learnt the movement. They concluded that the accelerometer was more suitable for its use on the shoulder or upper arm; however, the large degree of freedom of the distal end, and the forearm movement due to gravity affected its accuracy. On the other hand, the performance of the gyroscope on the shoulder was lower, due to the rotational limits of the joint; but higher on the distal end.

Motion Capture Systems

Motion capture systems have been largely used in research, since they provide highly accurate body kinematics that have been used traditionally for gait analysis. Usually, they require the placement of markers on the anatomical landmarks, which are processed offline to obtain the 3D coordinates. In literature, these methods have been mainly used as assessment for gait deviations, to build the baseline before the treatment, and compare its efficacy by measuring again after the treatment; another common use is as a gold standard to validate other measurement techniques.

Recently, other motion capture systems, such as the Microsoft Kinect, have arisen reducing the costs, removing the necessity of markers, and ultimately making the technology more accessible. Born as an interface for video-game platforms, biomedical research has taken advantage of this system, since it provides a marker-free estimation of the distances between moving objects. The workspace where the rehabilitation treatment can be applied is evidently reduced, but it also allows a spatial tracking transparent to the user. The already reported work of Exell et al. combined a Microsoft Kinect with an electrogoniometer, to assess in real time the arm and hand movements and to stimulate the upper-limb muscles accordingly (Exell., 2013). Another example is the work of Štrbac et al., who have integrated the Microsoft Kinect with a stimulation system for the biceps and triceps in tetraplegic subjects with impaired elbow control (Štrbac, 2013). The intensity of the stimulation pulses was controlled using the visual feedback coming from the estimation of the position of the hand. Due to the low cost, the freedom of the movement these systems allow, the reduced time to set up (no markers or sensors have to be placed on the subject), we expect that in future more applications based on these optical trackers will be designed.

FUTURE RESEARCH DIRECTIONS AND CONCLUSIONS

The framework provided by this review study is very motley. Many different approaches have been tested in the literature to get useful information in order to optimize the control of the stimulation parameters. Biological direct measures of the intention of the subjects have been proved to efficiently assure the synchronization, when possible, between the residual control of the muscles by the natural volition of the person, and the artificial contraction induced by the stimulation. Some very simple and technologically advanced sensors' solutions that would allow a direct and natural control of the neuroprosthesis are still scarcely investigated and exploited, such as the eye tracker and the voice control. The technological maturity achieved by these systems into different application domains, makes them promising solutions also in the field of neuroprosthetics. Many sensors have been tested to assure a closed-loop control of the stimulation parameters so as to adapt the stimulation level to possible positioning errors of the electrodes and to the time variant properties of the muscles themselves, which can change primarily due to fatiguing.

The selection of the best sensors to control a neuroprosthesis is anyway non univocal, and many aspects need to be considered: the task to be controlled, the final goal to be achieved by the system and the place where the system is supposed to work.

We can summarize the functional aspects that we consider fundamental to evaluate alternative solutions:

- The evaluation of the accuracy of the measurements,
- The stability of the signals over time,
- The reproducibility of the signals over subsequent sessions,
- The information rate, if real-time control is required.

Beyond these functional properties, a paramount role in the evaluation of the sensors is related to their usability, which includes:

- The compactness in size,
- The ease of use,
- The time to don and doff,
- The sensibility to positioning errors or inaccurate positions,
- The naturalness of the interaction.

Overall, the literature has demonstrated a lot of effort in the testing of the functional properties of the sensors, focusing most of the attention on the accuracy, the communication system, and the choice of the signals. Unfortunately, most of the solutions proposed have been tested mainly on healthy people, or eventually on very few target end-users.

Among these studies including end-users, only a couple have discussed the results of the tests on end-users not only in terms of functionality, but also in terms of user's acceptance and ease of use. The lack of a full demonstration of usability and efficacy over a significant sample of end-users is the major limit of the current situation and it is the main cause of the gap between the variety of complex research prototypes and the basic commercial devices that are currently available on the market or that are used into daily clinical practice. These latter are indeed mostly open-loop systems with very simple trigger inputs.

We are indeed convinced that there is a risk of proliferation of research outputs that just ends with the scientific publication: they do not result into realistic applications reaching the bedside of the patient and neither into following studies that proceed toward the final application.

Nevertheless, the level of complexity, of scientifically soundness, and of technological advances demonstrated by the current literature represent a very fruitful starting point for future translational research.

The most important ingredient to overcome the current weakness is the strong link between academia, research, clinicians and industries. Indeed, a real impact of research can be foreseen only by considering that the starting point of the research projects needs a debate to establish the technical specifications tailoring end-users and clinical needs. The integration must comprise both functional aspects and operability issues; and the outcome of the research prototypes needs to be their validation considering both technological results and user's feedbacks over significant sample groups.

REFERENCES

Abbott, W. W., & Faisal, A. A. (2012). Ultra-low-cost 3D gaze estimation: An intuitive high information throughput compliment to direct brain-machine interfaces. *Journal of Neural Engineering*, *9*(4), 046016. doi:10.1088/1741-2560/9/4/046016

Ambrosini, E., Ferrante, S., Ferrigno, G., Molteni, F., & Pedrocchi, A. (2012). Cycling induced by electrical stimulation improves muscle activation and symmetry during pedaling in hemiparetic patients. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *20*(3), 320–330. doi:10.1109/TNSRE.2012.2191574

Ambrosini, E., Ferrante, S., Pedrocchi, A., Ferrigno, G., & Molteni, F. (2011). Cycling induced by electrical stimulation improves motor recovery in postacute hemiparetic patients: A randomized controlled trial. *Stroke*, *42*(4), 1068–1073. doi:10.1161/STROKEAHA.110.599068

Ambrosini, E., Ferrante, S., Schauer, T., Ferrigno, G., Molteni, F., & Pedrocchi, A. (2010). Design of a symmetry controller for cycling induced by electrical stimulation: preliminary results on post-acute stroke patients. *Artificial Organs*, *34*(8), 663–667.

Ambrosini, E., Ferrante, S., Schauer, T., Klauer, C., Gaffuri, M., Ferrigno, G., & Pedrocchi, A. (2014). A myocontrolled neuroprosthesis integrated with a passive exoskeleton to support upper limb activities. *Journal of Electromyography and Kinesiology*, *24*(2), 307–317. doi:10.1016/j.jelekin.2014.01.006

Armstrong, T., & Olatunji, B. O. (2012). Eye tracking of attention in the affective disorders: A meta-analytic review and synthesis. *Clinical Psychology Review*, *32*(8), 704–723. doi:10.1016/j.cpr.2012.09.004

Barsi, G. I., Popovic, D. B., Tarkka, I. M., Sinkjaer, T., & Grey, M. J. (2008). Cortical excitability changes following grasping exercise augmented with electrical stimulation. *Experimental Brain Research*, *191*(1), 57–66. doi:10.1007/s00221-008-1495-5

Bergquist, A. J., Clair, J. M., Lagerquist, O., Mang, C. S., Okuma, Y., & Collins, D. F. (2011). *Neuromuscular electrical stimulation: Implications of the electrically evoked sensory volley*. Academic Press.

Bohs, L., McElhaney, J., Cooper, E., Joost, M., Han, D., & Clippinger, F. (1988). A voice controlled FES system for restoring hand functions in quadriplegics. In *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society, 1988*. IEEE.

Braz, G. P., Russold, M., & Davis, G. M. (2009). Functional electrical stimulation control of standing and stepping after spinal cord injury: A review of technical characteristics. *Neuromodulation: Journal of the International Neuromodulation Society*, *12*(3), 180–190. doi:10.1111/j.1525-1403.2009.00213.x

Burridge, J. H. (2001). Does the drop-foot stimulator improve walking in hemiplegia? *Neuromodulation: Journal of the International Neuromodulation Society*, *4*(2), 77–83. doi:10.1046/j.1525-1403.2001.00077.x

Cauraugh, J., Light, K., Kim, S., Thigpen, M., & Behrman, A. (2000). Chronic motor dysfunction after stroke: Recovering wrist and finger extension by electromyography-triggered neuromuscular stimulation. *Stroke*, *31*(6), 1360–1364. doi:10.1161/01.STR.31.6.1360

Chu, J.-U., Song, K.-I., Han, S., Lee, S. H., Kang, J. Y., & Hwang, D. et al. (2013). Gait phase detection from sciatic nerve recordings in functional electrical stimulation systems for foot drop correction. *Physiological Measurement*, *34*(5), 541–565. doi:10.1088/0967-3334/34/5/541

Comolli, L., Ferrante, S., Pedrocchi, A., Bocciolone, M., Ferrigno, G., & Molteni, F. (2010). Metrological characterization of a cycle-ergometer to optimize the cycling induced by functional electrical stimulation on patients with stroke. *Medical Engineering & Physics*, *32*(4), 339–348. doi:10.1016/j.medengphy.2010.01.005

Corbett, E. A., Körding, K. P., & Perreault, E. J. (2013). Real-time evaluation of a noninvasive neuroprosthetic interface for control of reach. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *21*(4), 674–683. doi:10.1109/TNSRE.2013.2251664

Cutti, A. G., Ferrari, A., Garofalo, P., Raggi, M., Cappello, A., & Ferrari, A. (2010). Outwalk: A protocol for clinical gait analysis based on inertial and magnetic sensors. *Medical & Biological Engineering & Computing*, *48*(1), 17–25. doi:10.1007/s11517-009-0545-x

Davoodi, R., Andrews, B. J., Wheeler, G. D., & Lederer, R. (2002). Development of an indoor rowing machine with manual FES controller for total body exercise in paraplegia. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *10*(3), 197–203. doi:10.1109/TNSRE.2002.802880

de Kroon, J. R., Ijzerman, M. J., Chae, J., Lankhorst, G. J., & Zilvold, G. (2005). Relation between stimulation characteristics and clinical outcome in studies using electrical stimulation to improve motor control of the upper extremity in stroke. *Journal of Rehabilitation Medicine*, *37*(2), 65–74. doi:10.1080/16501970410024190

De Luca, C. J. (1997). The use of surface electromyography in biomechanics. *Journal of Applied Biomechanics*, *13*(2), 135–163.

