

Topical Review

Biomimetic rehabilitation engineering: the importance of somatosensory feedback for brain–machine interfaces

David Perruchoud¹, Iolanda Pisotta², Stefano Carda³,
Micah M Murray^{1,4,5,6} and Silvio Ionta^{1,7}

¹The Laboratory for Investigative Neurophysiology (The LINE), Department of Radiology and Department of Clinical Neurosciences, University Hospital Center and University of Lausanne, Lausanne, Switzerland
²NeuroRobot Lab - Laboratory of Robotic NeuroRehabilitation, IRCCS Fondazione Santa Lucia, Rome, Italy

³Department of Neuropsychology and Neurorehabilitation, University Medical Centre of Lausanne (CHUV), 1011 Lausanne, Switzerland

⁴EEG Brain Mapping Core, Centre for Biomedical Imaging (CIBM) of Lausanne and Geneva, Switzerland

⁵Department of Hearing and Speech Sciences, Vanderbilt University, Nashville, TN, USA

⁶The Department of Ophthalmology, Jules Gonin Hospital, University of Lausanne, Switzerland

⁷Rehabilitation Engineering Laboratory, Institute of Robotics and Intelligent Systems, Swiss Federal Institute of Technology (ETHZ), Zurich, Switzerland

E-mail: ionta.silvio@gmail.com

Received 16 February 2015, revised 8 March 2016

Accepted for publication 11 April 2016

Published 25 May 2016



CrossMark

Abstract

Objective. Brain–machine interfaces (BMIs) re-establish communication channels between the nervous system and an external device. The use of BMI technology has generated significant developments in rehabilitative medicine, promising new ways to restore lost sensory-motor functions. However and despite high-caliber basic research, only a few prototypes have successfully left the laboratory and are currently home-deployed. **Approach.** The failure of this laboratory-to-user transfer likely relates to the absence of BMI solutions for providing naturalistic feedback about the consequences of the BMI's actions. To overcome this limitation, nowadays cutting-edge BMI advances are guided by the principle of biomimicry; i.e. the artificial reproduction of normal neural mechanisms. **Main results.** Here, we focus on the importance of somatosensory feedback in BMIs devoted to reproducing movements with the goal of serving as a reference framework for future research on innovative rehabilitation procedures. First, we address the correspondence between users' needs and BMI solutions. Then, we describe the main features of invasive and non-invasive BMIs, including their degree of biomimicry and respective advantages and drawbacks. Furthermore, we explore the prevalent approaches for providing quasi-natural sensory feedback in BMI settings. Finally, we cover special situations that can promote biomimicry and we present the future directions in basic research and clinical applications. **Significance.** The continued incorporation of biomimetic features into the design of BMIs will surely serve to further ameliorate the realism of BMIs, as well as tremendously improve their actuation, acceptance, and use.



Original content from this work may be used under the terms of the [Creative Commons Attribution 3.0 licence](https://creativecommons.org/licenses/by/3.0/). Any further distribution of this work must maintain attribution to the author(s) and the title of the work, journal citation and DOI.

Keywords: biomedical engineering, biomimicry, sensorimotor integration, brain, spinal cord injury, amputation, disconnection

1. Introduction

Every year in the United States of America alone, about two million people suffer from the consequences of spinal cord injury (250 thousand; Jackson *et al* 2004) or limb loss (1.6 million; Ziegler-Graham *et al* 2008). These, and other similar breakdowns in communication between the central nervous system and the body's periphery, result in a complex picture of symptoms including motor and/or somatosensory impairments. Despite the great technological developments in e.g. spinal cord repair (van den Brand *et al* 2012, Tabakow *et al* 2014), and even if some of the most advanced approaches are currently undergoing human clinical trials (Wang *et al* 2014), the new solutions are still far from being implemented as a part of standard rehabilitation procedures. Until clinical and non-clinical researchers identify treatments for each of these conditions and learn how to re-establish functions of a disconnected or uncontrolled limb, patients will continue to await novel solutions to re-acquire even the slightest part of their former mobility and autonomy.

Brain-machine interfaces (BMIs) are an approach that proposes bypassing the lesion or substituting the involved body segment and instead aims to restore at least part of the sensory-motor functions in patients suffering from movement disorders due to disconnection or loss. BMIs decode neural activity associated with motor intentions directly from the brain or nerves and feed it into an external device (see also Rupp *et al* 2014). The first BMI applications have been the control of robotic prostheses on the basis of invasive (Fetz 1969, Fetz and Finocchi 1971, Fetz and Baker 1973) or non-invasive recordings (Vidal 1973). The ensuing forty years have been marked by intensive worldwide research and growth of the field at an astonishing pace. After an initial phase of development and testing, BMI technologies are nowadays receiving increasing attention from clinics (Vaughan and Wolpaw 2006, Sellers *et al* 2010) and the media (Nicoletis and Servick 2014).

Here, we focus on the importance of generating matching somatosensory percepts when designing BMIs to restore lost motor functions. The present work summarizes the current biomedical engineering evidence on the different steps required to bridge the gap between the onset/appearance of a sensory-motor disease and its rehabilitation. In this vein, this review is organized in six independent but concatenated sections, each focused on a particular aspect of technology-based sensorimotor restoration. After an initial introduction (section 1, here), we focus on the first step of this restoration: the user's classification and the selection of the appropriate BMI approach (section 2). Second, the user needs to control the BMI system; here we review several techniques to decode neural activity and different means to exploit useful biological signals for BMI control (section 3). Third, the BMI system has to volley back information on its current state to the user; here we discuss current approaches to equip BMIs with

sensory feedback and mimic natural conditions to increase acceptance and incorporation (sections 4 and 5). In particular, we focus on the importance of biomimetic somatosensory feedback (section 4) and the available techniques to produce sensory-motor biomimicry (section 5). Finally, we review current limitations and future perspectives to further develop BMI systems (section 6).

2. User-BMI integration

The first step in clinically-applied BMIs is the classification of the user's needs, to find the best fit within the available BMI solutions. As the same BMI approach can address similar symptoms (despite different etiologies), the best user-BMI match could instead be based on the effects of disease. Three main classifications have been suggested (Wolpaw *et al* 2006): (1) mild and/or localized motor impairments, but presence of volitional movements—for this class of users, BMI technology likely has limited benefit since their residual muscular activity is sufficient to effectively control any assistive device; (2) some degree of volitional movements—users in this class (e.g. high cervical spinal cord injury) could benefit from a hybrid BMI/electromyographic (EMG) system; (3) no volitional movements at all—this class of users could rely entirely on BMIs.

