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Intracortical Brain-machine Interface for Restoring Sensory Motor Function: Progress and Challenges

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Abstract: Limb loss or paralysis due to spinal cord injury has a devastating impact on quality of life. One way to restore the sensory and motor abilities lost by amputees and quadriplegics is to provide them with implants that interface directly with the central nervous system. Such Brain-machine interfaces could enable patients to exert active control over the electrical contractions of prosthetic limbs or paralysed muscles. The parallel interface can transmit sensory information about these motor outcomes back to the patient. Recent developments in algorithms for decoding motor intention from neuronal activity, using biomimetic and adaptation-based approaches and methods for delivering sensory feedback through electrical stimulation of neurons have shown promise for invasive interfaces with sensorimotor cortex, although significant challenges remain.

Keywords: Brain-machine Interface; Sensorimotor Cortex; Decoding of Neuronal Activity; Cerebral Cortex.

1. Introduction

A study published in 1999 described training rats to access water [1] using two 16-electrode arrays implanted in the primary motor cortex (M1) and thalamus. Since this pioneering study, the functionality of Brain-machine interfaces (BMI) has expanded [2,3] significantly. Advances in microelectrodes, electronic science, and computing have made it possible to build electronic interfaces with the brain, allowing us to "read" and "decode" hundreds of neural signals from brain motor areas to control increasingly complex robotic arms. Recently, a person with tetraplegia was able to manipulate the seven degrees [4] of freedom of a complex anthropomorphic arm and hand using inputs from two 96-channel intracorporeal microelectrode arrays implanted in the primary motor cortex (M1). In this review, we explore the progress of intracortical Brain-machine interfaces since the first experiments to date by discussing studies that have led to significant increases in function in rodents, monkeys, and humans.

Current Brain-machine interfaces have a number of limitations. First, most Brain-machine interfaces involve only efferent neural interfaces, that is, they decodulate movement-related information from measured brain activity. Almost all Brain-machine interfaces are guided only by visual feedback and lack somatosensory feedback, which is a key component [5] of normal motor behavior. The absence of somatosensory feedback may largely contribute to the relatively poor quality of movement controlled by the BCI. Afferent interfaces are being developed to restore a patient's sense of touch and limb movement through a series of electrical stimuli delivered to electrodes in the somatosensory cortex (**Figure 1**). Eventually, Brain-machine interfaces will transfer information in both directions to restore motor and somatosensory functions.

Second, the currently developed BCI focuses on the "kinematics" of controlling actions, and very little research work has been done to develop the "dynamics" of controlling actions. The "kinetic" design of the control action controls the forces and muscle activity behind the action. While there have been many advances in controlling hand use, object grasping, and manipulation, large areas of the M1 cortex for the complex mechanisms that control hand use are currently unexplored.

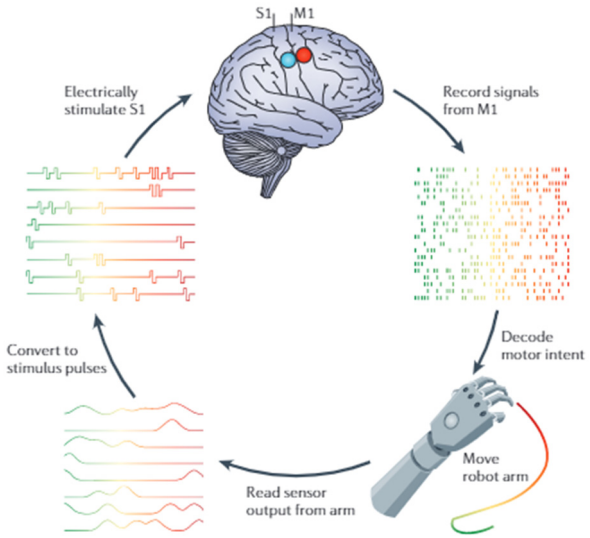


Figure 1. An ideal bidirectional Brain-machine interface for prosthetic control

Finally, most efferent Brain-machine interfaces rely on decoders that attempt to exploit the natural mapping between brain activity and limb movements - a process known as biomimetics [6,7]. Some afferent Brain-machine interfaces use a similar strategy in an attempt to produce natural patterns [8,9] of neuronal activation in the somatosensory cortex through electrical stimulation. However, under the current level of science and technology, perfect bionic mapping cannot be achieved by any kind of interface. An alternative approach is to employ a systematic but not necessarily bionic mapping between neuronal activation and limb states, which subjects then have to learn through adaptation, sometimes combined with synchronous adaptation [10, 11] by decoder algorithms. Ultimately, both biomimetics and adaptation may become important principles in the development of Brain-machine interfaces.

Due to space constraints, we focus in this review on methods that involve implanting intracorporeal electrode

arrays rather than minimally invasive methods using epidural, subdural, or scalp recordings. However, although intracortical approaches offer great potential for restoring sensorimotor function, they face considerable challenges. Perhaps the most critical challenge is that current intracortical electrode technology does not have the longevity [12] required for clinically viable efferent interfaces. Given that larger, lower impedance electrodes sample aggregate activity from thousands of neurons, the signal quality obtained by minimally invasive methods tends to remain longer, but they have poorer spatial resolution and produce fewer[13] independent signals. It may be possible to extend the recording lifetime of the intracortical Brain-machine interface by recording local field potentials rather than individual neuronal activity [14] and by recording multi-unit activity rather than single-unit activity. The lifespan of existing electrode techniques for stimulation is likely to be much longer than those for recording because stimulation is less affected by many of the factors that contribute to the degradation of recording quality. Another major challenge is that Brain-machine interfaces will eventually need to be applied to patients 24/7, rather than just in the lab. This goal has been difficult to achieve [15] with currently invasive intracortical Brain-machine interfaces.