Dutta, A., Kobetic, R., & Triolo, R. J. (2009). Gait initiation with electromyographically triggered electrical stimulation in people with partial paralysis. *Journal of Biomechanical Engineering*, *131*(8), 081002. doi:10.1115/1.3086356

Exell, T., Freeman, C., Meadmore, K., Kutlu, M., Hallewell, E., Hughes, A.-M., et al. (2013, February). *Goal Orientated stroke rehabilitation utilising electrical stimulation, iterative learning and Microsoft Kinect*. Retrieved from http://eprints.soton.ac.uk/350060/

Fujiwara, T., Kasashima, Y., Honaga, K., Muraoka, Y., Tsuji, T., & Osu, R. et al. (2008). Motor improvement and corticospinal modulation induced by hybrid assistive neuromuscular dynamic stimulation (HANDS) therapy in patients with chronic stroke. *Neurorehabilitation and Neural Repair*, *23*(2), 125–132. doi:10.1177/1545968308321777

Gandolla, M., Ferrante, S., Molteni, F., Guanziroli, E., Frattini, T., & Martegani, A. et al. (2014). Re-thinking the role of motor cortex: Context-sensitive motor outputs? *NeuroImage*, *91*, 366–374. doi:10.1016/j.neuroimage.2014.01.011

Graupe, D. (1989). EMG pattern analysis for patient-responsive control of FES in paraplegics for walker-supported walking. *IEEE Transactions on Bio-Medical Engineering*, *36*(7), 711–719. doi:10.1109/10.32103

Guger, C., Daban, S., Sellers, E., Holzner, C., Krausz, G., & Carabalona, R. et al. (2009). How many people are able to control a P300-based brain-computer interface (BCI)? *Neuroscience Letters*, *462*(1), 94–98. doi:10.1016/j.neulet.2009.06.045

Honiger, D., Micallef, J. P., Peruchon, E., Guiraud, D., & Rabischong, P. (2001). *A Robust, Economic and Ergonomic Sensor Device for Gate Phase Detection for an Implanted FES System*. Academic Press.

Inmann, A., & Haugland, M. (2004). Functional evaluation of natural sensory feedback incorporated in a hand grasp neuroprosthesis. *Medical Engineering & Physics*, *26*(6), 439–447. doi:10.1016/j.medengphy.2004.03.002

Inmann, A., Haugland, M., Haase, J., Biering-Sørensen, F., & Sinkjaer, T. (2001). Signals from skin mechanoreceptors used in control of a hand grasp neuroprosthesis. *Neuroreport*, *12*(13), 2817–2820. doi:10.1097/00001756-200109170-00013

Jiang, N., Falla, D., d'Avella, A., Graimann, B., & Farina, D. (2010). Myoelectric control in neurorehabilitation. *Critical Reviews in Biomedical Engineering*, *38*(4), 381–391. doi:10.1615/CritRevBiomedEng.v38.i4.30

Kimberley, T. J., Lewis, S. M., Auerbach, E. J., Dorsey, L. L., Lojovich, J. M., & Carey, J. R. (2004). Electrical stimulation driving functional improvements and cortical changes in subjects with stroke. *Expérimentation Cérébrale*, *154*(4), 450–460. doi:10.1007/s00221-003-1695-y

Kojović, J., Djurić-Jovicić, M., Dosen, S., Popović, M. B., & Popović, D. B. (2009). Sensor-driven four-channel stimulation of paretic leg: Functional electrical walking therapy. *Journal of Neuroscience Methods*, *181*(1), 100–105. doi:10.1016/j.jneumeth.2009.04.005

Kotiadis, D., Hermens, H. J., & Veltink, P. H. (2010). Inertial Gait Phase Detection for control of a drop foot stimulator Inertial sensing for gait phase detection. *Medical Engineering & Physics*, *32*(4), 287–297. doi:10.1016/j.medengphy.2009.10.014

Lauer, R. T., Peckham, P. H., & Kilgore, K. L. (1999). EEG-based control of a hand grasp neuroprosthesis. *Neuroreport*, *10*(8), 1767–1771. doi:10.1097/00001756-199906030-00026

Lee, R. G., & van Donkelaar, P. (1995). Mechanisms underlying functional recovery following stroke. *The Canadian Journal of Neurological Sciences*, *22*(4), 257–263.

Liberson, W. T., Holmquest, H. J., Scott, D., & Dow, M. (1961). Functional electrotherapy: Stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. *Archives of Physical Medicine and Rehabilitation*, *42*, 101–105.

Looned, R., Webb, J., Xiao, Z. G., & Menon, C. (2014). Assisting drinking with an affordable BCI-controlled wearable robot and electrical stimulation: a preliminary investigation. *Journal of Neuroengineering and Rehabilitation*, *11*(1), 51. doi:10.1186/1743-0003-11-51

Luinge, H. J., & Veltink, P. H. (2004). Inclination measurement of human movement using a 3-D accelerometer with autocalibration. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *12*(1), 112–121. doi:10.1109/TNSRE.2003.822759

Lyons, G. M., Sinkjaer, T., Burridge, J. H., & Wilcox, D. J. (2002). A review of portable FES-based neural orthoses for the correction of drop foot. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *10*(4), 260–279. doi:10.1109/TNSRE.2002.806832

Mele, M. L., & Federici, S. (2012). A psychotechnological review on eye-tracking systems: Towards user experience. *Disability and Rehabilitation. Assistive Technology*, *7*(4), 261–281. doi:10.3109/17483107.2011.635326

Merletti, R., Andina, A., Galante, M., & Furlan, I. (1979). Clinical experience of electronic peroneal stimulators in 50 hemiparetic patients. *Scandinavian Journal of Rehabilitation Medicine*, *11*(3).

Merletti, R., Knaflitz, M., & DeLuca, C. J. (1992). Electrically evoked myoelectric signals. *Critical Reviews in Biomedical Engineering*, *19*(4), 293–340.

Miura, N., Watanabe, T., Sugimoto, S., Seki, K., & Kanai, H. (2011). Fuzzy FES controller using cycle-to-cycle control for repetitive movement training in motor rehabilitation. Experimental tests with wireless system. *Journal of Medical Engineering & Technology*, *35*(6-7), 314–321. doi:10.3109/03091902.2011.591480

Moe, J. H., & Post, H. W. (1962). Functional electrical stimulation for ambulation in hemiplegia. *The Journal-Lancet*, *82*, 285–288.

Müller-Putz, G. R., Scherer, R., Pfurtscheller, G., & Rupp, R. (2005). EEG-based neuroprosthesis control: A step towards clinical practice. *Neuroscience Letters*, *382*(1-2), 169–174. doi:10.1016/j.neulet.2005.03.021

Nathan, R. H., & Ohry, A. (1990). Upper limb functions regained in quadriplegia: A hybrid computerized neuromuscular stimulation system. *Archives of Physical Medicine and Rehabilitation*, *71*(6), 415–421.

Park, E. J.,, & Lee, J. K. (2009). A fast quaternion-based orientation optimizer via virtual rotation for human motion tracking. *IEEE Transactions on Bio-Medical Engineering*, *56*(5), 1574–1582. doi:10.1109/TBME.2008.2001285

Pedrocchi, A., Ferrante, S., Ambrosini, E., Gandolla, M., Casellato, C., & Schauer, T. et al. (2013). MUNDUS project: MUltimodal Neuroprosthesis for daily Upper limb Support. *Journal of Neuroengineering and Rehabilitation*, *10*(1), 66. doi:10.1186/1743-0003-10-66

Pedrocchi, A., Ferrante, S., De Momi, E., & Ferrigno, G. (2006). Error mapping controller: A closed loop neuroprosthesis controlled by artificial neural networks. *Journal of Neuroengineering and Rehabilitation*, *3*, 25. doi:10.1186/1743-0003-3-25

Postans, N. J., & Granat, M. H. (2005). Effect of functional electrical stimulation, applied during walking, on gait in spastic cerebral palsy. *Developmental Medicine and Child Neurology*, *47*(1), 46–52. doi:10.1111/j.1469-8749.2005.tb01039.x

Raspopovic, S., Carpaneto, J., Udina, E., Navarro, X., & Micera, S. (2010). On the identification of sensory information from mixed nerves by using single-channel cuff electrodes. *Journal of Neuroengineering and Rehabilitation*, *7*, 17. doi:10.1186/1743-0003-7-17

Rushton, D. N. (2003). Functional electrical stimulation and rehabilitation--An hypothesis. *Medical Engineering & Physics*, *25*(1), 75–78. doi:10.1016/S1350-4533(02)00040-1

Saxena, S., Nikolic, S., & Popovic, D. (1995). An EMG-controlled grasping system for tetraplegics. *Journal of Rehabilitation Research and Development*, *32*(1), 17–24.

Scott, T. R., Peckham, P. H., & Kilgore, K. L. (1996). Tri-state myoelectric control of bilateral upper extremity neuroprostheses for tetraplegic individuals. *IEEE Transactions on Rehabilitation Engineering*, *4*(4), 251–263. doi:10.1109/86.547925

Seel, T., Schäperkötter, S., Valtin, M., Werner, C., & Schauer, T. (2013). Design and Control of an Adaptive Peroneal Stimulator with Inertial Sensor-based Gait Phase Detection. In *Proceedings of 18th Annual International FES Society Conference* (pp. 177–180). San Sebastian, Spain: FES.

Shalaby, R., Schauer, T., Liedecke, W., & Raisch, J. (2011). Amplifier design for EMG recording from stimulation electrodes during functional electrical stimulation leg cycling ergometry. *Biomedizinische Technik*, *56*(1), 23–33. doi:10.1515/bmt.2010.055

Sheffler, L. R., & Chae, J. (2007). Neuromuscular electrical stimulation in neurorehabilitation. *Muscle & Nerve*, *35*(5), 562–590. doi:10.1002/mus.20758

Shimada, Y., Ando, S., Matsunaga, T., Misawa, A., Aizawa, T., Shirahata, T., & Itoi, E. (2005). Clinical application of acceleration sensor to detect the swing phase of stroke gait in functional electrical stimulation. *The Tohoku Journal of Experimental Medicine*, *207*(3), 197–202. doi:10.1620/tjem.207.197

Shindo, K., Fujiwara, T., Hara, J., Oba, H., Hotta, F., & Tsuji, T. et al. (2011). Effectiveness of hybrid assistive neuromuscular dynamic stimulation therapy in patients with subacute stroke: A randomized controlled pilot trial. *Neurorehabilitation and Neural Repair*, *25*(9), 830–837. doi:10.1177/1545968311408917

Sinkjaer, T., Haugland, M., Inmann, A., Hansen, M., & Nielsen, K. D. (2003). Biopotentials as command and feedback signals in functional electrical stimulation systems. *Medical Engineering & Physics*, *25*(1), 29–40. doi:10.1016/S1350-4533(02)00178-9

Štrbac, M., Malesevic, N., Cobeljic, R., & Schwirtlich, L. (2013). Feedback control of the forearm movement of tetraplegic patient based on microsoft kinect and multi-pad electrodes. *Journal of Automatic Control*, *21*(1), 7–11. doi:10.2298/JAC1301007S

Tavella, M., Leeb, R., Rupp, R., & Millan, J. D. R. (2010). Towards natural non-invasive hand neuroprostheses for daily living. In *Proceedings of the Annual International Conference of the IEEE Engineering in Medicine and Biology Society*. IEEE.

