Stimulating Peripheral Activity to Relieve Conditions (SPARC)

Informational Webinar for RFA-RM-16-008

Data Coordination, Map Synthesis, and Simulation Cores for the SPARC Program

March 29, 2017

National Institutes of Health

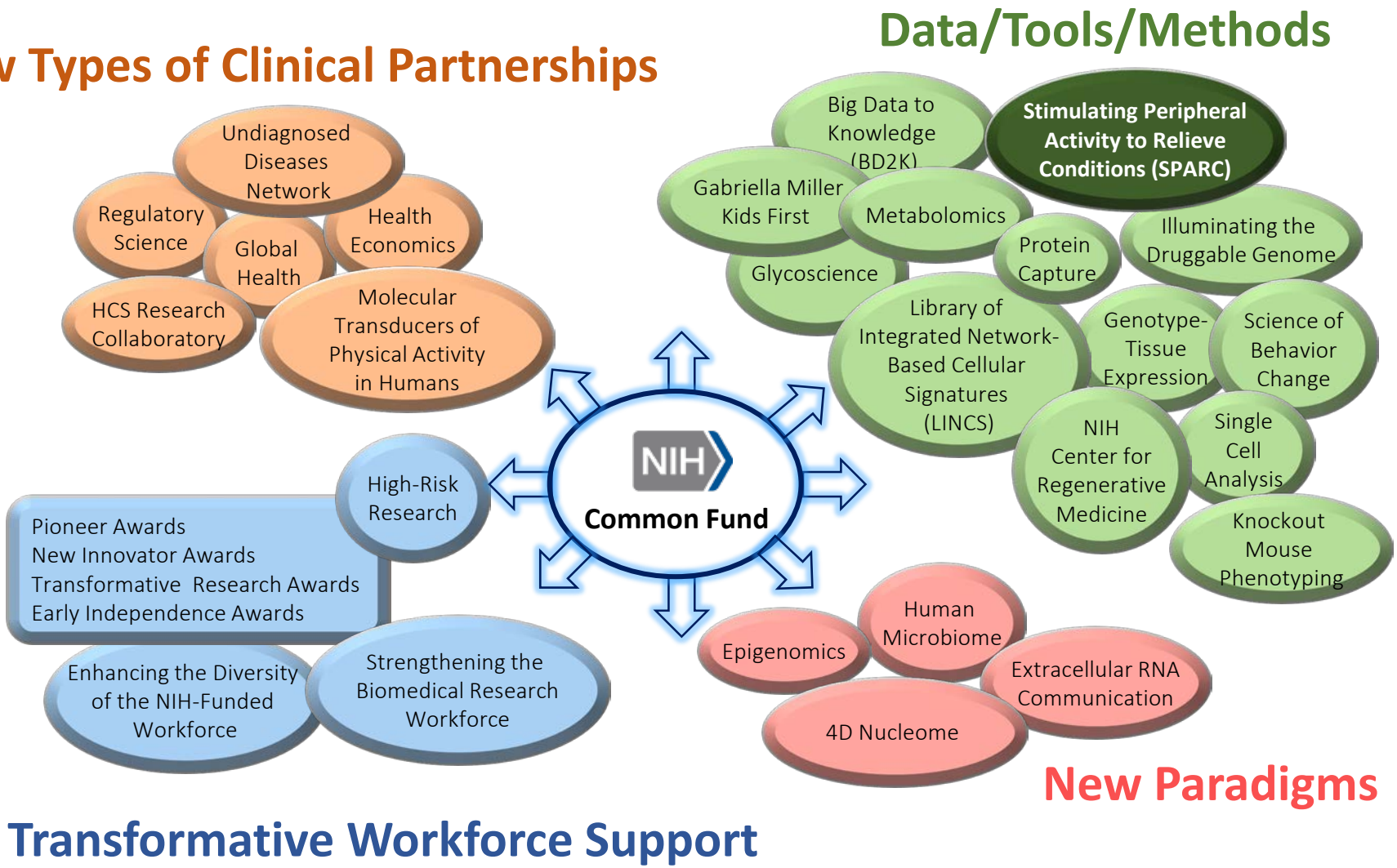
Office of Strategic Coordination - The Common Fund

Features of NIH Common Fund Programs

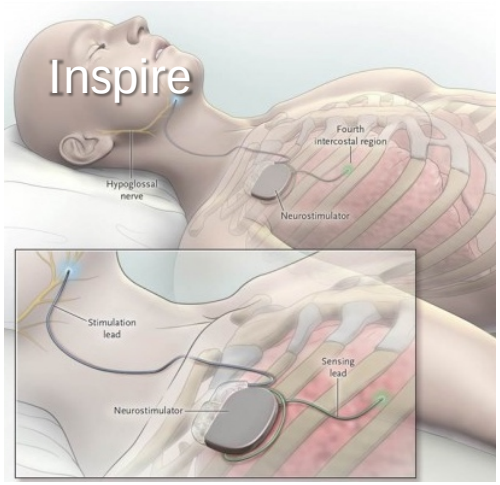
- Address important **challenges/obstacles** in biomedical research, and/or capitalize on **emerging scientific opportunities** where strategic investment can have an impact
- Are **catalytic**: Programs must achieve a defined set of high impact goals within 5-10 years
- Are **goal-driven**, with progress measured against concrete **milestones**
- Promote the missions of **multiple NIH Institutes and Centers (ICs)**
- Can require a high level of **coordination**