2. Movement is Controlled through Efferent Brain-machine Interfaces

2.1. Controlling Range of Motion

Movements controlled by Brain-machine interfaces have progressed in a short time from collecting water [1] droplets using a single-DOF robotic arm in rats to controlling cursor movement in two [7] or three [16] dimensions in monkeys. Each of the three pioneering studies used decoders based on data recorded during natural movement in an attempt to mimic existing mapping from M1 cortex to movement. In an ampuant or paralyzed person who is unable to produce actual movement, neuronal firing can be measured as he or she observes and attempts to mimic the movement of a robotic arm as it performs a series of preprogrammed movements. Together with the cursor trajectory, this neuronal activity is then used to compute an "observation-based" decoder. In fact, experiments with monkeys have shown that when the monkey watches and possibly tries to mimic the hand action represented by a moving cursor, many M1 neurons fire in a way that is at least qualitatively similar to firing when an actual limb movement is being made. This observation-based firing may partly reflect the activity of "mirror neurons," however, neurons with mirror properties make up less than 15% of neurons in the premotor cortex, and perhaps even fewer in M1, so they are unlikely to contribute significantly to decoding.

The use of observation-based decoders is increasingly being used to conduct experiments on nonparalyzed monkeys in an effort to mimic what paralyzed patients would encounter. However, this practice may not be ideal. Abolishing limb movements better mimics the clinical situation because it removes much of the sensory input [17,18] M1 receives from the moving limb. However, for a nonparalyzed monkey, imagining moving rather than actually moving involves large changes in its motor intention or downstream mechanisms to turn off cortical output. Since there is little evidence that such gating occurs, a nonparalyzed monkey that imagines but inhibits limb movement may not be a good model for a paralyzed person who is actually trying to move. Indeed, behavior-related changes in afferent input or movement intention could explain some of the changes in neural firing that occur when nonparalyzed subjects transition from actual limb movement to cerebral control of the robotic arm.

To date, the best clinical demonstration of robotic limb control by means of a Brain-machine interface was performed in a 52-year-old man with quadriplegia due to spinocerebellar degeneration (**Figure 2a-c**). The patient had two microelectrode arrays implanted in the motor cortex, which she used to control the anthropomorphic robotic arm (with the hand shown in **Figure 2d**) [19]. The decoder was initially recalculated daily in a two-step sequence. Neural recordings were made while the patient observed a series of limb movements that were used to calculate the observation-based decoder. She then uses this initial decoder to move the robotic arm herself, thereby generating the data needed to calculate a more accurate motion-based decoder. She achieved 3D control of hand position by the second day of training, progressing to four and finally seven degrees of freedom (six on the arm and one on the grasp) after 3-4 months. Early in the learning process, the trajectory of the prosthesis's movements was restricted to a simple, accurate path by the decoder computer. As the subject learns to control the limb and the complexity of the task increases, this computer assistance is adjusted to maintain a reasonable success rate. It is eventually eliminated completely (the red part of the trace in **Figure 2c**). The combination of a simple linear bionic decoder and this guided adaptation may be key to the success of this effort.

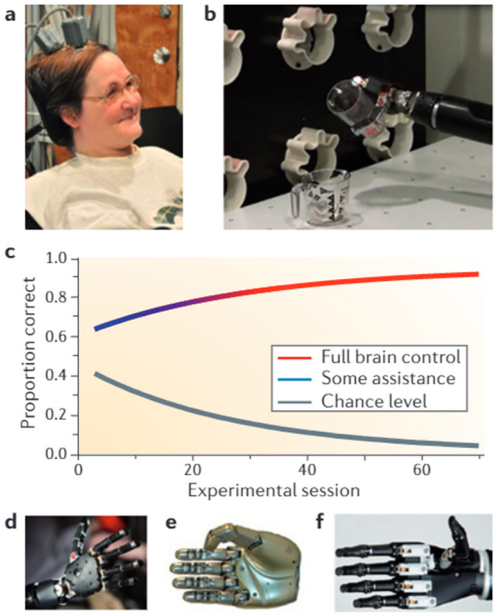


Figure 2. Seven degrees of freedom control of the prosthesis for reaching and grasping

2.2. Controlling the Grasp

Artificial hands are becoming increasingly anthropomorphic, and some of them are almost as versatile as human hands (**Figure. 2d-f**). Although considerable progress has been made in recent years in our understanding of the laws associated with grasping movements within the primary motor cortex, no Brain-machine interface currently achieves grip control that is more advanced than that achieved with a single degree of freedom. For example, the BrainGate experiment [20] used a linear discriminant classifier to determine whether neural activity in the primary motor cortex

represented an open or closed hand state. This enabled paralysed human patients to safely grasp objects using robotic hands (including the one shown in **Figure 2e)**.

While online control of hand motion is still very limited, offline decoding of hand kinematics is more advanced and points the way to future robotic hand improvements. The continuous decoder has also been used offline to predict a variety of high-dimensional, grasp-related motion signals. In one study, estimates [21] of hand position and 18 wrist and finger joint angles were calculated from recordings in M1, dorsal premotor cortex (PMd), and ventral premotor cortex (PMv). In another study, M1 activity was used to predict 25 joint angles [22] of the arm and hand as monkeys grasps different objects. Thus, achieving this level of control through Brain-machine interfaces is a feasible near-term goal.

Dexterous manipulation of objects requires more degrees of freedom than simple grasping. Extending control from two or three degrees of freedom to two or three degrees of freedom per finger, thus giving the ability to manipulate objects, will be quite a challenge for the next stage of Brain-machine interface development. Indeed, simply assessing whether a BCI-mediated grasp is successful may prove to be another challenge. It would be an important contribution [23] to the field by establishing a common set of metrics that can be applied across laboratories to assess the achievable performance of Bcis and, ultimately, to master experiments.

