Concept Clearance for the Common Fund Stimulating Peripheral Activity to Relieve Conditions Program (SPARC)
Phase 2 Concept: SPARC-VOX

Peripheral nerve stimulation to modulate organ function is rapidly developing as a therapeutic approach to a wide range of conditions. Clinical studies, often using a purely empirical approach, have yielded both promising successes and puzzling failures, highlighting an urgent need for clear mechanistic targets with a rational basis in anatomy and physiology. The SPARC program was launched in response to this need, with the goal of catalyzing the development of next-generation peripheral neuromodulation, or "bioelectronic medicine", by providing access to high-value datasets, maps, and predictive simulations.

SPARC phase 1 comprised five interdependent initiatives: 1) anatomical, physiological, and transcriptomic data collection across multiple organ systems; 2) development of new sensing and stimulating technologies; 3) data-rich clinical studies; 4) an online Data and Resource Center with core functionalities of data management, map synthesis, and computation and simulation; and 5) anatomical and functional characterization of neurovisceral circuits carrying pain signals, in association with the NIH HEAL Initiative. Over the past several months, the NIH SPARC working group has sought and received multifaceted feedback from numerous outside experts, and is proposing a phase 2 of the program, comprising three new initiatives.

In phase 2 of SPARC, the program's mapping focus will narrow to the human vagus nerve. Because the vagus nerve innervates many organs and modulates many autonomic functions, it is a target for both existing and potential neuromodulation therapies. **SPARC-V** will create circuit-level descriptions of human **V**agal anatomy and physiology. **SPARC-O** will develop a clinical-grade, modular **O**pen-source neuromodulation platform, empowering future researchers to prove out new therapeutic concepts. **SPARC-X** will support **X**-prize-like competitions to incentivize groundbreaking proof-of-concept demonstrations meeting specified benchmarks. The SPARC Portal will continue to be developed during SPARC phase 2, with the twin goals of distributing the data products of SPARC-V and completing a transition to sustainability by becoming the first-choice data repository and knowledgebase for the peripheral neuromodulation community.

SPARC-V will consist of two sub-initiatives. The goal of the first will be to create a circuit-level schematic, similar to a subway map, with at-least fascicular resolution of a large number of human vagal nerves at points of interest selected by the SPARC team, using a single sample-to-image-to-data pipeline across multiple work sites. The goal of the second will be to conduct a large clinical study using standardized stimulation parameters and endpoints across a large number of implanted patients. We expect that this influx of human data will lead to new VNS strategies that target specific vagal subcircuits, thereby showing the value of higher-resolution data in broadening the use cases for peripheral neuromodulation. The data and knowledge resulting from these studies will be shared with the scientific community through the existing SPARC Data and Resource Center and SPARC Portal.

Many academic researchers have expressed interest in a clinical grade neurostimulation platform that is not controlled by a large medical device firm. Numerous elements of such a platform (leads, connectors, batteries, hermeticity seals) are common to all neuromodulation applications. In SPARC-O the SPARC and BRAIN Initiative teams will work together to pilot an open-neurostimulation hardware initiative. This initiative will fund teams to create interoperable modules that can be combined into custom hardware profiles for new clinical studies.

SPARC-X, the final SPARC initiative, will consist of a series of increasingly difficult challenges designed to break new ground in VNS with greater specificity of effect, These challenges will range from developing plans to proofs of concept to reliability studies, and will be associated with increasing prize awards as the complexity increases. Ideally, the products of SPARC stage 1 and of the companion initiatives in SPARC stage 2 will prove essential in achieving the prize benchmarks. One example of such a benchmark might be the demonstration of independent vagal modulation of multiple endpoints, not usually studied together, in a large-animal model. The SPARC-X challenge prizes will draw new ideas and talent into the VNS community and end the program with a final catalytic burst of excitement to carry them forward.