invasive or noninvasive: understanding brain–machine interface technology

With this issue of the magazine, we are adding a new feature, "Conversations in BME," in which distinguished academics and researchers discuss a biomedical issue in depth, highlighting pros and cons of different approaches. Our goal for this feature is to promote discussion as a way to facilitate scientific growth in our community and, in particular, among students.

José del R. Millán

Jose M. Carmena

It is a pleasure to introduce the guests for this issue: Prof. José del R. Millán, Swiss Federal Institute of Technology, Lausanne, and Prof. Jose M. Carmena, University of California, Berkeley, who discuss how noninvasive and invasive cortical signals can be used to control robotic systems in a successful way and examine the potentials and limits of noninvasive and invasive cortical neural prostheses. Representing excellence in their respective fields, Dr. Millán and Dr. Carmena here share thoughtful ideas for the future of brain–machine interface technology.

—Silvestro Micera

The Promise of Brain-Machine Interface

Millán: The idea of controlling devices or interacting with our environment not by manual control but by mere thinking, i.e., by human brain activity, has fascinated researchers for the past 40 years. However, only recently have experiments shown the possibility of doing so [1]–[4]. This is a rapidly emerging field of multidisciplinary research called brain–machine interface (BMI) that has seen impressive achievements during the last years. A BMI monitors the user's brain activity, extracts specific features from the brain signals that reflect the intent of the subject, and translates these features into actions (such as moving a wheelchair or selecting a letter from a virtual keyboard), without using the activity of any muscle or peripheral nerve. The central tenet of a BMI is the capability to distinguish different patterns of brain activity, each being associated to a particular intention or mental task. Hence, adaptation is a key component of a BMI because users must learn to modulate their brainwaves voluntary, through appropriate feedback, so as to generate distinct brain patterns. In some cases, user training is complemented and accelerated with machine learning techniques to discover the individual brain patterns characterizing the mental tasks executed by the subject [5], [6].

What kind of brain signals can directly control devices? Electrical activity is the natural candidate because of its excellent time resolution—we can detect changes in brain activity at the millisecond range. We can record the electrical brain activity invasively or noninvasively. The former technique employs microelectrode arrays implanted in the brain that record the activity of single neurons [11], [12], [16], [17], [22]. The overall concerted activity of neuronal populations can also be recorded invasively with electrodes placed on the surface of the brain, the so-called electrocorticography (ECoG), which measures local field potentials [14]. Noninvasive BMIs, commonly referred as brain–computer interfaces (BCIs), mainly use electroencephalographic (EEG) activity recorded from electrodes placed on the scalp to measure the synchronous activity of thousands of cortical neurons [13], [18], [24]–[26], [30], [32]–[41].

Carmena: Since its origins, the primary goal of transforming thought into action and sensation into perception has been to improve the quality of life for the physically impaired. As a result, multiple groups around the globe have successfully demonstrated rodents, nonhuman primates, and humans controlling prosthetic devices in real-time through a diverse set of neural signals collected from the brain [7]–[22].

In addition to the paramount application as therapeutic technology, brain–machine interface (BMI) systems hold enormous potential as a tool for studying fundamental questions about how the brain learns and adapts to new environments, which in turn will contribute to improve design of the future BMI systems. In the BMI paradigm (Figure 1), the experimenter has full control of the motor transformation linking the spatiotemporal patterns of neural activity to the behavior or the sensory transformation linking a behavioral or external event to neural activity. For example, sensorimotor maps can be arbitrarily changed by the experimenter, allowing the neural adaptations to environmental changes to be studied in a controlled manner [19], [22], [23].

BMI systems can be divided with respect to the type of physiological signals recorded. At the microscopic level, the two types of signals available are: the single unit (spiking) activity (SUA) and the local (or intracortical) field

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potential (LFP). At the mesoscopic level, cortical field potentials can be subdural or epidural via electrocorticography (ECoG) and can also be recorded from the scalp via electroencephalography (EEG). Although there are other key attributes for classification of BMI systems, such as the decoding technique, control scheme, and prosthetic device to be controlled, the most typical classification of BMI systems refers to the level of invasiveness of the recording technique.

