Deep Brain Stimulation

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***Abstract*—Deep brain stimulation (DBS) is an established therapy for movement disorders such as Parkinson's disease, essential tremor and dystonia, and is increasingly explored for psychiatric conditions including OCD and depression. Despite its success, DBS remains constrained by its invasive implantation, limited accessibility, side effects from imprecise stimulation and the difficulty of programming fixed, open-loop systems that cannot adapt to symptoms. This report reviews the principles, mechanisms and clinical applications of DBS, and outlines the limitations of current technologies that drive innovation. It focuses on three emerging approaches: closed-loop adaptive DBS, segmented electrodes for directional stimulation and non-invasive temporal interference (tTIS), and describes how each aims to improve targeting precision, reduce side effects and personalise neuromodulation. Such developments point toward a future of more efficient, safe and patient-specific DBS therapies.**

I. Introduction

Deep brain stimulation (DBS) is a neurosurgical therapy in which electrodes are implanted into specific brain targets to deliver controlled electrical pulses from a subcutaneous neurostimulator placed in the chest. DBS is an established treatment for refractory movement disorders such as Parkinson's disease (PD), dystonia and essential tremor (ET), known as oscillopathies. In recent years, various studies are exploring its potential to treat neuropsychiatric conditions including major depression, epilepsy and obsessive–compulsive disorder (OCD).

Compared with traditional ablative surgery, DBS offers several advantages: it is non-lesional and reversible, enables millimetre-level targeting of deep brain structures and allows fine-tuning of stimulation parameters to optimize therapeutic outcomes. Moreover, modern DBS systems can record neural activity, providing a powerful tool to investigate the neural mechanisms of disease and refine circuit-based models of brain dysfunction.

However, DBD adoption is limited reflecting the invasiveness of the procedure, the risk of surgical complications and the challenges of selecting optimal targets and stimulation settings. These limitations highlight the need for technological and clinical innovations that can simplify patient selection, enhance targeting accuracy, reduce risks and expand access to DBS therapy. The following report reviews current DBS practices and emerging developments aimed at optimizing its clinical implementation.

II. DBS Principles and Hardware

A. Mechanism of action

The exact mechanism of action of DBS is still not fully understood and many theories have been proposed to explain how it alleviates motor symptoms. Early on, the observation that DBS and surgical ablation of the same target could produce similar clinical benefits led to the idea that DBS worked by inhibiting neural activity downstream of the stimulated nucleus and disrupting pathological circuit dynamics. However, later studies showed that high-frequency stimulation ($\sim$100 Hz) can actually increase the output activity of the target region. This contradiction led to the idea that downstream effects depend on whether the stimulated nucleus sends excitatory or inhibitory projections: activity in connected regions can be either upregulated or downregulated accordingly. More broadly, it is now common consensus that DBS modifies activity not only within the target nucleus, but also across its afferent and efferent networks [1].

For movement disorders such as PD and dystonia, also known as "oscillopathies", symptom severity is linked to low-frequency rhythmic activity in specific circuits localized in the basal ganglia. High-frequency DBS seems to suppress the propagation of these pathological oscillations, therefore, many theories focus on stimulation-induced disruption of abnormal brain rhythms at ionic, cellular, and network levels.

At the ionic level, a cathodic electrode creates an electric field that redistributes ions in the extracellular space, opening voltage-gated sodium channels and triggering action potentials in nearby axons. Many axons can reliably follow the high stimulation frequency, but synaptic transmission does not keep up: presynaptic terminals deplete their neurotransmitter and postsynaptic receptors become depressed. As a result, synapses behave like a filter reducing the transmission of signals, especially low-frequency activity that characterizes pathological oscillations. This "synaptic filtering" is thought to be a key component of the DBS mechanism.

Since DBS usually delivers regular trains of pulses, the information content of the evoked activity is minimal. This has led to the "information lesion" hypothesis, which proposes that DBS-induced action potentials override intrinsic activity in the stimulated neurons and limit the propagation of oscillatory activity through the network. Synaptic filtering and information lesion effects are likely to act together, resulting in robust suppression of pathological low-frequency activity. In PD, for example, basal ganglia–cortical circuits appear to be abnormally tuned to low-frequency rhythms (beta-band, 12-30 Hz); high-frequency stimulation blocks the propagation of these "bad oscillations" locally. This could explain why high-frequency DBS can improve symptoms across different disorders that share pathological low-frequency synchronization.

