Connecting cortex to machines: recent advances in brain interfaces

John P. Donoghue

Department of Neuroscience, Box 1953, Brown University, Providence, Rhode Island 02912, USA
Correspondence should be addressed to (John_Donoghue@Brown.edu)

Recent technological and scientific advances have generated wide interest in the possibility of creating a brain–machine interface (BMI), particularly as a means to aid paralyzed humans in communication. Advances have been made in detecting neural signals and translating them into command signals that can control devices. We now have systems that use externally derived neural signals as a command source, and faster and potentially more flexible systems that directly use intracortical recording are being tested. Studies in behaving monkeys show that neural output from the motor cortex can be used to control computer cursors almost as effectively as a natural hand would carry out the task. Additional research findings explore the possibility of using computers to return behaviorally useful feedback information to the cortex. Although significant scientific and technological challenges remain, progress in creating useful human BMIs is accelerating.

The creation of an interface between brain and machine—an old concept—has recently received a resurgence of attention. This renewed interest has emerged from a number of recent experiments that demonstrate the ability to read out or rapidly influence brain function, as well as from the first applications of new human devices. Terms like 'brain–machine interface', 'brain–computer interface', 'neural prosthetics' and 'neurorobotics' are appearing widely in both research publications and in the popular press.

How is this recent work new? For decades, neurophysiologists have coupled devices to the nervous system of alert primates and other animals to record its electrical activity, and thereby infer its function, or to modify its function by stimulating it electrically. Single-neuron recordings were already underway in humans[1] and in behaving monkeys[2] in the 1960s. Electrical stimulation has been used to influence brain function in alert monkeys and to treat neurological disorders in conscious humans since the 1950s (refs. 3,4). Today, implantation of physical devices into the brain is increasingly used to treat neurological disorders. Most noteworthy are deep brain stimulator implants, a remarkable therapy to relieve the tremor, rigidity and bradykinesia of Parkinson's disease by manipulating basal ganglia activity[5]. These and older uses of electrical stimulation provide physicians and investigators with a means to alter brain function by injecting a signal, but they do not establish a communication channel for the patient or subject.

Advances in BMI show that a new communication link between a functioning human brain and the outside world is feasible (**Fig. 1**). Such devices are potentially valuable for restoring lost neurological functions associated with spinal cord injury, degenerative muscular diseases, stroke or other nervous system injury. Although we are a long way from producing a fully functional BMI of this type for humans, recent work has moved this possibility nearer. These studies have centered around interfaces with the cerebral cortex, where it is widely believed that motor intent and sensory percepts are more readily accessed than elsewhere in brain. This review will focus on research that has dealt with these types of BMIs, with particular emphasis on efforts to derive command signals from the cortex.

Output BMIs

A major goal of an 'output BMI' is to provide a command signal from the cortex. This command serves as a new functional output to control disabled body parts or physical devices, such as computers or robotic limbs. Finding a communication link emanating from the cortex has been hindered by the lack of an adequate physical neural interface, by technological limitations in processing large amounts of data, and by the need to identify and implement mathematical tools that can convert complex neural signals into a useful command. BMIs that use neural signals from outside the cortex ('indirect BMIs') have already been developed for humans, and more recent efforts have produced 'direct BMIs' that use neural signals recorded from neurons within the cortex.

Indirect BMIs

An initial problem in the search for a BMI is to create a neural interface that can report brain activity. Standard EEG electrodes noninvasively record electrical signals, which form the basis of several indirect BMIs. Existing indirect BMIs use scalp recordings, which reflect the massed activity of many neurons. Signal quality is improved with more invasive recordings where similar electrodes are placed on the dura or on the cortical surface. Various brain signals are being used as command sources. Individuals can learn to modulate slow cortical potentials (on the 0.5–10 s time scale), adjust mu/beta EEG rhythms or use P300 as control signals[6]. These signals can be readily acquired, averaged and discriminated with standard computers, which serve as the decoding instrument. In present devices, the command output is displayed on a computer screen, which serves as the machine component of the BMI and translates intent into a desired action (**Fig. 1**). Such systems can be successfully used by