2.3. Control Limb Resistance and End-point Strength

When we reach for an object, our arms and hands move along a spatial trajectory that can be described by their position and their velocity at any point in time. This description of motion is called kinematics. But we're not just controlling the kinematics of an action. For example, we can apply precise forces to delicate objects, or large amounts of force to heavy tools, and stiffen the entire limb by contracting muscles together when greater stability is needed (this is often referred to as "impedance control." [24] These force-related properties are referred to as motion dynamics. Muscle forces that cause movement and regulate stiffness are richly represented in M1, and can be predicted from M1 records almost as well as, or in some cases better than, movement kinematics (FIG. **3)**. When monkeys used these hybrid kinesio-torque decoders to control movements with dynamics similar to those of natural limbs (i.e., stiffness, damping, and mass), they obtained movement trajectories that were straighter, smoother, and arguably more natural than movements with dynamics alone.

The difficulty in controlling movement using a pure torque decoder of neural signals is due in part to the inability to control the impedance [25] of the limb. For example, monkeys are unable to stiffen the limb at the end of a movement to stabilize the hand on the desired target. In principle, the necessary impedance control could be accomplished through a muscle-based Brain-machine interface. To test this possibility, another group used neural networks to indirectly reproduce limb movements and joint torques: they used the network to generate inputs to a musculoskeletal model of the arm, while training the network [26] solely on the resulting torque errors.

Although the system was only tested offline, it reproduced torques across different force-field loading conditions and was more accurate than a torque model that did not incorporate musculoskeletal mechanics. Importantly, the system also accurately captured the impedance of the limb under different conditions. Interestingly, the inputs to the musculoskeletal model generated by the neural network produced modulation patterns similar to the actual EMG signals in the monkey, despite the fact that the network was not explicitly trained. Several groups have begun exploring the possibility of using M1 recordings to directly control muscle activity, a strategy [27] that could be used to restore autonomic control over limb movement and impedance after SCI. In another study, monkeys were trained to control the activity of individual neurons in order to generate specific levels of isometric wrist moments [28] during nerve blocks through functional electrical stimulation of the flexor and extensor muscles.

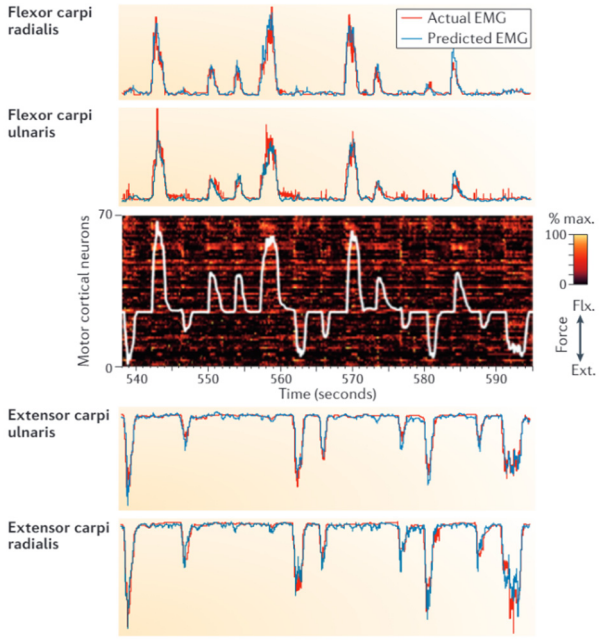


Figure 3. Offline EMG - Prediction based on flexion and extension isometric torques to the wrist

The results of these studies suggest that incorporating some form of BMI motion dynamics – (for example, torque prediction combined with impedance control or muscle activity prediction) - is feasible and may provide a way for patients to interact with their environment more naturally than with purely motor-powered Brain-machine interfaces.

2.4. The Role of Adaptability

Shapeable adaptive changes in the brain are fundamental to normal learning and recovery after injury. Adaptation may be most evident in the motor system when we practice new skills, but it also occurs[30] in the somatosensory system during skill acquisition and recovery after injury[29]. For example, when humans perform reach actions in response to force fields or rotational visual feedback, the initial error in reach direction becomes smaller and eventually disappears with repeated exposure to perturbations over tens of minutes. These adaptive processes also lead to changes in subjects' perception of their hand position and somatosensory evoked potentials. Patients almost certainly engage in similar motor and sensory adaptation processes as they learn to control a prosthetic limb.

As discussed above, two contrasting and complementary strategies have been used in BCI design. The biomimetic approach aims to preserve as much mapping as possible

between the natural patterns of neuronal activity and the state of the limb. The goal is to maximize performance and minimize the amount of learning required by the user. An alternative approach, often referred to as "adaptive," uses systematic, but not necessarily biomimetic, mapping between neural activity and limb states that the patient must learn. The rationale behind the adaptive approach is that attempts to mimic normal mapping are likely to achieve little, given the extraordinary adaptability of the brain and the relatively crude interface provided by the current state of technology.

Currently, most motor Brain-machine interfaces are designed to be bionic. In able-bodied monkeys, decoders can be calculated from neuronal activity recorded during actual limb movements. In paralyses, it is usually calculated[31] from neural firing during movement. However, even with a bionic decoder, the firing properties of M1 neurons gradually changed as able-fit monkeys switched from normal stretching maneuvers to Brain-machine interface exercises. Typically, the tuning curves of neurons used for Bcis become sharper, and they often shift to new preferred directions. If monkeys are tested in this way over a series of experimental sessions, the neuronal tuning curves tracked across sessions tend to shift by the same amount each time. Changes in neuronal firing may reflect changes in motor intention, as if the monkey were learning a new motor behavior.