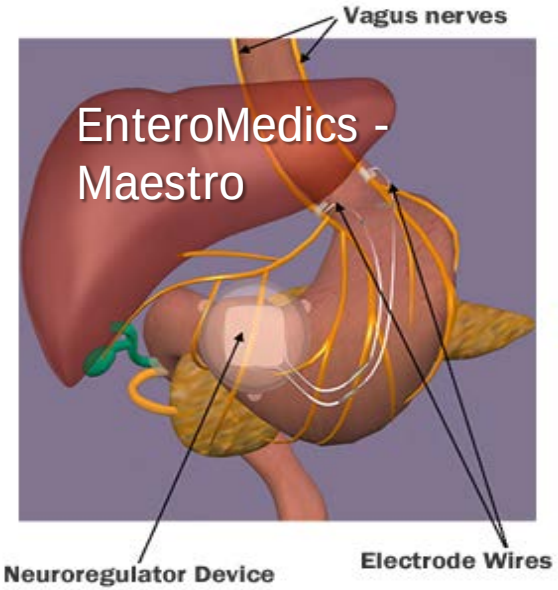
Each Common Fund program addresses unique scientific needs and opportunities, and so each program has a unique implementation plan driven by the science.

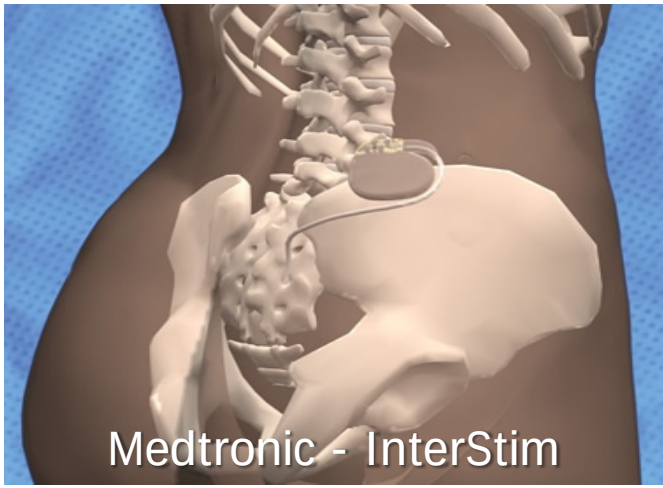
NIH Common Fund Programs

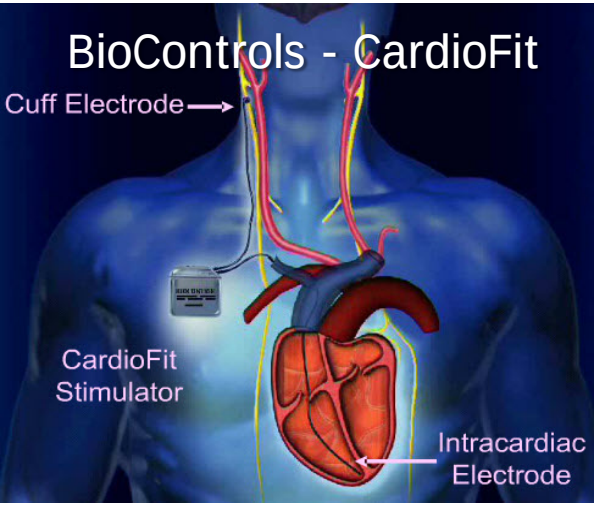


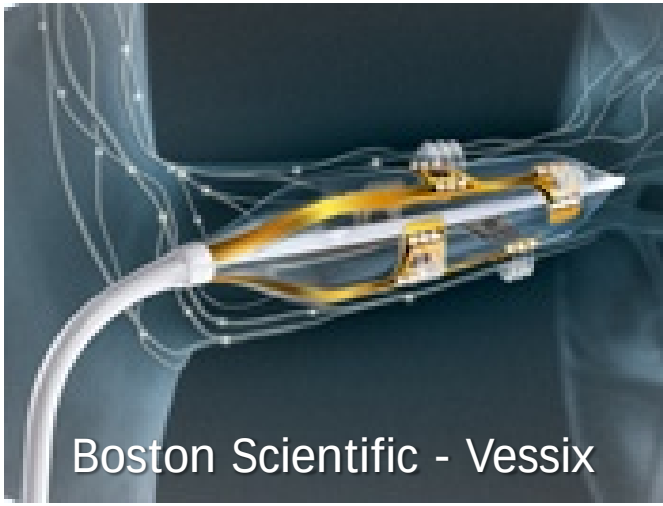
Recent FDA Market Approvals











Many randomized controlled trials miss their prespecified primary efficacy endpoints