Millán: Considering a Noninvasive Approach

Noninvasive EEG is a convenient, safe, and inexpensive recording method that is ideal to bring BMI technology to a large population. Indeed, the promise of BMI is to augment human capabilities by providing a new interaction link with the outside world and is particularly relevant as an aid for paralyzed humans, although it also opens up new possibilities for able-bodied people, for instance, in gaming and space applications. This promise is supported by the fact that researchers working with EEG signals have made it possible that human subjects mentally control a variety of devices: keyboards for writing messages [32], [34], [35] [37], brain games [34], [38], robots [18], hand orthoses [36] and wheelchairs [30]. Figures 2 and 3 show two of our noninvasive BMIs at use. The first one allows a person to control either software processes running in a computer or external devices such as a mobile robot. The second BMI demonstrated the feasibility of noninvasive BMI for space applications during a parabolic flight [24].

Yet, why have EEG-based BMIs not seen a widespread clinical application so far? Remember that the main source of the EEG is the synchronous activity of thousands of cortical neurons. Thus, EEG signals suffer from a reduced spatial resolution, and since they are recorded on the scalp, they are susceptible to artifacts generated by muscle contractions and ocular movements, as well as outside sources. Consequently, current EEG-based BMIs are limited by a low information transfer rate and are considered too slow for controlling complex devices. However, as mentioned previously, researchers have recently shown that online analysis of EEG signals, if used in combination with machine learning techniques and smart interaction designs, is sufficient for humans to do so. Furthermore, thanks to the principle of mutual learning, where the user and the BMI are coupled together and adapt to each other, humans learn to operate the brain-actuated device very rapidly, in a few hours normally split between a few days [5], [6].

Rapid user training is often associated with unstable control signals, but this is actually not the case. Many groups have reported that users keep a stable level of performance over months and even years. Moreover, these groups have largely demonstrated that subjects are able to operate different brain-actuated devices by triggering the same EEG patterns they have learned to modulate; they need to know only the association

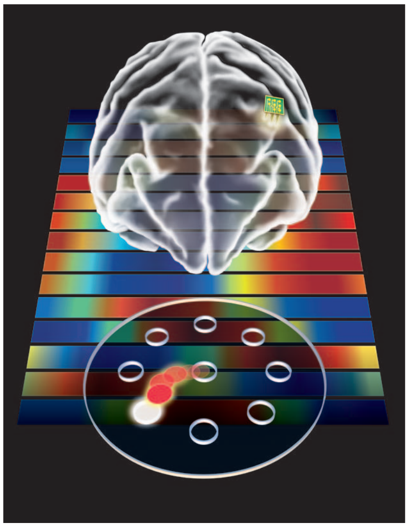

Fig. 1. Schematic description of a cortically controlled computer cursor performing a center-out task. Color map in the background depicts a stable cortical map for prosthetic function (16). (Illustration copyright John Blanchard.)

Fig. 2. Noninvasive BMI based on the analysis of EEG signals, i.e., the brain electrical activity recorded from electrodes placed on the scalp (colored spots in the red cap worn by the person). The user is mentally driving a mobile robot between rooms in a house-like environment, making it turn or move forward. Alternatively, he can control some software processes running in the computer by triggering the same EEG patterns as for the interaction with the robot.

between EEG patterns and the mental commands. And last, but not least, some subjects have demonstrated that they can deliver appropriate mental commands only when they wish to do so and while performing other tasks such as speaking. This is possible because of the use of machine learning techniques at two levels. First, to discover discriminant EEG patterns that users rapidly learn to modulate at will. Second, to make an intelligent analysis of the continuous EEG signals to deliver a mental command only when the BMI has accumulated enough evidence for it, thus effectively supporting idle (or non-intentional control) states where subjects do not want to operate the device.