Especially in the third class of users, the ability to generate specific brain signals is crucial, because the BMI will be controlled on this basis. However, some clinical conditions (e.g. locked-in syndrome) can deteriorate this ability, leading to so-called 'illiteracy' for the BMI (Guger *et al* 2003, Vidaurre and Blankertz 2010). One possible solution is 'co-adaptation' (Vidaurre *et al* 2011), in which both users and BMIs dynamically adapt to each other (Millan *et al* 2010, Wolpaw and Wolpaw 2012). That is, the BMI system regularly updates its decoding algorithm based on new neural data from the user, and the users optimize their strategies based on the performance of the BMI device. In most cases, this closed-loop system results in steeper learning curves and/or generally improved BMI efficiency (Bryan *et al* 2013, Mattout *et al* 2015). However, it should be noted that in such cases the users evaluate the performance of BMI devices exploiting only visual information. In other words, to determine whether the BMI outcome corresponds to their intentions they can only look at the device.

How can co-adaptation be further ameliorated? In this regard, it is crucial to consider the concept of biomimicry: 'the elicitation of naturalistic patterns of neuronal activation' (Bensmaïa and Miller 2014). In natural conditions, even the simplest motor act triggers a cascade of complex multisensory afferents (vision, hearing, somatosensation) resulting in a broad panel of neural activity patterns. Thus, extending and specifying previous definitions, here we refer to biomimicry as the attempt to artificially emulate these multisensory

spatio-temporal features of biological processes. On this basis, we define as ‘biomimetic’ any approach aiming at using artificial stimulation to reproduce naturalistic patterns of neuronal activity associated with normal sensory sensations and bodily control; namely the artificial recreation of the neural activity naturally occurring during normal experiences. Far from being an all-or-none phenomenon, we propose that biomimicry is a graded process and it can be progressively augmented, e.g. in today’s BMIs. Under this conceptualization, a BMI system in which only vision is available to evaluate its performance is *less* biomimetic than a *more* biomimetic one exploiting both visual and somatosensory feedback, and therefore eliciting patterns of neural activity more closely corresponding to natural conditions.

Thus one possibility to ameliorate co-adaptation is to increase the biomimicry of BMIs by providing more channels of communication from the BMI to the user including additional sensory modalities, e.g. somatosensation. The tight relationship between biomimicry and co-adaptation is particularly evident in the context of movements (Tabot *et al* 2015) because the implementation of techniques able to recreate somatosensations are increasing the biomimicry of old-fashioned BMIs (Berg *et al* 2013, Tabot *et al* 2013), augmenting their co-adaptation abilities. Relying on such more naturalistic and complex multisensory neural schemes, we postulate that future biomimetic systems will be experienced more intuitively by the users, facilitating the user-BMI co-adaptation, and easing the BMI acceptance and integration into daily routines.

3. Neuroprosthetic control

After establishing the user-BMI communication channel (section 2), the second step consists in providing users with intuitive ‘control’, i.e. the ability to voluntarily change the states of a dynamic system in order to achieve specific tasks and desired goals (see also Tucker *et al* 2015). To this aim, distinguishable brain signals have to be extracted and two classes of techniques can be used to this aim: non-invasive and invasive.

Within the non-invasive category, despite some approaches exploiting electromyography (Scheme and Englehart 2011, Ambrosini *et al* 2014, Memberg *et al* 2014) or the electroculogram (Usakli *et al* 2010), the most common procedure for BMI control relies on electroencephalography (EEG) (Birbaumer *et al* 2014, Bortole *et al* 2014). It can be combined with advanced decoding algorithms to overcome possible drops in signal quality (e.g. due to the resistance of the skull) (Wolpaw and McFarland 2004). EEG-based BMIs have been used to move wheelchairs (Carlson and Millán 2013), spell words (Hwang *et al* 2012, Yin *et al* 2013), and estimate the kinematics of hand movements (Bradberry *et al* 2010) and locomotion (Presacco *et al* 2011). Building on the effectiveness of mental simulation in activating specific neural mechanisms (Ionta *et al* 2010), simulation of hand and foot movements has also been shown to enable BMI control (McFarland *et al* 2010).

Invasive techniques tend to provide less noisy signals with better spatial resolution. However, they present downsides due to surgical implantation, limited number of channels, risk of infection, and cellular isolation or death. The most common invasive techniques are intraneural recording, electrocorticography (ECoG), and intracortical electrodes. Being directly inserted inside the nerve fascicles, intraneural electrodes can record peripheral activity (Rossini *et al* 2010, Micera *et al* 2010a, 2010b) to exploit relevant tasks, such as natural grasping (Micera *et al* 2011, Di Pino *et al* 2012). Surgically inserting grids or strips of subdural electrodes directly on the cortex, ECoG relies on the same principles as EEG but avoids many sources of signal blurring. Being able to encode the neural activity associated with movement planning and control (Halje *et al* 2015), ECoG can be used to control software (Schalk *et al* 2008, Leuthardt *et al* 2011, Milekovic *et al* 2012, Wang *et al* 2013), robotic devices (Kwak *et al* 2015), and restore motor functions (Wang *et al* 2013). Finally, intracortical recording is based on the surgical insertion of high-density electrode microarrays to record the activity of single neurons (Campbell *et al* 1991). At present, intracortical recordings performed in humans have entailed pilot trials (Hochberg *et al* 2006, Simeral *et al* 2011, Hochberg *et al* 2012, Collinger *et al* 2013), and most of the BMI work on intracortical recording has been carried out on non-human mammals (Serruya *et al* 2002, Velliste *et al* 2008, O’Doherty *et al* 2009, Ethier *et al* 2012, Flint *et al* 2012). This particular technique raises the issue of long-term signal stability, as signal quality tends to decrease with time (Takmakov *et al* 2015) due to the emergence of inflammation and fibrotic tissues that isolate the electrodes as a natural immune response of the neuroglia (Polikov *et al* 2005). Nevertheless, a new generation of biocompatible flexible electrodes decreases the risk of rejection and provides stable signals for longer periods (Marin and Fernandez 2010). The most notable recent applications of intracortical BMI for humans include giving a tetraplegic patient a point-and-click ability up to 1000 days after implantation (Simeral *et al* 2011), or the natural control of a seven degrees-of-freedom neuroprosthesis (Hochberg *et al* 2012, Collinger *et al* 2013).

Altogether, multiple approaches can be considered for BMI control, each of which is best-suited for a different population of patients. The highest BMI performance is still obtained using invasive recording techniques, but recent advances in EEG signal processing are rapidly filling the gap (Chavarriaga *et al* 2010) and might provide similar results within a cheap, non-invasive, and perfectly safe framework in the upcoming decades (Leeb *et al* 2013).