Boston Scientific NECTAR Trial (Vagal Nerve Stimulation, Heart Failure)

BioControls INOVATE Trial (Vagal Nerve Stimulation, Heart Failure)

Medtronic SYMPLICITY (Renal Denervation, Hypertension)

CVRx® Rheos (Baroreflex Activation Therapy)

Apnex (Hypoglossal Nerve Stimulation, Sleep Apnea)

St. Jude BROADEN Trial (DBS Area 25, Depression)

Medtronic RECLAIM Trial (DBS Ventral Capsule/Ventral Striatum, Depression)

Medtronic SANTE Trial (DBS ANT, Epilepsy)

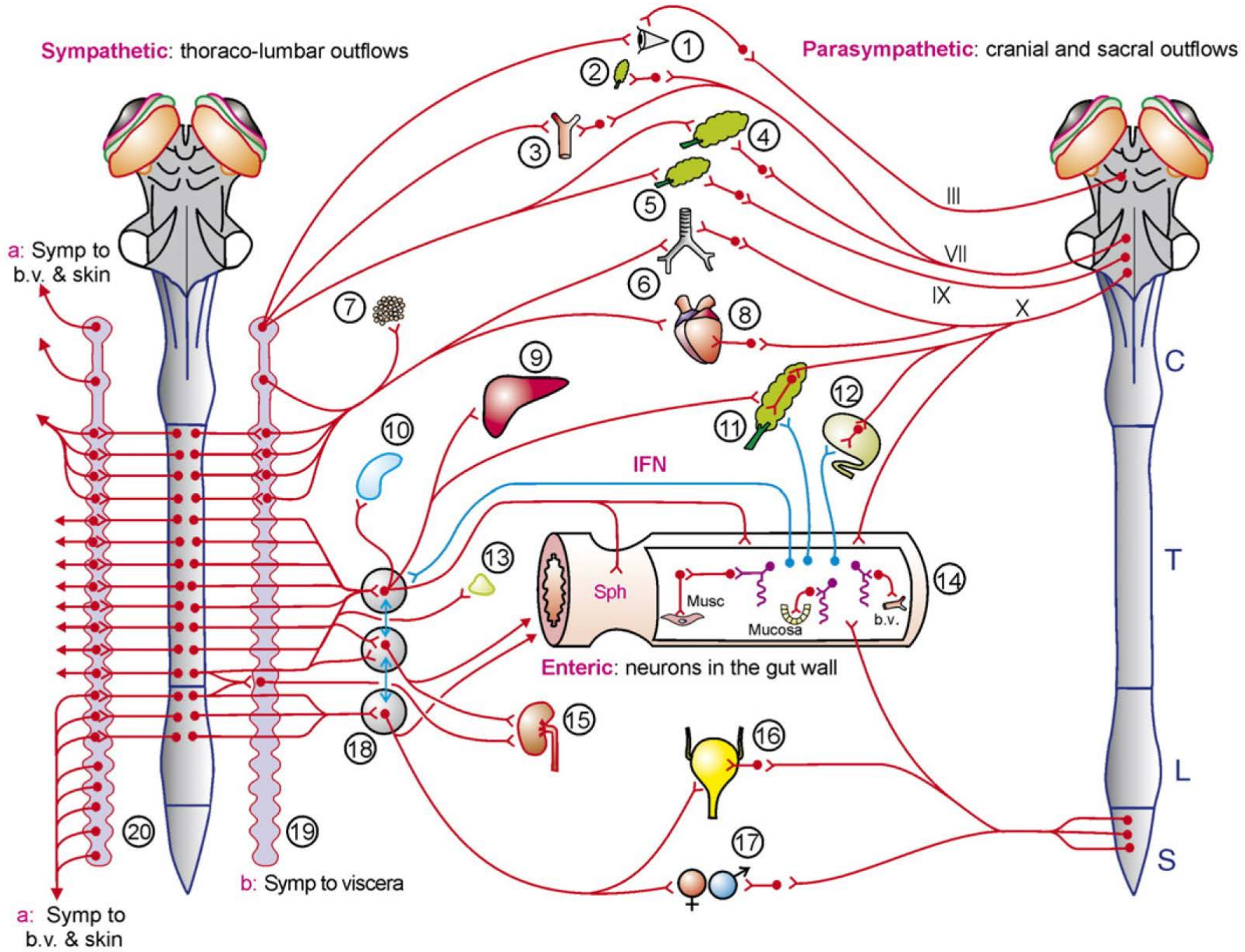
Common Themes:

