Handbook of Clinical Neurology, Vol. 168 (3rd series)
Brain-Computer Interfaces
N.F. Ramsey and J. del R. Millán, Editors
https://doi.org/10.1016/B978-0-444-63934-9.00025-1

Chapter 25

Industrial perspectives on brain-computer interface technology

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Abstract

Neuromodulation therapies offer a unique opportunity for *translating* brain-computer interface (BCI) technologies into a clinical setting. Several diseases such as Parkinson's disease are effectively treated by invasive device stimulation therapies, and the addition of sensing and algorithm technology is an obvious *evolutionary* expansion of capabilities. In addition, this infrastructure might enable a roadmap of novel BCI technologies. While the initial applications are focused on epilepsy and movement disorders, the technology is potentially transferable to a broader base of disorders, including stroke and rehabilitation. The ultimate potential of BCI technology will be determined by forthcoming chronic evaluation in multiple neurologic disorders.

INTRODUCTION

The ultimate goal of a bioelectronic therapy is to restore more normative function in patients with disease by using an adjunctive electronic circuit that seamlessly integrates into the compromised physiologic system. From a bioengineering point-of-view, many biologic systems are comprised of a "dynamic control loop" (Feldman and Del Negro, 2006; Fowler et al., 2008). These loops serve to provide adaptive feedback to keep a physiologic activity at a target set point determined by a higher-level system. These control loops exist across many spatial and temporal scales, from the molecular to the organ system and from milliseconds to months. A bioelectronic system dynamically interacts with the physiologic system to functionally restore, reinstate, or repair a control loop compromised by a disease state (Birmingham et al., 2014). To be successful, a bioelectronic system must integrate with the physiology at the appropriate scales of space and time. This chapter will discuss how brain-computer interfaces (BCIs) might help to implement more advanced bioelectronic systems in the future as well as the opportunities and challenges that should be considered for industrial translation.

Please note that at the time of this writing, all applications of BCI described in this chapter are still limited by law to investigational use cases only.

COMMERCIAL PERSPECTIVES ON BRAIN-COMPUTER INTERFACES

New technologies often face hurdles in their commercialization journey. Economists often capture this as part of the "technology adoption lifecycle (TALC)" (Rogers, 2003). As illustrated in Fig. 25.1, the TALC is often represented as a diffusion of innovation that proceeds from innovators and early adopters into the population majority. Refinements to this model are proposed when the new technology is disruptive, meaning a technology that requires an entirely new way of performing a task (Moore and McKenna, 2006). Technologies that are disruptive often face major hurdles when trying to make

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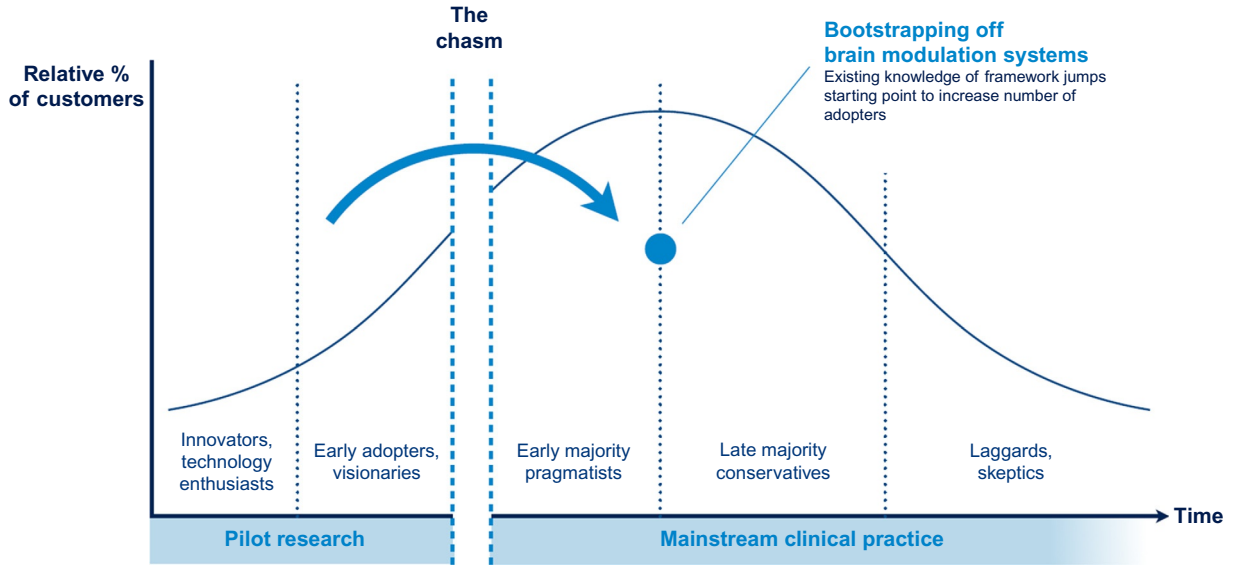

Fig. 25.1. Considering the technology adoption lifecycle (TALC) and implications for translating brain-computer interfaces into the clinic.

the leap across the "chasm" between early adopters, often found in advanced academic communities, and the general population. While innovators and early adopters might feel content to explore the capabilities of a technology for its own sake, the pragmatic view of the early majority requires a different value proposition. This large group of practitioners needs stronger assurance of economic and therapy success.

From an industry perspective, we must think carefully about how we introduce brain–machine interfacing technology. For example, neural prosthetic control would likely require new implant interfaces and procedures that are more invasive than commercialized brain modulation systems. While some progress has been made on neural prostheses (e.g., the revolutionary prosthesis project from DARPA, Collinger et al., 2013; Downey et al., 2016; BrainGate, Hochberg et al., 2006; Ajiboye et al., 2017), more than a decade and many millions of dollars later, there is still no viable fully implantable system that is approved by regulators for commercial marketing or by reimbursement agencies for commercial viability. The chasm between early adopters and the general population for this application will probably prove to be quite large. An alternative is to look for applications where invasive brain interfacing already exists, including the robust environment of manufacturers and regulators. Brain modulation systems, shown in Fig. 25.2, might provide such a pathway.