These adaptive processes have been further investigated in experiments in which the BMI decoder was deliberately disrupted. In one example, monkeys were trained to use a bionic decoder to move the cursor before and after all inputs to the decoder were swapped randomly (so that the decoder [10] was no longer bionic). Under these conditions, the monkey's performance initially declined and then gradually returned to the level achieved by the original bionic decoder after a few sessions. The change in success rate correlated with a gradual change in the tuning curve of the neurons.

In another set of experiments, half of the tuning curve used for control was intentionally rotated 90 degrees [32] around a common axis, so that any attempt to move toward a given target displayed in a 3D VR environment would cause the cursor to move in the wrong direction, much like classical visual rotation experiments. Although slower and less complete than the natural adaptation experiment, the monkeys learned to compensate for this perturbation in a single training session. Most neurons changed their firing patterns in some way, suggesting that the monkeys simply learned to aim at different targets. Another study found that neurons used for Brain-machine interface-based cursor movement control experienced greater changes [33] in the transition from actual hand control to brain control than neurons whose responses were recorded but not used in the decoder. Thus, in both experiments, monkeys apparently learned to selectively modulate the activity of individual neurons to improve the control function of the Brain-machine interface.

These changes occurred automatically, probably through normal motor learning mechanisms. A different approach might be to train animals to directly control the activation of individual neurons. If monkeys were offered rewards based on the desired firing rate, they could learn to adapt to the firing of M1 neurons. Interestingly, monkeys can learn to control the activation of individual motor cortex neurons, regardless of any prior relationship those neurons may have with movement. In fact, monkeys even learned to modulate neurons [34] recorded in the somatosensory cortex. When signals were recorded from pairs of neurons but rewards were given based on the firing of only one of the two neurons, the firing rate of the second unrewarded cell generally did not correlate with the firing rate of the reward neuron, suggesting that the monkey was not using a strategy that involves indiscriminantly activating many neurons. In fact, monkeys can even learn to control two neurons [35] independently if they are given different rewards.

The first implementation of intracortical interfaces in human patients essentially used this approach. Two locked patients with advanced ALS learned, with at least some success [36], to control the movement of the cursor that provided the communication interface. The extent to which this approach can be scaled up to include a larger number of neurons and more complex movements remains to be determined.

Monkeys, and possibly humans, can thus learn novel mappings between neuronal activity and movement in a process that may resemble normal motor learning. Notably, these results suggest that some learning occurs even at the level of individual neurons during BCI control. Still, one might expect that a bionic decoder that is very close to the normal mapping from brain to motion would yield faster learning rates compared to a non-bionic map, and might yield better final performance, but this remains an important issue for future research.

3. Somatosensory Feedback is Delivered Via a Brain-machine Interface

Movement is usually guided by somatosensory and visual feedback. The lack of somatosensory feedback in current Brain-machine interfaces undoubtedly limits the quality of motion produced. Below, we discuss the importance of touch and proprioception in motor control and describe methods for restoring somatosensory feedback through intracranial electrical stimulation (ICMS).

3.1. The Importance of Somatosensory Feedback

Loss of somatosensory - both touch and proprioception - has devastating effects on motor ability. Signals from mechanosensory afferents in our skin convey information about the location[37] of contact and the force applied to the skin when we grasp an[38] object. Skin afferents also send signals[39] when our grasp on an object slips. Without these afferents, we would normally crush or drop the object we are gripping. The importance of proprioception in motor control has been most strikingly revealed in injury and clinical studies. Damage or inactivation of the primary sensory cortex (S1) in monkeys results in discoordinated finger movements and coarse and exaggerated grasping behavior, the latter possibly an adaptive response to compensate for diminished sensation [40]. The loss of proprioception largely eliminates the ability [41] to plan limb movement dynamics. In addition to its importance in motor control, somatosensory plays an important role in our emotional lives. Indeed, the sensory experience of the position and movement of our limbs in space, as well as the events that strike our skin, give the limbs a reification, so that they are experienced as part of the "me".

The importance of somatosensory feedback spurred the development of the first bidirectional Brain-machine interface, which guided monkeys to use the efferent interface [42] by stimulating the somatosensory cortex.

3.2. Somatosensory Perception is Elicited by Cortical Stimulation

In the 1930-1940s, Wilder Penfield provided the first example [43] of somatosensory perception elicited by electrical stimulation. He evoked tactile sensations by applying electrical stimulation to the exposed brains of patients undergoing neurosurgery. These sensations are "felt" in body regions whose location is systematically correlated [44] with the stimulation site on the cortical surface. In recent years, in pioneering experiments using electrical stimulation in monkeys, Romo and colleagues elicited the perception of skin fibrillation at frequencies corresponding to those of intracranial electrical stimulation pulses, demonstrating that the temporal structure of the electrical stimulation pulse train shapes the evoked sensation [45] in a systematic way. These studies pave the way for attempts to elicit a wider range of sensations through electrical stimulation in S1, with the hope of one day restoring tactile and proprioceptive perception to these senseless patients.

One approach to restoring somatosensory feedback through Brain-machine interfaces is to try to elicit perception through stimuli that approximate the sensory experiences that arise in everyday behavior, as is the case with biomimetic approaches to motor Brain-machine interfaces. This involves restoring different aspects of touch and proprioception in different ways, depending on our understanding of the relevant natural somatosensory coding. In one example of such biomimetics mapping in rodents, electrical stimulation is delivered to a location in the barrel cortex as long as the corresponding whiskers of a rat pass through a specific spatial location, even though it touches nothing. The mice were able to use this artificial sense to locate the virtual object in a way that mimicked the sensory experience[46] of the mice when they brushed the physical target. A similar example of a biomimetic approach in primates is the use of orthography to convey information about the position of hand contact. Electrical stimulation in S1 evokes perceptions that can be highly localized, down to a single palm thread or fingertip (**Figurer**. **4a**). This somatic organization can be used to signal which areas of the prosthesis are in contact with objects: activation of sensors on the prosthesis can be used to drive activation of neurons in S1 with corresponding receptive fields.