followed successful open label studies

large sham arm effect

remarkable response in some patients

Autonomic Nervous System



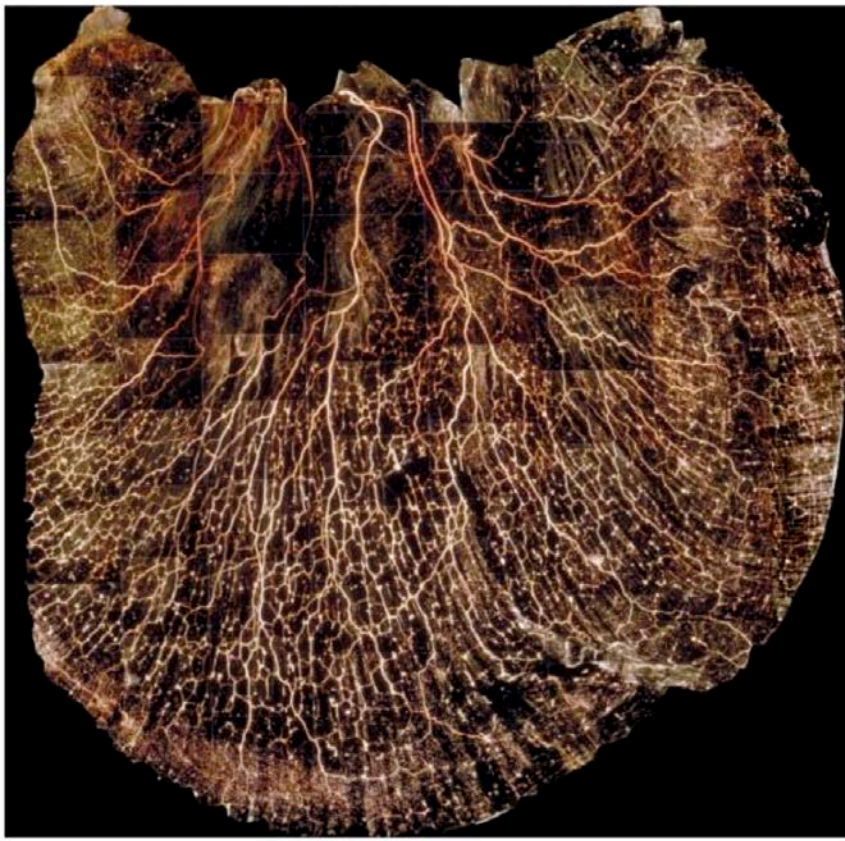
Furness 2006

SPARC - Stimulating Peripheral Activity to Relieve Conditions

Opportunity: Neuromodulation of organ function holds promise in treating many diseases.

Challenge: The mechanisms of action for neuromodulation therapies remain poorly understood.

Program Goals: Provide a scientific foundation that enables better understanding of the neural control of organ function, spurring development of the next-generation of therapeutic closed-loop neuromodulation devices.



~$238 million investment over 7 years

SPARC Components

SPARC1 Anatomical and Functional Mapping of the Innervation of Major Internal Organs

