BRAIN-MACHINE INTERFACE

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Contents

Summary

Brain-machine interfaces (BMIs) strive to restore neural functions to disabled individuals by linking brain circuitry to artificial devices, such as computers, prosthetic limbs, wheelchairs and communication systems. The BMI field has advanced considerably during the last two decades, driven by the developments in neural recording methods, computer science, robotic engineering and medical technology. BMIs are often classified by their function as sensory, motor or sensorimotor (bidirectional). Motor BMIs extract motor commands from brain signals and redirect them to artificial actuators. Sensory BMIs aim to restore sensory functions – hearing, vision, sense of touch and limb position – by interfacing neural structures with artificial sensors. Sensorimotor BMIs combine sensory and motor components. Additionally, cognitive BMIs have been proposed to decode higher-order brain signals, such as decisions, thoughts and memories. Depending on the degree of interference with the biological tissue, BMIs are classified as noninvasive or invasive. Noninvasive BMIs, for example those utilizing electroencephalography (EEG), are safe to use, but their bandwidth is limited. Invasive BMIs employ electrodes implanted in the brain to get access to highly informative neural signals produced by single neurons and their populations. Many decoding algorithms have been proposed for extraction of

information from brain activity and its utilization in BMIs. In addition to clinical goals, BMIs provide insights on fundamental brain mechanisms.

1. Introduction

1.1. Neural Control and When Things Go Wrong

Motor movements are essential for the interaction of living organisms with each other and with the external world. Indeed, all forms of mental activity – from relatively simple to highly sophisticated – are eventually expressed through muscle contractions and relaxations. Muscles move our limbs, rotate our eyes, produce facial expressions, and generate speech. Properly controlled muscle activity is essential not only for motor behaviors, but also for sensory functions. We actively seek sensations: reach toward objects with our arms; touch and grasp these objects to appreciate their texture and shape. As the body as a whole and its individual parts move, their displacements are monitored by numerous sensory receptors located in the skin, muscles, tendons and joints, as well as by the vestibular apparatus and vision. These continuous streams of sensory and motor information are processed by multiple neural structures richly interconnected with each other. We are consciously unaware of the majority of details of this immense neural processing and take for granted that we can effortlessly perform such complex tasks as maintenance of balance, bipedal walking, dexterous hand movements, speech and many others.

Unfortunately, neural trauma, disease or limb loss may seriously disrupt normal physiological functions. Destruction of just a few millimeters of nervous tissue may leave a person unable to move and feel. Spinal cord injury (SCI) breaks communication pathways between the brain and the spinal cord and produces devastating sensorimotor deficits, often a complete paralysis of large portions of the body. Neurological stroke can entail profound motor and sensory deficits. In Parkinson's disease, degeneration of dopamine neurons in substantial nigra pars compacta – a relatively small subcortical nucleus – dramatically damages sensorimotor and cognitive functions. Amyotrophic lateral sclerosis (ALS), a motor neuron disease, results in paralysis, muscle atrophy and eventually death.

Strikingly, higher brain functions often remain intact in many of these dire neurological conditions. Thus, in SCI and locked-in syndrome, patients are unable to produce muscle contractions, but remain mentally able and awake.

Currently, there is no cure for many devastating neurological conditions, such as SCI and ALS. Millions of paralyzed patients are bound to their beds or wheelchairs for the rest of their life. The development of efficient treatments for neurological trauma and disease is clearly one of the most important and difficult challenges for the medical science today.

1.2. Connecting the Brain to Machines

Brain machine interfaces (BMIs) represent an ambitious attempt to revolutionize treatment of paralysis and other neurological conditions. BMI is an artificial system that enables communication between the brain and artificial devices, such as computers, limb prostheses and neural stimulators (Lebedev and Nicolelis 2006; Nicolelis and Lebedev 2009; Nicolelis 2011; Schwartz et al. 2006; McFarland et al. 2006; Hatsopoulos and Donoghue 2009) (Figure 1). Therapeutic BMIs strive to bypass the site of neural damage and to establish a direct functional connection between an intact brain area and an assistive device. For example, it has been proposed that SCI patients may be able to regain motor function if they are aided with a BMI that extracts signals from the motor cortex and directs these signals to robotic limbs, exoskeletons, or functional electrical stimulation (FES) devices connected to paralyzed muscles (Lebedev and Nicolelis 2006; Wolpaw et al. 2002). In addition to medical applications, BMIs can be employed by healthy people to enhance certain neural and physiological functions.