Another characteristic of EEG is that, although it is possible to achieve accurate two-dimensional movement control of cursors and wheelchairs, it naturally reflects more abstract information such as intended targets, intended actions, and preferences. This makes it an ideal control signal whenever we follow shared control principles to design smart interaction devices, where the user conveys high-level commands that the devices interpret and execute in the most appropriate way to achieve the goal because of their knowledge about the task and the current situation. This is particularly effective for the control of robots and neuroprostheses [18], [24].

Still another advantage of EEG is that it allows researchers to monitor the ongoing activity all across the brain. This, in principle, should facilitate the design of BMIs that combine different brain processes, each engaging different cortical areas or requiring an orchestrated activity of a complex network of cortical areas. In addition, and perhaps more importantly, the EEG not only conveys information about the subject's intent (the mental commands) but also about cognitive states that are crucial for a purposeful interaction. All this is done in parallel. An example of such a cognitive state is the user's awareness to errors made by the BMI. The associated brain correlate of this cognitive state is called an error-related potential (ErrP). Recently, we have demonstrated its online use embedded in a BMI, which yields enormous increases in performance [25], [26]. The principle is to stop the execution of the wrong BMI response if an ErrP is detected a few milliseconds afterward. In general, detection of some cognitive states such as errors can directly trigger automatic responses of the intelligent brain-controlled device, whereas other kinds of states can customize the interaction according to, for instance, the user's mental workload [39] or alertness [40].

Carmena: Considering an Invasive Approach

On the invasive side, two main recording technologies dominate the BMI spectrum: ECoG and cortically implanted microelectrode arrays that record from ensembles of SUA. The nature of the signals recorded via ECoG is similar to EEG, since they measure electrical potentials, resulting from the spatial average of a large area of the brain, and hence use a large group of neurons. However, the fact that the recording electrodes that are placed under the dura leads to higher spatial resolution than do EEG (i.e., tenths of millimeters versus centimeters), broader bandwidth (i.e., 0–500 Hz versus 0–50 Hz), higher characteristic amplitude (i.e., 50–100 μV versus 10–20 μV), and far less vulnerability to artifacts, such as EMG or ambient noise. The main drawback with respect to EEG is the invasiveness of the procedure, as it requires opening the skull and, in the case of subdural implants, also opening the dura mater [27].

Microelectrode arrays are the most invasive of the techniques used in BMI systems. To date, this is the only recording technique that allows decoding the intended movements of the subject's limb with high accuracy. This technique allows recording SUA from large populations of neurons from multiple areas of the brain simultaneously. Arrays are chronically implanted in cortical areas of the brain. Typical areas include the primary motor cortex (M1), the dorsal premotor cortex (PMd), and the posterior parietal cortex (PPC). Of great concern with this technique is the long-term stability of the recordings. The brain

Fig. 3. Validation of a non-invasive brain–machine interface for space applications during a parabolic flight (note a person floating in the top left corner). The subject needs to operate the BMI in different gravity conditions, including microgravity. This study was run in collaboration with the European Space Agency's Advanced Concept Team.

tends to protect itself by creating a layer of scar tissue around the electrodes, leading to a slow decrease of the signal-to-noise ratio (SNR). Moreover, micromotion of the electrodes within the brain can lead to changes in the observed waveforms and to a below-threshold SNR. Nevertheless, chronic SUA recording techniques have improved in recent years, with studies reporting up to several years of continuous recordings with lasting cell yield, isolation quality, and stability through time [22], [28].

BMIs based on cortical field potentials (such as EEG and ECoG) typically use nonbiomimetic decoders (i.e., not generated from arm movement data) and rely on operant learning through visual feedback to master control of the prosthetic device. Similarly, recent results with invasive BMIs recording from SUA suggest that biomimetic decoding may not be necessary if constant conditions in the ensemble and decoder structure are maintained [20], [22]. While some EEG studies have demonstrated comparable functionality to SUA studies with respect to the kind of task achieved (e.g., target hitting) [13], typical drawbacks are the lengthy training required, and that only a fraction of the subjects are typically capable of performing the task. In other words, achieving prosthetic control remains more natural with SUA. This, of course, comes at the high price of the invasive technique, which, today, still makes it inaccessible for most patients.