Thorsen, R., Spadone, R., & Ferrarin, M. (2001). A pilot study of myoelectrically controlled FES of upper extremity. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *9*(2), 161–168. doi:10.1109/7333.928576

Tong, K. Y., Mak, A. F. T., & Ip, W. Y. (2003). Command control for functional electrical stimulation hand grasp systems using miniature accelerometers and gyroscopes. *Medical & Biological Engineering & Computing*, *41*(6), 710–717. doi:10.1007/BF02349979

Upshaw, B., & Sinkjaer, T. (1998). Digital signal processing algorithms for the detection of afferent nerve activity recorded from cuff electrodes. *IEEE Transactions on Rehabilitation Engineering*, *6*(2), 172–181. doi:10.1109/86.681183

Vodovnik, L., & Grobelnik, S. (1977). Multichannel functional electrical stimulation--Facts and expectations. *Prosthetics and Orthotics International*, *1*(1), 43–46.

Yeom, H., & Chang, Y.-H. (2010). Autogenic EMG-controlled functional electrical stimulation for ankle dorsiflexion control. *Journal of Neuroscience Methods*, *193*(1), 118–125. doi:10.1016/j.jneumeth.2010.08.011

ADDITIONAL READING

Chae, J., Sheffler, L., & Knutson, J. (2008). Neuromuscular electrical stimulation for motor restoration in hemiplegia. *Topics in Stroke Rehabilitation*, *15*, 412–426. doi:10.1310/tsr1505-412

Chowdhury, R. H., Reaz, M. B. I., Ali, M. A. B. M., Bakar, A. A. A., Chellappan, K., & Chang, T. G. (2013). Surface electromyography signal processing and classification techniques. *Sensors (Basel, Switzerland)*, *13*(9), 12431–12466. doi:10.3390/s130912431

De Luca, C. J., & Knaflitz, M. (1992). *Surface electromyography: what's new?* CLUT.

Díaz, I., Gil, J. J., & Sánchez, E. (2011). Lower-Limb Robotic Rehabilitation: Literature Review and Challenges. *Journal of Robotics*, 2011.

Doucet, B. M., Lam, A., & Griffin, L. (2012). Neuromuscular electrical stimulation for skeletal muscle function. *The Yale Journal of Biology and Medicine*, *85*, 201–215.

Gerwin, S., & Mellinger, J. (2010). *A Practical Guide to Brain-Computer Interfacing with BCI2000*. Springer.

Kandel, E. R., Schwartz, J., Jessell, T., Siegelbaum, S., & Hudspeth, A. J. (2012). *Principles of Neural Science* (5th ed.). McGraw Hill Professional.

Kirtley, C. (2006). *Clinical Gait Analysis: Theory and Practice*. Elsevier Health Sciences.

Knaflitz, M., & Merletti, R. (1988). Suppression of simulation artifacts from myoelectric-evoked potential recordings. *IEEE Transactions on Bio-Medical Engineering*, *35*, 758–763. doi:10.1109/10.7278

Merletti, R., & Parker, P. J. (2004). Electromyography: Physiology, Engineering, and Non-Invasive Applications. Hoboken, NJ: Wiley. doi:doi:10.1002/0471678384

Mikołajewska, E., & Mikołajewski, D. (2012). Neuroprostheses for increasing disabled patients' mobility and control. *Advances in clinical and experimental medicine: official organ Wroclaw Medical University*, 21(2), 263–272.

Popović, D. B., Sinkaer, T., & Popović, M. B. (2009). Electrical stimulation as a means for achieving recovery of function in stroke patients. *NeuroRehabilitation*, *25*(1), 45–58.

Rattay, F. (1990). *Electrical nerve stimulation: theory, experiments and applications*. Berlin: Springer-Verlag.

Rueterbories, J., Spaich, E. G., Larsen, B., & Andersen, O. K. (2010). Methods for gait event detection and analysis in ambulatory systems. *Medical Engineering & Physics*, *32*(6), 545–552. doi:10.1016/j.medengphy.2010.03.007

Tao, W., Liu, T., Zheng, R., & Feng, H. (2012). Gait analysis using wearable sensors. *Sensors (Basel, Switzerland)*, *12*(2), 2255–2283. doi:10.3390/s120202255

Wolpaw, J., & Wolpaw, E. W. (2012). Brain-Computer Interfaces: Principles and Practice Hardcover. Oxford, UK: Oxford University Press. doi:doi:10.1093/acprof:oso/9780195388855.001.0001

KEY TERMS AND DEFINITIONS

Electroencephalogram: Technique to measure the electrical activity of the neurons of the brain through electrodes placed on the scalp.

Electrogoniometer: Sensor to measure angles, consisting of two ends connected by a transducer, usually a strain gauge.

Electromyogram: Technique to measure the electrical activity of muscles; it is the result of the summation of the action potentials discharged by the active muscle fibers.

Force Sensitive Resistor: Sensor built with a conductive polymer that changes its resistance when a force is applied on it.

Functional Electrical Stimulation (FES): Electrical stimulation of an intact lower motor neuron to activate plegic or paretic muscle in a precise sequence so as to directly accomplish or support functional tasks.

Inertial Measurement Unit: Device that combines an accelerometer, a gyroscope and sometimes a magnetometer, with sensor fusion algorithms that create a more robust measurement and obtain the 3D orientation of the sensor with respect to a reference global frame.

Neuroprosthesis: A device based on FES to activate the neuromuscular system in order to improve or substitute motor or sensory functions of an impaired central nervous system.

Sensor: A device able to measure a physical magnitude, and transform it into an electrical variable easier to understand, acquire and process by an observer.

Journal of NeuroEngineering and Rehabilitation

BioMed Central

Methodology

Open Access

Error mapping controller: a closed loop neuroprosthesis controlled by artificial neural networks

Alessandra Pedrocchi*, Simona Ferrante, Elena De Momi and Giancarlo Ferrigno

Address: Nitlab, Bioengineering Department, Politecnico di Milano, Milano, Italy

Email: Alessandra Pedrocchi* - alessandra.pedrocchi@polimi.it; Simona Ferrante - simona.ferrante@polimi.it; Elena De Momi - elena.demomi@polimi.it; Giancarlo Ferrigno - giancarlo.ferrigno@polimi.it

* Corresponding author

Published: 09 October 2006

Journal of NeuroEngineering and Rehabilitation 2006, **3**:25 doi:10.1186/1743-0003-3-25

Received: 28 March 2006
Accepted: 09 October 2006

This article is available from: http://www.jneuroengrehab.com/content/3/1/25

Abstract

Background: The design of an optimal neuroprostheses controller and its clinical use presents several challenges. First, the physiological system is characterized by highly inter-subjects varying properties and also by non stationary behaviour with time, due to conditioning level and fatigue. Secondly, the easiness to use in routine clinical practice requires experienced operators. Therefore, feedback controllers, avoiding long setting procedures, are required.

Methods: The error mapping controller (EMC) here proposed uses artificial neural networks (ANNs) both for the design of an inverse model and of a feedback controller. A neuromuscular model is used to validate the performance of the controllers in simulations. The EMC performance is compared to a Proportional Integral Derivative (PID) included in an anti wind-up scheme (called PIDAW) and to a controller with an ANN as inverse model and a PID in the feedback loop (NEUROPID). In addition tests on the EMC robustness in response to variations of the Plant parameters and to mechanical disturbances are carried out.

Results: The EMC shows improvements with respect to the other controllers in tracking accuracy, capability to prolong exercise managing fatigue, robustness to parameter variations and resistance to mechanical disturbances.

Conclusion: Different from the other controllers, the EMC is capable of balancing between tracking accuracy and mapping of fatigue during the exercise. In this way, it avoids overstressing muscles and allows a considerable prolongation of the movement. The collection of the training sets does not require any particular experimental setting and can be introduced in routine clinical practice.

Background

Nowadays neuromuscular electrical stimulation allows simple clinical practice of rehabilitation therapy, even if some of its initial promises have failed. Indeed, the complex motor control performed by the Central Nervous System (CNS) is hard to reproduce by any artificial controller, even to recover a single function like gait, sit to stand or grasping.

Several studies were presented in the last years aiming at controlling such motor tasks by stimulation [1-4] and some commercial products are available in the market [5-8]. Functional stimulation allows conditioning muscular tone, reducing joint stiffness, increasing peripheral vascularisation, preventing ulcers and providing a good cardiorespiratory training. In addition functional neuromuscular stimulation provides the CNS with a complete afference of the motor function to be re-learnt offering promising advantages in the rehabilitation of incomplete spinal cord injured, stroke and ataxia patients [9,10].

In this frame, the development of sophisticated control systems is a crucial point in the design of neuroprostheses. Namely, the control should be able to let the limb track accurately the desired movement and to repeat the exercise as long as possible, even if fatigue occurs. The problem of fatigue is actually particularly amplified for artificial contraction because muscular fibres are activated synchronously, at higher frequency and in the opposite order with respect to the natural contraction.

A neuroprosthesis should be specifically calibrated on a single subject and even on a single session of each subject. The design has to face the well-known difficulties of controlling the human neuromuscular apparatus: non linear, time varying, redundant and very difficult to model analytically. In addition to these typical bioengineering problems, there is another crucial aspect in the design of a neuroprosthesis, i.e., making it easy to use in clinics. The real widespread use in clinical practice as well as the probability of being accepted by many patients strongly depend on short preparation and on exercise procedures being easy.

Most controllers available for functional neuroprostheses in clinical practice are feedforward (FF) [11-13]. They predefined a fixed stimulation pattern during the motor task. By definition, a FF controller did not include any correction on the basis of the current performance, limiting the possibility to track the time variability of the neuromuscular apparatus. On the contrary, several feedback (FB) controllers were proposed. Adaptive controllers [14] and PID controllers were designed for the purpose [15]: Veltink showed that the good tracking performance of PID controllers was offset by a considerable time lag between reference and actual joint angle, which became more marked when exercises were protracted in time. In order to reduce the time lag and to give the PID a FF guess, model-based controllers were combined with PID [1]. These included a neuro-musculo-skeletal model of the system to be controlled. Unfortunately, the large quantity of parameters required for the identification of the system to be controlled was difficult to be experimentally determined and, anyway, a long preparation for each patient was needed in each session. An attempt to reduce this problem was the replacement of the physiological model with a non-linear black-box model, such as an artificial neural network (ANNs). Chang et al. [16] proposed a NEUROPID controller composed by a neural network trained to behave as inverse model in the FF line and a fixed-parameter PID feedback controller, thereby making adjustments for residual errors, due to external disturbances, or to erroneous model identification. Results demonstrated an improvement of tracking performance with respect to Veltink [15], especially because of the reduction of the PID time lag. However, such controller still required long preparation for the PID setting and when fatigue increased, the controller was overstressing the stimulation inducing itself a very fast fatigue increase.