4. Biomimicry and (somato)sensory reproduction

Section 3 highlighted how an ideal BMI should translate brain signals related to biological movements into computational commands to activate mechanical movements (Pistohl *et al* 2012). However, not only pure motor disorders, but also deficits associated with sensory loss can dramatically affect movement execution (Sainburg *et al* 1995). In traditional

BMIs, sensory feedback is primarily visual and is linked to the mere observation of the movement. However, vision alone does not provide important information on objects' material properties, such as their texture, stiffness, slipperiness, weight, roughness, compliance, etc. In addition, visual information is pointless for cutaneous senses, such as pressure during isometric muscle activity, in which a modulation of the applied force does not translate into actual movement (for example while grasping a stiff object). Thus, despite the indisputable importance of vision for motor performance (Johansson and Flanagan 2009), visual feedback alone cannot satisfy the requirements for the effective manipulation of a neuroprosthesis. Instead, kinesthetic senses are an inescapable source of information to properly interact with the environment. Through senses such as proprioception or touch, objects' material properties are continuously extracted during manipulation and are mediated by the appropriate somatosensory afferents, which allow a fine-tuned movement recalibration in real-time. Thus in natural conditions, any movement is indissolubly associated with a cascade of, at least, visual and kinesthetic consequences, which are used to evaluate the results of the action and possibly correct some or all components of the movement itself (e.g. preserving direction but correcting force).

Mimicking this complex and multisensory scenario, the combination of visual and kinesthetic feedback can increase the biomimicry of modern BMIs (Callier *et al* 2015). At the neural level this combination can biomimetically improve the similarity between reproduced and natural neural activity. This aspect can help the users to recognize the device as more natural, based on the correspondence between expected and perceived multisensory consequences of a given BMI movement. Indeed, the artificial reproduction of natural somatosensations associated with or following consequently from a motor act is an important component to help users diminish the differences between natural functions and BMI reproductions. A real-time artificial somatosensory feedback needs to be provided to the user as a consequence of the prosthetic movement (Yanagisawa *et al* 2012), augmenting the system's biomimicry. This feedback could help the user to identify appropriate mental strategies to adjust brain activity according to the device's performance. In addition, based on this feedback, the BMI system could use advanced machine-learning algorithms (1) to continuously adapt the prosthesis to the user (Vidaurre *et al* 2011) and (2) to receive real-time feedback of its own performance through, for example, the detection of error-related brain activity patterns (Ferrez and Millán 2005, Ferrez and del 2008, Chavariaga and Millán 2010, Combaz *et al* 2012). In order to close this user-BMI-user loop, efficient control and real-time sensory feedback have to be properly integrated (Pisotta *et al* 2015). For instance, recent evidence showed that congruent sensory feedback (visuo-tactile) is crucial to properly represent our body (Ionta *et al* 2013) and can boost the sense of ownership also for a prosthesis (Marasco *et al* 2011), leading to acceptance and recognition of the prosthesis as part of one's own body.

Along these lines, BMIs' biomimicry is continuously increased, promoting more naturalistic interactions with the environment, including somatosensory signals (Ramos-Murguialday *et al* 2012). The transition from only visual to a more biomimetic multisensory feedback is starting to yield its first results. Building on previous evidence on the effectiveness of mental simulation in activating sensory-motor pathways (Fourkas *et al* 2006), Cincotti *et al* (2007) integrated either visual or vibrotactile real-time feedback while participants mentally simulated the movement of their right or left hand, focusing on kinesthetic aspects. All participants reported a more natural feeling while using vibrotactile feedback (Cincotti *et al* 2007). The potential interference between somatosensory stimulation and movement control was evaluated in another study in which mental simulation of left or right hand movements coincided with vibrotactile feedback on the left or right arm (Chatterjee *et al* 2007). The results showed that the ipsilateral vibrotactile feedback yielded better results, while the incongruent contralateral vibrotactile feedback generated greater distraction (Chatterjee *et al* 2007). Based on current models of healthy (Borich *et al* 2015) and aberrant (Perruchoud *et al* 2014) sensory-motor integration, this subjective preference for tactile feedback might arise from the tight relationship between the motor and somatosensory (instead of visual) systems.

In summary, the effective implementation of somatosensory feedback in standard BMIs is an important step towards the creation of better biomimetic conditions, but still requires technological developments to produce closed-loop systems between output (prosthetic movement) and input (feedback regarding the movement itself). In the majority of current BMIs, this output-input balance cannot be reached because of unnatural or modality-mismatching feedback, and indeed the need of somatosensory feedback is one bottleneck for future BMIs (Lebedev and Nicolelis 2006).

5. Sensory-motor biomimicry

The improvements in BMIs have raised the possibility to completely bypass a defective sensory organ and directly stimulate (upstream) the nervous system. Building on intraneural recording of peripheral neural activity (section 3), this approach can be used to stimulate peripheral nerves and biomimetically elicit sensory percepts to be coordinated with motor routines. Non-human primate research has shown that BMIs' biomimetic ability to reproduce neural natural conditions can be based on the combination of intraneural recordings and nerve stimulation. For instance, by means of intraneural recordings, the efferent signals from the brain (e.g. to an amputated hand) can be decoded and used to control and move a prosthetic hand. Simultaneously, nerve stimulation can be used to encode the afferent signals from the prosthesis and transmit information on the states of the robotic hand to the brain as a form of sensory feedback about the prosthetic movement (Ledbetter *et al* 2013). In humans, a similarly biomimetic approach can be used to restore (prosthetic) motor control and somatosensation after amputation (Saal and

Bensmaia 2015). This approach can improve the detection of objects' features, such as shape and stiffness even in absence of visual and auditory information (Raspovic *et al* 2014), produce stable somatosensory percepts (Tan *et al* 2015), and alleviate phantom pain (a chronic painful sensation from the missing limb; Knecht *et al* 1996) as measured by structured interviews (Di Pino *et al* 2012).