Modulating neural activity through stimulation is an effective treatment for several neurologic diseases, such as Parkinson's disease and essential tremor, and is being explored for several new indications. Opportunities for improving neuromodulation include reducing the burden of optimizing stimulation parameters, objectively measuring efficacy over time, and continuously adjusting therapy to optimize patient outcomes. Achieving these goals is challenged by practical issues, including the paucity of human data related to disease states, poorly validated patient state estimators, and evolving nonlinear mappings between estimated patient state and optimal stimulation parameters (Ryu and Shenoy, 2009). The application of brain–machine interface (BMI) technology to existing stimulator architectures could help address these issues and potentially enable smarter "prosthesis" systems in the future for neural circuits impacted by disease.

When well designed, these building blocks can be integrated as a whole to restore a physiologic function or create new synthetic "reflexes" for therapeutic benefit. Before detailing specific examples of these potential use cases, we briefly highlight other additional practical considerations in designing a translational BCI that works within a medical device system. These factors include both the clinical evidence and regulatory environment, which motivate considerations of risk management, maintenance of quality management processes, and a consideration of the therapy value vs cost, as well as technical considerations such as power management, information management like data privacy, and interface management like materials biocompatibility and biostability.

Considering the systems perspective, successful bioelectronic devices incorporating a BCI will demonstrate a favorable balance across at least six factors (Fig. 25.3):

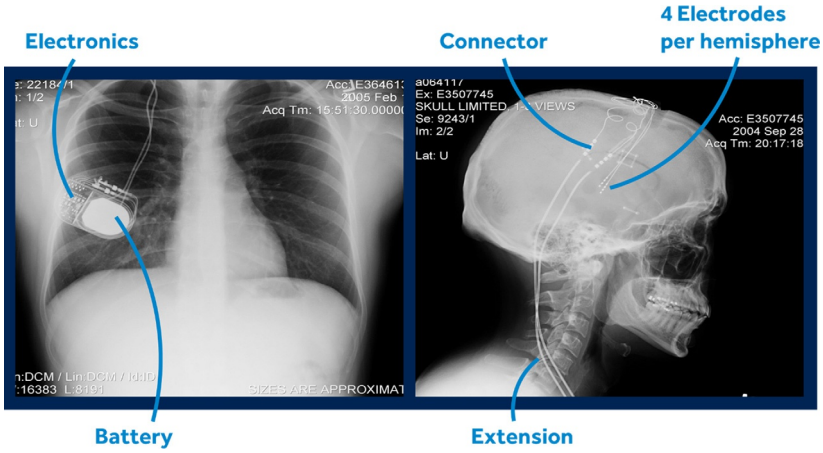

Fig. 25.2. An example of a fully implanted brain–interface system for treating neurologic disorders. The required systems for deep brain stimulation are already in place: from physical device systems to implant planning support, to regulatory adoption (for stimulation in movement disorders), to reimbursement. More than a hundred thousand systems have been deployed to date. The use of sensing signals to optimize therapy is arguably a natural extension of the technology and clinical practice, as opposed to a disruptive innovation.

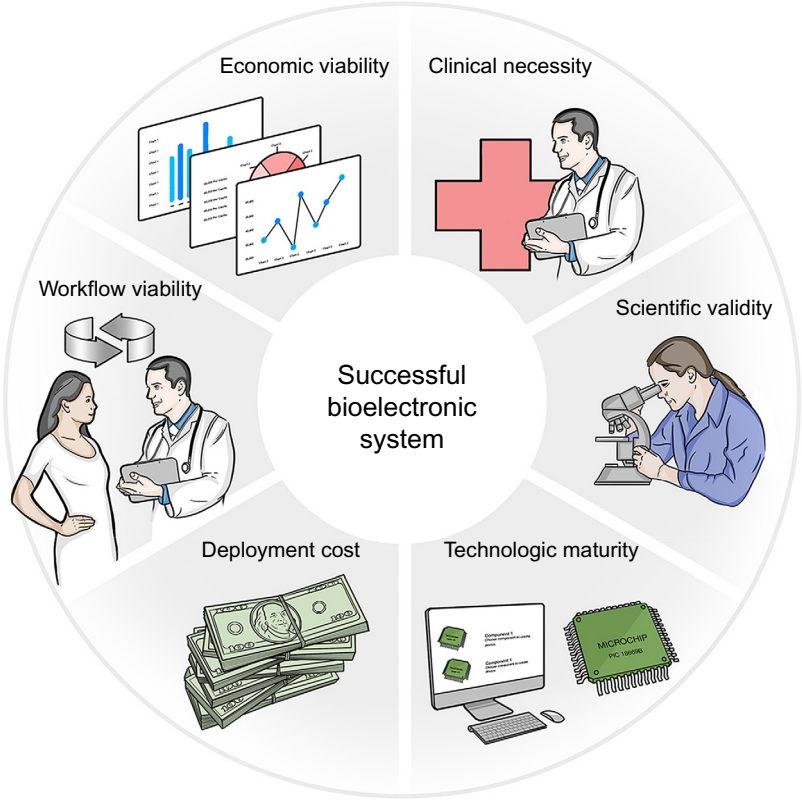

Fig. 25.3. Practical translation constraints for a successful bioelectronic system.

1. *Clinical necessity*: This is a clinical problem that is currently inadequately met by existing therapies and affects a significant number of patients to justify application of the technology. For instance, the need to reduce tremor in a Parkinson's disease or drug-refractory essential tremor patient is a key motivation for deep brain stimulation (DBS) therapy.
2. *Scientific validity*: This is the theory of operation or mechanism of action of the therapy that relates to the disease state pathophysiology. It is captured in the

transfer function and can be used to identify patient subgroups that would most benefit from the technology. Tools such as microelectrode recordings and functional imaging are often used to elucidate mechanisms of action in neurologic disorders (Hart et al., 2015).