Some studies indicate that during subthalamic or pallidal DBS, elements of sensorimotor modulation are still preserved in the stimulated region. This supports a view in which DBS acts as a filter that selectively suppresses pathological low-frequency oscillations while permitting some physiologically relevant modulation to pass through. The information lesion hypothesis can be reconciled with these findings if normal basal ganglia function relies more on other forms of information encoding than on synchronization, which is what DBS supposedly supresses.

Finally, the mechanisms described above mainly account for the acute effects of DBS in certain movement disorders. In many psychiatric indications, there is less evidence of pathologically synchronized low-frequency activity, suggesting that additional mechanisms must be involved. One emerging area of interest is the effect of DBS on astrocytes, which regulate synaptic transmission and plasticity. Clinically, DBS effects often develop gradually over time, consistent with longer-term neuroplastic changes. These may include DBS-induced alterations in the expression of trophic factors and synaptic proteins, leading to a durable reorganization of the pathological circuits [3].

B. Electrodes Design and Stimulation Programming

To provide electrical stimulation, electrodes are chronically implanted in specific brain regions. These electrodes are inserted using stereotactic techniques, which combine radiological guidance and electrophysiological mapping to accurately localize the target structure[2]. The crucial characteristics of a DBS electrode include biocompatibility, inertness, long-term stability, surgical feasibility, suitable current delivery and spatial configuration. Additional considerations include MRI compatibility and the potential for sensing. DBS electrodes typically consist of platinum–iridium wires and nickel alloy connectors encased in a polyurethane sheath; platinum–iridium is chosen because of its minimal toxicity and excellent conduction properties [6].

Traditionally, cylindrical electrodes with four contacts are used, designed to generate a symmetrical electric field and homogeneously stimulate the target area. Stimulation can be delivered from 4 to 8 cylindrical band contacts at the distal end of the electrode lead; a common example is the Medtronic 3387/3389 quadripolar lead, which has a diameter of 0.27 mm and a height of 1.5 mm per contact. Beyond these traditional cylindrical designs, recent innovations include thin-film electrodes and segmented electrodes, in which the contacts are no longer continuous rings but are divided into separate segments. Both of these technologies are described in more detail in Section V.

The electrodes are connected to a pulse generator, a subcutaneous neurostimulator that delivers pulse trains programmable in amplitude, pulse width and frequency. The programming parameters are chosen to maximize the effect of DBS on the fiber pathways that mediate the clinical benefit of the therapy, while avoiding the recruitment of fibers associated with adverse effects and minimizing energy consumption to prolong device longevity. In current clinical practice, parameter settings are empirically selected with typical ranges of 130–180 Hz for stimulation frequency, 60–90 μs for pulse width, and 1–4 V for stimulation amplitude[1]. The traditional stimulation pattern is regular and monotonic, consisting of a continuous monopolar cathodic pulse train at high frequency, with the neurostimulator casing used as the reference electrode. However, for PD and tremor, non-regular patterns have also been investigated. These include pulses with short pulse-free intervals, short bursts of pulses, highly non-regular pulse trains with a log-normal distribution of instantaneous pulse frequencies and patterns with the same average stimulation frequency as the clinically optimal settings but with an overall 20% coefficient of variation. In PD, biphasic stimulation has been shown to facilitate charge recovery and improve clinical scores in several domains, although at the cost of increased power consumption and reduced battery life. By contrast, non-regular patterns have not provided therapeutic benefit in treating ET, suggesting that tremor may be better controlled with regular stimulation patterns [2].

C. Signal Path

Once a target area has been selected, the choice of stimulating contacts and electrode design, together with the adjustment of stimulation parameters, is used to shape the volume of tissue activated (VTA) so that it matches the intended target as closely as possible. The VTA around the electrode critically depends on the number of active contacts, the use of monopolar versus bipolar configurations, the stimulation parameters, such as amplitude and pulse width and the properties of the surrounding tissue. In particular, whether the tissue is isotropic or anisotropic strongly affects the resulting VTA. In an isotropic medium, stimulation with cylindrical electrodes generates a symmetrical, omnidirectional VTA around the lead; side effects can be reduced by decreasing the duration or intensity of stimulation or by switching to bipolar stimulation. In contrast, in an anisotropic medium the symmetry of the electric field is lost, and the VTA becomes distorted. In this context, electrodes that enable field steering improve the precision of the VTA, and segmented electrodes with independent control of each contact allow the current to be directed toward a specific region, thereby reducing off-target effects [2].