Remaining at the peripheral level, in combination with classic BMI approaches, the so-called 'targeted reinnervation' is substantially improving the biomimicry of neuroprostheses and has already demonstrated robust results in restoring sensory and motor functions. This technique allows the re-implantation of residual nerves after amputation into denervated muscles (Kuiken *et al* 2004, 2009). After arm amputation the nerves are redirected and re-implanted into the denervated ipsilateral chest area, creating a biomimetic bidirectional communication channel. Downstream, voluntary motor commands (normally traveling from the brain to the missing limb) create muscular activity in the reinnervated chest muscles, which function as bio-amplifiers and produce the signals on the basis of which a BMI system can translate neural information into prosthetic commands (Kuiken *et al* 2007b). Upstream, afferent channels can transmit information from the reinnervated mechanoreceptors (in the chest) to the brain regions representing the amputated limb (Kuiken *et al* 2007a). Thus, the user-BMI-user biomimetic sensory-motor loop is closed. Mimicking natural conditions, this innovative technique initiated a substantial improvement in the biomimicry of BMI robotic prostheses, leading to impressive results. For instance, patients with reinnervated skins are as accurate as with normal skin in the identification of gratings and force levels (Marasco *et al* 2009), in point localization on the skin (Marasco *et al* 2009, Sensinger *et al* 2009), and in grip force control based on biomimetically reproduced sensations of touch, pressure, shear, and temperature (Kim and Colgate 2012). One of the main outcome of the augmented biomimicry of a BMI system based on targeted reinnervation is the increased sense of ownership for a prosthetic device, based on both self-reports and physiological measurements of the prosthesis's embodiment, including vibrations and temperature changes robotically delivered to the reinnervated skin (Marasco *et al* 2011). Another important result of the biomimicry increase in BMIs based on targeted reinnervation is the restoration of hand maps at the cortical levels to represent both motor and somatosensory aspects of information incoming from and outgoing to the prosthetic hand (Hebert *et al* 2014). These examples highlight the need of constant development of biomimetic solutions based on the improvement of existing sensors, able to detect and transmit a broad range of relevant signals (different degrees of shearing, pressure, temperature and humidity), such as the artificial skin recently developed by Kim *et al* (2014).

Similarly, another solution to produce a much broader, and therefore biomimetic, panel of percepts is via intracortical microstimulation (ICMS). It is based on the same principles as intracortical recording, but employs electrode arrays instead of single electrodes (Romo *et al* 1998). Using ICMS, sensations can be induced by stimulating specific cortical

areas with particular parameters. For example, after specific ICMS-based training, owl monkeys are able to solve a binary forced-choice task, solely based on specific patterns of ICMS cues (Fitzsimmons *et al* 2007). Classic intracortical stimulation and ICMS can be carried out over longer periods with respect to intracortical recording (Callier *et al* 2015), because the electrodes' physiologic isolation due to fibrotic tissues can be circumvented by modulating the stimulation parameters (Bensmaia and Miller 2014). In this vein, the combination of ICMS (for somatosensory encoding) with BMI (for prosthetic control) can sensibly increase the biomimicry of bi-directional sensory-motor integration systems. For instance, rhesus monkeys can control a cursor based on signals from motor cortex, while the consequences of the task itself are encoded as specific ICMS patterns in the sensory cortex (O'Doherty *et al* 2009). As an extension of this study, the same approach has also been used to have rhesus monkeys control more complex situations as virtual hands (O'Doherty *et al* 2012) as well as to reproduce proprioceptive signals and guide arm movements in the absence of vision (Dadarlat *et al* 2015). Using this approach, non-human primates become able to identify virtual textures within the same time-scale as for natural tactile exploration (Lebedev *et al* 1994, Liu *et al* 2005). Similarly, recent work has shown that ICMS can be used to faithfully encode the force of skin indentation in the hand and can be easily interfaced with a robotic prosthetic hand, rendering de facto native and prosthetic body parts more equivalent in terms of tactile discrimination (Berg *et al* 2013), location, pressure, and timing (Tabot *et al* 2013). Finally, ICMS can augment perceptual abilities, e.g. invisible (infrared) inspection, by regulating intracortical stimulation as a function of signals created by implanted infrared detectors (Thomson *et al* 2013).

6. Future perspectives

6.1. Translational research

Nature inspires countless ways to manipulate technology, in order to restore lost functions and progressively reduce consequent limitations. For example, mimicking signals naturally encoded by the retina improves efficacy of ocular implants (Nirenberg and Pandarinath 2012), supporting the standpoint that common technological and scientific advances can ameliorate the sensory feedback for neuroprosthesis. However, natural perceptions require a precise combination of numerous parameters such as frequency, duration, intensity, temporal patterns, and localization (Cincotti *et al* 2007, Bensmaia and Miller 2014). Specific combinations of these features might elicit a broad range of different percepts and the complete mapping of all parameters' combinations with the corresponding percepts can be extremely laborious, if not impossible, in animal models. Conversely, this process can be reverse-engineered in humans, by having the participant reporting the sensation elicited by exhaustive combinations of features, and identifying the corresponding combination for each investigated sensory feedback. Therefore, future

directions will have to attempt the transition from animal research to human clinical trials, following the line drawn by biomimicry principles.

6.2. Cortical maintenance

Not only can physical tasks be improved by augmenting the biomimicry of BMIs, but also neurological conditions such as phantom referral tactile sensation, resulting from reinnervation and/or cortical reorganization. The proximity of the hand and face areas in the cerebral cortex is probably the reason why many upper arm amputees get referral sensations in their phantom hand while stimulating their face. Thanks to biomimetic BMIs, a proper somatosensory stimulation can be associated with specific prosthetic movements, thus re-establishing a somatotopic correspondence between motor intentions and sensory feedback and therefore limiting sprouting of cortical maps (Antfolk *et al* 2012, 2013). Future work will be required to precisely individuate the best type of BMI-based somatosensory restoration to preserve functional somatotopic cortical maps.

6.3. Users

The number of BMI research studies has steadily grown and the scientific community has started to ponder on philosophical, ethical, and social issues, including responsibility (Lucivero and Tamburrini 2008, Grübler 2011), psychological implications (Hildt 2010), dissemination of results (Haselager *et al* 2009), and safety (Denning *et al* 2009). Yet, it is important to incorporate the subjective experience of the users, as they can provide important information on the BMI's performance, including positive effects of augmented biomimicry. For example, one user described: 'After a few days I have a greater perception of my left hand, and I can use it in a more spontaneous way!'; or 'The illusion of the movement of my own hand made me feel stimulated to continue the training'; or 'I appreciate the technology, I experienced it to be useful for motor recovery' (Grübler *et al* 2014).

6.4. Scalability

In future BMIs, another important aspect that will need further attention concerns the concept of scalability. Scalability can be defined as the ability of a system to handle and accommodate variable amounts of information (Bondi 2000). Therefore, a system whose output changes proportionally to the environmental input is said to be a scalable system (Duboc *et al* 2006). At present, one of the main limitations of current BMIs is the inability to scale different degrees of single components for complex behaviors. For example, as a function of contextual factors, in naturalistic situations many different forces can be applied to perform the same action (e.g. grasping an object). We are effortlessly able to dose this force based on the object's characteristics, but the BMI might trigger the same prosthetic movement for grasping e.g. a fragile or a heavy object. Thus, future biomimetic BMI developments will include flexibility (in terms of measurable

output) and ease of reconfiguration to better address progressively more complex behaviors.

