Platform Research Tools and Deployment Strategies to Accelerate Translational Discovery

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Neurological disease has a significant impact at the personal, economic, and societal levels. Brain disease alone affects well over 100M people globally and is a major contributor to the cost of healthcare; diseases such as Stroke, Brain Tumor, Parkinson's disease, Epilepsy, Brain Injury, Alzheimer's, and Depression rank among the leading causes of death and disability in the world. While promising in-roads for treatment have been made for some conditions, engineers can help play a key role in developing new therapy concepts and bringing them to the clinical market to address critical unmet needs.

Reflecting on the evolution of medical technology, there are many parallels between the current state of most neuromodulation therapies and early cardiac pacing devices. The first generation of cardiac pacemakers operated as "metronomes," asynchronously delivering fixed-rate stimulation regardless of the intrinsic heart function. In a similar way, the first generation of neuromodulation systems used adapted circuits from cardiac pacers to provide tonic, fixed-rate stimulation to discrete neural circuits, leveraging electrode locations that were derived from established stereotactic neurosurgical targets for radiofrequency lesioning. Technological developments in cardiac systems have since evolved to include onboard diagnostics, programmability, and responsive pacing, which are all supported by a foundational understanding of the heart and its bioelectrical properties. As neuroengineers look to advance the treatment of neurological disease using similar technology concepts, the field needs to establish a similar physiological basis for how the nervous system operates, goes awry with disease, and how interventions might restore function. *These goals align well with the NAE grand challenges of "building tools for scientific discovery," "reverse engineering the brain," and "engineering better medicines."*

For the many neurological diseases, the mechanism of action for therapy is still not yet completely clear, which confounds the optimization of the medical technology. To help bridge translation of devices across these unknowns, teams are creating investigational research tools that can be chronically implanted as part of existing care pathways. These new tools permit the active probing of diseased neural circuits by observing how they respond to both electrical and concomitant pharmaceutical interventions (Figure 1). The platforms are enabled by a system architecture that harnesses an existing neurostimulator's capability to provide instrumentation with chronic access to the nervous system, while seamlessly maintaining the predicate therapy capability. Deployed with clinician-researcher collaborators (Figure 2), these instrumentation toolkits can bootstrap off existing clinical care pathways to facilitate exploration of novel therapeutic concepts and generate a pipeline of innovations.

The successful deployment of such a strategy requires a complete innovation ecosystem, and additional catalysts include public-private partnerships between clinicians, industry and government bodies like the National Institutes of Health. Working as a team for gathering key scientific knowledge, and then applying this know-how to prototyping of pragmatic therapeutic innovations, engineers in partnership with clinician-researchers can create the next generation of medical technology for addressing neurological disorders.

This talk will provide a technical perspective on the state-of-the-art, promising areas for exploration, and challenges that remain.