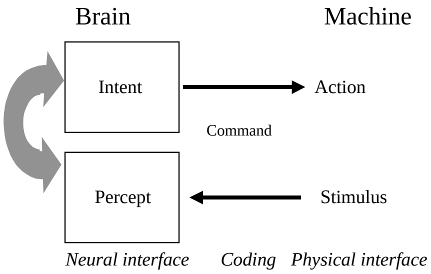

Fig. 1. The organization of a brain–machine interface (BMI). In the output BMI, a neural interface detects the neurally coded intent, which is processed and decoded into a movement command. The command drives a physical device (computer) or a body part (paralyzed limb) so that the intent becomes an action. For input, a stimulus is detected by a physical device, coded into an appropriate signal and then delivered by its interface to the user to elicit a percept (such as touch or vision). The use of these inputs and outputs is determined by the individual through the voluntary interplay between percept and desired action.

paralyzed humans to move a cursor on a computer screen or to indicate discrete choices[6].

Although current indirect BMIs provide an important new functional output channel for paralyzed individuals, they still have many shortcomings. In particular, they are cumbersome to attach and are very slow compared to natural behavior. Multi-electrode EEG systems can take an hour to attach and typically allow only a few choices per minute. The output signal often depends on repeated samples, although changes in EEG frequency can provide some degree of real-time computer cursor control. The slowness of the system emerges from the indirect nature of the signals and the relatively long time (often several seconds) it takes for the user to modify those signals. It impossible for these BMIs to obtain a direct readout of movement intent because neural spiking that carries this information is lost by averaging and filtering across the scalp. Thus, the EEG signal used in indirect BMIs is a substitute for the actual neural signal that encodes movement. The user must therefore learn how to relate this arbitrary signal to an intended action, and because the signal is attention-related, use of the BMI can interfere with other activities and control can be degraded by distractors.

Nevertheless, indirect BMIs are important communication channels that are now available for individuals who otherwise have extremely limited ability to communicate intent. Beyond many important scientific advances, research on these BMIs has also provided an important test-bed for the development of mathematical methods to derive command signals from brain activity, methods of multiple-channel signal processing and for methods for testing useful computer interfaces (for a review of the problems and advantages of each technology, see ref. 6).

Direct BMIs

Direct BMIs are intracortical recording devices designed to capture the action potentials of many individual neurons, especially those that code for movement or its intent. This constraint immediately requires a more demanding neural interface, more sophisticated signal processing and more computationally intensive algorithms to decode neural activity into command signals. Gaining access to the action potentials of individual neurons is particularly challenging because microelectrode tips require close proximity to the signal source. To obtain a successful signal, electrodes must remain stable for long periods, or robust algorithms must be identified to deal with shifting populations. One alternative is to record a more degenerate (and more easily obtained) signal from local field potentials[7]. However, this signal may be considerably limited in its information content in comparison to action potentials[8]. Furthermore, the nature of information coding in the cortex has the added challenge of recording from many neurons simultaneously, especially if higher-order commands and high signal fidelity are desired. Reliable chronic multielectrode recording methods for the cerebral neocortex are at relatively early stages of development.

In recent years, however, several technologies have advanced to the point where recordings can be made in tens to hundreds of neurons for months. Assemblies of small wires, termed 'microwires', have been used for many years for chronic cortical recordings. These have proven to be a very useful experimental tool to study cortical activity[1,9,10]. More advanced multiple electrode array systems are also being developed using advanced manufacturing and design methods[11–13], which is desirable for a reliable human medical device (**Fig. 2**). These neural interfaces—plus microribbon cables, connectors and telemetry devices—are necessary for successful multiple neuron recordings in humans. Miniaturization is necessary to place devices in the confines of the skull; small, high density connectors are essential to interconnect components, and telemetry is needed to move signals to remote processors or effectors too large to be in or on the head[9,12,14]. Each of these components is under development, but they present formidable technical challenges.