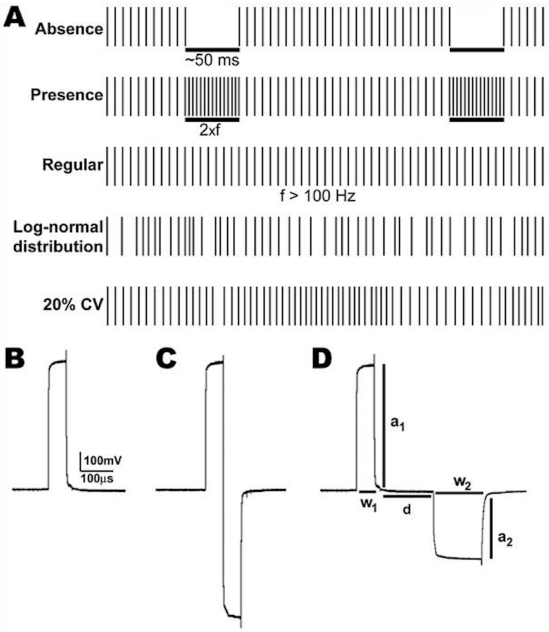

Fig. 1: A) Stimulation patterns used in DBS. B) Monopolar pulse. C) Balanced biphasic pulse. D) Parameters of biphasic pulse. [2].

In clinical practice, DBS is generally applied without direct visualization of the spread of stimulation or the VTA, making it difficult to precisely control the stimulated regions and potentially leading to side effects. To address this limitation, 3D software tools have been introduced to visualize the VTA as a function of stimulation parameters and electrode position in the brain. These models provide the VTA as a function of the active contact, amplitude, pulse width, frequency, electrode geometry and impedance, and have proven essential for guiding lead implantation and contact selection, as well as for optimizing spatial and temporal stimulation patterns to maximise therapeutic benefit while limiting side effects due to off-target stimulation.

III. Clinical Applications

Deep brain stimulation is now an established therapy for several movement disorders, most notably PD, ET and dystonia. In PD, DBS is typically offered to patients with medication-refractory motor symptoms such as bradykinesia, rigidity and tremor, with the subthalamic nucleus (STN) and globus pallidus (GPi) serving as the primary stimulation targets. For ET, electrodes are implanted into the ventral intermediate nucleus (VIM) of the thalamus, while GPi stimulation is commonly used for dystonia. Eligibility generally requires that patients exhibit disabling symptoms despite optimal pharmacological therapy, retain sufficient cognitive and psychiatric stability and demonstrate favorable response to Levodopa (in PD cases). Beyond movement disorders, DBS is increasingly explored as a neuromodulatory therapy for treatment-resistant psychiatric and

neurological conditions, including obsessive-compulsive disorder (OCD), major depressive disorder and Alzheimer's disease (AD), although these applications remain largely experimental and are still under clinical investigation.

IV. Limitations

Deep brain stimulation has transformed the treatment of movement disorders, with over 160,000 patients worldwide benefitting from its reversible, non-lesional therapy [2]. Yet, despite its promise, DBS faces significant hurdles. Only about 2% of PD patients undergo DBS, largely due to the invasive nature of the neurosurgical procedure, high cost and limited access to specialised surgical teams [1]. Its success depends heavily on patient selection and precise electrode placement; even slight deviations can reduce therapeutic effects and increase off-target effects, which occur in up to 50% of patients (with varying severity) [1]. Traditional open-loop systems deliver a fixed stimulation that cannot respond to fluctuations in symptoms, often leading to unnecessary current spread, faster battery depletion and incomplete control over complex issues such as gait impairment or cognitive decline [2]. On top of this, clinicians have to contend with technical hurdles including stimulation artifacts, a limited understanding of underlying DBS mechanisms and the need for extensive trial-and-error to determine optimal stimulation parameters. This makes programming and patient management time-consuming and demanding for the clinical team. Surgical risks such as hemorrhage, infection, skin erosion and hardware malfunction add further constraints. While improvements in device miniaturisation and battery longevity have helped, these challenges have driven the development of next generation DBS technologies, including closed-loop control, segmented electrodes and less invasive stimulation approaches, all designed to deliver therapy more precisely and safely.