3. *Technologic maturity*: This is the development of robust designs, including scientific instrumentation, which can safely and reliably interact with the body.
4. *Deployment cost*: This is the cost to bring a medical technology to the marketplace, including the ability to secure intellectual property, satisfy regulatory constraints, and distribute to physicians and patients.
5. *Workflow viability*: This is the ability for the technology to satisfy relevant clinical and patient stakeholders without prohibitive adjustments or burden.
6. *Economic viability*: This is a clear value proposition for the technology that demonstrates economic value to the healthcare continuum. This can be accomplished in a number of ways, including: reducing the price of technology, expanding access to care, improving therapy efficacy, and reducing time to receive care.

A common method for optimizing these factors is the "biodesign" approach (Zenios et al., 2009). This approach is useful to identify impactful medical technology opportunities and invent solutions that efficiently address unmet needs.

BCI TAXONOMY AND REPRESENTATIVE USE CASES

A framework (Fig. 25.4) based upon use cases and risk profile could be useful in facilitating communication between investigators, manufacturers, and medical device regulators to allow for setting initial expectations of data needed to support device safety and effectiveness. A four-class taxonomy is presented in what follows, illustrating a range of applications from classical BCIs to restorative neural "coprocessors" that are an evolution of current DBS therapies.

IMPLANTED TECHNOLOGY LANDSCAPE

The Medtronic Activa PC+S® is an investigational bidirectional neural interface system that illustrates many

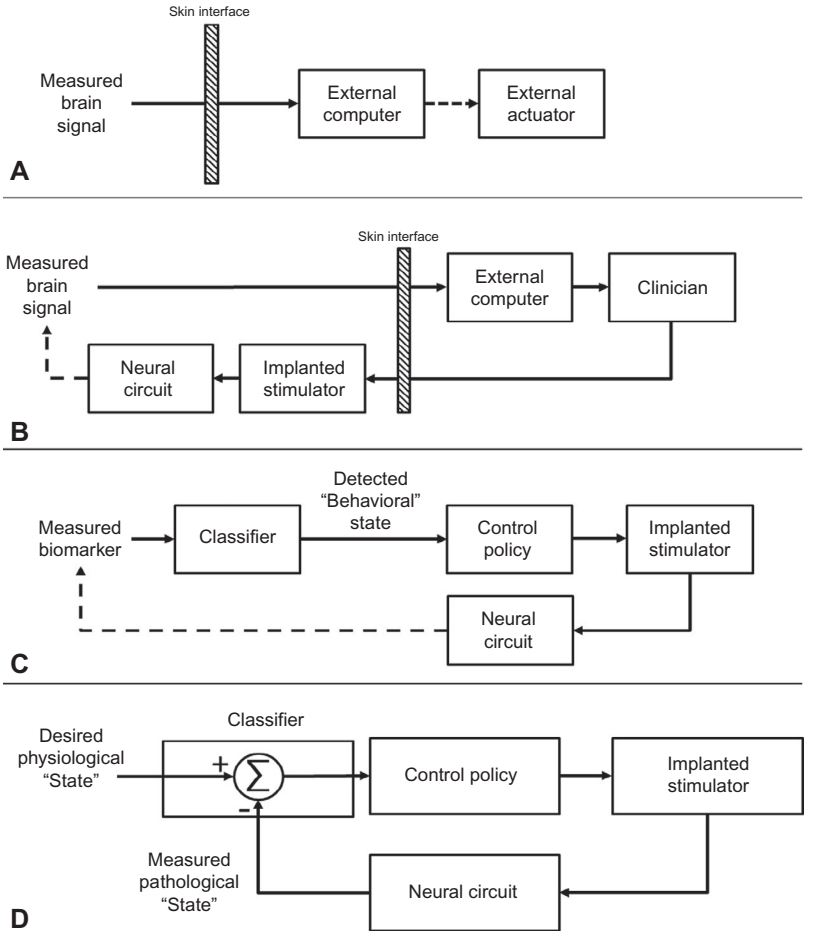

Fig. 25.4. Framework for BCIs based on implanted neural stimulators.