In addition to the term "BMI", systems interfacing neural tissue with external devices are called brain-computer interfaces (BCIs), mind-machine interfaces, neural interfaces, brain implants or neural prostheses. Although this terminology is commonly used interchangeably, some authors make strict distinction between specific BMI subtypes. In this chapter the term "BMI" is used in its most generic meaning.

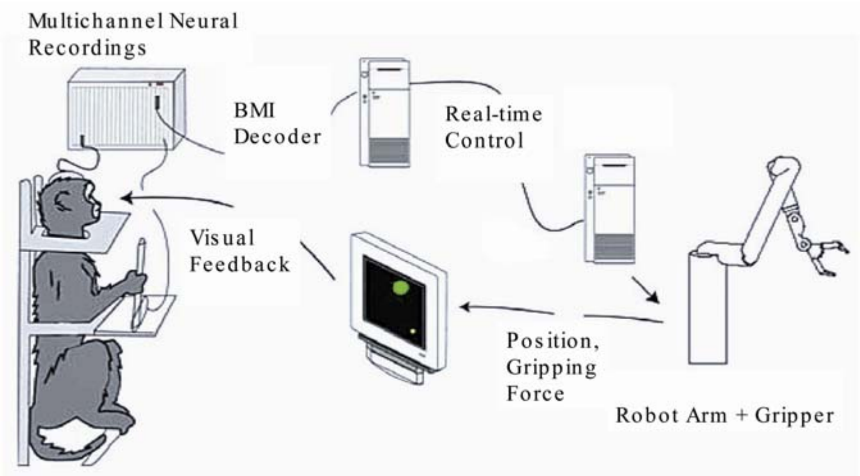

Figure 1. Brain-machine interface for reaching and grasping. Neuronal ensemble activity was recorded in multiple cortical areas in a rhesus monkey and translated into reaching and grasping movements performed by a robotic arm. The experimental setup included the data acquisition system, the computer running BMI decoders, the robot arm, and the visual display which provided feedback of the robot movements. Adapted from Carmena et al. (2003)

BMIs introduce artificial components into neural circuitry: sensors for sampling neural signals, electronic chips that decode and transform neural activity, neural stimulation devices, robotic limbs with sensors of touch and position, wireless transmitters, and other components. In science fiction, biological organisms that receive artificial parts are called cyborgs. Whereas BMI-based cyborgs, as envisioned by futuristic writers, may emerge in the future, current BMI research considers medical treatment as the priority and major practical goal. Many branches of this clinically oriented research, particularly research on invasive BMIs, are still at the stage of animal experiments or preliminary human trials. Considerable effort will be required in these areas to develop fully functional clinical neural prostheses. The major challenges that hinder the progress in clinical BMIs include the need to improve neural recording methods, problems of biocompatibility, the task of making BMIs fully implantable, development of advanced BMI decoders, incorporation of artificial sensation in BMI systems, and engineering of advanced robotic prostheses (Lebedev and Nicolelis 2006). One notable exception is the cochlear implant, which has already entered the clinical world and has helped hundreds of thousands patients to regain hearing (Shannon 2012; Wilson and Dorman 2008)).

In addition to medical applications, BMIs have emerged that are intended for healthy people. These are, for example, BMI devices for computer gaming that allow users to play simply by thinking instead of using a joystick or a keyboard (Tangermann et al. 2009). Additionally, BMIs can provide useful biofeedback of neural signals that people cannot perceive through their normal senses. For example, a safety system for a long-distance driver continuously samples encephalographic (EEG) activity and issues a warning if signs of drowsiness are detected (Lin et al. 2010). In the future, consumer BMIs may allow humans to exceed many of normal abilities: computational power, accuracy, consistency, reaction time and physical strength.

BMI research has experienced a spectacular growth since the 1990s, driven by the progress in multichannel neural recordings, computer technologies and robotic engineering. Many ideas previously entertained only by science fiction are becoming a reality.