7. Conclusions

The broad scope of BMI spreads across countless applications, including entertainment, monitoring of physiological states (Lal *et al* 2003), as well as augmenting physical and sensory abilities (Wodlinger *et al* 2015). Here, we reviewed the existing literature on control and feedback for medical BMI, with a particular focus on the importance of biomimicry-relevant signals. The willingness of disabled people to enter BMI rehabilitation programs (Blabe *et al* 2015) should be further supported by the developments of means to ease the incorporation of the prosthesis into the user's body representation, considering the (possibly deteriorated) biological and psychological sense of bodily self (Ionta *et al* 2016). This is a critical step for efficient rehabilitation and is enhanced by engaging naturally-occurring control and sensory systems (Glannon 2014). An efficient incorporation of the device can be significantly reinforced via biomimicry-relevant somatosensory and proprioceptive feedback (Gallagher 2005). However, artificially re-created sensory percepts run the risk of overloading or distorting natural information processing (Lenay *et al* 2003) and, in contrast to normal situations, are not constrained by cognitive mechanisms, e.g. attention (Spence 2014). This is one of the most challenging present limitations, in order to control noisy and distracting signals as in natural conditions (reciprocal inhibition). Future work will have to render BMIs able to self-regulate their activity as a function of attentional and cognitive states. This is a core reason why understanding and developing the concept of biomimicry will be crucial for the upcoming deployment of BMIs and their laboratory-to-user transition.

Acknowledgments

This work was supported by the Swiss National Science Foundation (grant PZ00P1_148186 to Silvio Ionta and 320030-149982 to Micah Murray). The procedures followed for selecting evidence and writing the manuscript were independent from the funding source. All authors confirm that there are no known conflicts of interest associated with this publication.

References

- Ambrosini E, Ferrante S, Schauer T, Klauer C, Gaffuri M, Ferrigno G and Pedrocchi A 2014 A myocontrolled neuroprosthesis integrated with a passive exoskeleton to support upper limb activities *J. Electromyogr. Kinesiology : Official J. Int. Soc. Electrophysiol. Kinesiology* **24** 307–17
- Antfolk C, Bjorkman A, Frank S O, Sebelius F, Lundborg G and Rosen B 2012 Sensory feedback from a prosthetic hand based on air-mediated pressure from the hand to the forearm skin *J. Rehabil. Med.* **44** 702–7

- Antfolk C, D'Alonzo M, Rosen B, Lundborg G, Sebelius F and Cipriani C 2013 Sensory feedback in upper limb prosthetics *Expert Rev. Med. Devices* **10** 45–54
- Bensmaïa S J and Miller L E 2014 Restoring sensorimotor function through intracortical interfaces: progress and looming challenges *Nat. Rev. Neurosci.* **15** 313–25
- Berg J A *et al* 2013 Behavioral demonstration of a somatosensory neuroprosthesis *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **21** 500–7
- Birbaumer N, Gallegos-Ayala G, Wildgruber M, Silvoni S and Soekadar S R 2014 Direct brain control and communication in paralysis *Brain Topogr.* **27** 4–11
- Blabe C H, Gilja V, Chestek C A, Shenoy K V, Anderson K D and Henderson J M 2015 Assessment of brain–machine interfaces from the perspective of people with paralysis *J. Neural Eng.* **12** 043002
- Bondi A B 2000 Characteristics of scalability and their impact on performance *Proc. 2nd Int. Workshop on Software and Performance:* (New York: ACM) pp 195–203
- Borich M R, Brodie S M, Gray W A, Ionta S and Boyd L A 2015 Understanding the role of the primary somatosensory cortex: opportunities for rehabilitation *Neuropsychologia* **79** 246–55
- Bortole M, Controzzi M, Pisotta I and Ubeda A 2014 *Emerging Therapies in Neurorehabilitation* ed L J Pons and D Torricelli (Berlin: Springer) 235–47
- Bradberry T J, Gentili R J and Contreras-Vidal J L 2010 Reconstructing three-dimensional hand movements from noninvasive electroencephalographic signals *J. Neurosci.: Official J. Soc. Neurosci.* **30** 3432–7
- Bryan M J, Martin S A, Cheung W and Rao R P 2013 Probabilistic co-adaptive brain–computer interfacing *J. Neural Eng.* **10** 066008
- Callier T, Schluter E W, Tabot G A, Miller L E, Tenore F V and Bensmaïa S J 2015 Long-term stability of sensitivity to intracortical microstimulation of somatosensory cortex *J. Neural Eng.* **12** 056010
- Campbell P K, Jones K E, Huber R J, Horch K W and Normann R A 1991 A silicon-based, three-dimensional neural interface: manufacturing processes for an intracortical electrode array *IEEE Trans. Biomed. Eng.* **38** 758–68
- Carlson T and Millán J d R 2013 Brain-controlled wheelchairs: a robotic architecture *IEEE Robot. Auton. Mag.* **20** 65–73
- Chatterjee A, Aggarwal V, Ramos A, Acharya S and Thakor N V 2007 A brain–computer interface with vibrotactile biofeedback for haptic information *J. Neuroeng. Rehabil.* **4** 40