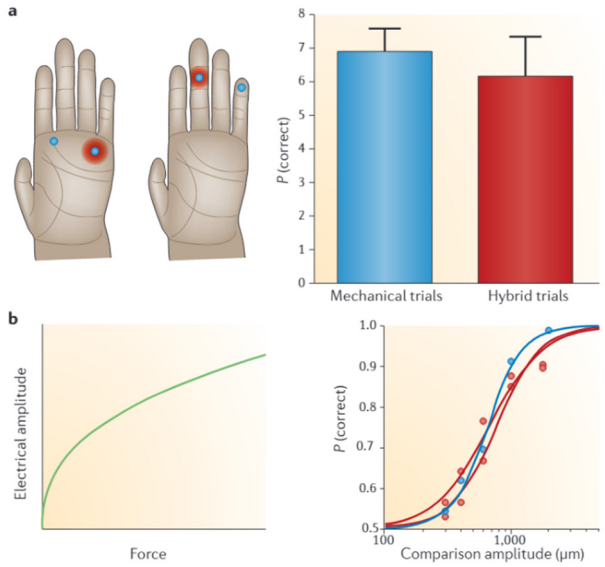


Figure 4. Use of biomimetic methods to convey information about contact location and pressure

One may ask how a "body-surface appropriate" mapping between the sensor on the prosthetic hand and the stimulating electrode in S1 can be achieved in an amputor or quadriplegic. In these patients, while the limb is missing or no longer connected to the brain, the part of the brain that responds to limb movement or tactile stimulation is still intact. In fact, amputees often experience sensations that project to the so-called "phantom limb"; That is, feeling the sensation [47] of being located where the missing limb used to be. One possible approach to sensor-electrode mapping is to deliver electrical stimulation through a single electrode while the patient reports where on the phantom or deafferent-block limb he or she "feels" the evoked sensation.

In addition to position information, biomimetic approaches can be used to convey information about the pressure that a prosthesis is exerting on an object by translating the output of a force sensor into a train of intracranial electrical stimulation pulses to evoke perception [48] of the appropriate amplitude (**Figure 4b**). In addition, information about different stimulus properties (for example, surface texture or direction of limb motion) can be conveyed by stimulating different groups of neurons in S1. [49]For example, some S1 mid-neurons signal the direction in which the tactile stimulus moves across the skin, while others signal the direction of the edge pressed into the skin, and still others [50] indicate the position and movement of the limb. [51] Thus, targeted stimulation of specific S1 neurons could in principle elicit the perception of skin motion, shape, or limb movement.

It is currently not possible to activate large numbers of neurons individually. Therefore, to evoke a specific perceptual quality requires that neurons that are activated together by training with a given intracranial electrical stimulation all have similar receptive field properties so that they convey consistent information. Even low-current intracranial electrical stimulation involves synchronous activation of populations of neurons, some of which may be distant [52] from the electrode. These more distant neurons may exhibit very different response dynamics than neurons near the tip of the electrode. With this in mind, efforts to generate biomimetic patterns of neuronal activation seem doomed to failure. Fortunately, there is some evidence of functional clustering of tactile [53] and proprioceptive [54] representations in the primary motor cortex. Nonetheless, it remains unclear whether these functional clusters are sufficiently separated to electrically activate large enough and homogeneous populations of neurons to elicit well-defined sensations with specific properties. Biophysical models may provide some insight into the effects of stimulation on neuronal activity and thus help improve stimulation protocols needed to produce realistically similar patterns of neuronal activation. Stimulation through a large number of electrodes, each with a very low current, could be one way to do this.[55] Optogenetic stimulation can activate neurons more selectively than electrical stimulation.[56] However, technological advances alone cannot address the fact that neurons are embedded in networks, and our understanding of network dynamics and how they relate to perception and behavior is still primitive. Thus, although biomimetics is an intuitive way to convey sensory feedback, it faces considerable technical and scientific challenges. Sensory Brain-machine interfaces, like motor Brain-machine interfaces, will also benefit from the brain's ability to adapt; In this case, it is necessary learn to compensate for the

limitations of the authenticity or intuition of artificial perception.

3.3. Adaptation of Sensory Brain-machine Interfaces

An "adaptive" approach requires a systematic mapping between the sensors on the prosthesis and the patterns of electrical stimulation applied to the brain. As a result, patients must learn to associate sensations evoked by different stimulation patterns with corresponding sensory events. The idea is that patients can learn mapping as long as different states of sensor activation evoke distinguishable perceptions. Animals have been trained to discriminate some patterns of electrical stimulation applied to the somatosensory cortex (Figure 5). [57]