Progress in invasive BMI systems is expected to greatly accelerate over the next years, as more research groups across multiple disciplines join this exciting quest. In the short-/mid-term, BMIs will improve the quality of life for millions of people by restoring communication and sensorimotor function in patients suffering from spinal-cord injuries and other neurological disorders. Moreover, the impact of this technology in the clinical realm may drive the field to the next level: augmentation of sensory, motor, and cognitive capabilities in healthy subjects. Yet, for this to happen, major breakthroughs will be needed to improve the implantable technology currently available.

Efforts are being pursued along these lines at various institutions around the globe (see [29] for an example). A key stepping stone is the development of fully integrated, ultra low-power, wireless neural interface systems that will perform real-time processing of a large number of channels and different types of physiological signals at the microscopic (SUA and LFP) and mesoscopic levels (ECoG). However, perhaps the biggest milestone for the invasive BMI approach to become the standard in the clinical realm is at the biophysical interface. The fields of materials science and bioengineering are positioned to be the game changers. Progress in these fields could relax some of the constraints and risks associated with invasive BMI technology, such as infection and tissue damage, and bring it to the level of the pacemaker, the cochlear implant, or the more recent deep-brain stimulator, making the invasiveness worth the risk for the final user.

The Future of BMI

Millán: Is EEG the ultimate signal for BMI? Despite all its current advantages and expected future progress, the answer is still open. I think that if we were constrained to use only one brain signal modality for a given human patient, the choice would be dictated by the degree of paralysis and control the patient has over the different signals. However, the most efficient solution in the future will be a combination of all modalities—from multiunit recordings for accurate continuous control to EEG for discrete goal-oriented tasks—to achieve the final goal of providing natural real-time control of complex prosthetic devices that replace the missing limbs. Nevertheless, we need to first design robust and principled BMI systems based on each single modality before addressing the fusion of all of them.

Carmena: Taking the wine glass problem as the standard (i.e., using a BMI to reach for and grasp a glass of wine in 3-D space), the main problem for BMIs today is how to scale up in task complexity. In other words, how do we move from the proof-of-concept level, "Can such a system ever be built?" to the real world application, "How do we build it?" Scalability holds the key for determining which technique proves to be the most ideal for interfacing with the brain.

BMIs are evolving toward a shared-control regime in which the system will combine decoded information from neural signals with knowledge about the prosthetic device and the environment, distributed across sensor networks, to improve control of the prosthetic device and to reduce the cognitive load.

A potential future limitation of noninvasive BMIs will be the delivery of feedback from the prosthetic device, i.e., bidirectional data flow (brain–machine–brain). In fact, one of the hottest areas in today's invasive BMI research aims at incorporating sensory feedback from the prosthesis via intracortical microstimulation (ICMS) to allow a patient to feel the prosthetic device as an extension of his/her own body. The expectation is that successful encoding of tactile and proprioceptive feedback from the prosthetic device will lead to realistic sensations and thereby increase performance accuracy.

Perhaps a debate about which approach (invasive versus noninvasive) is best does not make much sense today. In fact, the BMI field benefits from the availability of both approaches. With today's techniques, it would be fair to say that the choice of invasive or noninvasive approach will be determined by the physical condition (e.g., degree of paralysis) of the patient. However, this scenario may change as the constraints of invasive techniques relax.

Ultimately, dramatic improvements on several parallel fronts will be needed to achieve the milestones required to bring BMI technology to the clinical realm and to explore and build real-world future applications with this technology. Thus, we ought to continue with the invasive BMI approach and investigate it further before we can even begin arguing which approach is the best compromise. We cannot afford to cease invasive work until we test its limits and exploit its potential. Moreover, since each approach informs the subject in different ways, a combination of several techniques may be necessary to build high-end BMI systems (i.e., those that will make it through the scalability problem). In the long term, the ultimate BMI system may very well become a hybrid of microscopic and mesoscopic neural signals, exploiting both SUA and ECoG and, thus, being able to benefit from local, high-resolution signals (e.g., for generating motor commands) and more global information (e.g., cognitive states, such as arousal, level of attention, and error-related potentials). Thus, the right question may not be which technique is better but which type of neural signal (or combination of) will be used by the ultimate BMI?