Current arrays are nevertheless reasonable prototypes for a human BMI. They are relatively small in scale and some have been successfully used for chronic recording. For example, individual electrodes in the Utah electrode[12] are tapered to a tip, with diameters <90 µm at their base, and they penetrate only 1–2 mm into the brain; these electrodes record for long periods in monkey cortex[15,16]. Intracortical arrays are tiny (**Fig. 2b**) compared to devices such as intraventricular catheters to treat hydrocephalus (approximately 2–3 mm in diameter) or deep brain stimulator electrodes, which are now accepted as safe human brain implants. Nevertheless, safety testing will be important to determine if intracortical arrays can remain effectively in long-term contact with neural tissue and still provide a useful signal, without creating significant damage. Neurotrophic recording electrodes are also being tested[17]. These electrodes, which have been used to record from human motor cortex, are small glass cones inserted individually into the motor cortex; each cone contains recording wires and factors that induce neural process ingrowth. The technologies described here are the most advanced candidates for a direct human cortical interface. Devices that detect action potentials without displacing neural tissue are highly desirable, but no such method is available.

After recording neural signals, one must derive a useful command signal from them. Multiple neuron recordings provide a significantly more challenging decoding problem than EEG signals, both because the signal is complex and because the processing demands are immense[9]. Electrical activity must be digitized at high rates (>20 kHz) for many channels, action potentials must be sorted from noise, and decoding algorithms must process neural activity into a useful command signal within a meaningful time frame—on the order of 200 ms. A further challenge is to extract a command signal that represents movement intent. A vast body of literature documents that populations of neurons carry considerable information about movement commands. Neural firing rate or pattern in motor areas carries sensory, motor, perceptual and cognitive informa-

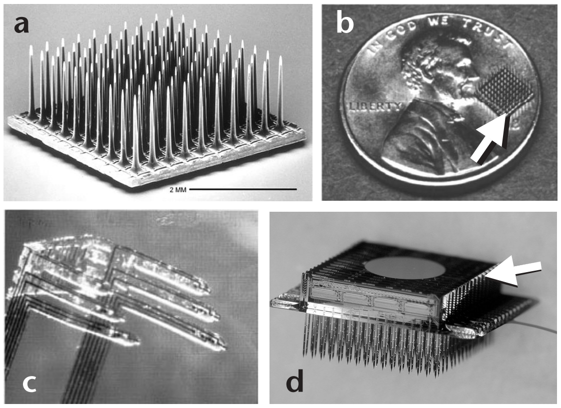

Fig. 2. Examples of intracortical electrode arrays under development. (**a**) Silicon 100 electrode array; each is separated by 400 µm (courtesy of B. Hatt, Cyberkinetics, Inc.). (**b**) Silicon array shown against a common scale to illustrate the size of these devices (courtesy of E. Maynard, University of Utah). (**c**) Polyamide 'bioactive electrode' array (courtesy of D. Kipke, University of Michigan). (**d**) Michigan thin film 256-shank array of 1024 multiplexed sites with mounted signal processing electronics (arrow; courtesy of K. Wise, University of Michigan).

tion. Pioneering work has demonstrated that motor cortical neurons can provide reliable estimates of motor intentions, including force and direction[2,18,19].

Recently however, three groups have demonstrated that hand trajectory can be recovered from the activity of populations of neurons in motor cortex[16,20,21]. These same groups also developed mathematical methods and took advantage of technological enhancements to demonstrate real-time reconstruction of monkey hand motion as it unfolds in a reaching task. Mathematical decoding methods, such as linear regression, population vector and neural network models, have been implemented by these groups to show that the firing rate of motor cortex populations provides a remarkably good—though not perfect—estimate of how the hand is moving through space. Although these mathematical techniques are themselves not new, it is a significant achievement to identify approaches and modify them to deal with large neural data sets. These advances resulted in the discovery that brain output connected to robot arms or computer cursors can mimic a monkey's ongoing arm movements as they occur[16,20,21]. This proved that neural decoding is fast and accurate enough to be a spatial control command. Ongoing efforts in mathematical decoding suggest that both the quality and form of movement reconstructions may be further improved when interactions among neurons[15] or additional signal features[22] are considered. However impressive, these signals are far from providing the full repertoire of movements that the arm can produce, such as manipulative movements of the fingers or grip control. Moreover, dealing with more complex actions or the simultaneous control of multiple, independent body parts will likely require more electrodes and more arrays.