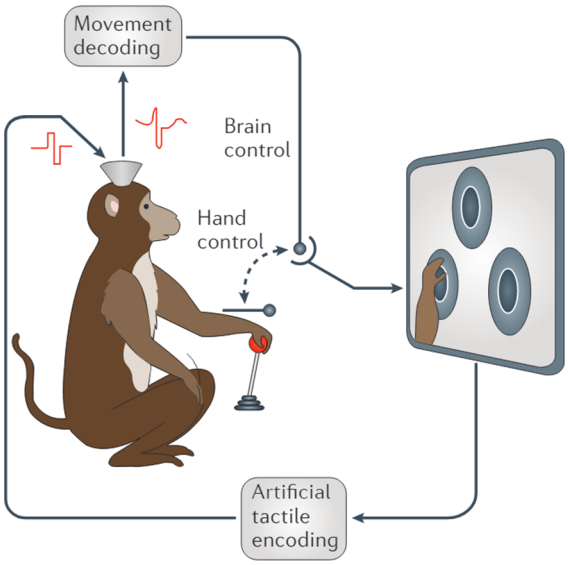


Figure 5. Bidirectional interface based on learning associations

Continuously modulated stimuli are used to guide the ongoing movement. In one study, the intensity of electrical stimulation in the whisker region of the somatosensory cortex of rats was modulated according to the distance of the rat's head from an infrared ray located above the water mouth. The closer the rat's head was to the port, the stronger the electrical stimulation. Although the somatosensory areas of the rats' brains were activated in an entirely new way compared to the patterns typically elicited during stirring, they learned to locate the outlet [58]. In another experiment, a monkey learned to guide the movement of a cursor across a screen based on the strength of somatosensory electrical stimuli delivered through eight electrodes. The intensity of the electrical stimulation was modulated according to the error vector directed from the cursor to the target. The stimulation frequency at each of the eight electrodes was determined by projecting the error vector onto one of eight evenly spaced unit vectors. The monkey learned the mapping over a period of several months, during which the electrical stimuli were paired with visual signals that carried the same target-related information. In both studies, the animals were able to perform the task even though the stimuli provided information that was not normally encoded by these brain regions.

Importantly, the real limb has a large number of proprioceptive states, and the number of combinations of skin events that can affect the limb is also almost unlimited. The main question regarding the feasibility of adaptation approaches is whether the adult brain can learn a mapping between the complex space of such possible states and the corresponding pattern of electrical stimulation. However, even the most ardent enthusiast of bionics must acknowledge that the fidelity of artificial perception is limited and that patients will have to rely at least in part on learning and plasticity to master the use of sensory prostheses.

A study involving targeted innervation provides a compelling example of the synergy between biomimicry and adaptation. In this study, amputors underwent surgery to reimplant the nerves that once innervated the amputated limb into the remaining skin and muscle sites. When touching this newly innervated skin, these individuals experience tactile [59] sensations projected to the phantom limb. Two of the patients underwent an experiment in which the newly innervated skin was mechanically stimulated each time the corresponding "receptive field" on the prosthesis was touched. Repeated pairing resulted in perception going from being experienced on the phantom limb to being experienced on the prosthesis, as determined [60] by self-report and body measurements.

Similar to the case with motor Brain-machine interfaces, biomimetic feedback may be more intuitive to use initially and require little learning to master, which may affect patient acceptance of sensory Brain-machine interfaces. However, based on the current state of the art, the ability to activate neurons in natural patterns is extremely limited. Therefore, learning and adaptation will play an important role in artificial sensory feedback. Research within the framework of biomimetics will tell us how similar artificial perceptions really are, while adaption-based research will tell us how far learning can take us.

4. Conclusion

Since the realization of a brain-controlled single-degree-of-freedom robotic arm, the research on Brain-machine interface (BCI) has been rapidly evolving. However, BCI is still largely limited to the execution of reaching, grasping and other movements under visual guidance. In the future, major challenges for the next generation of Brain-machine interfaces include integrating somatosensory feedback through afferent interfaces to control limb impedance and end-point forces. Therefore, understanding and exploiting biomimetics and decoder-based adaptive roles is critical to achieve these functions.

In the future, BCI technology must also move out of the laboratory and into clinical applications. Therefore, percutaneous leads must be eliminated to solve safety, aesthetics, and convenience issues. At the same time, the overall reliability of Brain-machine interfaces must be improved, especially given the limited lifetime of existing microelectrode arrays. Alternatively, the portability of BCI needs to be improved so that they can be used 24 hours a day without the need for ongoing technical support. It can be seen that the challenges facing the field of BCI are enormous, but the opportunities it provides are also unprecedented. In the next 5 to 10 years, the technology's ability to enter the clinical arena will depend on how these challenges are successfully addressed.

References

[1] Chapin, J. K., Moxon, K. A., Markowitz, R. S. & Nicolelis, M. A. L. Real-time control of a robot arm using simultaneously recorded neurons in the motor cortex. NATURE NEUROSCIENCE 2, 664-670 (1999).

[2] Carmena, J. M. et al. Learning to control a Brain-machine interface for reaching and grasping by primates. PLOS BIOLOGY 1, 193-208 (2003).

[3] Velliste, M., Perel, S., Spalding, M. C., Whitford, A. S. & Schwartz, A. B. Cortical control of a prosthetic arm for self-feeding. NATURE 453, 1098-1101 (2008).

[4] Collinger, J. L. et al. High-performance neuroprosthetic control by an individual with tetraplegia. LANCET 381, 557-564 (2013).

[5] Johansson, R. S. & Flanagan, J. R. Coding and use of tactile signals from the fingertips in object manipulation tasks. NATURE REVIEWS NEUROSCIENCE 10, 345-359 (2009).

[6] 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).

[7] Wessberg, J. et al. Real-time prediction of hand trajectory by ensembles of cortical neurons in primates. NATURE 408, 361-365 (2000).

[8] Venkatraman, S. & Carmena, J. M. Active Sensing of Target Location Encoded by Cortical Microstimulation. IEEE TRANSACTIONS ON NEURAL SYSTEMS AND REHABILITATION ENGINEERING 19, 317-324 (2011).

[9] 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).

[10] Ganguly, K. & Carmena, J. M. Emergence of a Stable Cortical Map for Neuroprosthetic Control. PLOS BIOLOGY 7 (2009).

[11] Chase, S. M., Kass, R. E. & Schwartz, A. B. Behavioral and neural correlates of visuomotor adaptation observed through a Brain-machine interface in primary motor cortex. JOURNAL OF NEUROPHYSIOLOGY 108, 624-644 (2012).