Anatomical and functional neural circuit maps for multiple major organs

Novel electrode designs, surgical procedures, and stimulation protocols

SPARC2 Next Generation Tools and Technologies

Novel and adapted technologies to define PNS control of organ function

Next generation neuromodulation therapies

SPARC3 Use of Existing Market-Approved Technology for New Market Indications

New indications for existing, approved devices

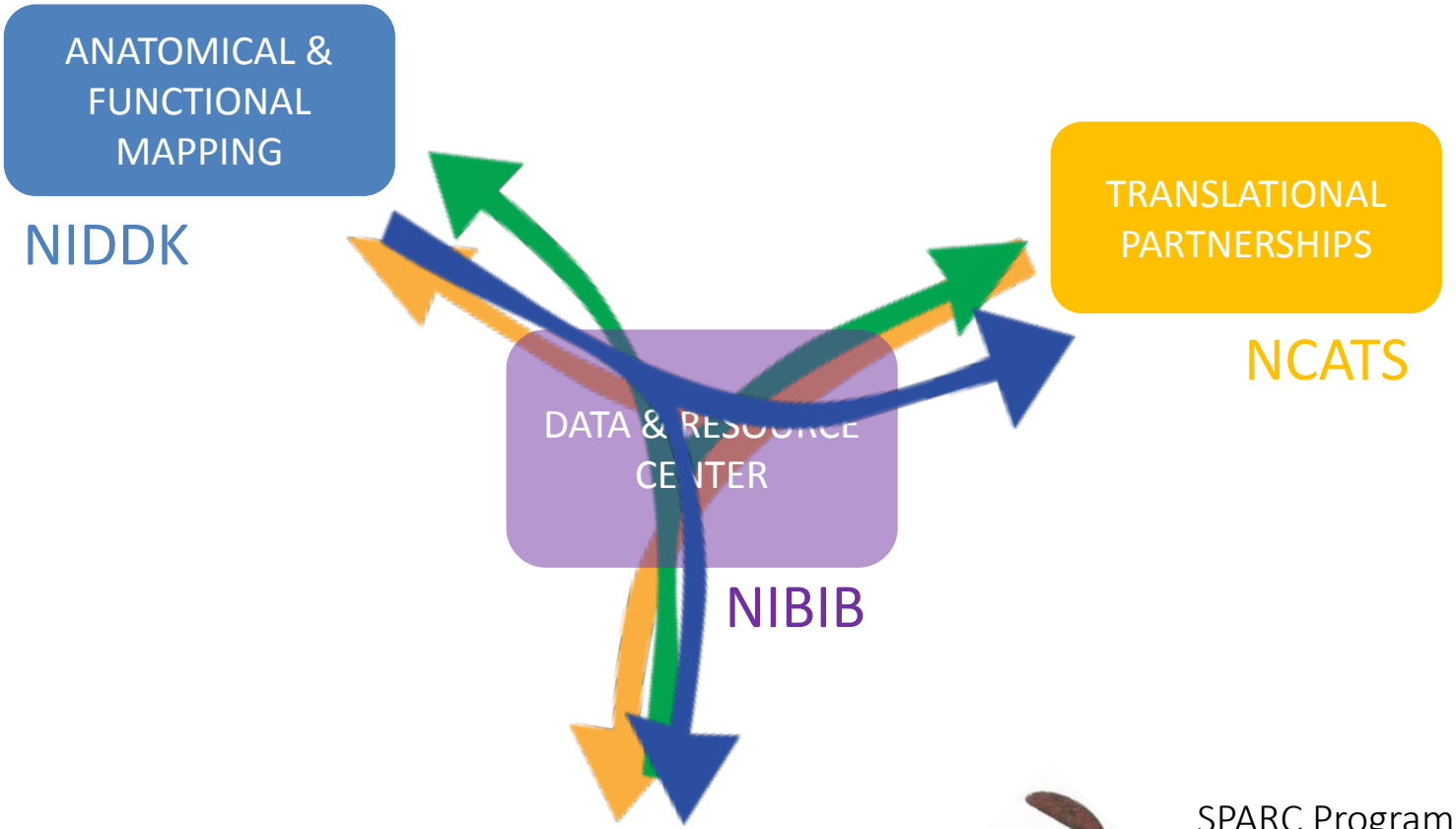
New therapeutic opportunities and methodologies

SPARC4 Data Resource Center (Data Coordination, Mapping, and Modeling)

Public data resource containing SPARC data

Integrated, predictive, anatomical, and functional neural circuit maps

SPARC Components



SPARC Program Manager and Staff set overall vision and make adjustments

Other Transactions

https://commonfund.nih.gov/sparc/OtherTransactions

Unique funding mechanism that is neither a grant, cooperative agreement, nor a contract

Funding Announcement

- Publication on the SPARC website and/or Grants.gov
- Encourages nontraditional partners

Review

- Interactive discussion with Program staff
- New reviewer voices
- Selection of pieces of a proposal
- Reviewer input considered by the SPARC Program Manager in award selection