1.3. Ethical Considerations and Cognitive BMIs

The prospect of BMI systems being able to reproduce virtually any brain function brings up a number of philosophical and ethical issues (Farah 2002; Vlek et al. 2012). Is it ethical to intrude into a person's mind with a BMI? Is there a danger that BMIs may interfere with the representation of self and free will? Even though many of these questions seem far-fetched, research has already started on BMIs that extract higher-order cognitive signals from brain activity, such as decisions (Andersen et al. 2010) and memories (Berger et al. 2005).

1.4. BMI Types by Function

Currently, the major focus of BMI research is on systems that handle motor and sensory signals. These BMIs hold promise to provide practical solutions for restoration of vital functions to people with disabilities. BMI systems of this type are often classified as: (i) motor, (ii) sensory, or (iii) bidirectional (sensorimotor). This classification resembles a simplified description of the layout of the nervous system as an arrangement of sensory areas, motor areas and their interconnections. In actuality, there is no clear-cut separation between sensory and motor areas in the brain. For instance, cortical areas – even the ones called primary motor and primary sensory – process both motor and sensory information and therefore are best described as sensorimotor (Lilly 1956; Evarts 1973). It is quite possible that with the advancement of the BMI field, BMIs will be incorporating sensorimotor modules instead of segregating motor and sensory processing. Recently demonstrated bidirectional BMIs represent the first step in this development (O'Doherty et al. 2011).

1.5. Invasive and Noninvasive BMIs

Safety is an important consideration when choosing a BMI system. The safest, nonivasive BMIs, utilize sensors (e.g., EEG electrodes) that may come in contact with the skin, but do not penetrate the body. Although such systems are safe to use, their information bandwidth is limited, often resulting in insufficient speed and accuracy of performance (Lebedev and Nicolelis 2006; Wolpaw et al. 2002).

Nonivasive recording methods, such as EEG, utilize weak neural signals detected at a distance from their source. These recordings often have low spatial resolution (the ability to discriminate signals from nearby brain sites) and/or low temporal resolution (the ability to detect rapid neural modulations), but they can be implemented much more easily than invasive recordings. Consequently, noninvasive BMIs have been extensively studied in humans. Many practical noninvasive systems have been developed, such as BMIs for communication, prosthetic control and wheelchair navigation (Galán et al. 2008; Muller-Putz and Pfurtscheller 2008; Nicolas-Alonso and Gomez-Gil 2012; Sellers et al. 2010).

Invasive BMIs hold promise to achieve a much higher bandwidth compared to noninvasive systems. An invasive surgical procedure is required to bring recording sensors close to brain neurons, the signal source. Extracellular activity or single neurons is usually recorded with microwires (typically 10-50 microns in diameter) implanted in the brain (Lebedev and Nicolelis 2006; Nicolelis and Lebedev 2009). In addition to single-unit recordings, microwires can be also used to record local field potentials (LFPs), which represent combined spiking activity and dendritic potentials of many neurons.

Much of invasive BMI research has been conducted in experimental animals (rodents and primates). Human clinical research on invasive BMIs has recently started, with promising results (Hanson et al. 2012; Hochberg et al. 2012; Collinger et al. 2013). Several issues still hinder the acceptance of invasive BMIs in clinic, most importantly the need to achieve reliability and long-term performance of invasive implants and the need to transition from tethered to wireless recordings (Lebedev and Nicolelis 2006).

Electrocorticography (ECoG) is a safer alternative to implanted microwires. This is a minimally invasive recording method that utilizes electrodes placed on the brain surface. Craniotomy is required, but the risk of neural damage is decreased. ECoG recordings cannot resolve discharges of single neurons, but they work well to detect synchronous electrical activity of large populations of neurons.

2. History of Research and Commercialization

2.1. The Birth of BMI Field

The first experiments in which multiple electrodes were implanted in the brain date back to the 1950s when John Lilly implanted 25 to 610 electrodes in monkey cortex at intervals from one to two millimeters apart. He then applied electrical stimulation through these electrodes to elicit movements (Lilly 1956). Lilly observed that movements occurred even when he stimulated cortical areas presumed to be purely sensory. He concluded that each cortical area was best characterized as sensorimotor rather than purely sensory or purely motor.