Direct cortical control of devices

Beyond simply decoding motor intent, recent work has shown that cortically derived command signals can substitute for hand motion in behavioral tasks[16,20]. Monkeys were able to move a cursor to targets displayed on a computer monitor solely by brain output. In both of these studies, neural control of the cursor could continue whether or not the original tracking hand motions were present. It is tempting to conclude from these findings that monkeys understood that the brain directly controlled the cursor, but one cannot fully rule out the possibility that the monkey learned some covert action to achieve cursor control. There has been great interest in knowing whether humans might be able to gain direct control over their own neurons, both from its fascinating implications and from a practical perspective for paralyzed patients. This question can be more readily resolved by recording in paralyzed humans, where it has been specifically addressed. For example, voluntarily generated neural activity in the motor cortex of a patient with near-total paralysis has been demonstrated[17]. Using activity obtained through a few channels from implanted cone electrodes, the patient was able to move a cursor on a computer screen. So far, the level of control using the cone electrode has not matched that seen in monkeys; human control has been slower and with more limited dimensionality, on par with that seen in the indirect BMIs. The reasons for this discrepancy are not clear.

Input BMIs

Converting motor intent to a command output signal can restore the ability to act upon the environment. However, sensory input will also be essential for normal interaction, especially when outcomes of behavior are unreliable or unpredictable. An ideal communication interface for patients lacking intact somatic sensory pathways would be able to deliver signals to the cortex that are indistinguishable from a natural stimulus. Two recent findings indicate the potential to return meaningful information to the cortex by using local electrical microstimulation within the cortex. For example, microstimulation of the somatic sensory cortex can substitute for skin vibration in a perceptual task requiring frequency discrimination based on either skin or electrical stimulation[23]. Similarly, rats can use electrical stimulation to their cortical whisker areas as a directional cue for left–right motions[24]. These findings and related work[25] suggest that it will be possible to construct stimulation patterns that humans can use in a meaningful way to form percepts when natural systems are not available. It is important to note the difference between these types of electrical stimulation, which are intended to replace the natural percept, and other forms of stimulation which have attempted to drive behavior or modify brain function without the recipient's cognitive intervention[4].

Cortical input BMIs may also be applied to other forms of sensory loss. Of particular interest is the visual prosthesis designed to restore sight by direct stimulation of the visual cortex. Both cortical surface and intracortical stimulation have been shown to generate phosphenes, although considerable research is needed to understand how to move from spots of light to restoration of useful images of the world. The status of this field is too extensive to be reviewed here, but the state of this interface can be obtained from several recent papers[26–30].

Promises of a BMI

An obvious application of an output BMI is as motor neuroprosthetic device for paralyzed individuals who are unable to deliver movement intentions to the muscles. Spinal cord injuries that damage descending corticospinal pathways or neuromuscular disorders such as amyotropic lateral sclerosis (Lou Gehrig's disease) are among the most common causes of severe paralysis afflicting millions[6]. In these disorders, the cerebral structures necessary to formulate and command movement are often operational, but the means to enact motor intent are gone. Medical cures are unavailable for many forms of neural and muscular paralysis (see ref. 31 for a patient's perspective on living without the ability to move). The enormity of the deficits caused by paralysis is a strong motivation to pursue BMI solutions. The current necessity for an invasive interface for optimal BMIs is a significant barrier, but one that may not be greater than those that were present for procedures that are becoming widely accepted for disorders such as Parkinson's disease.