- Chavarriaga R, Biasucci A, Forster K, Roggen D, Troster G and Millan Jdel R 2010 Adaptation of hybrid human–computer interaction systems using EEG error-related potentials *Conf. Proc. IEEE Engineering Medicine Biology Society* vol 2010 pp 4226–9
- Chavarriaga R and Millán J R 2010 Learning from EEG error-related potentials in noninvasive brain–computer interfaces *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **18** 381–8
- Cincotti F *et al* 2007 Vibrotactile feedback for brain–computer interface operation *Comput. Intell. Neurosci.* **2007** 48937
- Collinger J L, Wodlinger B, Downey J E, Wang W, Tyler-Kabara E C, Weber D J, McMorland A J, Velliste M, Boninger M L and Schwartz A B 2013 High-performance neuroprosthetic control by an individual with tetraplegia *Lancet* **381** 557–64
- Combaz A, Chumerin N, Manyakov N V, Robben A, Suykens J A and Van Hulle M M 2012 Towards the detection of error-related potentials and its integration in the context of a P300 speller brain–computer interface *Neurocomputing* **80** 73–82
- Dadarlat M C, O'Doherty J E and Sabes P N 2015 A learning-based approach to artificial sensory feedback leads to optimal integration *Nat. Neurosci.* **18** 138–44
- Denning T, Matsuoka Y and Kohno T 2009 Neurosecurity: security and privacy for neural devices *Neurosurg. Focus* **27** E7
- Di Pino G, Benvenuto A, Cavallo G, Denaro L, Denaro V, Rossini L and Tombini M 2012 *Grasping the Future: Advances in Powered Upper Limb Prosthetics* ed V Parenti Castelli and M Troncossi (Charjah: Bentham Science Publishers) pp 28–38
- Duboc L, Rosenblum D S and Wicks T 2006 A framework for modelling and analysis of software systems scalability *Proc. 28th Int. Conf. on Software Engineering* (New York: ACM) pp 949–52
- Ethier C, Oby E R, Bauman M J and Miller L E 2012 Restoration of grasp following paralysis through brain-controlled stimulation of muscles *Nature* **485** 368–71
- Ferrez P and Millán J d R 2005 You are wrong!—automatic detection of interaction errors from brain waves *Proc. 19th Int Joint Conf Artificial Intelligence (Lausanne, EPFL-CONF)*
- Ferrez P W and del R M J 2008 Error-related EEG potentials generated during simulated brain–computer interaction *IEEE Trans. Biomed. Eng.* **55** 923–9
- Fetz E B and Finocchi D V 1971 Operant conditioning of specific patterns of neural and muscular activity *Science* **174** 431
- Fetz E E 1969 Operant conditioning of cortical unit activity *Science* **163** 955–8
- Fetz E E and Baker M A 1973 Operantly conditioned patterns on precentral unit activity and correlated responses in adjacent cells and contralateral muscles *J. Neurophysiol.* **36** 179–204
- Fitzsimmons N A, Drake W, Hanson T L, Lebedev M A and Nicolelis M A 2007 Primate reaching cued by multichannel spatiotemporal cortical microstimulation *J. Neurosci.* **27** 5593–602
- Flint R D, Lindberg E W, Jordan L R, Miller L E and Slutzky M W 2012 Accurate decoding of reaching movements from field potentials in the absence of spikes *J. Neural Eng.* **9** 046006
- Fourkas A D, Ionta S and Aglioti S M 2006 Influence of imagined posture and imagery modality on corticospinal excitability *Behav. Brain Res.* **168** 190–6
- Gallagher S 2005 *How the Body Shapes the Mind* (Oxford: Clarendon)
- Glannon W 2014 Prostheses for the will *Front. Syst. Neurosci.* **8** 79
- Grübler G 2011 Beyond the responsibility gap discussion note on responsibility and liability in the use of brain–computer interfaces *AI Soc.* **26** 377–82
- Grübler G, Al-Khodairy A, Leeb R, Pisotta I, Riccio A, Rohm M and Hildt E 2014 Psychosocial and ethical aspects in non-invasive EEG-based BCI research—a survey among BCI users and BCI professionals *Neuroethics* **7** 29–41
- Guger C, Edlinger G, Harkam W, Niedermayer I and Pfurtscheller G 2003 How many people are able to operate an EEG-based brain–computer interface (BCI)? *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **11** 145–7
- Halje P, Seeck M, Blanke O and Ionta S 2015 Inferior frontal oscillations reveal visuo-motor matching for actions and speech: evidence from human intracranial recordings *Neuropsychologia* **79** 206–214
- Haselager P, Vlek R, Hill J and Nijboer F 2009 A note on ethical aspects of BCI *Neural Netw.* **22** 1352–7
- Hebert J S, Olson J L, Morhart M J, Dawson M R, Marasco P D, Kuiken T A and Chan K M 2014 Novel targeted sensory reinnervation technique to restore functional hand sensation after transhumeral amputation *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **22** 765–73
- Hildt E 2010 Brain–computer interaction and medical access to the brain: individual, social and ethical implications *Studies Ethics Law Technol.* **4** 5
- Hochberg L R *et al* 2012 Reach and grasp by people with tetraplegia using a neurally controlled robotic arm *Nature* **485** 372–5
- Hochberg L R, Serruya M D, Friehs G M, Mukand J A, Saleh M, Caplan A H, Branner A, Chen D, Penn R D and Donoghue J P