[12] Millan, J. D. & Carmena, J. M. invasive or noninvasive: understanding Brain-machine interface technology. IEEE ENGINEERING IN MEDICINE AND BIOLOGY MAGAZINE 29, 16-22 (2010).

[13] Hwang, E. J. & Andersen, R. A. The utility of multichannel local field potentials for Brain-machine interfaces. JOURNAL OF NEURAL ENGINEERING 10 (2013).

[14] Flint, R. D., Wright, Z. A., Scheid, M. R. & Slutzky, M. W. Long term, stable brain machine interface performance using local field potentials and multiunit spikes. JOURNAL OF NEURAL ENGINEERING 10 (2013).

[15] Chestek, C. A. et al. Long-term stability of neural prosthetic control signals from silicon cortical arrays in rhesus macaque motor cortex. JOURNAL OF NEURAL ENGINEERING 8 (2011).

[16] Taylor, D. M., Tillery, S. I. H. & Schwartz, A. B. Direct cortical control of 3D neuroprosthetic devices. SCIENCE 296, 1829-1832 (2002).

[17] Cheney, P. D. & Fetz, E. E. CORTICOMOTONEURONAL CELLS CONTRIBUTE TO LONG-LATENCY STRETCH REFLEXES IN THE RHESUS-MONKEY. JOURNAL OF PHYSIOLOGY-LONDON 349, 249-272 (1984).

[18] Asanuma, H. FUNCTIONAL-ROLE OF SENSORY INPUTS TO THE MOTOR CORTEX. PROGRESS IN NEUROBIOLOGY 16, 241-262 (1981).

[19] Johannes, M. S. et al. An Overview of the Developmental Process for the Modular Prosthetic Limb. JOHNS HOPKINS APL TECHNICAL DIGEST 30, 207-216 (2011).

[20] Hochberg, L. R. et al. Reach and grasp by people with tetraplegia using a neurally controlled robotic arm. NATURE 485, 372-U121 (2012).

[21] Aggarwal, V., Mollazadeh, M., Davidson, A. G., Schieber, M. H. & Thakor, N. V. State-based decoding of hand and finger kinematics using neuronal ensemble and LFP activity during dexterous reach-to-grasp movements. JOURNAL OF NEUROPHYSIOLOGY 109, 3067-3081 (2013).

[22] Vargas-Irwin, C. E. et al. Decoding Complete Reach and Grasp Actions from Local Primary Motor Cortex Populations. JOURNAL OF NEUROSCIENCE 30, 9659-9669 (2010).

[23] Yuan, P. et al. A study of the existing problems of estimating the information transfer rate in online Brain-machine interfaces. JOURNAL OF NEURAL ENGINEERING 10 (2013).

[24] Hogan, N. ADAPTIVE-CONTROL OF MECHANICAL IMPEDANCE BY COACTIVATION OF ANTAGONIST MUSCLES. IEEE TRANSACTIONS ON AUTOMATIC CONTROL 29, 681-690 (1984).

[25] Burdet, E., Osu, R., Franklin, D. W., Milner, T. E. & Kawato, M. The central nervous system stabilizes unstable dynamics by learning optimal impedance. NATURE 414, 446-449 (2001).

[26] Kim, H. K. et al. The muscle activation method: An approach to impedance control of Brain-machine interfaces through a musculoskeletal model of the arm. IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING 54, 1520-1529 (2007).

[27] Santucci, D. M., Kralik, J. D., Lebedev, M. A. & Nicolelis, M. A. L. Frontal and parietal cortical ensembles predict single-trial muscle activity during reaching movements in primates. EUROPEAN JOURNAL OF NEUROSCIENCE 22, 1529-1540 (2005).

[28] Moritz, C. T., Perlmutter, S. I. & Fetz, E. E. Direct control of paralysed muscles by cortical neurons. NATURE 456, 639-U663 (2008).

[29] Xerri, C., Merzenich, M. M., Jenkins, W. & Santucci, S. Representational plasticity in cortical area 3b paralleling tactual-motor skill acquisition in adult monkeys. CEREBRAL CORTEX 9, 264-276 (1999).

[30] Qi, H. X., Chen, L. M. & Kaas, J. H. Reorganization of Somatosensory Cortical Areas 3b and 1 after Unilateral Section of Dorsal Columns of the Spinal Cord in Squirrel Monkeys. JOURNAL OF NEUROSCIENCE 31, 13662-13675 (2011).

[31] Wahnoun, R., He, J. P. & Tillery, S. I. H. Selection and parameterization of cortical neurons for neuroprosthetic control. JOURNAL OF NEURAL ENGINEERING 3, 162-171 (2006).

[32] Jarosiewicz, B. et al. Functional network reorganization during learning in a Brain-machine interface paradigm. PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 105, 19486-19491 (2008).

[33] Ganguly, K., Dimitrov, D. F., Wallis, J. D. & Carmena, J. M. Reversible large-scale modification of cortical networks during neuroprosthetic control. NATURE NEUROSCIENCE 14, 662-U164 (2011).

[34] Moritz, C. T. & Fetz, E. E. Volitional control of single cortical neurons in a Brain-machine interface. JOURNAL OF NEURAL ENGINEERING 8 (2011).

[35] Fetz, E. E. & Baker, M. A. OPERANTLY CONDITIONED PATTERNS OF PRECENTRAL UNIT-ACTIVITY AND CORRELATED RESPONSES IN ADJACENT CELLS AND CONTRALATERAL MUSCLES. JOURNAL OF NEUROPHYSIOLOGY 36, 179-204 (1973).