V. Emerging Technologies for Improved DBS

A. Closed-loop DBS

Traditional DBS delivers continuous stimulation without regard to the patient's state. Closed-loop DBS offers a dynamic alternative that adjusts stimulation timing and intensity based on real-time biomarkers of disease severity (Fig. 2). The most commonly used biomarkers are local field potentials (LFPs), recorded at the stimulation site, which reflect local neuronal activity, such as beta-band oscillations (∼20Hz) in the motor cortex for PD. LFPs provide good spatial resolution and long-term stability, but recording and stimulating through the same electrode introduces artifacts that can obscure biomarkers signals. To address this, additional electrodes, such as electrocorticograph (ECoG) strips placed over the primary motor cortex can record clean neural activity. Alternatively, peripheral sensors can provide external feedback for symptoms like tremor or gait disturbances, though such wireless communication introduces concern for energy loss.

In closed-loop systems, the biomarker signal is conditioned, digitized and processed using machine-learning algorithms to determine the optimized stimulation parameters. This allows the system to augment stimulation when symptoms worsen (e.g. in PD, a rise in beta activity amplitude) and reduce when unnecessary, such as during sleep or specific gait phases. Compared to its open-loop counterparts, this approach improves therapeutic outcomes, reduces side effects and extends battery life.

However, challenges remain in its application including defining safe stimulation limits, managing power consumption for the added on-board sensing and processing units, and ensuring biomarker reliability. The recent FDA approval of the Medtronic Percept PC closed-loop system represents a major milestone for adaptive DBS, bringing this precision neuro-modulation approach closer to routine clinical use [5].

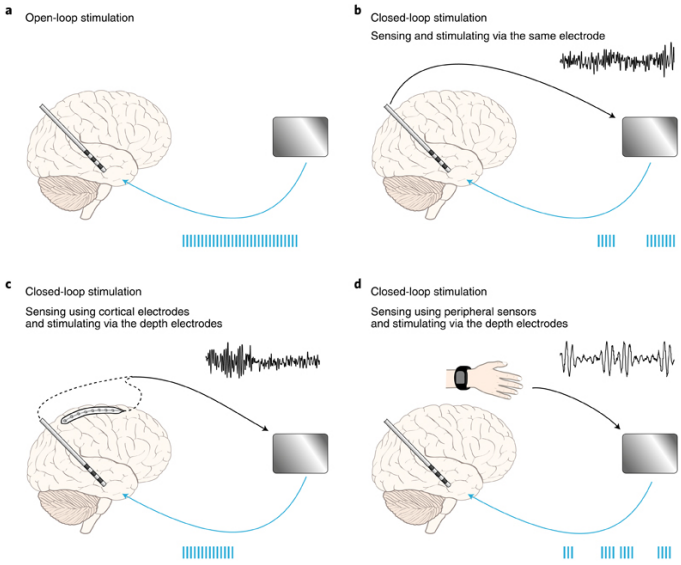

Fig. 2: Overview of open- and closed-loop DBS strategies. A) Fixed, clinician-adjusted B) LFP-based adaptive DBS. C) ECoG-based with separate sensing/stimulation. D) Peripheral-sensor processes biomarkers to modulate stimulation [1].

B. Segmented Electrodes

Segmented electrodes are a recent innovation in DBS lead design, introduced to enable more precise targeting by supporting field steering, thus improving the spatial specificity and accuracy of the lead–tissue interface. In current commercial designs, this is achieved by replacing the two cylindrical middle contacts of a traditional quadripolar lead with three segmented contacts, increasing the total number of programmable contacts from four to eight and enabling three radial directions of stimulation separated by 120°. As illustrated in Fig. 3, three designs from Aleva, Boston Scientific and Abbott–St. Jude Medical implement this architecture, with the common goal of steering current toward therapeutic targets while avoiding regions associated with side effects. Fig. 3 also shows a design from Medtronic–Sapiens, which features ten rows of four electrodes each, with alternating rows offset by 45°. This configuration enables stimulation in eight radial directions and allows the VTA to be shaped by selecting different combinations of independently active contacts [2].

Overall, these high-resolution leads allow clinicians to adjust side-effect thresholds and widen the therapeutic window between symptom suppression and side-effect induction.

Upcoming technologies, such as thin-film planar arrays, may further enhance spatial specificity for both stimulation and recordings by reducing contact size and increasing the number of available contacts.

In parallel, strategies are being explored that access the nervous system via less invasive vascular routes, potentially avoiding cranial burr holes and tissue-disrupting lead insertions.