Abbas et al. [17-19] proposed a control system which used a combination of adaptive FF and FB control techniques. The FF adaptive controller was a pattern generator/pattern shaper (PG/PS), in which PG generated a stable oscillatory rhythm while PS (a single-layer neural network) took its input from PG and provided the muscles with stimulation. A fixed-parameter proportional-derivative (PD) FB controller enhanced disturbance resistance and supplemented the action of the FF controller. This controller showed a good performance both in simulation and in experimental sessions, with a good capability of controlling different subjects. The adaptive controller was demonstrated only to repeat one-pattern sequences. However, no particular evidences were reported by the authors about the efficacy of the controller in tracking fatigue. Even if it could be used with many patterns, this could strongly decrease the efficiency and velocity of the adaptive controller, being the architecture of PS multiplied by the number of patterns. In the study proposed by Jezernik et al. [20], a sliding mode controller was developed and demonstrated a good stability and robustness to parameter variations in an early stage of the movement, before the occurrence of fatigue. As discussed by the authors themselves, one of the main drawbacks of the controller is the time required for the tuning phase of the great number of parameters.

In a previous study developed by our research group [21], an adaptive control system (NEURADAPT) based on ANNs was designed to control the knee joint angle in accordance with desired trajectories, by stimulating quadriceps muscles. This strategy included an inverse neural model of the stimulated limb in the FF line and a ANN trained on-line to learn a PID behaviour in the feedback loop. Despite the encouraging results, the ANN in the feedback loop still relied on a PID: it needed the PID parameters identification phase and it also produced a considerable time lag between the reference and actual joint angle, due to the intrinsic delay of the integrative part of the PID function.

With the presented literature and these previous results as a starting point, the control strategy developed and presented in this study is totally free of a PID controller.

In order to combine the engineering requirements along with the clinical specifications, we designed a control system for a neuroprosthesis, called Error Mapping Controller (EMC), for a simple motor task such as knee flexion and extension. This neuroprosthesis was completely designed to identify the controller in the normal steps of clinical use of electrical stimulation, avoiding extra complex protocol procedures to the therapist and the patient.

Methods

EMC structure is reported in Figure 1. It included a FF ANN inverse model (ANNIM) of the system to be controlled and a neural network trained to compensate the fatigue effects in the FB loop, Neuro Feedback (NF). ANNIM stored a stable scheme of the motor apparatus and it was able to convert the planned desired movement (trajectory) into motor commands (pulse width of the stimuli). FB controller (NF) provided the correction of the motor command depending on the current error of the executed movement and on the estimation of the current fatigue level.

Neuro-muscular skeletal model

In order to simulate neuromuscular skeletal features of the lower limb of a paraplegic subject, a biomechanical model, adapted from Riener and Fuhr [4], was implemented in Matlab Simulink® (MathWorks, Inc. Massachusetts). The Plant was constrained to move in the sagittal plane and the knee was assumed to be an ideal hinge joint. The movement considered was the flexion extension of the knee. Inputs to the Plant were the pulse width of the stimuli delivered to the quadriceps through surface electrodes. The Plant output was the knee joint angle. Five muscle groups were considered: hamstrings (i.e. semimembranosus, semitendinosus, biceps femoris long head), bicep femoris short head, rectus femoris, vasti muscles, lateral and medial gastrocnemius.

Muscle groups could be treated independently and were characterized by activation and contraction parameters. Muscular activation included the effect of spatial summation (through the recruitment curve), the effect of temporal summation (through the calcium dynamics) and the muscular fatigue. When the quadriceps were stimulated with a pulse width greater than the recruitment threshold (100 μs), other muscles still contributed to limb dynamics by their passive viscous and elastic properties. The dynamic modellization took the elastic and the viscous torque into account (for more details see [4]).

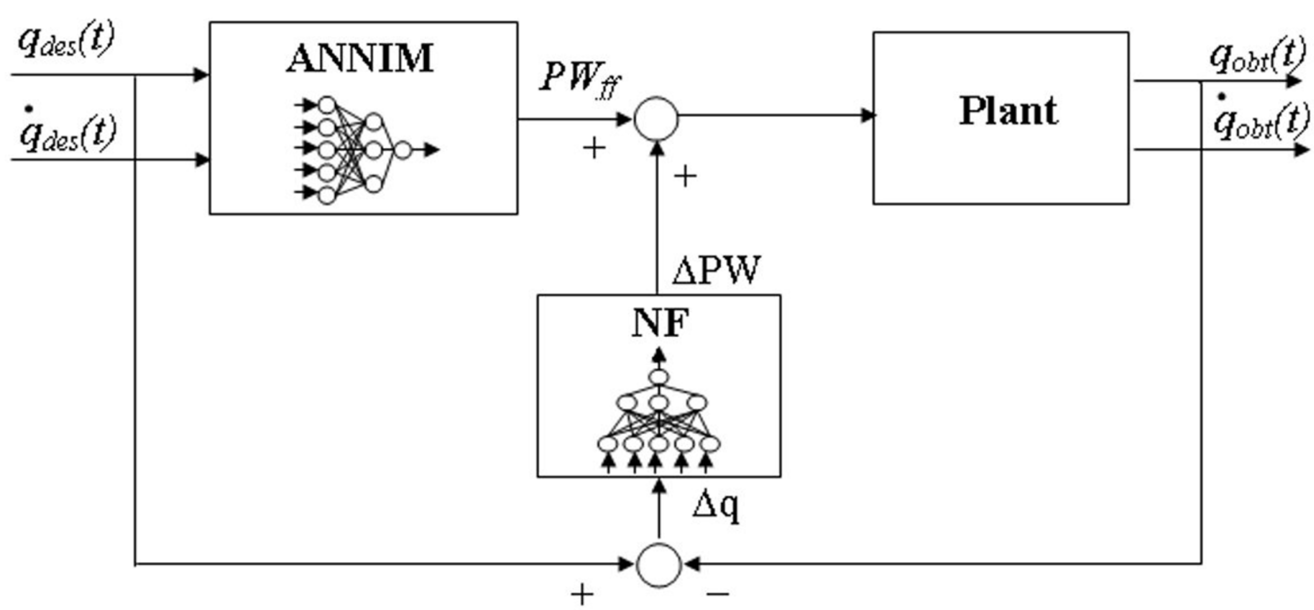


Figure 1
EMC controller. EMC structure.

To describe the effect of fatigue/recovery, a fitness function $fit(t)$ was used [4]. It can be expressed by the following first order relation:

$$\frac{dfit(t)}{dt} = \frac{(fit_{\min} - fit(t))a(t)\lambda(f)}{T_{fat}} + \frac{(1 - fit(t))(1 - a(t)\lambda(f))}{T_{rec}} \quad \text{(eq. 1)}$$

where $a(t)$ was the activation of the not fatigued muscle and fit_{min} was the minimum fitness parameter. The time constants for fatigue (T_{fat}) and for recovery (T_{rec}), as well as fit_{min}, were estimated from stimulation experiments [4].

The term $\lambda(f)$ was introduced by Riener and Fuhr [4] to better account for the fact that muscle fatigue rate strongly depends on stimulation frequency and it was expressed by the following relation:

$$\lambda(f) = 1 - \beta + \beta\left(\frac{f}{100}\right)^2 \quad \text{for } f < 100 \text{ Hz} \qquad \text{(eq. 2)}$$

In our stimulations the stimulation frequency f was always fixed at 40 Hz and β was a shape factor not dependent on frequency or muscles.

Finally, the activation of the tiring muscle was given by:

$$a_{fat}(t) = a(t) * fit(t) \qquad \text{(eq. 3)}$$

The fatigue occurrence showed a decrease of the muscle input gain to 50% of its nominal value over 100 s, comparable to [17].

Artificial Neural Network Inverse Model

Following direct-inverse modelling approach [22], the pulse width waveforms, used as ANNIM desired outputs, were rectified sinusoids and triangles of different duration and amplitude. The ANNIM inputs were obtained stimulating the nominal Plant, i.e., not including the fatigue effects ($fit(t)$ = 1), in response to the chosen pulse width signals. In order to take the system dynamics into account, ANNIM inputs were augmented with signals corresponding to past inputs. Therefore, ANNIM inputs were the actual knee angle and velocity and their 4 previous samples (q(t), q(t-1), ..., q(t-4)) and ($\dot{q}$ (t), $\dot{q}$ (t - 1), ..., $\dot{q}$ (t - 4)). It has already been established that adding noise to the training data in artificial neural learning improves the quality of learning, as measured by the trained networks ability to maximize exploration of the input/output space, avoid overfitting and generalise [23]. Therefore, a white noise was added to the input signals (mean 0, standard deviation equal to 5% of the maximum pulse width value). Several networks were trained and the smallest network architecture that gave good RMSE and similar performance between training and testing data was chosen, as reported in details in a previous article of the authors [21]. The ANNIM was a multilayer FF perceptron with 10 input neurons, 10 neurons in hidden layer and 1 neuron in the output layer. We chose the hyperbolic tangent as the activation function of the hidden layer and the logarithmic sigmoid function in the output layer, mapping the non linearity of the Plant and the bounded stimulation range. The Levenberg-Marquardt learning algorithm was used to train ANNIM [24].

Neuro feedback

NF training set was obtained using a setup including the series of ANNIM, Plant and another ANNIM (Figure 2). This scheme was aimed at obtaining the relationship between the angular error and the pulse width signal during a repeated movement sequence, where the effect of muscular fatigue, as well as any time variant occurrence, was evident. Desired angle (q_{des}) was input to the ANNIM, that had already been trained, producing the corresponding desired pulse width (PW_{des}) as an output. PW_{des} was then given as an input to the Plant, where fatigue was modelled. Output of the Plant was the actual angle (q_{act}), i.e., the angle generated stimulating a Plant in which the fatigue effect was included. After that, q_{act} was used as an input to the second ANNIM, which was exactly a copy of the first one, converting it in the PW domain producing PW_{act}. PW_{act} was the nominal pulse width corresponding to the actual movement q_{act}. Therefore, the angular error $\Delta q = q_{act} - q_{des}$ was correlated to an estimation of the current fatigue level expressed in the pulse width domain: $\Delta PW = PW_{act} - PW_{des}$.

These two signals were used as input/output couples for NF training set. Thus NF was trained to produce ΔPW as an output, when it received as an input the correspondent angular error Δq. This training set allowed NF to work as a predictor and a compensator of the fatigue effect: when the Plant was getting tired, the angular error (Δq) increased and NF gave an extra pulse width (ΔPW). Once trained NF allowed estimating the fatigue level and mapping the actual angular error into a needed correction in the pulse width domain.

The signal used to build the training set of NF (q_{des} in Figure 2) was a repeated sequence of consecutive flexion extension trajectories lasting 100 s. The training set included 12 angular trajectories lasting 100 s, having different profiles, durations and amplitudes; some examples of the first angular oscillation are reported in Figure 3.

