Topical Review

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

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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.

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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 (Nicolesis 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’ (Bensmaia 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, Membarg et al 2014) or the electroculeogram (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, intraneuronal 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
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, Chavarriga 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 effenter 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 (Raspopovic 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 reinnervation is the increased sense of ownership for a prosthetic device, based on both self-reports and physiological

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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, IMCS 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.

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