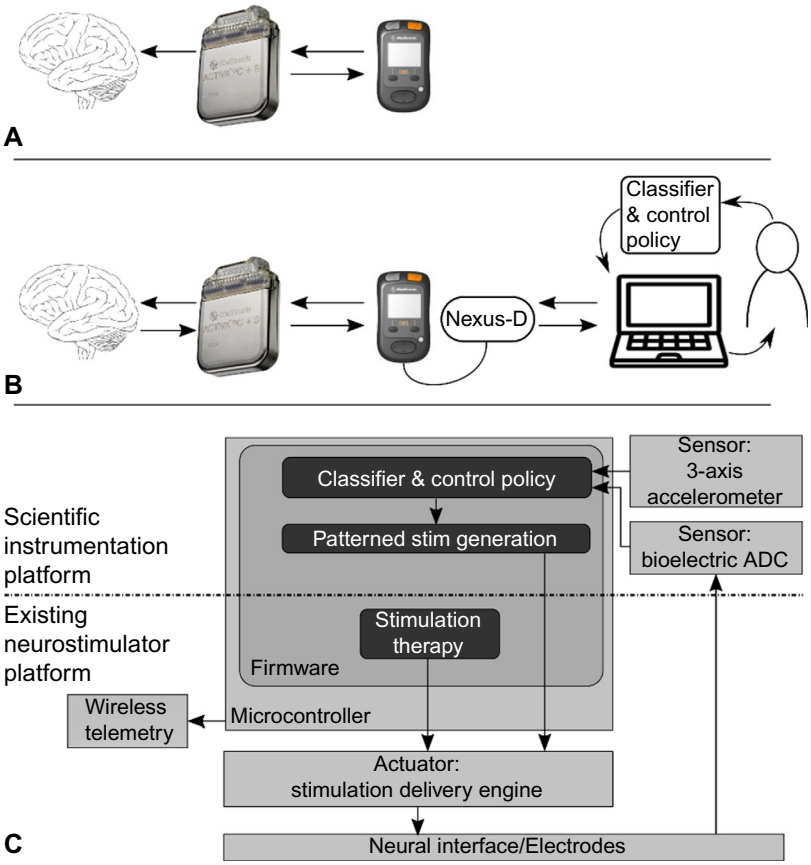

Fig. 25.5. (A) The design of a typical neuromodulation system, including the patient activator (*right*). (B) Leveraging typical neuromodulation components to implement a computer-in-the-loop closed-loop prototyping system. (C) Embedded scientific instrumentation (e.g., bioelectric sensing, accelerometer) and upgradable firmware allow typical systems to act as a vehicle for both delivering therapy and investigational research.

of these the core bioelectronic design principles in action. The Activa PC+S® system was developed for gathering basic neuroscience information to better understand future neuromodulation-based therapy opportunities. The Activa PC+S® is CE-marked for epilepsy, Parkinson's disease, essential tremor, and dystonia, and was designed with the strategies outlined for bioelectronic research tools (note: it is not approved for commercial use in the United States). A block diagram of the system architecture is shown in Fig. 25.5. The system architecture leverages an existing, approved neurostimulator system, the Activa PC® as the foundation for the bioelectronic system; all predicated therapy capabilities for DBS are preserved in the research tool. The research capability is enabled by a scientific payload that is embedded as a peripheral inside the device. The design is modular at multiple scales; e.g., the science payload is activated as an independent entity by the researcher to mitigate the risk of compromising the predicate therapy while gathering data. Information flow is also modular: critical sensing interfaces such as amplification of local field potentials (LFPs) and inertial sensing and stimulation delivery, including novel pulse trains, are allocated to the implant. Simple biomarker calculations such as spectral analysis (i.e., digital signal processing-based Fourier transforms) and control policies can be embedded within the implant (Stanslaski et al., 2012), while for more complex signal analysis, such as phase-amplitude coupling (de Hemptinne et al., 2015) and fusion of external signals for control policies, the use of the bidirectional telemetry is employed to leverage the distributed architecture and offload processing to an external system. The flexible firmware platform allows for configuration of the device for different use cases.

The design of the external system, employing a computer-in-the-loop, includes additional features for facilitating algorithm research. For example, all data can be streamed to an external data collection portal rather than stored on the device and requiring subsequent upload. The external interfacing to the device also uses an application programming interface (API), which enables users to rapidly prototype new classifiers and control policy algorithms. Rapid prototyping is enabled by providing the API abstraction layer that allows simplified interfacing to the system with applications such as

Matlab® and LabVIEW™. Leveraging an external computing platform also allows the system to link to secure web portals for annotation, data sharing, and analysis. Once an acceptable algorithm is found, the firmware can be upgraded noninvasively through a wireless link to enable new features such as investigational closed-loop algorithms that enable de novo reflex arcs.

The investigational examples cited in each class of the BCI framework illustrate how the Activa PC+S® bioelectronic system is being used to support a variety of BCI applications using commercially viable building blocks.

CLASS A

Class A includes BCI applications that record signals from the brain to interface with an external system due to motor impairment from neurologic disease or injury (e.g., spinal cord injury, amyotrophic lateral sclerosis (ALS), brainstem stroke). These external systems include but are not limited to communication software, environmental controls, wheelchairs, and prosthetic limbs. This category excludes applications in which brain recordings directly influence operation of an implanted neural stimulator (INS), and can be thought of as a classical BCI. The benefit of Class A applications in this patient population is to provide a robust, chronically stable, cosmetically acceptable mechanism to tap into intact neural structures for functional restoration. An investigational example of a fully implanted communication interface for a patient with locked-in syndrome (LIS) is described in the following section.

Cortical recording for communication in locked-in syndrome

LIS is characterized by an inability to exert voluntary control over muscles in the presence of intact cognition, resulting in quadriplegia and aphonia. Despite their physical impairment, people with LIS often report a high quality of life (Rousseau et al., 2015), but this parameter is strongly affected by the ability to communicate adequately. When that is not possible, e.g., in late-stage ALS, vertical eye movements or blinks only allow for caregiver-initiated yes/no communication or selection of letters one at a time (i.e., alphabet board), leaving limited or no options for self-initiated and private communication. Recent years have seen a surge in research on decoding neuronal signals from brain implants, with quite impressive achievements, where paralyzed people succeeded in moving a robotic or paralyzed arm using their brain signals. To date, however, such systems have been far away from being fully functional for autonomous use in real life, which is a key consideration for translation (Huggins et al., 2011).

Recently, the first fully implantable BCI communication system for home use (Vansteensel et al., 2016) was demonstrated. Subdural electrode strips were implanted through burr holes on target areas in the left dorsolateral prefrontal cortex and left sensorimotor area and connected to the Activa PC+S®. The participant controlled the BCI by attempting to move the fingers of the right hand. The signals recorded over the hand region of the sensorimotor area showed a strong increase in high frequency band (65–95 Hz) power and a strong task-related decrease in low frequency band power during attempted hand movement (Fig. 25.6A). Performance on the