The NF was a non-adaptive multilayered perceptron with 10 input neurons, 8 neurons in the hidden layer and 1 in

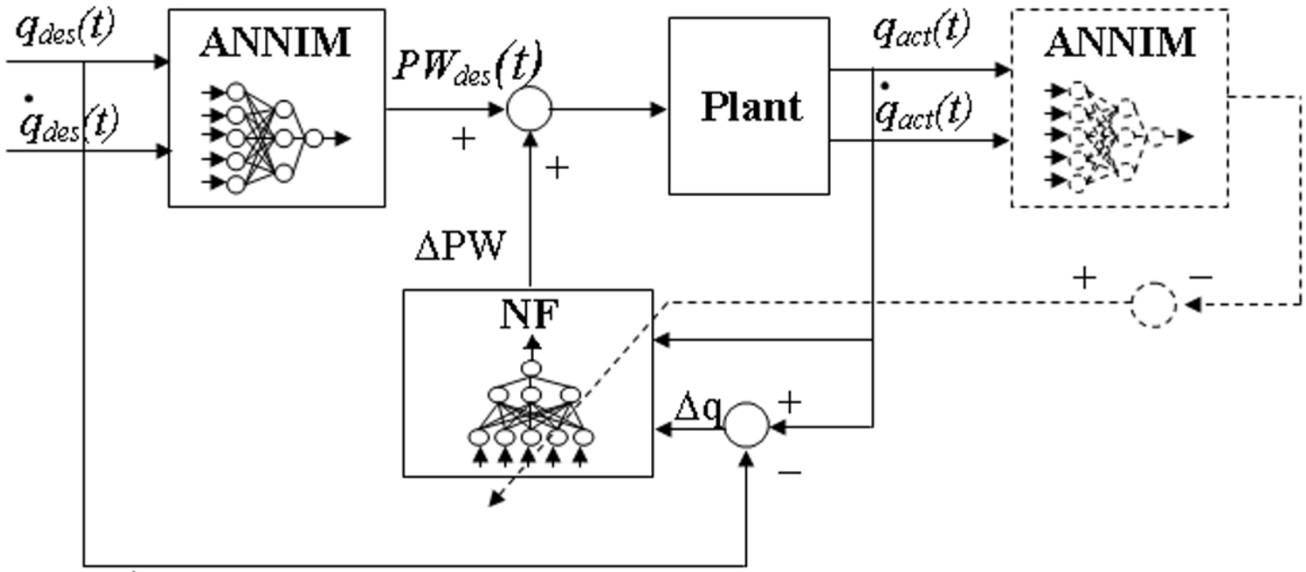


Figure 2
NF Training scheme. Scheme used to collect the training set of NF.

the output layer. We chose the hyperbolic tangent as the activation function in order to allow positive and negative corrections of pulse width. The introduction of past inputs allowed the network to map the dynamic nature of the system. The training algorithm was Levenberg-Marquardt [24].

Capability to resist to mechanical disturbances
More than the tracking performance and the capability to manage fatigue occurrence, the EMC controller proved its resistance to internal disturbances that could occur during the stimulation. Such disturbances could be caused by internal spastic muscle contractions or external loading of the limb. In order to model a mechanical disturbance such as a spasm, a square wave lasting for two seconds was delivered to the simulator with the limb in different positions during the simulated movement. The spasm amplitude ranged between 20% and 30% of the maximal total torque of the knee: the spasm model was analogous to [17].

An additional test on the effect of a distributed noise on the knee torque was designed to check the capability of the controller to face random variations in the Plant. This test could simulate an error in the stimulation or in the electrodes coupling with the skin. Random noises uniformly distributed between ± 25%, ± 30%, ± 35%, ± 40%, ± 45% and ± 50% of the maximal knee torque were tested, as in Abbas et al. [17].

EMC robustness
EMC capabilities to track time varying physical parameters, indicating an increase or a decrease of the fitness level of the subject, were tested as a second aspect of this methodological study. In particular, the robustness of our controller was tested changing the following parameters: the damping property of the leg, the time constant of fatigue and recovery and the weight of the limb. The values of these coefficients were fixed "a priori" in the model. For this reason, the training of the ANNs of EMC was not including any variation of such parameters. Anyway, ANNs generalization capability could partly adapt to these possible variations.

All these parameters were changed up to ± 50% of their nominal value and the angular RMSE on the 1st (not fatigued) and the 5th (fatigued) flexion extension of a repetitive trial were assessed.

Reference controllers anti wind-up PID (PIDAW) and NEUROPID
In order to prove advantages of EMC strategy, a comparison with two reference controllers was performed: a traditional closed loop controller PID and the model-based neural controller, NEUROPID, proposed by Chang [16].

The PID controller general form in the time domain is given by:

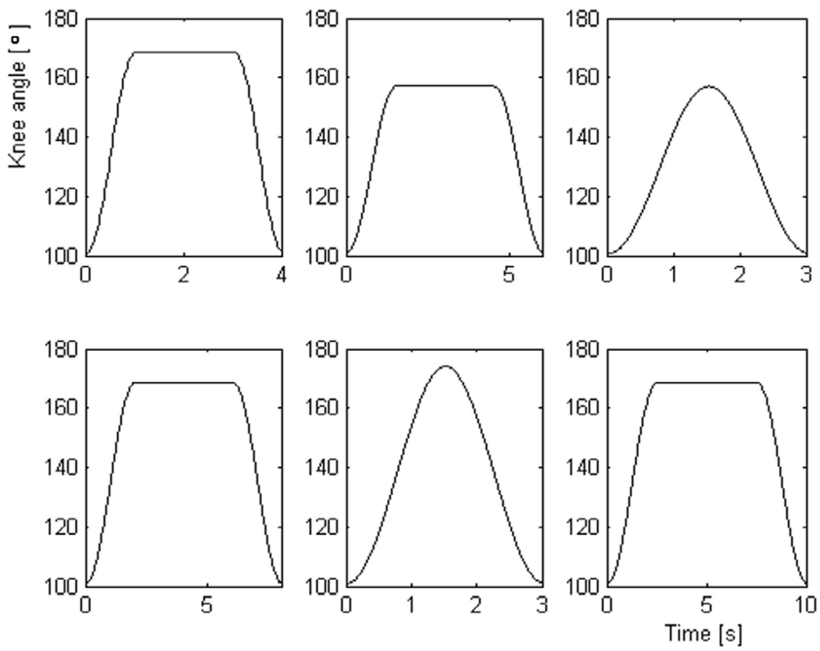


Figure 3
Examples of the NF training signals. Some examples of the first 10 seconds of the signals used to build the NF training set are reported in this figure. Each trajectory was delivered for 100 s to the setup reported in Figure 2 in order to obtain the Δq and ΔPW signals.

$$u(t) = K_P(t) + K_i \int_0^t e(\tau)d\tau + K_d \frac{de(t)}{dt}$$

where: $e(t)$ is the difference between the reference and the actual value of the controlled variable, and Kp, Ki, Kd, are the proportional, integrative and derivative parameters respectively.

The PID controller parameters were first identified using an iterative procedure based on the minimization of Root Mean Square Error (RMSE) [25], where the initial estimation of the optimization was derived from the Ziegler-Nichols rules [26]. Then the transfer function of the PID was discretized in view of a digital implementation of the control algorithm.

A saturation block was added between the output of the PID controller and the stimulator input in order to limit the pulse width values between 0 and 500 μs. The use of integral action in the PID controller combined with actuator saturation can give undesirable effects: if the error signal is so large that the integrator saturates the actuator, the feedback path will be broken because the actuator would remain saturated even if the Plant output changed. The integrator, being an unstable system, may then integrate up to large values. When the error is finally reduced, the integration may be so large that it will take much time before the output of the integrator falls to a normal value. This effect is called integrator wind-up. To avoid it, a PID was introduced in an anti wind-up scheme [27], in the following PIDAW.

The NEUROPID controller, developed by Chang at al. [16], included an ANN in the FF loop, which was the inverse model of the system, and a PID in the feedback loop, which was able to adjust the pulse width signal in case of error between the desired and the actual angle.

In order to compare the three listed controllers (PIDAW, NEUROPID, EMC), we simulated controlled repeating sequences of flexion extension movements lasting 100 s and we computed the RMSE between actual and desired angular values.

A non parametric Kruskal-Wallis test ($p < 0.05$) was carried out to highlight significant differences between the RMSE obtained by the three controllers at different levels of fatigue. A Dunn-Sidak post hoc test was performed to understand which pairs of effects were significantly different.

Results

Tracking performance

In Figure 4 the tracking performance of the three controllers (EMC, PIDAW and NEUROPID) is shown in the case of no fatigue.

Without fatigue, the tracking capability of EMC was very similar to the NEUROPID one, while the PIDAW showed the typical time lag. The RMSE between the desired and actual trajectory shown in Figure 4 was about 1,7° for EMC, 7,7° for the PIDAW and 3.2° for NEUROPID.

Fatigue mapping

In order to test fatigue mapping capabilities, the comparison of the three controllers was performed in terms of the RMSE obtained in response to simulations of 100 s using 6 different angular trajectories (repeated oscillations of different amplitudes, from 40 to 70 degrees and each oscillation lasted from 2 to 10 seconds). In Figure 5 an example of the performance of the three controllers with fatigue is reported. In this case, the three controllers behaved very differently: PIDAW and NEUROPID increased the stimulation pulse width rapidly, due to the increasing tracking error. Within the third cycle, the pulse width raised up to the limit (500 μs) and in the next repetition it remained saturated for more time. Unfortunately, due to fatigue, such stimulation did not achieve the correct tracking of the desired path and it was greatly tiring out the Plant. In addition, in between two successive cycles, those two controllers were not suspending the stimulation but they only reduced it. The continuous stimulation did not permit the possibility of recovery. In contrast, the EMC was always able to keep the stimulation at lower levels. In this way, the fatigue was increasing more slowly and the exercise was repeated with more amplitude for much longer. The EMC avoided over-stimulating the Plant in reaching the desired trajectory when fatigue was too strong and it always had an interval of no stimulation in between waves, which was fundamental for recovery. In this way, it was able to prolong the exercise with satisfying extensions.