Final Thoughts

Millán: Dr. Carmena has made a very compelling case for invasive BMIs that I can easily subscribe to, but not fully! We share many of the views concerning the current state of the art and future of BMI. To start with, I agree that we need to continue research on both invasive and noninvasive BMIs to explore their respective limits and advance our knowledge. A second point of confluence is in the major role that shared control will play to bring BMIs to practical use. We are also in accord that a mid- to long-term milestone for BMI technology is the development of better technology to measure brain signals in a safe, robust, and accurate way, which applies to invasive and noninvasive BMIs. Because the achievements of noninvasive BMIs are attracting a growing interest from funding agencies and industry, significantly more efforts will be devoted to develop new generations of electrodes. It is likely that a large number of such electrodes, in combination with embedded signal processing algorithms, will overcome many of the limitations of today's EEG, which has not changed much for the last 50 years!

Two additional points of agreement are the fundamental role of sensory feedback from the neuroprosthesis to the subject and that the ultimate BMI will likely exploit different kinds of neural signals, microscopic and mesoscopic. However, in this article, here I diverge from Dr. Carmena's views. Concerning the first issue, he assumes that the only way to deliver rich tactile and proprioceptive feedback is via intracortical microstimulation. However, this is not really the case. There exists a large body of research on neuroplasticity that shows how people can acquire new sensory brain maps through peripheral stimulation (for a popular review, see [41]). The challenge is to design appropriate transducers that convey the state of the neuroprosthesis through the body surface, or peripheral nerves, and to couple them with the BMI to allow people to develop brain maps for such an external device.

Regarding the combination of microscopic and mesoscopic neural signals, Dr. Carmena states that the best option is to exploit single unit activity (SUA) and ECoG, both invasive signals, and discards EEG. It can be argued that if one could implant electrodes everywhere in the brain safely and robustly, then there would be no need for noninvasive BMI. However, I doubt this will be the case, even in the long term. Most probably, brain implants will be limited to a few per patient and not for every subject. There are, of course, ethical and medical reasons to limit the use of invasive BMI. However, the fact that up-to-date, noninvasive BMIs have achieved similar levels of performance as invasive BMIs for tasks once considered inapplicable is compelling. Indeed, the only BMIs actually used by disabled people in their daily life are noninvasive. A prominent example is Birbaumer and colleagues' work [32] with paralyzed patients. I contend that the next generation of noninvasive BMI will also be capable of decoding the intended movement of the subject's prosthetic limb to reach and grab a glass. This will be possible because such a future noninvasive BMI will combine several neural correlates associated to movement control—identification of intended targets with a relatively good resolution, recognition of when subjects decide to start/end an action, and even generations of acceptable trajectories—with advanced shared control architectures. Stay tuned!

Carmena: Dr. Millán brings very important points regarding the widespread utility of EEG-based BMI systems. I fully agree that noninvasive BMIs will always have their niche due to the accessibility of the technique. In cases in which invasiveness is not an option, EEG-based BMIs will be the only technology available. Moreover, other realms such as the video-game industry have already started incorporating noninvasive BMI headsets with their products at an affordable price. For basic neuroscience research, however, the utility and potential of the invasive approach is better positioned than noninvasive because all relevant signals—SUA, LFP, and ECoG—are accessible with the same technique.

For future high-end prosthetics that will require sensory feedback to feel the prosthetic device, EEG-based BMIs are more limited. Both invasive and noninvasive approaches currently rely on visual feedback to close the loop. However, noninvasive BMIs lack the potential that invasive techniques possess, such as using ICMS to evoke natural perception in the subject by stimulation of sensory neurons. The noninvasive BMIs will need to be complemented by other options such as sensory encoding through vibrotactile displays on other parts of the body (e.g., the neck).