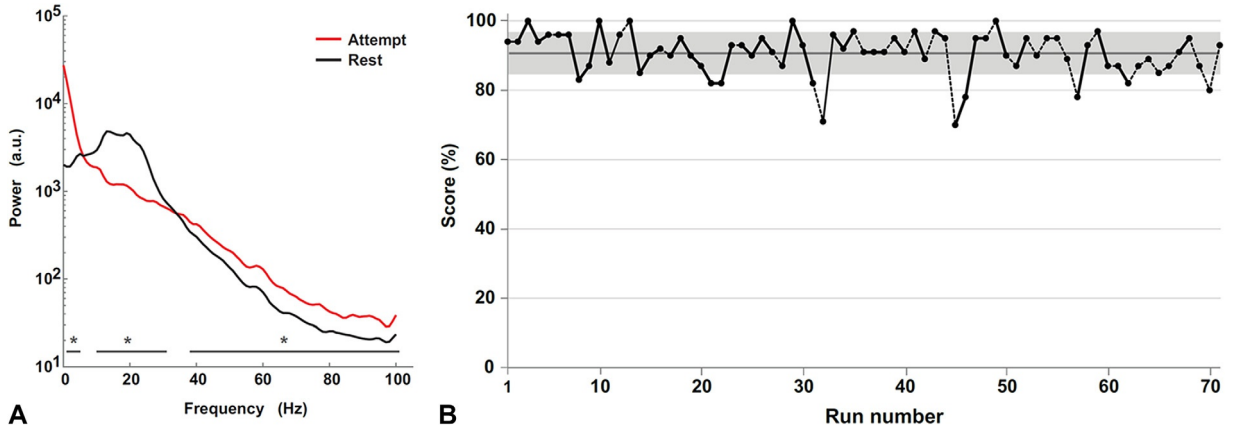

Fig. 25.6. (A) Spectral power distribution of attempted movement (*red*) and rest (*black*) of sensorimotor cortical brain signals. (B) Two target task performance development over >6 months after implantation. *Every black dot* represents a single, 300-s run. Multiple runs on the same day are indicated by *connecting black lines between the dots*. *Black dashed lines* connect runs on different days. Mean and SD of performance are indicated by a *horizontal gray line and gray shading*, respectively. Adapted from Vansteensel, M.J., Pels, E.G.M., Bleichner, M.G., et al., 2016. Fully implanted brain-computer interface in a locked-in patient with ALS. N Engl J Med 375, 2060–2066. doi: 10.1056/NEJMoa1608085.

standard BCI two-target task was high (>90% correct) and was stable for more than 6 months (Fig. 25.6B). Every black dot represents a single, 300 s, run. Multiple runs on the same day are indicated by connecting black lines between the dots. Black dashed lines connect runs on different days. Mean and SD of performance are indicated by a horizontal gray line and gray shading, respectively. After optimization of parameters, performance on training games and spelling was stable at high levels: 74% in a continuous feedback task, 87% in a discrete "clicking" task, and an information transfer rate of 13 ± 3 bit/min during spelling. The participant is currently using the system at home without the help of the research team or other experts. This case study provides direct evidence supporting the utility of an implantable system that clinicians can configure to tap into neural circuits for control of an external actuator or system.

CLASS B

Class B is defined to include component applications that provide quantitative information (i.e., neural or inertial data collected from the INS) to the clinician for assistance in optimizing therapy. This category requires manual intervention by the clinician to change the operation of the neural stimulator; applications where the brain signals themselves directly influence the operation of the INS are excluded. The benefits of these Class B use cases are to improve the information available to a clinician to optimize therapy while minimizing their burden. Though not an automated closed-loop system, it improves the manual feedback loop involving the clinician. An investigational example of providing guidance on optimal therapeutic stimulation settings by applying the measured physiologic signals through a machine learning prediction algorithm is described in the following section.

DBS electrode selection in Parkinson's disease

Currently, selection of effective stimulation parameters for DBS therapy can be time consuming for both the physician and the patient, as the programming process relies upon iterative observation of behavioral responses. It is possible that leveraging neurophysiologic symptoms correlated to clinical symptoms may provide a method to guide effective DBS programming. In the example illustrated in Fig. 25.7, data from a new patient is recorded and compared to a database to determine optimal DBS settings based on historical outcomes of patients with similar neural features.

In a pilot study, LFP recordings were obtained from 15 patients with Parkinson's disease with DBS leads in the subthalamic nucleus using the Activa PC+S® system (Connolly et al., 2015). These recordings were then used for a preliminary investigation into whether characteristics of the recordings correlate with the contacts selected by the attending physician for the patient's DBS therapy. During device implantation and follow-up sessions extending out to 6 months, recordings were saved from the DBS leads with the patient at rest in the

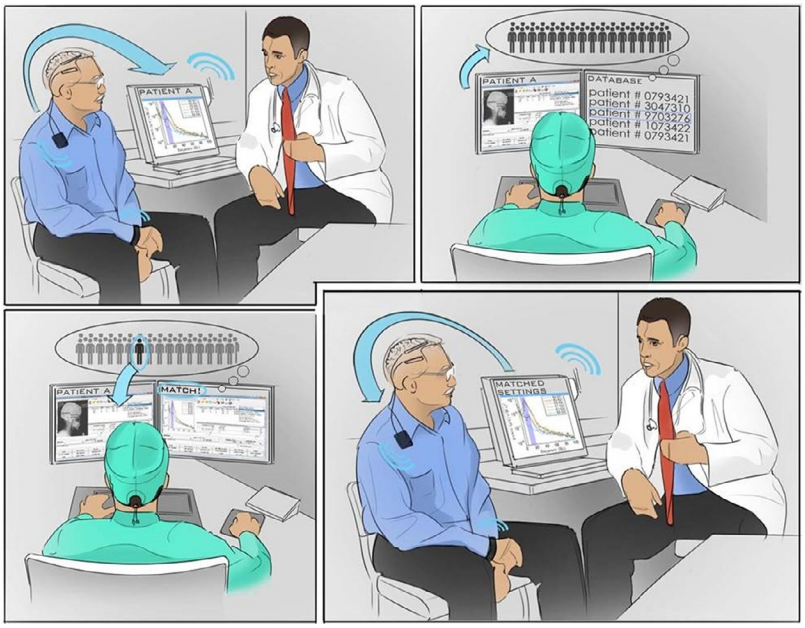

Fig. 25.7. Example clinical decision support tool that leverages brain sensing. Data from a new patient is recorded and compared to a database to determine optimal DBS settings based on historical outcomes of patients with similar neural features.