- 2006 Neuronal ensemble control of prosthetic devices by a human with tetraplegia *Nature* **442** 164–71
- Hwang H J, Lim J H, Jung Y J, Choi H, Lee S W and Im C H 2012 Development of an SSVEP-based BCI spelling system adopting a QWERTY-style LED keyboard *J. Neurosci. Methods* **208** 59–65
- Ionta S, Fourkas A D and Aglioti S M 2010 Egocentric and object-based transformations in the laterality judgement of human and animal faces and of non-corporeal objects *Behav. Brain Res.* **207** 452–7
- Ionta S, Sforza A, Funato M and Blanke O 2013 Anatomically plausible illusory posture affects mental rotation of body parts *Cogn. Affect. Behav. Neurosci.* **13** 197–209
- Ionta S, Villiger M, Jutzeler C R, Freund P, Curt A and Gassert R 2016 Spinal cord injury affects the interplay between visual and sensorimotor representations of the body *Sci. Rep.* **6** 20144
- Jackson A B, Dijkers M, Devivo M J and Poczatek R B 2004 A demographic profile of new traumatic spinal cord injuries: change and stability over 30 years *Arch. Phys. Med. Rehabil.* **85** 1740–8
- Johansson R S and Flanagan J R 2009 Coding and use of tactile signals from the fingertips in object manipulation tasks *Nat. Rev. Neurosci.* **10** 345–59
- Kim J *et al* 2014 Stretchable silicon nanoribbon electronics for skin prosthesis *Nat. Commun.* **5** 5747
- Kim K and Colgate J E 2012 Haptic feedback enhances grip force control of sEMG-controlled prosthetic hands in targeted reinnervation amputees *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **20** 798–805
- Knecht S, Henningsen H, Elbert T, Flor H, Hohling C, Pantev C and Taub E 1996 Reorganization and perceptual changes after amputation *Brain* **119** 1213–9
- Kuiken T A, Dumanian G, Lipschutz R, Miller L and Stubblefield K 2004 The use of targeted muscle reinnervation for improved myoelectric prosthesis control in a bilateral shoulder disarticulation amputee *Prosthet. Orthot. Int.* **28** 245–53
- Kuiken T A, Li G, Lock B A, Lipschutz R D, Miller L A, Stubblefield K A and Englehart K B 2009 Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms *J. Am. Med. Assoc.* **301** 619–28
- Kuiken T A, Marasco P D, Lock B A, Harden R N and Dewald J P 2007a Redirection of cutaneous sensation from the hand to the chest skin of human amputees with targeted reinnervation *Proc. Natl Acad. Sci. USA* **104** 20061–6
- Kuiken T A, Miller L A, Lipschutz R D, Lock B A, Stubblefield K, Marasco P D, Zhou P and Dumanian G A 2007b Targeted reinnervation for enhanced prosthetic arm function in a woman with a proximal amputation: a case study *Lancet* **369** 371–80
- Kwak N S, Muller K R and Lee S W 2015 A lower limb exoskeleton control system based on steady state visual evoked potentials *J. Neural Eng.* **12** 056009
- Lal S K, Craig A, Boord P, Kirkup L and Nguyen H 2003 Development of an algorithm for an EEG-based driver fatigue countermeasure *J. Safety Res.* **34** 321–8
- Lebedev M A, Denton J M and Nelson R J 1994 Vibration-entrained and premovement activity in monkey primary somatosensory cortex *J. Neurophysiol.* **72** 1654–73
- Lebedev M A and Nicolelis M A L 2006 Brain-machine interfaces: past, present and future *Trends Neurosci.* **29** 536–46
- Ledbetter N M, Ethier C, Oby E R, Hiatt S D, Wilder A M, Ko J H, Agnew S P, Miller L E and Clark G A 2013 Intrafascicular stimulation of monkey arm nerves evokes coordinated grasp and sensory responses *J. Neurophysiol.* **109** 580–90
- Leeb R, Perdakis S, Tonin L, Biasucci A, Tavella M, Creatura M, Molina A, Al-Khodairy A, Carlson T and Millan J D 2013 Transferring brain-computer interfaces beyond the laboratory: successful application control for motor-disabled users *Artif. Intell. Med.* **59** 121–32
- Lenay C, Gapenne O, Hanneton S, Marque C and Genouëlle C 2003 Sensory substitution: limits and perspectives *Touching for Knowing* ed Y Hatwell, A Streri and E Gentaz (Amsterdam: John Benjamins Publishing Co) pp 275–92
- Leuthardt E C, Gaona C, Sharma M, Szrama N, Roland J, Freudenberg Z, Solis J, Breshears J and Schalk G 2011 Using the electrocorticographic speech network to control a brain-computer interface in humans *J. Neural Eng.* **8** 036004
- Liu Y, Denton J M and Nelson R J 2005 Neuronal activity in primary motor cortex differs when monkeys perform somatosensory and visually guided wrist movements *Exp. Brain Res.* **167** 571–86
- Lucivero F and Tamburrini G 2008 Ethical monitoring of brain-machine interfaces *AI Soc.* **22** 449–60
- Marasco P D, Kim K, Colgate J E, Peshkin M A and Kuiken T A 2011 Robotic touch shifts perception of embodiment to a prosthesis in targeted reinnervation amputees *Brain* **134** 747–58
- Marasco P D, Schultz A E and Kuiken T A 2009 Sensory capacity of reinnervated skin after redirection of amputated upper limb nerves to the chest *Brain* **132** 1441–8
- Marin C and Fernandez E 2010 Biocompatibility of intracortical microelectrodes: current status and future prospects *Front. Neuroeng.* **3** 8
- Mattout J, Perrin M, Bertrand O and Maby E 2015 Improving BCI performance through co-adaptation: applications to the P300-speller *Ann. Phys. Rehabil. Med.* **58** 23–8
- McFarland D J, Sarnacki W A and Wolpaw J R 2010 Electroencephalographic (EEG) control of three-dimensional movement *J. Neural Eng.* **7** 036007
- Memberg W D, Polasek K H, Hart R L, Bryden A M, Kilgore K L, Nemunaitis G A, Hoyen H A, Keith M W and Kirsch R F 2014 Implanted neuroprosthesis for restoring arm and hand function in people with high level tetraplegia *Arch. Phys. Med. Rehabil.* **95** 1201–11
- Micera S *et al* 2011 Decoding of grasping information from neural signals recorded using peripheral intrafascicular interfaces *J. Neuroeng. Rehabil.* **8** 53
- Micera S, Carpaneto J and Raspopovic S 2010a Control of hand prostheses using peripheral information *IEEE Rev. Biomed. Eng.* **3** 48–68
- Micera S, Citi L, Rigosa J, Carpaneto J, Raspopovic S, Di Pino G, Rossini L, Yoshida K, Denaro L and Dario P 2010b Decoding information from neural signals recorded using intraneural electrodes: toward the development of a neurocontrolled hand prosthesis *Proc. IEEE* **98** 407–17
- Milekovic T, Fischer J, Pistohl T, Ruescher J, Schulze-Bonhage A, Aertsen A, Rickert J, Ball T and Mehring C 2012 An online brain-machine interface using decoding of movement direction from the human electrocorticogram *J. Neural Eng.* **9** 046003
- Millan J D *et al* 2010 Combining brain-computer interfaces and assistive technologies: state-of-the-art and challenges *Front. Neurosci.* **4** 161
- Nicolelis M and Servick K 2014 Interview Kickoff looms for demo of brain-controlled machine *Science* **344** 1069–70
- Nirenberg S and Pandarinath C 2012 Retinal prosthetic strategy with the capacity to restore normal vision *Proc. Natl Acad. Sci. USA* **109** 15012–7
- O'Doherty J E, Lebedev M A, Hanson T L, Fitzsimmons N A and Nicolelis M A 2009 A brain-machine interface instructed by direct intracortical microstimulation *Front. Integrative Neurosci.* **3** 20
- O'Doherty J E, Lebedev M A, Li Z and Nicolelis M A L 2012 Virtual active touch using randomly patterned intracortical microstimulation *IEEE Trans. Neural Systems Rehabil.* **20** 85–93
- Perruchoud D, Murray M M, Lefebvre J and Ionta S 2014 Focal dystonia and the sensory-motor integrative loop for enacting (SMILE) *Front. Human Neurosci.* **8** 458