What might an ideal BMI look like? Optimally, a complete BMI should be able to provide a control signal that restores natural movement of paralyzed body parts without extensive learning. Control should emerge from the voluntary intent to carry out an action. Furthermore, it should be able to deliver useful sensory signals. These signals would be perceived naturally without disturbing behavior more than does the arrival of a sensory signal in the intact nervous system. Feedback of limb position and touch will also be essential. The device would also be noninvasive. At present, these are all major challenges. In particular, noninvasive single-neuron recording or microstimulation, which seem to be the only means capable of meeting these goals, are not feasible. Getting these signals to produce natural-seeming movements of paralyzed limbs will require further understanding of how muscles interact to produce complex movements. In the case of walking, this will also require a way to integrate vestibular signals. Finally, for feedback to work, a considerably better understanding of how electrical stimulation may substitute for natural pathway activation is essential. These challenges suggest that there will be a long process of intermediate steps before ideal physical replacements for lost functions are available, but this process has indeed begun.

One initial use of BMIs is to provide an outlet for severely paralyzed individuals to communicate with the world through a computer interface. However, a next step for paralysis treatment might be to connect cortical output directly to paralyzed muscles. One FDA-approved interface to generate arm movements exists[32]. This device can control hand grasp via very primitive commands delivered from an external switch controller to muscle stimulating electrodes. An EEG-based neural command has already been coupled to this device, although it suffers from the difficulties inherent to indirect BMIs[33]. If direct neuromuscular BMIs are successful, they will provide extraordinary options for those who have lost major neural pathways. Future BMIs may further complement biological solutions to repair the damaged nervous system, using approaches such as gene or stem cell therapy. One can further envision even more imaginative uses of BMIs. For example, they could be used to augment human capabilities by providing novel information input–output channels or added memory capacity. However, the neural augmentation prospects of BMIs resurrect important ethical and social issues that have been raised in the past[4]. Discussion on these topics should resume.

There are considerable barriers to overcome before it is possible for a paralyzed individual to fully interact with the world, with the full range of capabilities afforded to an intact system. Nevertheless, renewed interest in BMIs, as well as technological advances and progress in understanding neural coding, are now moving this field forward at a considerable pace.

Acknowledgments

The author would like to acknowledge support from the NIH/NINDS, DARPA and the Keck Foundation.

Competing interests statement

The authors declare competing financial interests; see the Nature Neuroscience website (http://www.nature.com/natureneuroscience) for details.