off-medication and off-stimulation state. LFP recordings were taken from each of the six possible pairwise combinations of the four electrode contacts, and at the end of each clinical visit, the neurologist programmed the patient's DBS therapy, choosing, from among other parameters, the stimulation contact(s) (C0, C1, C2, C3, or some combination thereof) to provide stimulation. A total of 83 distinct recordings were made. Spectral features (i.e., power in several frequency bands) were extracted from the LFP recordings offline, and a number of machine learning algorithms (e.g., linear discriminant analysis, *k*-nearest neighbors, classification trees, and support vector machines) were trained to predict which contact the clinician selected based upon some combination of the spectral features. The support vector machine method yielded a low misclassification rate (7/83) using a minimal set of spectral features (i.e., power in 3–5 Hz θ-band, and 10–20 Hz β-band) (Fig. 25.8). In Fig. 25.8, each dot represents the clinician-selected contact for each observation. The black *x*'s show misclassified observations and the vertical location shows the predicted contact/group.

While there is certainly a need for larger scale validation, these results suggest that it may be possible to develop an algorithm that uses LFP recordings from DBS leads to guide the identification of the contact nearest the physiologic sweet spot for effective DBS in the STN and greatly improve efficiency and simplify DBS programming. As newer DBS systems with larger numbers of stimulation contacts emerge, the practical time savings afforded by automatic programming may prove to be a critical component of clinical adoption and optimizing patient outcomes.

CLASS C

Class C includes BCI applications that analyze signals recorded from neural circuits to detect behavioral events and trigger stimulation based upon the detection of these events. The behavioral events of interest include but are not limited to sleep/awake cycles, body posture, initiation and termination of voluntary movement, and gait. The key characteristic of Class C configurations is the use of algorithms that detect these events based upon neural data and control policies that deliver stimulation based upon the detected events. That is, the brain signals are used as a proxy for behavior and directly influence the operation of the INS. In principle, this can be considered an automated adjustment of the patient programmer since signals are triggered by signals denoting intention, but bypassing the need for overt manual intervention. The benefit of a Class C application is the ability of the stimulator to respond more quickly and specifically to patient needs, while greatly minimizing their burden. An investigational example of this class of closed-loop strategies applied to adaptive control of DBS for treatment of essential tremor is presented in the following section.

Cortical recording for closed-loop control of DBS in essential tremor

Current DBS for ET uses implanted leads in the ventral intermediate nucleus of the thalamus to deliver constant high frequency stimulation to mitigate tremor. Given that these patients only experience tremor during volitional movement, a feasible goal for a closed-loop system would be to limit stimulation to periods of intentional movement. This could result in a system that preserves power, reduces the frequency of replacement surgeries, and reduces side effects by only delivering stimulation on an as-needed basis. A simplified form of a closed-loop system is shown in Fig. 25.9, where sensors are collecting information (i.e., brain signals) from the patient, classifiers identify the patient state (i.e., detect when the patient is moving), and a control policy dictates the action that the actuator takes in each state (i.e., stimulation turns on when the patient is voluntarily moving and turns off at rest). In this example, when the patient is at rest, the stimulator is off (Fig. 25.9A). When motor planning is initiated, brain rhythms (e.g., β) change (Fig. 25.9B). Detection of changes in these neural signatures then triggers stimulation during intentional motion (Fig. 25.9C). Finally, when the patient returns to rest, brain rhythms return to baseline and stimulation ceases (Fig. 25.9D).

Several approaches can be adapted for detection of patient movement as a trigger for stimulation. Wrist-worn inertial sensors and limb electromyography have already been used to trigger stimulation changes in

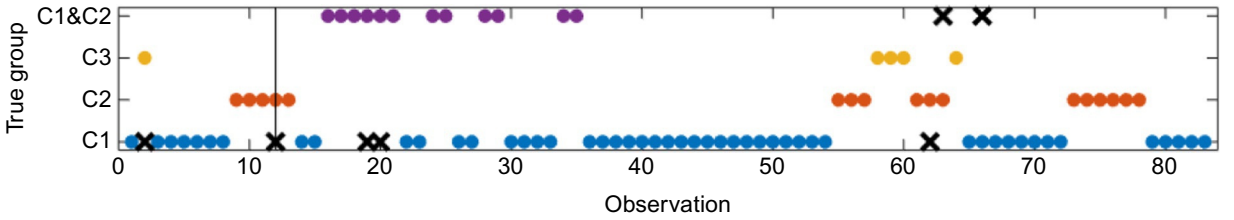

Fig. 25.8. Automated stimulation contact selection based on brain sensing (Connolly et al., 2015).