- Pisotta I, Perruchoud D and Ionta S 2015 Hand-in-hand advances in biomedical engineering and sensorimotor restoration *J. Neurosci. Methods* **246** 22–9
- Pistohl T, Schulze-Bonhage A, Aertsen A, Mehring C and Ball T 2012 Decoding natural grasp types from human ECoG *NeuroImage* **59** 248–60
- Polikov V S, Tresco P A and Reichert W M 2005 Response of brain tissue to chronically implanted neural electrodes *J. Neurosci. Methods* **148** 1–18
- Presacco A, Goodman R, Forrester L and Contreras-Vidal J L 2011 Neural decoding of treadmill walking from noninvasive electroencephalographic signals *J. Neurophysiol.* **106** 1875–87
- Ramos-Murguialday A, Schurholz M, Caggiano V, Wildgruber M, Caria A, Hammer E M, Halder S and Birbaumer N 2012 Proprioceptive feedback and brain computer interface (BCI) based neuroprostheses *PLoS One* **7** e47048
- Raspopovic S *et al* 2014 Restoring natural sensory feedback in real-time bidirectional hand prostheses *Sci. Translational Med.* **6** 222ra19
- Romo R, Hernandez A, Zainos A and Salinas E 1998 Somatosensory discrimination based on cortical microstimulation *Nature* **392** 387–90
- Rossini P M *et al* 2010 Double nerve intraneural interface implant on a human amputee for robotic hand control *Clin. Neurophysiol.* **121** 777–83
- Rupp R, Kleih S C, Leeb R, Millan J d R, Kübler A and Müller-Putz G R 2014 *Brain–Computer–Interfaces in their Ethical, Social and Cultural Contexts* (Berlin: Springer) pp 7–38
- Saal H P and Bensmaia S J 2015 Biomimetic approaches to bionic touch through a peripheral nerve interface *Neuropsychologia* **79** 344–53
- Sainburg R L, Ghilardi M F, Poizner H and Ghez C 1995 Control of limb dynamics in normal subjects and patients without proprioception *J. Neurophysiol.* **73** 820–35
- Schalk G, Miller K J, Anderson N R, Wilson J A, Smyth M D, Ojemann J G, Moran D W, Wolpaw J R and Leuthardt E C 2008 Two-dimensional movement control using electrocorticographic signals in humans *J. Neural Eng.* **5** 75–84
- Scheme E and Englehart K 2011 Electromyogram pattern recognition for control of powered upper-limb prostheses: state of the art and challenges for clinical use *J. Rehabil. Res. Dev.* **48** 643–59
- Sellers E W, Vaughan T M and Wolpaw J R 2010 A brain–computer interface for long-term independent home use *Amyotrophic Lateral Sclerosis: Official Publ. World Fed. Neurology Res. Group Motor Neuron Diseases* **11** 449–55
- Sensinger J W, Schultz A E and Kuiken T A 2009 Examination of force discrimination in human upper limb amputees with reinnervated limb sensation following peripheral nerve transfer *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **17** 438–44
- Serruya M D, Hatsopoulos N G, Paninski L, Fellows M R and Donoghue J P 2002 Instant neural control of a movement signal *Nature* **416** 141–2
- Simeral J D, Kim S P, Black M J, Donoghue J P and Hochberg L R 2011 Neural control of cursor trajectory and click by a human with tetraplegia 1000 days after implant of an intracortical microelectrode array *J. Neural Eng.* **8** 025027
- Spence C 2014 The skin as a medium for sensory substitution *Multisensory Res.* **27** 293–312
- Tabakow P *et al* 2014 Functional regeneration of supraspinal connections in a patient with transected spinal cord following transplantation of bulbar olfactory ensheathing cells with peripheral nerve bridging *Cell Transplant* **23** 1631–55
- Tabot G A, Dammann J F, Berg J A, Tenore F V, Boback J L, Vogelstein R J and Bensmaia S J 2013 Restoring the sense of touch with a prosthetic hand through a brain interface *Proc. Natl Acad. Sci. USA* **110** 18279–84
- Tabot G A, Kim S S, Winberry J E and Bensmaia S J 2015 Restoring tactile and proprioceptive sensation through a brain interface *Neurobiol. Dis.* **83** 191–8
- Takmakov P, Ruda K, Scott Phillips K, Isayeva I S, Krauthamer V and Welle C G 2015 Rapid evaluation of the durability of cortical neural implants using accelerated aging with reactive oxygen species *J. Neural Eng.* **12** 026003
- Tan D W, Schiefer M A, Keith M W, Anderson J R and Tyler D J 2015 Stability and selectivity of a chronic, multi-contact cuff electrode for sensory stimulation in human amputees *J. Neural Eng.* **12** 026002
- Thomson E E, Carra R and Nicolelis M A 2013 Perceiving invisible light through a somatosensory cortical prosthesis *Nat. Commun.* **4** 1482
- Tucker M R, Olivier J, Pagel A, Bleuler H, Bouri M, Lambercy O, Millan Jdel R, Riener R, Vallery H and Gassert R 2015 Control strategies for active lower extremity prosthetics and orthotics: a review *J. Neuroeng. Rehabil.* **12** 1
- Usakli A B, Gurkan S, Aloise F, Vecchiato G and Babiloni F 2010 On the use of electrooculogram for efficient human computer interfaces *Comput. Intell. Neurosci.* **2010** 135629
- van den Brand R *et al* 2012 Restoring voluntary control of locomotion after paralyzing spinal cord injury *Science* **336** 1182–5
- Vaughan T M and Wolpaw J R 2006 The third international meeting on brain–computer interface technology: making a difference *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **14** 126–7
- Velliste M, Perel S, Spalding M C, Whitford A S and Schwartz A B 2008 Cortical control of a prosthetic arm for self-feeding *Nature* **453** 1098–101
- Vidal J J 1973 Toward direct brain–computer communication *Annu. Rev. Biophys. Bioeng.* **2** 157–80
- Vidaurre C and Blankertz B 2010 Towards a cure for BCI illiteracy *Brain Topogr.* **23** 194–8
- Vidaurre C, Sannelli C, Muller K R and Blankertz B 2011 Co-adaptive calibration to improve BCI efficiency *J. Neural Eng.* **8** 025009
- Wang S *et al* 2014 Design and control of the MINDWALKER exoskeleton *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.*
- Wang W *et al* 2013 An electrocorticographic brain interface in an individual with tetraplegia *PLoS One* **8** e55344
- Wodlinger B, Downey J E, Tyler-Kabara E C, Schwartz A B, Boninger M L and Collinger J L 2015 Ten-dimensional anthropomorphic arm control in a human brain–machine interface: difficulties, solutions, and limitations *J. Neural Eng.* **12** 016011
- Wolpaw J and Wolpaw E W 2012 *Brain–Computer Interfaces: Principles and Practice* (Oxford: Oxford University Press)
- Wolpaw J R, Loeb G E, Allison B Z, Donchin E, do Nascimento O F, Heetderks W J, Nijboer F, Shain W G and Turner J N 2006 BCI Meeting 2005—workshop on signals and recording methods *IEEE Trans. Neural Syst. Rehabil. Eng.: Publ. IEEE Eng. Med. Biol. Soc.* **14** 138–41
- Wolpaw J R and McFarland D J 2004 Control of a two-dimensional movement signal by a noninvasive brain–computer interface in humans *Proc. Natl Acad. Sci. USA* **101** 17849–54
- Yanagisawa T, Hirata M, Saitoh Y, Kishima H, Matsushita K, Goto T, Fukuma R, Yokoi H, Kamitani Y and Yoshimine T 2012 Electrocorticographic control of a prosthetic arm in paralyzed patients *Ann. Neurology* **71** 353–61
- Yin E, Zhou Z, Jiang J, Chen F, Liu Y and Hu D 2013 A novel hybrid BCI speller based on the incorporation of SSVEP into the P300 paradigm *J. Neural Eng.* **10** 026012
- Ziegler-Graham K, MacKenzie E J, Ephraim P L, Travison T G and Brookmeyer R 2008 Estimating the prevalence of limb loss in the United States: 2005 to 2050 *Arch. Phys. Med. Rehabil.* **89** 422–9