Award Management

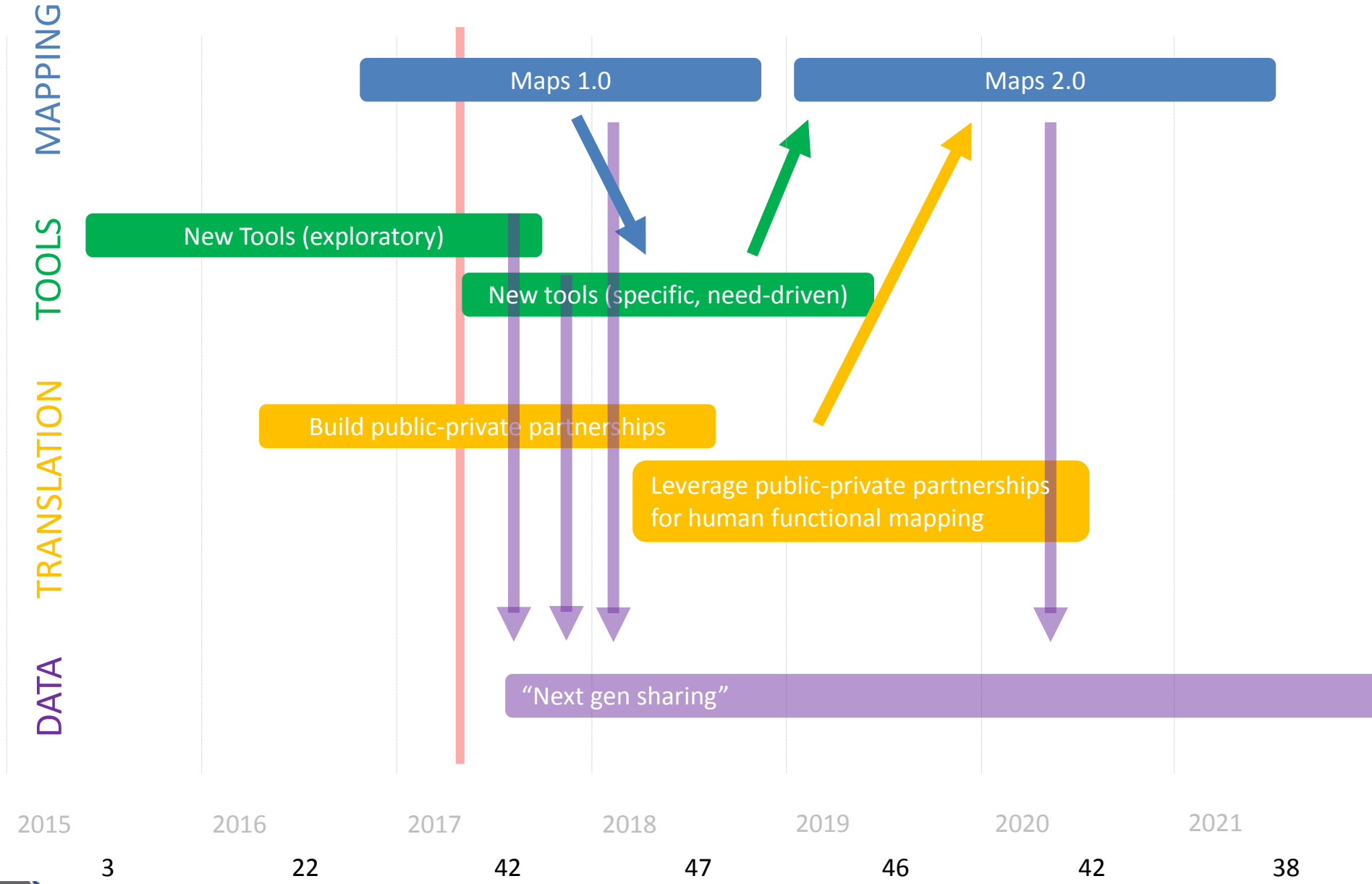
Awarded activity can be:

- Expanded
- Modified
- Partnered
- Not supported
- Discontinued

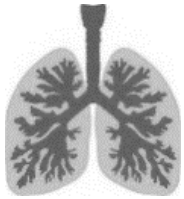
Based on:

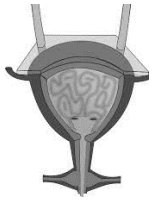
- Program needs
- Emerging methods
- Technologies or approaches
- Availability of funds

SPARC Timeline



SPARC Snapshot, March 2017

ETC

Mapping

Comprehensive (Shivkumar/UCLA)
Auricular branch of vagus (Napadow/MGH)

Superior Cervical Ganglion(Lewis/Case Western)

Comprehensive (Bolser/U FL)
Pulmonary neuroepithelial cells (Sun/UCSD)

Comprehensive (Powley/Purdue)

Comprehensive (Howard/Toledo)
Transcriptome (Southard-Smith/Vanderbilt)
Enteroendocrine cells (Shen/Duke)

Foundational maps (Keast/Melbourne)

Pancreas (Campbell-Thompson/U FL)
Spleen (Campbell-Thompson/U FL)
Adipose tissue (Muenzberg-Gruening/Pennington; Zeltser/Columbia)

Translation

Canning (Hopkins)/Nuviant
Synapse VNS for asthma

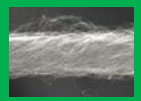
Chen (Hopkins)/Boston Sci
SCS for gastric motility

Yin (Transtimulation)/CVRx
VNS for diabetes

Tools

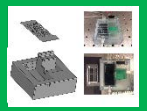
Cardioneural mapping Electrodes (Ardell/UCLA)

Intrafascicular nanowire (Durand/Case)



Rabbit OSA model (Strohl/CWRU)

Ephys/IR mapping (Horn/Pitt)



Implantable gastric platform (Farajidavar/NYIT)

Ultrasound modulation (Okusa/UVA)

Mouse lines for ENS study (Howard/Toledo)

Human GI organoids (Wells/Cinncinnati)

Conformal bladder electronics (Gereau/WashU)

Bladder monitoring (Damaser/Cleveland Clinic)

Spinal root interface (Bruns/U Mich)

Viral bladder tools (Davis/Pitt)