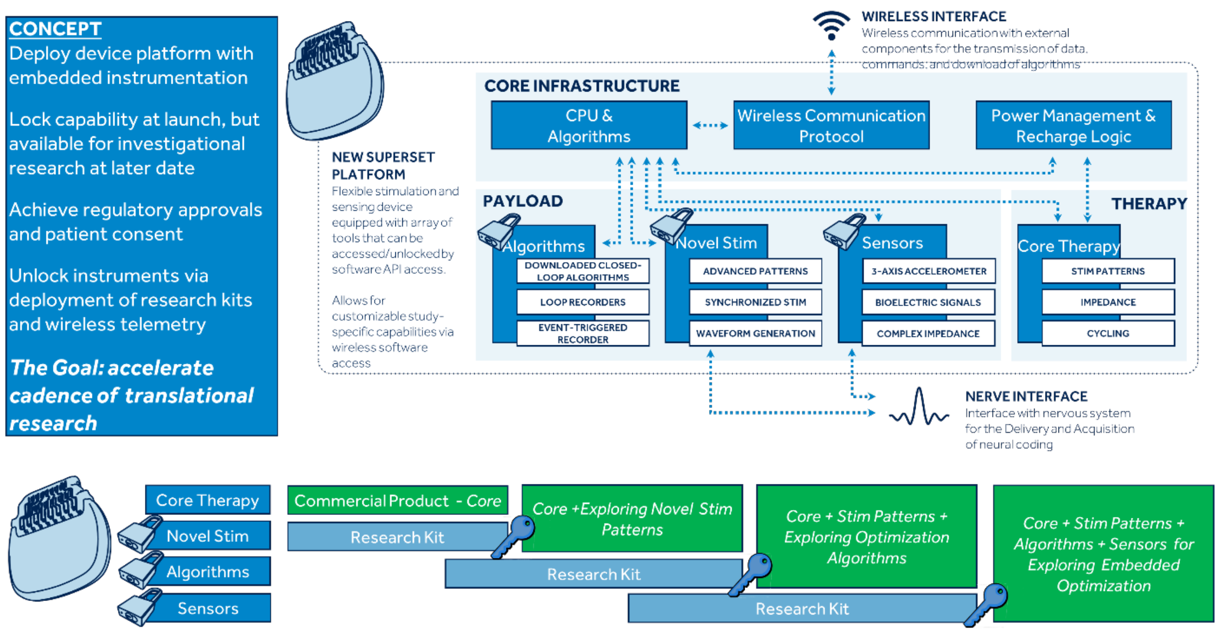

Figure 1. Examples of an investigational hardware platform for use as a clinical research tool. The system is built on the foundation of a core therapy system that supports existing clinical practice, with the addition of scientific instrumentation that can be unlocked to allow for gathering neuroscience data and prototyping future advanced therapy concepts. Using such an architecture allows for continuous, iterative development of new therapy concepts with clinician partners, through investigational studies that are enabled with wireless, reversible, firmware updates that enable expanded instrumentation capability.

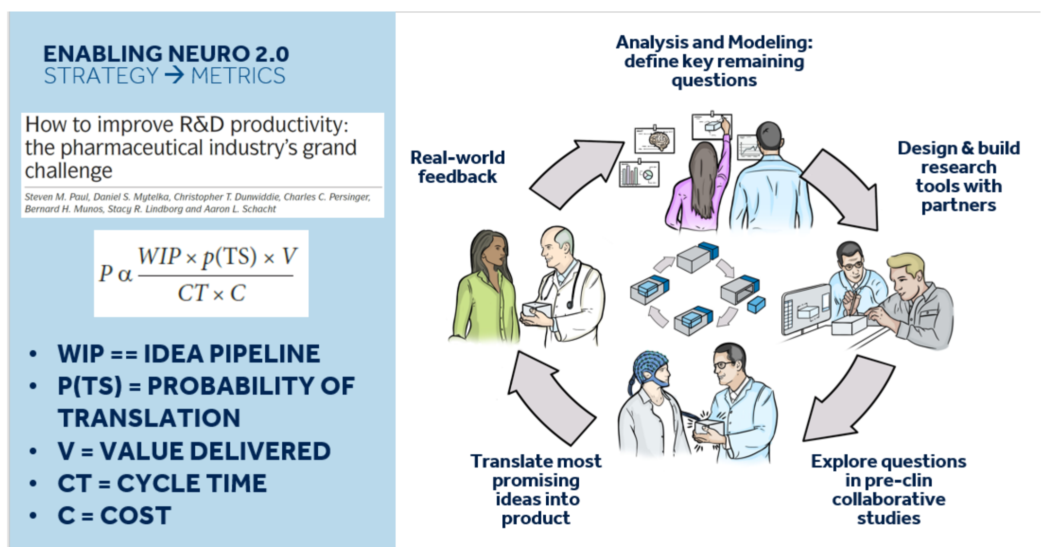

Figure 2. Drawing on concepts from pharmaceutical R&D strategies (Nature Reviews of Drug Discovery (9)2010), research tool platforms are used in collaboration with key partners to prototype and accelerate next generation therapies. As opposed to a linear funnel, one can argue with bioelectronic systems translational discovery can be viewed as an iterative feedback loop. If successful, the application of the research tool platforms will increase research productivity by broadening access to the idea pipeline through public-private partnerships, improving the probability of translation through iterative, longitudinal experiments, reducing cycle time by leveraging firmware updates, and containing cost by major reuse of established practice.