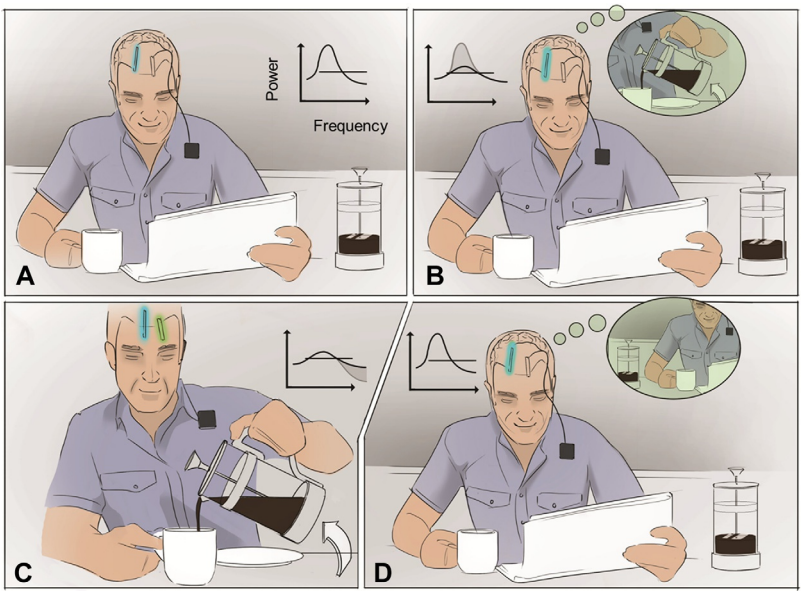

Fig. 25.9. Adaptive stimulation reflex schemes for essential tremor. (A) When the patient is at rest, the stimulator is off. (B) Brain rhythms (e.g., β, γ) change when motor planning is initiated. (C) Detection of changes in neural signal features triggers stimulation during intentional motion. (D) When the patient returns to rest, brain rhythms return to baseline and stimulation ceases. Note that the leads for sensing (*blue*) and stimulation (*green*) are drawn separately for illustrative purposes.

DBS patients (Herron et al., 2017). However, these sensors are worn externally and may be uncomfortable or undesirably attract attention to a patient. Additionally, they would need to communicate wirelessly with the INS to trigger stimulation changes, which would consume additional power. An alternative to using limb-based sensors would be to make use of known neural phenomena that can be used to indicate when a patient is performing volitional movements. As described in the Class A example of using a BCI for communication, desynchronization (i.e., decrease in power) is observed in the β-band during movement when electrodes are placed over the primary motor cortex. In the context of essential tremor, this enables a simple, robust threshold scheme to distinguish periods of volitional motion from periods of rest. The output of this classifier could then toggle between states of a controller that delivers full clinical stimulation (i.e., the amplitude used for open-loop tremor suppression) during movement and no stimulation during rest.

An initial proof-of-concept of this control paradigm was recently completed (Fig. 25.10) by leveraging the Activa PC+S® system with an external computer-in-the-loop via the Nexus-D system (Herron et al., 2017). Stimulation was ramped up when power in the β-band decreased below a lower threshold and ramped down when power in the β-band increased above an upper threshold. These thresholds were empirically determined during the experimental session. On the left are two spirals drawn with the dominant hand before and after

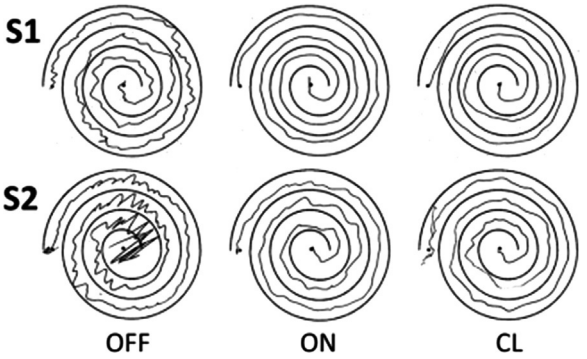

Fig. 25.10. Patient drawn spirals collected as part of clinical tremor assessment (Herron et al., 2017).

DBS implant. On the right are spirals collected on the day of the experiment in each of the three stimulation states. Differences in tremor between no stimulation at 4 months post-op and experimental day are attributed to day to day tremor variation. Note tremor in the upper right and lower left quadrants of the spiral in the experimental no stimulation case. Comparatively there are few deviations from normal spirals in the open-loop and closed-loop cases.

CLASS D

In contrast to Class C, where neural signals are used as an indirect measure of behavioral events that trigger stimulation, Class D component arrangements leverage a closed-loop approach that is more similar to the

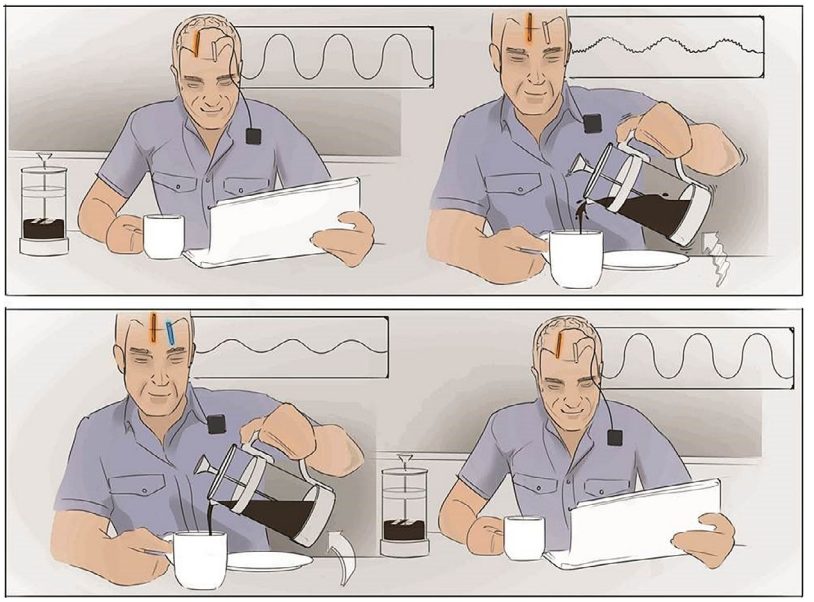

Fig. 25.11. Concept diagram illustrating a restorative brain coprocessor for DBS therapy.

traditional engineering principle of feedback control. That is, Class D includes applications in which neural signals are part of a feedback loop that delivers stimulation to regulate the signals themselves (Fig. 25.11). In these arrangements, the neural signals are an indirect measure of the underlying pathologic state. In the example shown in Fig. 25.11, implanted hardware senses brain rhythms (recording electrode shown in orange, top left). A disturbance in these rhythms, corresponding to a change in patient state, is then detected (top right). This disturbance triggers delivery of stimulation (stimulating electrode shown in blue, bottom left). Finally, when sensed brain rhythms return to normative state, stimulation is terminated (bottom right).