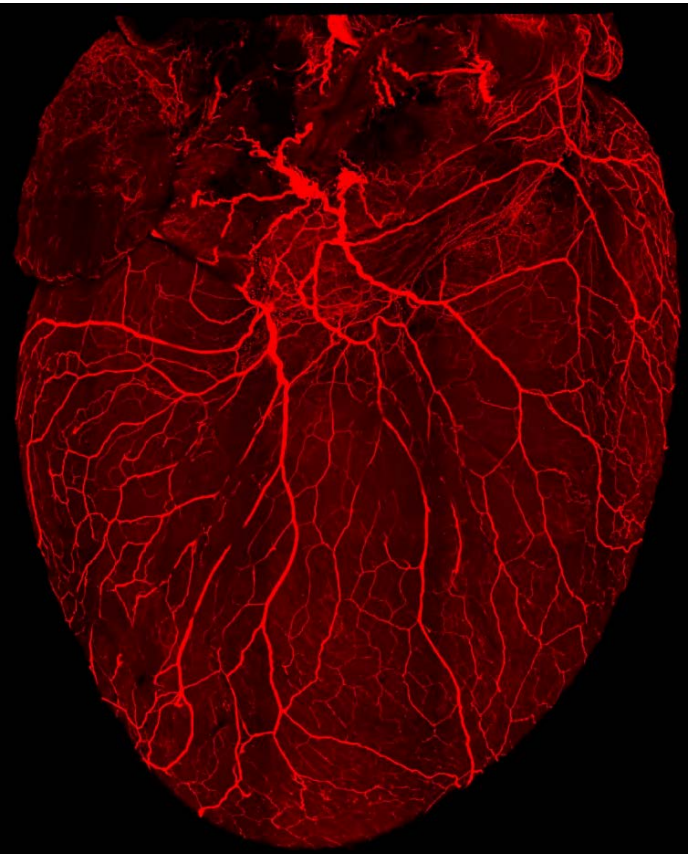
Optical prove (Weir/U Colorado)

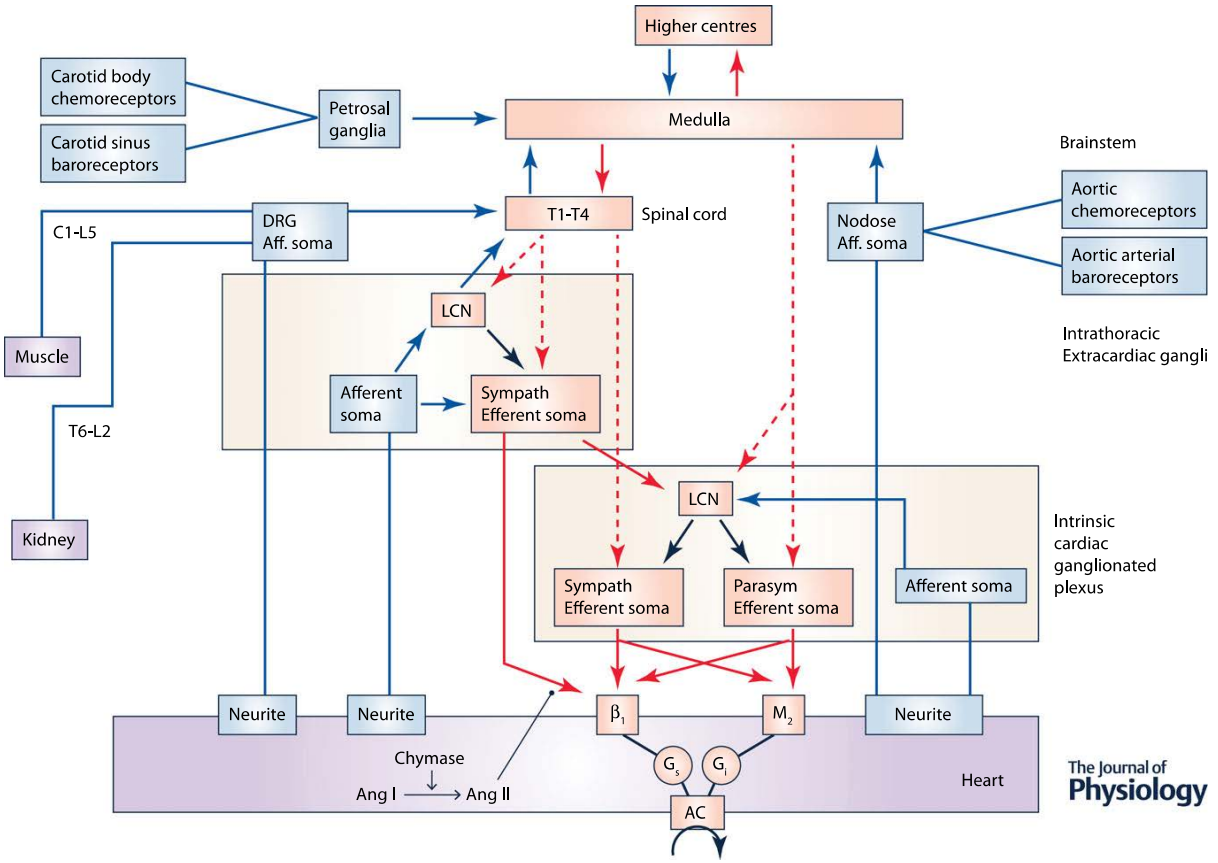
Viral tools (Vulchanova/UMN)

Data

TBD TBD TBD TBD – APPLY!