The three controllers were tested in response to different testing signals lasting 100 s not included in the training set of both the ANNs of the EMC. Between 90 and 100 s the mean value of the RMSE with respect to the desired knee

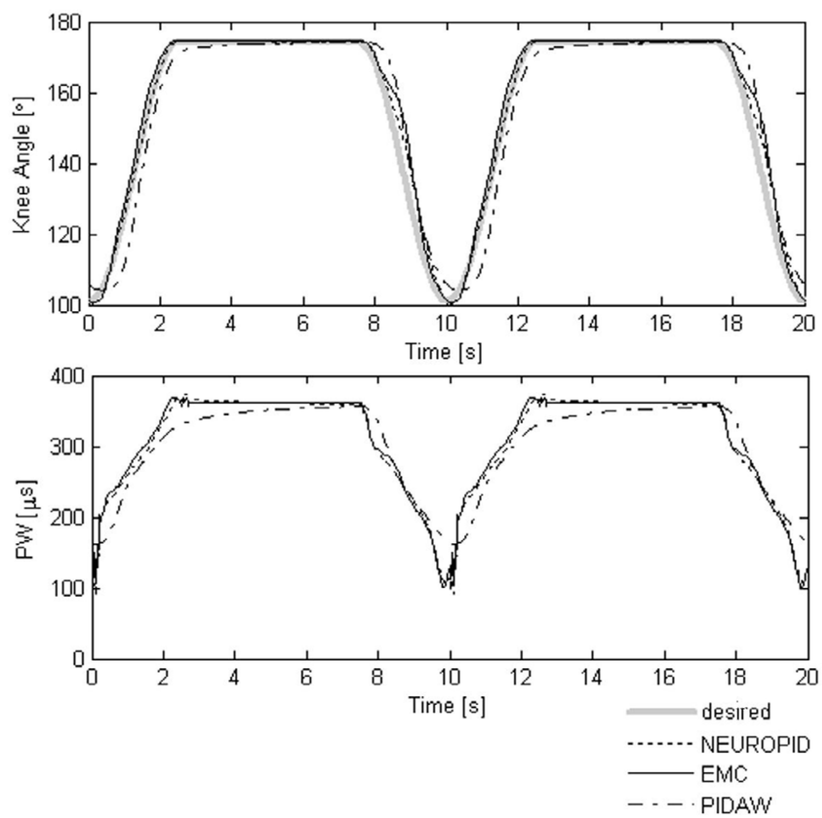


Figure 4
EMC vs traditional controllers without fatigue. A comparison of the performance obtained by the three controllers in term of angular trajectories and pulse width without considering the muscular fatigue effect.

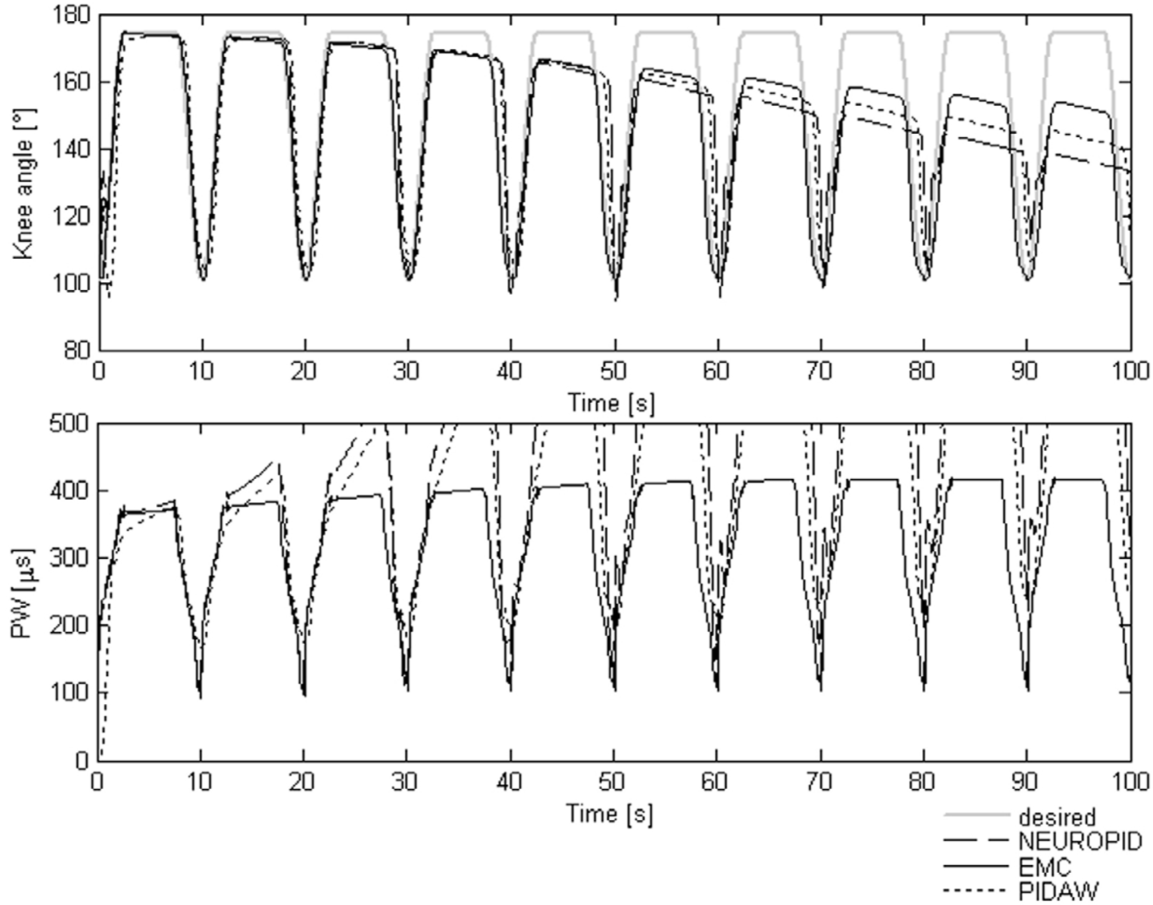


Figure 5
EMC vs traditional controllers with fatigue. An example of the comparison of the performance obtained by the three controllers in terms of angular trajectories and pulse width. The testing signal lasted 100 s and during the trial fatigue was strongly affecting the Plant performance.

angle trajectories tested was about 14° for the EMC, while it was about 21° for the PIDAW and 23° for the NEUROPID.

The results of the Kruskal Wallis test is reported in Figure 6 and highlighted that there were significant statistical differences between the RMSE obtained by the three controllers in three different periods of time (0–30 s, 30–60 s, 60–90 s). The Dunn-Sidak post hoc test showed that a significant difference was present between all the controllers in all the time periods.

Resistance to disturbances

In order to test resistance to internal mechanical disturbances (like occurring spasms), the comparison of the three controllers was performed in terms of the RMSE during flexion extension movements lasting 100 s. Six spasms occurrences, each lasting 2 s, were randomly added to the Plant knee torque during the 100 s simulation, both during the extension and flexion. For each spasm, different amplitudes were tested (between 20% and 30% of the maximal total torque of the knee). Performances of the three controllers are reported in Figure 7. The increase of the RMSE due to the spasms, evidenced by the lines crossing each column in Figure 7, was very similar for the three controllers in the early spasms as well as in the later ones, independently from the phase of the cycle. These results demonstrated that even if the EMC was never trained to respond to such disturbances both the stability of the system and its capability to generalize to unknown events was comparable to the other two reference controllers, keeping anyway the specific advantages on fatigue estimation.

In order to test resistance to random noises of different amplitudes (ranging from 25% to 50% of the knee torque), the comparison of the three controllers was performed in terms of the RMSE during flexion extension

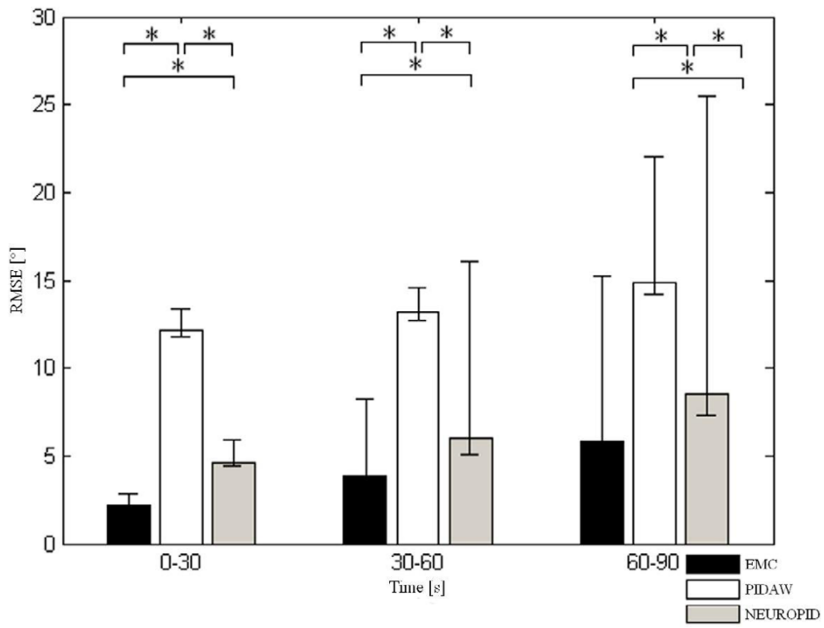


Figure 6
Statistical comparison of EMC vs traditional controllers. Comparison of the performance obtained by EMC, PIDAW and NEUROPID in terms of the median and the quartiles of the RMSE obtained on 6 different testing angular trajectories. Such comparison was divided in three periods (0–30 s, 30–60 s and 60–90 s). The Kruskal-Wallis test highlighted significant differences between the controllers. The asterisks indicate that the Dunn-Sidak post-hoc test showed a significant difference between the RMSE.

movements lasting 100 s. A random noise was added to the whole sequence. The EMC had the best performance reducing evidently fatigue effect and tracking discrepancy, both in the initial oscillations (without fatigue) and for the last oscillations (9–10th) when fatigue is strongly affecting the Plant performances (Figure 8).

Robustness

EMC robustness with respect to changes in the Plant parameters was tested by calculating the error in tracking performance and the results are shown in Figure 9. The circles represent the error on the first flexion extension (wave1), while asterisks represent the values of the RMSE on the fifth flexion extension, i.e., after about 50 s of stimulation (wave 5).

Modifications in the viscoelastic properties, i.e., damping value, of the Plant were compensated very well by the EMC, damping changes of 50% affected the results less than 1° both in the first and in the fifth leg movement. Analogously, the EMC coped with the changes in the time required for recovery from fatigue, (T_{rec}), well. As expected a slight increase of the RMSE was obtained when T_{rec} was increased. Naturally, the first wave was not affected much by the variation of this parameter, like the variation in T_{fat}, because fatigue was not yet present at this stage of the movement. The effect of variations of T_{fat} was much more evident, when negative variations of T_{fat} were simulated (meaning a faster occurrence of fatigue) and in fact the RMSE increases exponentially in the left part of the panel referred to as T_{fat} in Figure 9. On the contrary, positive variations of T_{fat} reduced the error. Indeed, the EMC was trained to face fatigue up to the defined value of T_{fat}; higher values of T_{fat} indicated a slower fatiguing, well addressed by the EMC. Lower values of T_{fat}, on the contrary, were not in anyway included in the training set. The robustness of the controller when lower leg mass was simulated, was good in the case of a reduction of the mass. In this case, while an overshooting was shown at the first cycle, once the error was detected by the feedback, NF correction reduced the error (asterisks lower than circles). On the contrary, in case of an increase of the mass of the leg, the effect was very similar to when fatigue occurred faster, showing a quick increase of the error. However, positive variations of 20% led to error of less than 10°.