Dr. Millán points to limited spatial resolution, muscle-related artifacts, and low information transfer rate as the main reasons why EEG-based BMIs have not seen a widespread clinical application, and that decoding techniques that involve mutual learning (or coadaptation) between the user and the BMI are helping with these problems. While I fully agree with Dr. Millán's point, in my opinion, this also brings up a different issue, which is that the potential for EEG-based BMIs to make quantum leap improvements is saturating, whereas invasive BMIs, in principle, have a larger unexplored territory and much room for improvement. This is reflected in the number of studies conducted with both approaches. In the case of EEG-based BMIs, both the easy accessibility to neural signals and the fact that they have been used for a longer period of time have resulted in the number of studies conducted around the world being significantly larger than for invasive BMIs. To a certain extent, we know what sort of signals can be decoded from the scalp and the level of volitional modulation that the subject can achieve through EEG. This is clearly not the case in SUA-based BMIs in which the invasiveness of the technique has constrained the number of studies demonstrating online cortical control of prosthetic devices to just over a dozen. Thus, an exponential increase in the number of these studies could result in dramatic progress and change the current application space in which EEG is dominant.

Finally, Dr. Millán agrees that a combination of both mesoscopic and microscopic signals will probably be the ideal scenario. The subtle difference in the argument is that, in my opinion, should SUA prove to be a fundamental part of a high-end BMI system, there will be no reason for recording the EEG instead of the ECoG. A hybrid BMI combining SUA and ECoG signals, as well as ICMS for prosthetic sensory feedback, may very well be the consummate approach that the field is missing.

José del R. Millán received his Ph.D. degree in computer science from the Universitat Politècnica de Catalunya (Barcelona, Spain) in 1992. He is the Defitech Professor at the Center for Neuroprosthetics of the Swiss Federal Institute of Technology in Lausanne [Ecole Polytechnique Federale de Lausanne (EPFL)], where he explores the use of brain signals for multimodal interaction and, in particular, the development of noninvasive brain-controlled robots and neuroprostheses. In this multidisciplinary research effort, he is bringing together his pioneering work on BCIs and adaptive intelligent robotics. He was also a research scientist at the Joint Research Center of the European Commission in Ispra, Italy, and a senior researcher at the Idiap Research Institute in Martigny, Switzerland. He was named Research Leader 2004 by Scientific American for his work on brain-controlled robots. He was a finalist of the European Descartes Prize 2001 for his research on BCIs and is the coordinator of a number of European projects on BCIs.

Jose M. Carmena received the B.S. and M.S. degrees in electrical engineering from the Polytechnic University of Valencia, Spain, in 1995 and the University of Valencia, Spain, in 1997. He received the M.S. degree in artificial intelligence and the Ph.D. degree in robotics, both from the University of Edinburgh, Scotland, United Kingdom, in 1998 and 2002, respectively. From 2002 to 2005, he was a postdoctoral fellow at the Department of Neurobiology and the Center for Neuroengineering at Duke University, Durham, North Carolina. In the summer of 2005, he was appointed as an assistant professor in the Department of Electrical Engineering and Computer Sciences, the Program in Cognitive Science, and the Helen Wills Neuroscience Institute at the University of California (UC), Berkeley. He is a Senior Member of the IEEE [Robotics and Automation (RA), Systems, Man, and Cybernetics (SMC), and Engineering and Medicine Biology (EMB) societies], Society for Neuroscience, and the Neural Control of Movement Society. He has been the recipient of the Sloan Research Fellowship (2009), the Okawa Foundation Research Grant Award (2007), the UC Berkeley Hellman Faculty Award (2007), and the Christopher Reeve Paralysis Foundation Postdoctoral Fellowship (2003). His research interests include systems neuroscience (neural basis of sensorimotor learning and control; neural ensemble computation) and neural engineering (BMIs; neuroprosthetics; and biomimetic robotics).

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