In the 1960s and 1970s, David Nowlis, Joe Kamiya, Abraham Black, Maurice Sterman and their colleagues experimented with EEG as a source of biofeedback that enabled subjects (both animals and humans) to gain control over their own brain rhythms (Lebedev and Nicolelis 2006).

In 1963, Grey Walter conducted a study which can be considered the first demonstration of a real-time BMI (Dennett 1992). He implanted electrodes in the motor cortex of patients undergoing neural surgery. The patients advanced a slide projector by pushing a button with their hands. These voluntary button presses were preceded by readiness potentials in the motor cortex. To create a direct link between the brain and the projector, Walter disconnected the button and made cortical potentials advance the slides. The patients continued to press the disconnected button, but the control signal came directly from the brain. Remarkably, their direct cortical control often worked before they initiated hand movements.

About the same time, a team of National Institutes of Health (NIH) scientists led by Karl Frank formulated the goal of building neurally controlled prosthetic devices. Frank wrote, "We will be engaged in the development of principles and techniques by which information from the nervous system can be used to control external devices such as prosthetic devices, communications equipment, teleoperators ... and ultimately perhaps even computers" (Frank 1968). The NIH team was able to achieve promising results. In 1970, team members Humphrey, Schmidt and Thompson simultaneously recorded 3-8 neurons with five electrodes inserted in the motor cortex of monkeys performing wrist flexions and extensions (Humphrey et al. 1970). The recordings were stored on tape. In an offline analysis of these data, the researchers were able to extract movement traces from the neuronal rates using multiple linear regression. A decade later, Schmidt recorded from monkey cortex with a 12-electrode array that stayed implanted for 37 months (Schmidt 1980). Schmidt's monkeys learned to move a cursor on a LED display by modulating their cortical activity.

In parallel with this work, pioneering studies on volitional control of single cortical neurons were conducted by Ebernhard Fetz at the University of Washington. His monkeys voluntarily modulated the activity of single cortical neurons in order to attain a particular firing rate (Fetz 1969).

Research on sensory BMIs started at about the same time as the work on motor BMIs. The development of cochlear implants was especially successful (Wilson and Dorman 2008). This work was pioneered in 1957 by Djourno and Eyriès who developed an implant that applied single-channel stimulation to the auditory nerve. The stimulation frequency was up to 1 kHz, and their patient eventually was able to detect pitch differences and recognize words. The first multichannel cochlear stimulator was developed by Blair Simmons in 1964. In the 1970s, William House and Jack Urban introduced a carrier frequency of 16 kHz to the stimulation signal. Their work eventually resulted in clinical device that received FDA approval. Additionally, Robin

Michelson's work contributed to improved implantation methods. Over several decades, cochlear implants have improved and have become widely accepted in clinic. More than 200,000 people have been implanted worldwide with these devices.

Also in the late 1960s – early 1970s, research has started on sensory BMI for restoration of vision. In these early studies conducted by the groups of Brindley and Dobelle (Brindley and Lewin 1972; Dobelle et al., 1974), electrical stimulation was applied through electrodes placed on the surface of the visual cortex in totally blind individuals. The subjects reported phosphens, i.e. appearances of light spots in their visual field. Moreover, they were able to recognize simple patterns and letters composed of such phosphens. These pioneering studies demonstrated the feasibility of a visual prosthesis for the blind.

2.2. Rapid Development and Key Players

In the late 1990s – early 2000s BMI research markedly accelerated, facilitated by progress in multielectrode recording methods and computer technologies. Several researchers became notable players in the BMI field.

Miguel Nicolelis, John Chapin and their colleagues at Hahnemann University pioneered an invasive BMI that converted extracellular activity of neuronal populations recorded in rat cortex and thalamus into one-dimensional movements of a robot (Chapin et al. 1999).