Discussion

The EMC showed good tracking performance when fatigue phenomenon was not present or stayed at low levels. In those cases, the EMC was more accurate with respect to the other two controllers tested, especially in avoiding the PID time lag. Similar levels of angular errors

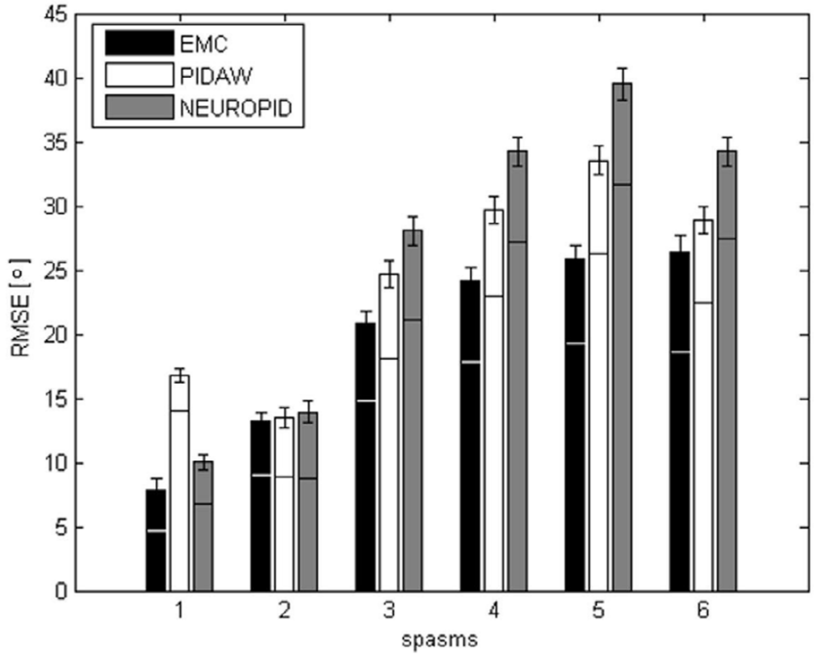


Figure 7

Capability to react to spasms. Comparison of the three controllers (EMC, PIDAW and NEUROPID) performed in terms of the RMSE during flexion extension lasting 100 s. X axis represents the events indicating spasms occurrence during the movement. 6 spasms were randomly added to the 100 s angular trajectories. Each spasm lasted 2 s and its amplitude was varied from 20% and 30% of the maximal total torque of the knee.

were showed by other controllers proposed in literature, like the Sliding Mode Controller [20]. Namely, the EMC tracking error on the same trajectories used by Jezernik was about 4.5°, which is quite comparable to the best result reported by those authors (about 3°).

However, the most significant advantage of the EMC was visible when fatigue was great. The behaviour of the EMC during the process of tiring was completely different to the other two controllers, PIDAW and NEUROPID, reducing the RMSE by a third after 100 s.

The EMC achieved such different performance because the NF correction considered tracking of the desired trajectory as well as the level of fatigue. The training solution of the EMC translated the angular error into pulse width correction estimating the differences between the actual fatigued performance with respect to the nominal one. In this way, the EMC corrected the stimulation parameters by giving an extra pulse width correlated to the level of fatigue. The main effect of this strategy was that stimulation parameters grew much more slowly during repeated flexion extensions, thereby not saturating and not overstressing the stimulated muscle. This behaviour was exactly contrary to PID based controllers [1,15,16,21]. The latter stimulated the muscle to a maximum, depending only on the angular error and not evaluating the feasibility of tracking. This solution, once fatigue was too strong to permit proper tracking, caused an over-stimulation of the muscle, inducing an even more rapid fatigue ramp. Analogously, the PG/PS controller proposed by Reiss and Abbas [19] had the same philosophy of the PID, being the adaptive controller tuned by a PD controller on the angular error only. Anyway, not a complete test on fatigue managing was available for the PG/PS controller, being fatigue included in the muscle model only in the simulations discussed in [17], where the testing trajectory was very small in amplitude (25°), lasted just 10 s, with a stimulation frequency of 20 Hz. Such testing trajectory is completely different from those used in EMC training and testing and, anyway, is not adequate to verify the capability of coping the fatigue occurrence as specifically aimed in the EMC design.

In addition, the EMC was able to resist well to mechanical disturbances, even if such occurrences were not included in the examples used for training. This property was similar to PID based controller, thereby maintaining the advantage of the best fatigue mapping learnt by the EMC.

Robustness in the model parameters was tested and the satisfactory results obtained ensured good generalization

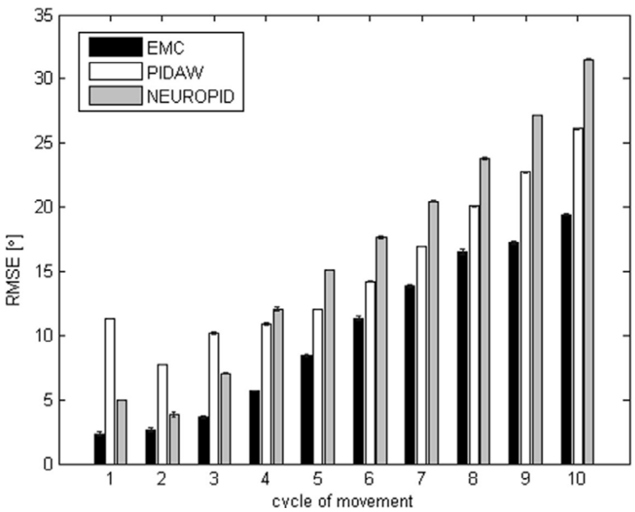


Figure 8
Capability to react to distributed noise. Comparison of the three controllers performed in terms of the RMSE during flexion extension sequence of 10 oscillations for a total duration of 100 s. Random noises of different amplitudes were added on the knee torque (ranging from 25% to 50% of the maximum knee torque values). The RMSE was evaluated separately for each oscillation of the angular trajectory (X axis), hence at different levels of fatigue.

for successive sessions on the same subject, especially in the case of a good muscle conditioning. It has to be mentioned that offline, after each single session, depending on the observed errors, an extra training of NF could be performed if necessary.

To verify the stability of the EMC controller for step and ramp knee movements, analogously to Jezernik *et al*. [20] and the EMC remained always stable. Instability was never observed in all the experiments carried out in this study.

EMC training on the preparation of the exercise is a crucial point in the clinical applicability of the controller. Actually, in order to train the inverse model (ANNIM) the subject needs to be stimulated with a variety of pulse width shapes and the corresponding knee angle are recorded. The set of pulse width/angle forms the training set of the ANNIM when the task is done in nominal conditions (no fatigue) or in initial single movements with long rest phases in between. Once such network is trained, the subject is stimulated longer, inducing fatigue, in a following session. A set of trajectory errors will be used as training input of the NF neural network and the corresponding desired output will be built using the replication of the ANNIM (Figure 2). These ANN training sets could be collected during the conditioning period, when patients usually become familiar with electrical stimulation and increase muscular tone. In such a way, a conditioning period, which normally takes place before the controlled stimulation session, is exploited for controller training. By the way these collection procedures do not globally change the programme for patients and do not require any specific setup except the one which will be used for the functional neuroprosthesis, simplifying therapists' efforts. This aspect is one important advantage with respect to other controllers discussed in literature, such all those based on PID [17-19,25,26] as well as model based controllers [25] and sliding mode controllers [20].

The last point concerns the possibility to generalize the EMC control strategy to more complex motor tasks. In these experiments, we utilized a cyclic joint angle tracking task to evaluate the performance of the control system. This task, which has been used in the evaluation of several neuroprosthesis control systems in the past [1,15-21,25] may represent a simplified version of practical actions that could be performed with FES systems, such as: FES exercise systems that utilize cyclic movements and lower-extremity FES systems for generating patterned movements such as gait, side-stepping, and stair-climbing. More importantly, however, the task used in these experiments demonstrates the ability of the controller to automatically account for the subject-specific musculo-skeletal input/output properties, and for fatigue occurrence that would be exhibited in many FES tasks.

Supporting a good translational property of EMC over multiple muscles and more complex tasks two points should be considered: first, EMC do not use any extra setup to identify the parameters of the controller. Second, neural networks can process many inputs and have many outputs; they are readily applicable to multivariable systems.

Conclusion
We proposed a controller, called EMC, for neuromuscular stimulation of knee flexion extension which is composed by a feedforward inverse model and a feedback controller, both implemented using neural networks. The training of the networks is conceived to avoid to a therapist and a patient any extra experiment, being the collection of the training set included in the normal conditioning exercises. The EMC philosophy differs from classical feedback controllers because it does not merely react to the error in the tracking of the desired trajectory, but it estimates also the actual level of fatigue of the muscles. This solution allows to prolong the exercise improving the conditioning effects. In addition, the controller robustness was tested, demonstrating a good capability of generalizing and thus reducing the time consuming for re-training, especially if subjects conditions are improving.

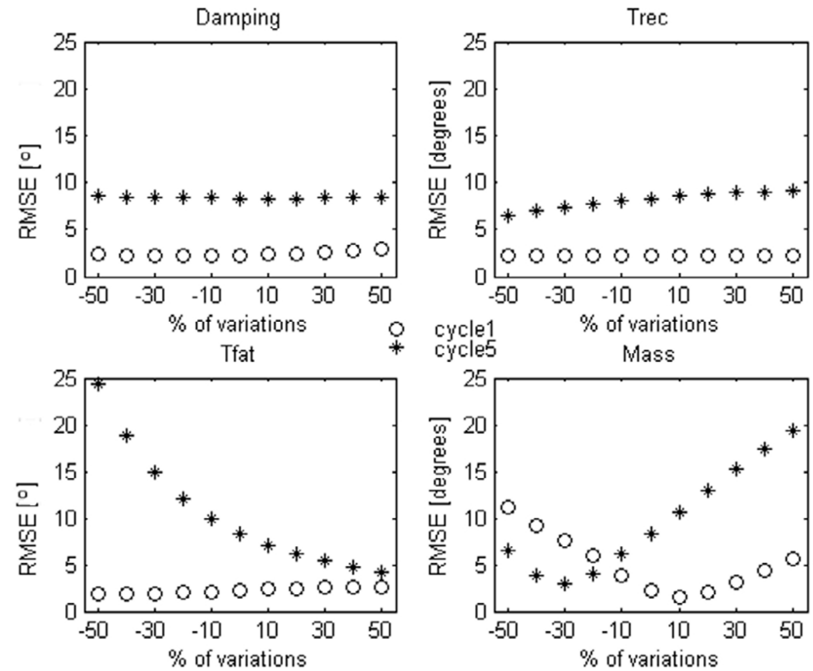


Figure 9
EMC robustness. EMC generalization performance obtained changing 4 parameters: damping, T_{rec}, T_{fat} and the limb mass. The horizontal axis indicates the percent by which the parameter has been varied, the vertical axis indicates the RMSE error. The errors in the first oscillation (wave 1, reported in circles) and in the fifth (wave 5 reported in asterisks) of a repetitive angular trajectory are shown.