An analogy of this type of system from daily life is a thermostat that controls room temperature. Thermostats measure temperature and use an actuator (i.e., furnace, boiler, or air conditioner) to drive the temperature toward a defined set point. In this way, Class D controllers may be thought of as thermostats that use an actuator (i.e., implanted stimulator) to regulate certain brain rhythms to maintain them within a homeostatic window. Once again, this can be considered an automated adjustment of the patient programmer, but now input signals are based on physiologic signals correlated with disease state. Similar to Class C, automated titration of signals in Class D again bypasses the need for overt manual intervention. The benefit of a Class D application is the ability to respond more quickly and specifically to a patient's needs, including signals of which they might not be consciously aware, while greatly minimizing their burden. It is important to consider, however, the relative amplitude of these signals and the proximity to therapeutic electrodes, as less favorable signal to noise characteristics due to stimulation artifact can impact performance (Stanslaski et al., 2012; Swann et al., 2018). An investigational example of this sort of closed-loop strategy is described in the following section.

Cortical recording for closed-loop control of DBS in Parkinson's disease

Recently, the Activa PC+S® system was used to obtain multisite long-term recordings on two patients with Parkinson's disease who experienced frequent dyskinesia (Swann et al., 2016). The patients were studied both at rest and during voluntary movement. It was demonstrated that dyskinesia is associated with a narrowband γ oscillation in the motor cortex between 60 and 90 Hz, a similar, though weaker, oscillation in the subthalamic nucleus, and strong phase coherence between the two (Fig. 25.12). The finding of a brain rhythm reliably associated with dyskinesia has translational potential as a control signal in closed-loop DBS (Fig. 25.12, middle) that has been evaluated during short-term in-clinic testing (Swann et al., 2018).

REFLECTIONS AND FUTURE DIRECTIONS

The treatment of neural disease continues to be an area of intense research and opportunity. While progress has been made in better understanding these diseases, we believe the underlying pathophysiology and quantifiable disease metrics continue to be elusive, most notably due to lack of chronic human data in representative use conditions. While BCI technology offers an avenue

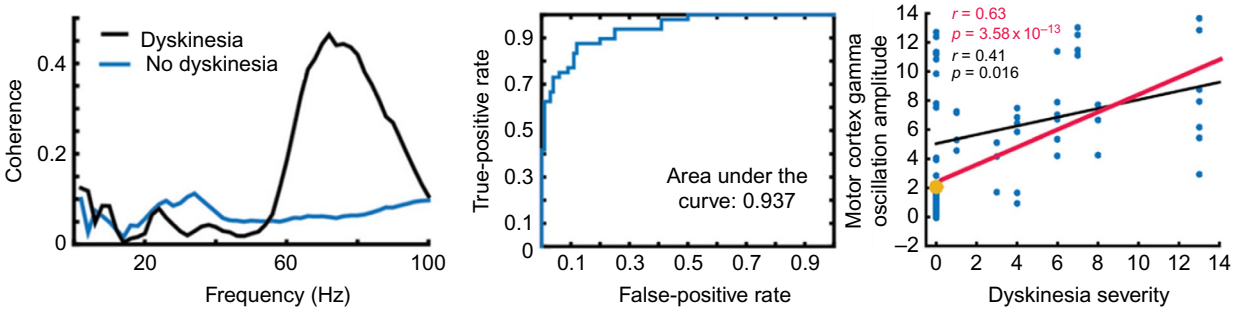

Fig. 25.12. γ oscillations distinguish dyskinetic and nondyskinetic states. Example phase coherence from one subject at rest on medication (*left*). Receiver operating characteristic curve using phase coherence as a biomarker for dyskinesia (*middle*). Correlation between γ oscillation amplitude and dyskinesia severity (*right*). Adapted from Swann, N.C., De Hemptinne, C., Miocinovic, S., et al., 2016. Gamma oscillations in the hyperkinetic state detected with chronic human brain recordings in Parkinson's disease. J Neurosci 36, 6445–6458. doi: 10.1523/JNEUROSCI.

to generate data and investigate these diseases from an engineering perspective, it is challenged by having to satisfy multiple other factors in order to be viable.

Besides the scientific challenges of biomarker identification and the need for advancement in our understanding of physiologic systems, remaining engineering challenges in translational BCI include longevity of devices, security of data and communications, and the standardization of connectivity and infrastructure. The longevity of devices depends largely on the materials that interface with the tissue and the energy storage technology. The challenges at the tissue interface include reaction of the tissue to the materials and breakdown of the device materials resulting in a degradation of the device's structure and intrusion of fluids into circuitry. Limitation on longevity due to energy storage either relate to the finite charge capacity of primary cells of a given battery chemistry and size or the number of recharge cycles that rechargeable designs can under go before charge capacity drops or catastrophic failure occurs. The emergence of smart, connected devices is already having a transformational impact on competition in a variety of markets, requiring companies to build and support an entirely new technology infrastructure (Porter and Heppelmann, 2014, 2015). This technological boom has led to growing security concerns, highlighted in the media through cases such as car hacking in the auto industry and retail credit card hacks. Bioelectronic devices might not only carry sensitive personal data; if their function is compromised, health and safety are at risk. Thus, communication security is a logical first step toward securing device access and data contents. On-device data encryption is another area to be explored, in the event that devices are stolen or covertly accessed. Finally, while many emerging BCI devices are exploring low energy communication protocols, such as Bluetooth Low Energy, many other proprietary communication protocols exist today, and further standardization of communication will foster growth and innovation of applications that promote health and lifestyle improvements.

The application of BCI as a discovery tool can be achieved by adding scientific instrumentation to proven therapy platforms, thereby enabling research tools for streamlined and ethical investigation of neural systems. As with other major innovations of societal importance, overcoming these challenges demands the collaboration of government, academia, industry, and willing and informed volunteers, to realize the common goals of better understanding disease and improving the lives of patients.

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