Nicolelis then moved to Duke University where he started BMI research in nonhuman primates. He and his colleagues pioneered several BMIs that utilized large-scale neuronal activity recorded from multiple cortical areas to control external actuators. Aided by these BMIs, monkeys learned to control robot arms that performed reaching movements (Wessberg et al. 2000) and reaching and grasping movements (Carmena et al. 2003; Lebedev et al. 2005). Nicolelis and his colleagues also pioneered cortical microstimulation as a method to provide artificial tactile feedback for a BMI that controlled arm reaching (O'Doherty et al. 2011). Furthermore, the Nicolelis laboratory extended their BMI approach to bipedal locomotion (Fitzsimmons et al. 2009).

Philip Kennedy is another prominent figure in the BMI field. He and his colleagues implanted an ALS patient with a neurotrophic electrode that induces growth of myelinated fibers into the recording tip. The patient was able to achieve an on/off control with neural signals (Kennedy and Bakay 1998).

John Donoghue heads a BMI research group at Brown University. The group conducts invasive-BMI experiments in monkeys and in human patients. They were the first to implant paralyzed patients with multielectrode arrays in the motor cortex. These human studies demonstrated real-time BMI control of a computer cursor (Hochberg et al. 2006) and a robotic manipulator (Hochberg et al. 2012).

Andrew Schwartz, first at Arizona State University and then at the University of Pittsburg, developed invasive BMIs for the control of three-dimensional movements of cursors (Taylor et al. 2002) and robots (Velliste et al. 2009). His laboratory also develops invasive BMIs for humans (Collinger et al. 2013).

The other notable players in the invasive BMI research are Richard Andersen at California Institute of Technology, Krishna Shenoy at Stanford University and Elon Vaadia at the University of Jerusalem.

In parallel with the development of invasive BMIs, noninvasive BMIs (often called BCIs) achieved impressive progress since the late 1990s. Many practical applications have been developed for assisting disabled patients in using a computer, controlling a wheelchair and restoring mobility of paralyzed limbs. Among the leading researchers in this field are Niels Birbaumer (University of Tübingen), Gert Pfurtscheller (Graz University of Technology), Theresa Vaughan (Wadsworth Center), Klaus-Robert Müller (Fraunhofer Institute for Intelligent Analysis and Information Systems), Gerwin Schalk (Wadsworth Center), Christa Neuper (University of Graz), Andrea Kübler (Eberhard-Karls-University), Jonathan Walpaw (Wadsworth Center) and Jose Millan (EPFL).

2.3. Commercialization

Several companies have emerged that commercialize BMI technology. Philip Kennedy founded Neural Signals, which is a research company focused on the development of communication devices for paralyzed patients. John Donoghue and his colleagues founded Cyberkinetics, a company that developed BMI components and marketed recording equipment. Cyberkinetics was then sold to Braingate. William Dobelle founded Avery Biomedical Devices to develop visual implants, but this work slowed down after his death. Several companies develop EEG-based BMIs: Guger Technologies, Interactive Productline, NeuroSky, Emotiv Systems, Starlab and OCZ Technology. Two major manufactures of cochlear implants are Cochlear Corporation and Advanced Bionics Corporation.

3. Information Encoding in the Brain

3.1. Factors that Allow Decoding of Neural Signals

Notwithstanding many remarkable advances made by neuroscientists, we still have a poor understanding of brain computations that underlie motor control, sensory processing and cognition. Luckily for BMI scientists, this poor understanding does not prevent them from trying and succeeding in extraction of useful information from the brain.

Numerous neurophysiological studies have shown that individual neurons and their populations modulate their discharge rates when the brain processes information. Even though the exact functional role of these neural activities is unknown in many cases, BMI researchers still can develop algorithms that discover correlations between neural signals and behavioral parameters of interest and employ these correlations to extract behavioral parameters from brain activity.

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Biographical Sketch

Mikhail Lebedev received his undergraduate degree in Physics from Moscow Institute of Physics and Technology and his PhD degree in Neurobiology in University of Tennessee, Memphis. He conducted research on motor control and neurophysiology at the Institute for Information Transmission Problems, Moscow, University of Tennessee, Memphis, La Scuola Internazionale Superiore di Studi Avanzati, Trieste and National Institute of Mental Health, Bethesda. He is currently a Senior Research Scientist at Duke University Center for Neuroengineering. Research interests include system neurosciences, primate motor control and cognition and brain-machine interfaces.