Together, these technological trends are expected to converge with advances in brain stimulation, making DBS less invasive and potentially reducing infection risk in clinical settings. However, the

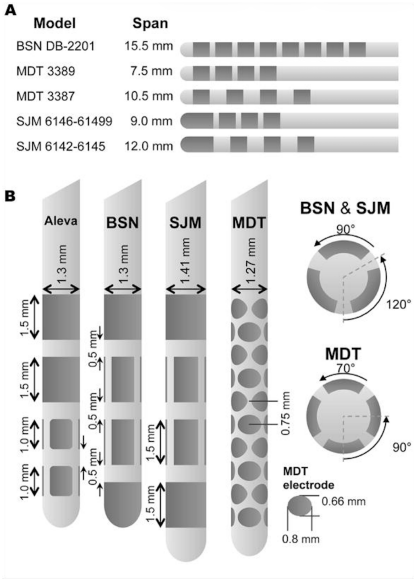

Fig. 3: A) Current clinical DBS leads. B) Emerging DBS segmented electrode lead designs [2].

gain in precision and flexibility substantially expands the degrees of freedom in programming and thus the workload for the clinical team. This burden can be mitigated by automated tools that assist in identifying optimal stimulation parameters. In particular, approaches that integrate electrode location, anatomical landmarks and patient-specific diffusion tensor imaging can provide additional constraints and help reduce the effective parameter space for DBS programming.

C. Non-invasive DBS: Transcranial Temporal Interference Stimulation

Transcranial Temporal Interference Stimulation (tTIS) is a recently developed non-invasive deep brain stimulation technique designed to selectively modulate deep brain structures and their associated neural circuits using electric fields. Its main advantage over other non-invasive approaches is the potential for greater spatial selectivity, with reduced stimulation of off-target regions.

tTIS operates by delivering two slightly different high-frequency currents (e.g. 2.00 and 2.01 kHz) through scalp electrodes. These currents interact in the brain to produce an amplitude-modulated electric field with a kilohertz carrier frequency and a lower-frequency envelope (Fig. 4). Neurons generally do not respond to the very high carrier frequency but can follow the lower envelope frequency (e.g. 10 Hz). The interference pattern creates a focal area of peak strength that can be positioned in deep brain areas by adjusting the electrodes location on the scalp. Similarly to DBS, stimulation parameters and electrode placement determine which regions and circuits are preferentially engaged.

In practice, tTIS is typically delivered at envelope frequencies depending on the oscillatory dynamics of the target region: for instance, theta-range stimulation for hippocampus and striatum in memory tasks, beta-range stimulation for primary motor cortex and striatum in motor control, or 130 Hz stimulation of the basal ganglia to parallel high-frequency DBS paradigms used in PD. Preliminary studies in PD and ET suggest that tTIS targeting basal ganglia can produce acute improvements in motor symptoms, particularly tremor, rigidity and bradykinesia. This raises the possibility that tTIS may replicate some effects of DBS modulating pathological oscillations. However, larger randomized controlled trials are needed to determine whether these acute effects are robust and reproducible across multiple sessions and over longer follow-up periods.

In healthy participants, tTIS has shown modest effects on motor performance, such as improvements in jump performance or motor learning. There is also evidence that tTIS may help counteract age-related plasticity declines: some studies report accelerated motor adaptation in older adults, suggesting that tTIS could serve as an adjunct to motor rehabilitation in aging populations or individuals with motor impairments.

Overall, tTIS is a promising technique that, with further technical refinement and clinical validation, could contribute to the treatment of motor symptoms and emulate some of the therapeutic benefits of DBS avoiding the need for invasive neurosurgery[7].

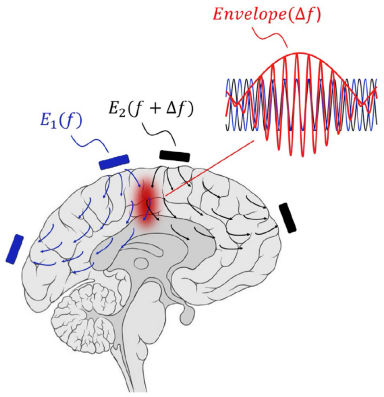

Fig. 4: Schematic on the functioning of tTIS. [8]

VI. Conclusion

To sum up, the understanding of the cellular and network mechanisms behind motor movement disorders are leading the development of next-generation DBS systems. Directional segmented electrodes and tools that accurately estimate the VTA contribute to a more controlled engagement of pathological circuits, while closed-loop systems enable stimulation to be dynamically adjusted to the individual patient. And finally, the development of non-invasive techniques, such as tTIS, supports the prospect that DBS will be offered to a larger patient population. Furthermore, as DBS evolves into an increasingly powerful neurotechnology, attention to ethical, privacy and data-security issues is essential. These considerations must evolve in parallel with technological progress, minimizing unintended consequences and ensuring clinical benefits of DBS.

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