RECEIVED 16 JULY; ACCEPTED 16 SEPTEMBER 2002

1. Marg, E. & Adams, J. E. Indwelling multiple micro-electrodes in the brain. *Electroencephalogr. Clin. Neurophysiol.* **23**, 277–280 (1967).
2. Evarts, E. V. Pyramidal tract activity associated with a conditioned hand movement in the monkey. *J. Neurophysiol.* **29**, 1011–1027 (1966).
3. Cooper, I. S. Twenty-five years of experience with physiological neurosurgery. *Neurosurgery* **9**, 190–200 (1981).
4. Delgado, J. M. *Physical Control of the Mind* (Harper and Rowe, New York, 1969).
5. Benabid, A. L. *et al.* Deep brain stimulation for Parkinson's disease. *Adv. Neurol.* **86**, 405–412 (2001).
6. Wolpaw, J. R., Birbaumer, N., McFarland, D. J., Pfurtscheller, G. & Vaughan, T. M. Brain–computer interfaces for communication and control. *Clin. Neurophysiol.* **113**, 767–791 (2001).
7. Pesaran, B., Pezaris, J. S., Sahani, M., Mitra, P. P. & Andersen, R. A. Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nat. Neurosci.* **5**, 805–811 (2002).
8. Donoghue, J. P., Sanes, J. N., Hatsopoulos, N. G. & Gaal, G. Neural discharge and local field potential oscillations in primate motor cortex during voluntary movements. *J. Neurophysiol.* **79**, 159–173 (1998).
9. Moxon, K. A., Morizio, J., Chapin, J. K., Nicolelis, M. A. & Wolf, P.D. in *Neural Prostheses for Restoration of Sensory and Motor Function* (eds. Chapin, J. K. & Moxon, K. A.) 179–219 (CRC Press, Boca Raton, Florida, 2000).
10. Palmer, C. A microwire technique for recording single neurons in unrestrained animals. *Brain Res. Bull.* **3**, 285–289 (1978).
11. Bai, Q. & Wise, K. D. Single-unit neural recording with active microelectrode arrays. *IEEE Trans. Biomed. Eng.* **48**, 911–920 (2001).
12. Maynard, E. M., Nordhausen, C. T. & Normann, R. A. The Utah Intracortical Electrode Array: a recording structure for potential brain-computer interfaces. *Electroencephalogr. Clin. Neurophysiol.* **102**, 228–239 (1997).
13. Rousche, P. J. *et al.* Flexible polyimide-based intracortical electrode arrays with bioactive capability. *IEEE Trans. Biomed. Eng.* **48**, 361–371 (2001).
14. Nicolelis, M. A. L. Actions from thoughts. *Nature* **409**, 403–407 (2001).
15. Maynard, E. M. *et al.* Neuronal interactions improve cortical population coding of movement direction. *J. Neurosci.* **19**, 8083–8093 (1999).
16. Serruya, M. D., Hatsopoulos, N. G., Paninski, L., Fellows, M. R. & Donoghue, J. P. Instant neural control of a movement signal. *Nature* **416**, 141–142 (2002).
17. Kennedy, P. R., Bakay, R. A., Moore, M. M., Adams, K. & Goldwaithe, J. Direct control of a computer from the human central nervous system. *IEEE Trans Rehabil. Eng.* **2**, 198–202 (2000).
18. Humphrey, D. R., Schmidt, E. M. & Thompson, W. D. Predicting measures of motor performance from multiple cortical spike trains. *Science* **170**, 758–762 (1970).
19. Georgopoulos, A. P. Population activity in the control of movement. *Int. Rev. Neurobiol.* **37**, 103–119 (1994).
20. Taylor, D. M., Tillery, S. I. & Schwartz, A. B. Direct cortical control of 3D neuroprosthetic devices. *Science* **296**, 1829–1832 (2002).
21. Wessberg, J. *et al.* Real-time prediction of hand trajectory by ensembles of cortical neurons in primates. *Nature* **408**, 361–365 (2000).
22. Gao, Y., Black, M. J., Bienenstock, E., Shoham, S. & Donoghue, J. Probabilistic inference of hand motion from neural activity in motor cortex. *Proc. Adv. Neural Info. Processing Systems* **14**, The MIT Press, 2002.
23. Romo, R., Hernandez, A., Zainos, A., Brody, C. D. & Lemus, L. Sensing without touching: psychophysical performance based on cortical microstimulation. *Neuron* **26**, 273–278 (2000).
24. Talwar, S. K. *et al.* Rat navigation guided by remote control. *Nature* **417**, 37–38 (2002).
25. Wickersham, I. & Groh, J. M. Neurophysiology: electrically evoking sensory experience. *Curr. Biol.* **8**, R412–R414 (1998).
26. Dobelle, W. H. Artificial vision for the blind by connecting a television camera to the visual cortex. *ASAIO J.* **46**, 3–9 (2000).
27. Hambrecht, F. T. Visual prostheses based on direct interfaces with the visual system. *Baillieres Clin. Neurol.* **4**, 147–165 (1995).
28. Maynard, E. M. Visual prostheses. *Annu. Rev. Biomed. Eng.* **3**, 145–168 (2001).
29. Normann, R. A., Maynard, E. M., Rousche, P. J. & Warren, D. J. A neural interface for a cortical vision prosthesis. *Vision Res.* **39**, 2577–2587 (1999).
30. Schmidt E. M. *et al.* Feasibility of a visual prosthesis for the blind based on intracortical microstimulation of the visual cortex. *Brain* **119**, 507–522 (1996).
31. Bauby, J.-D. *The Diving-Bell and the Butterfly* (Knopf, New York, 1997).
32. Mauritz, K. H. & Peckham, H. P. Restoration of grasping functions in quadriplegic patients by functional electrical stimulation (FES). *Int. J. Rehabil. Res.* **10** (**Suppl. 5**) 57–61 (1987).
33. Lauer, R. T., Peckham, P. H. & Kilgore, K. L. EEG-based control of a hand grasp neuroprosthesis. *Neuroreport* **10**, 1767–1777 (1999).