Competing interests
The author(s) declare that they have no competing interests.

Authors' contributions
AP and SF have made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data and manuscript drafting; EDM have made part of acquisition of data, analysis and interpretation of data and have been involved in drafting the manuscript; and GF have made substantial contributions to conception and design and interpretation of data and have given final approval of the version to be published.

Acknowledgements
The authors wish to thank Marco Iannò and the students who collaborated to part of the activities.

References
1. Ferrarin M, Palazzo F, Riener R, Quintern J: **Model-based control of FES-induced single joint movements.** *IEEE Trans Neural Syst Rehabil Eng* 2001, **9(3):**245-257.
2. Chen J, Yu N, Huang D: **Applying fuzzy logic to control cycling movement induced by functional electrical stimulation.** *IEEE Trans on Rehab Eng* 1997, **5(2):**158-169.
3. Hunt K, Stone B, Negard N: **Control strategies for integration of electric motor assist and functional electrical stimulation in paraplegic cycling: utility for exercise testing and mobile cycling.** *IEEE Trans Neur Sys Rehab Eng* 2004, **12(1):**89-101.
4. Riener R, Fuhr T: **Patient-driven control of fes-supported standing-up: a simulation study.** *IEEE Trans Rehab Eng* 1998, **6:**113-124.
5. Wieler M, Stein RB, Ladouceur M, Whittaker M, Smith AW: **Multicenter evaluation of electrical stimulation systems for walking.** *Arch Phys Med Rehabil* 1999, **80:**495-500.
6. Haugland M, Larsen B, Burridge JH, Svaneborg N, Iversen H: **A preliminary non-randomised study to evaluate the safety and performance of the acti-gait implanted drop-foot stimulator in established hemiplegia.** *Proceedings of 9th Annual Conf Int FES Soc: 6–9 September 2004; Bournemouth UK* 2004:153-55.
7. Smith B, Peckham P, Keith M, Roscoe D: **An externally powered, multichannel, implantable stimulator for versatile control of paralyzed muscle.** *IEEE Trans Biomech* 1987, **34(7):**499-508.
8. Ijzerman M, Stoffers T, In 't Groen F, *et al.*: **The ness handmaster orthosis: restoration of hand function in c5 and stroke patients by means of electrical stimulation.** *J Rehabil Sci* 1996, **9:**86-89.
9. Vitenzon AS, Mironov EM, Petrushanskaya KA: **Functional electrostimulation of muscles as a method for restoring motor functions.** *Neurosci Behav Physiol* 2005, **35(7):**709-14.
10. Stein RB, Chong SL, James KB, Kido A, Bell GJ, Tubman LA, Bélanger M: **Electrical stimulation for therapy and mobility after spinal cord injury.** *Prog Brain Res* 2002, **137:**27-34.
11. Lan N, Crago PE, Chizeck HI: **Control of end-point forces of a multijoint limb by functional electrical stimulation.** *IEEE Trans Biomed Eng* 1991, **38:**953-965.
12. Marsolais EB, Kobetic R: **Functional electrical stimulation for walking in paraplegia.** *J Bone Joint Surg* 1987, **69-A(5):**728-733.
13. Peckham PH, Keith MW: **Motor prostheses for restoration of upper extremity function.** In *Neural Prostheses: Replacing Motor Function After Disuse or Disability* Edited by: Stein RB, Peckham PH, Popovic D. London, UK: Oxford Univ. Press; 1992:162-190.

14. Hatwell MS, Oderkerk BJ, Sacher CA, Inhar GF: **The development of a model reference adaptive controller to control the knee joint of paraplegics.** *IEEE Trans on Automatic Control* 1991, **36:**683-691.
15. Veltink P: **Control of fes-induced cyclical movements of the lower leg.** *Med Biol Eng Comput* 1991, **29:**8-12.
16. Chang G, Luh J, Liao G: **A neuro-control system for the knee joint position control with quadriceps stimulation.** *IEEE Trans Rehabil Eng* 1997, **5:**2-11.
17. Abbas J, Chizack H: **Neural network control of functional neuromuscular stimulation systems: Computer simulation studies.** *IEEE Trans Biomed Eng* 1995, **42(11):**1117-1127.
18. Riess J, Abbas J: **Adaptive neural network control of cyclic movements using functional neuromuscular stimulation.** *IEEE Trans Rehab Eng* 2000, **8(1):**42-52.
19. Riess J, Abbas J: **Adaptive control of cyclic movements as muscles fatigue using functional neuromuscular stimulation.** *IEEE Trans on Neural Syst and Rehab Eng* 2001, **9(3):**326-330.
20. Jezernik S, Wassink RGV, Keller T: **Sliding Mode Closed-Loop Control of FES: Controlling the Shank Movement.** *IEEE Trans on Biomed Eng* 2004, **51(2):**263-272.
21. Ferrante S, Pedrocchi A, Iannò M, De Momi E, Ferrarin M, Ferrigno G: **Functional electrical stimulation controlled by artificial neural networks: pilot experiments with simple movements are promising for rehabilitation applications.** *Funct Neurol* 2004, **19(4):**243-252.
22. Kumpaty S, Narendra K, Parthasarathy K: **Identification and control of dynamical systems using neural networks.** *IEEE Trans Neural Networks* 1990, **1:**4-27.
23. Matsuoka K: **Noise injection into inputs in back-propagation learning.** *IEEE Transactions on Systems, Man and Cybernetics* 1992, **22(3):**436-440.
24. Hagan M, Menhaj M: **Training feedforward networks with the Marquardt algorithm.** *IEEE Trans Neural Networks* 1994, **5(6):**989-993.
25. Quintern J, Riener R, Rupprecht S: **Comparison of simulation and experiments of different closed-loop strategies for functional electrical stimulation: experiments in paraplegics.** *Artif Organs* 1997, **21:**232-235.
26. Ferrarin M, D'Acquisto E, Mingrino A, Pedotti A: **PID controller for knee movement restoration with closed-loop fes system.** *Proceedings of the 18th Annual International Conference of the IEEE Engineering in Medicine and Biology Society: 31 October–3 November 1996; Amsterdam, The Netherlands* 1996:453-454.
27. Ferrante S, Previdi F, Ferrigno G: **Model identification for fes supported standing up and sitting down.** *Proceedings of 9th Annual Conf Int FES Soc: 6–9 September 2004; Bournemouth UK* 2004:210-212.

Journal of NeuroEngineering and Rehabilitation

BioMed Central

Correction

Open Access

Correction: Error mapping controller: a closed loop neuroprosthesis controlled by artificial neural networks

Alessandra Pedrocchi*, Simona Ferrante, Elena De Momi and Giancarlo Ferrigno

Address: Nitlab, Bioengineering Department, Politecnico di Milano, Via Garofalo, 39, 20133, Milano, Italy

Email: Alessandra Pedrocchi* - alessandra.pedrocchi@polimi.it; Simona Ferrante - simona.ferrante@polimi.it; Elena De Momi - elena.demomi@polimi.it; Giancarlo Ferrigno - giancarlo.ferrigno@polimi.it

* Corresponding author

Published: 20 April 2007

Journal of NeuroEngineering and Rehabilitation 2007, **4**:9 doi:10.1186/1743-0003-4-9

Received: 22 January 2007
Accepted: 20 April 2007

This article is available from: http://www.jneuroengrehab.com/content/4/1/9

After the publication of this work [1], we noticed in figure 2 (see Figure 1) the signal indicated as the desired output to train NF was not correctly reported in the figure. The training signal is the result of the difference between PW_{act} and PW_{des} as it is explained in the text, and as it is shown in the new figure we are showing here.

We apologize for the inconvenience that this inaccuracy in the paper might have caused to the readers.

References

1. Pedrocchi A, Ferrante S, De Momi E, Ferrigno G: **Error mapping controller: a closed loop neuroprosthesis controlled by artificial neural networks.** *Journal of NeuroEngineering and Rehabilitation* 2006, **3**:25.

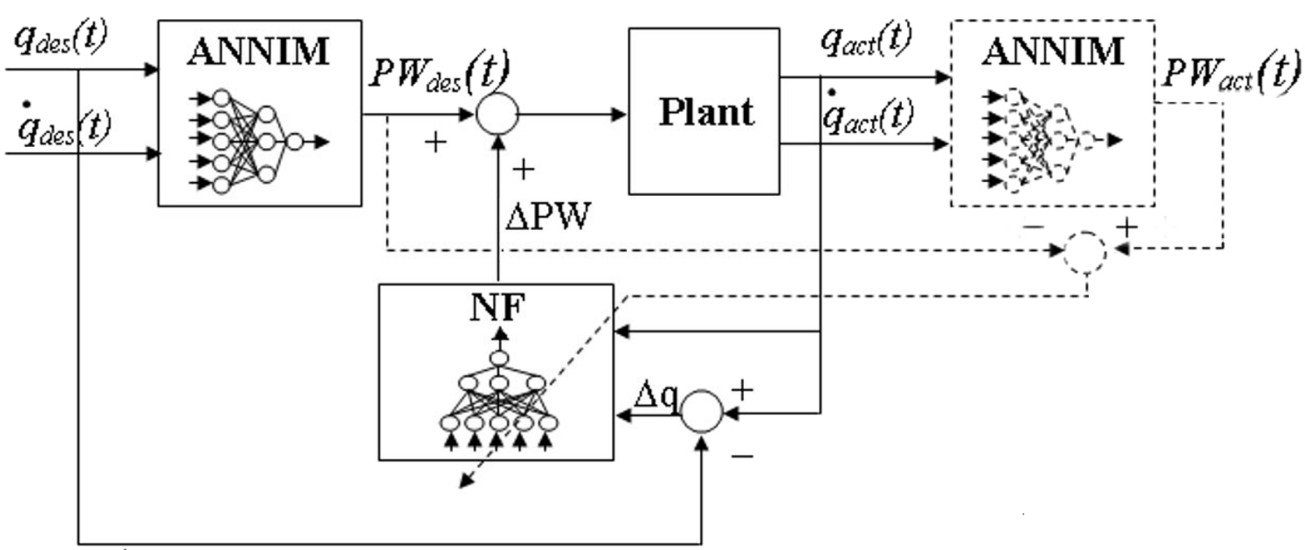


Figure 1
NF Training scheme. Scheme used to collect the training set of NF. The training output signal of NF is the difference between PW_{act} and PW_{des} and not the PW_{act} as it was wrongly indicated in figure 2 of the original paper.