[36] Kennedy, P. R., Bakay, R. A. E., Moore, M. M., Adams, K. & Goldwaithe, J. Direct control of a computer from the human central nervous system. IEEE TRANSACTIONS ON REHABILITATION ENGINEERING 8, 198-202 (2000).

[37] Ochoa, J. & Torebjork, E. SENSATIONS EVOKED BY INTRANEURAL MICROSTIMULATION OF SINGLE MECHANORECEPTOR UNITS INNERVATING THE HUMAN HAND. JOURNAL OF PHYSIOLOGY-LONDON 342, 633-654 (1983).

[38] Knibestol, M. STIMULUS-RESPONSE FUNCTIONS OF SLOWLY ADAPTING MECHANORECEPTORS IN HUMAN GLABROUS SKIN AREA. JOURNAL OF PHYSIOLOGY-LONDON 245, 63-80 (1975).

[39] Johansson, R. S. & Westling, G. ROLES OF GLABROUS SKIN RECEPTORS AND SENSORIMOTOR MEMORY IN AUTOMATIC-CONTROL OF PRECISION GRIP WHEN LIFTING ROUGHER OR MORE SLIPPERY OBJECTS. EXPERIMENTAL BRAIN RESEARCH 56, 550-564 (1984).

[40] Brochier, T., Boudreau, M. J., Pare, M. & Smith, A. M. The effects of muscimol inactivation of small regions of motor and somatosensory cortex on independent finger movements and force control in the precision grip. EXPERIMENTAL BRAIN RESEARCH 128, 31-40 (1999).

[41] Sainburg, R. L., Ghilardi, M. F., Poizner, H. & Ghez, C. CONTROL OF LIMB DYNAMICS IN NORMAL SUBJECTS AND PATIENTS WITHOUT PROPRIOCEPTION. JOURNAL OF NEUROPHYSIOLOGY 73, 820-835 (1995).

[42] O'Doherty, J. E. et al. Active tactile exploration using a Brain-machine-brain interface. NATURE 479, 228-U106 (2011).

[43] Penfield, W. & Boldrey, E. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. BRAIN 60, 389-443 (1937).

[44] Rasmussen, T. & Penfield, W. THE HUMAN SENSORIMOTOR CORTEX AS STUDIED BY ELECTRICAL STIMULATION. FEDERATION PROCEEDINGS 6, 184-185 (1947).

[45] Romo, R., Hernandez, A., Zainos, A. & Salinas, E. Somatosensory discrimination based on cortical microstimulation. NATURE 392, 387-390 (1998).

[46] O'Connor, D. H. et al. Neural coding during active somatosensation revealed using illusory touch. NATURE NEUROSCIENCE 16, 958-U238 (2013).

[47] Ramachandran, V. S. & Hirstein, W. The perception of phantom limbs - The D.O. Hebb lecture. BRAIN 121, 1603-1630 (1998).

[48] Berg, J. A. et al. Behavioral Demonstration of a Somatosensory Neuroprosthesis. IEEE TRANSACTIONS ON NEURAL SYSTEMS AND REHABILITATION ENGINEERING 21, 500-507 (2013).

[49] Pei, Y. C., Hsiao, S. S., Craig, J. C. & Bensmaia, S. J. Shape Invariant Coding of Motion Direction in Somatosensory Cortex. PLOS BIOLOGY 8 (2010).

[50] Bensmaia, S. J., Denchev, P. V., Dammann, J. F., Craig, J. C. & Hsiao, S. S. The representation of stimulus orientation in the early stages of somatosensory processing. JOURNAL OF NEUROSCIENCE 28, 776-786 (2008).

[51] London, B. M. & Miller, L. E. Responses of somatosensory area 2 neurons to actively and passively generated limb movements. JOURNAL OF NEUROPHYSIOLOGY 109, 1505-1513 (2013).

[52] Histed, M. H., Bonin, V. & Reid, R. C. Direct Activation of Sparse, Distributed Populations of Cortical Neurons by Electrical Microstimulation. NEURON 63, 508-522 (2009).

[53] Mountcastle, V. B. & Powell, T. P. S. CENTRAL NERVOUS MECHANISMS SUBSERVING POSITION SENSE AND KINESTHESIS. BULLETIN OF THE JOHNS HOPKINS HOSPITAL 105, 173-200 (1959).

[54] Weber, D. J. et al. Limb-State Information Encoded by Peripheral and Central Somatosensory Neurons: Implications for an Afferent Interface. IEEE TRANSACTIONS ON NEURAL SYSTEMS AND REHABILITATION ENGINEERING 19, 501-513 (2011).

[55] Zaaimi, B., Ruiz-Torres, R., Solla, S. A. & Miller, L. E. Multi-electrode stimulation in somatosensory cortex increases probability of detection. JOURNAL OF NEURAL ENGINEERING 10 (2013).

[56] Diester, I. et al. An optogenetic toolbox designed for primates. NATURE NEUROSCIENCE 14, 387-397 (2011).

[57] Costanzo, R. M. & Gardner, E. P. MULTIPLE-JOINT NEURONS IN SOMATOSENSORY CORTEX OF AWAKE MONKEYS. BRAIN RESEARCH 214, 321-333 (1981).

[58] Thomson, E. E., Carra, R. & Nicolelis, M. A. L. Perceiving invisible light through a somatosensory cortical prosthesis. NATURE COMMUNICATIONS 4 (2013).

[59] Marasco, P. D., Schultz, A. E. & Kuiken, T. A. Sensory capacity of reinnervated skin after redirection of amputated upper limb nerves to the chest. BRAIN 132, 1441-1448 (2009).

[60] Marasco, P. D., Kim, K., Colgate, J. E., Peshkin, M. A. & Kuiken, T. A. Robotic touch shifts perception of embodiment to a prosthesis in targeted reinnervation amputees. BRAIN 134, 747-758 (2011).