SPARC1 – Neurocardiac Circuitry
Shivkumar – UCLA

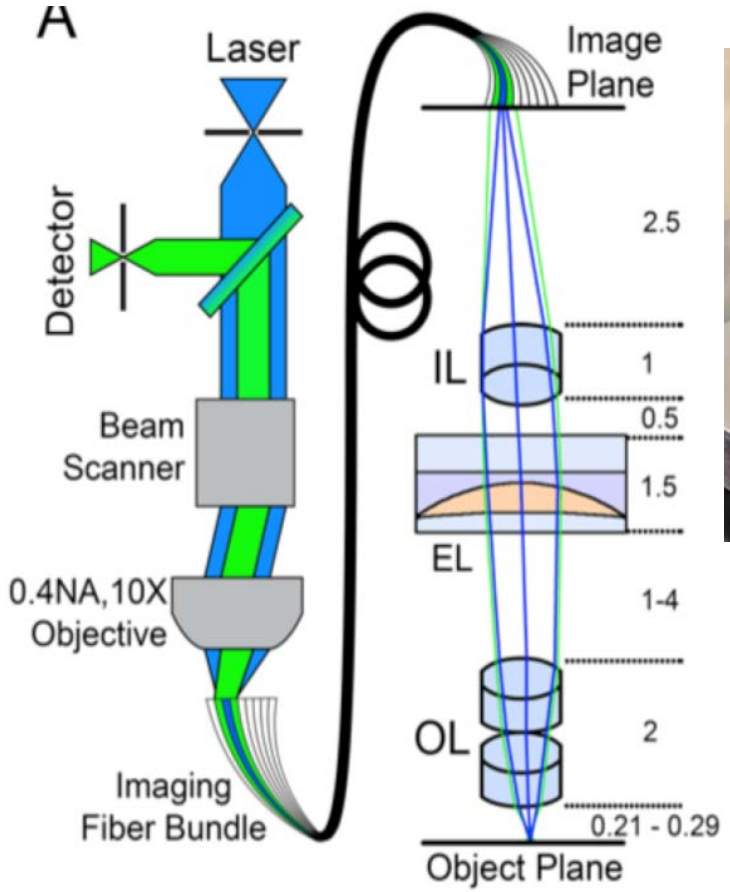




Shivkumar group, UCLA

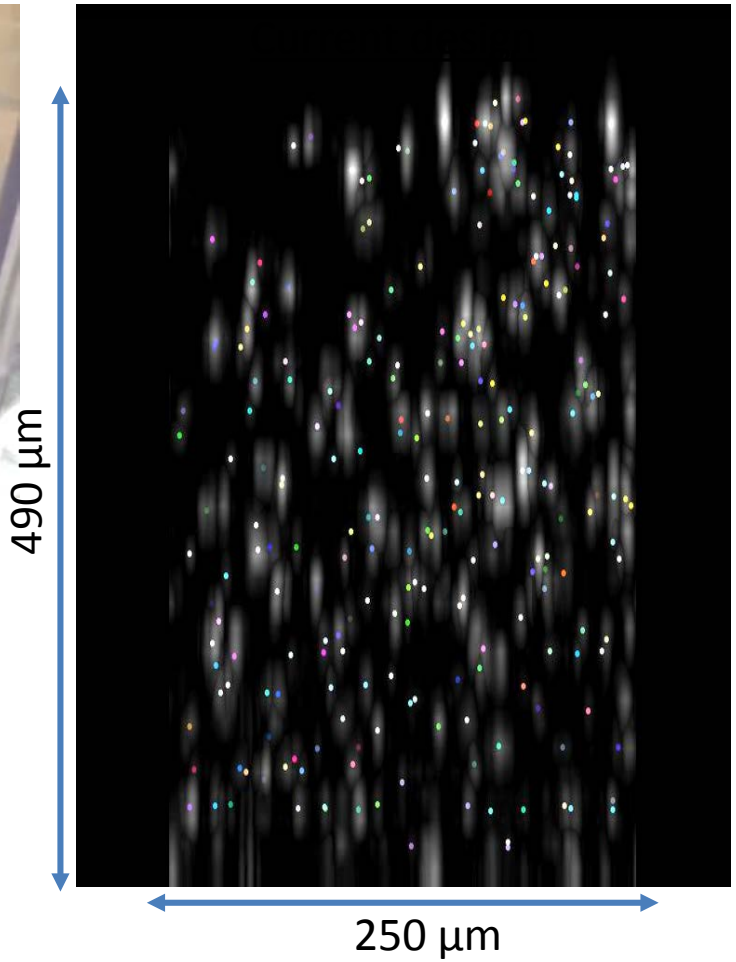
Ardell et al 2016 *J Physiol*

SPARC2 – Miniature Multiphoton Microscope
Weir – U Colorado



Preliminary device

Cells in volume: > 200



http://dx.doi.org/10.1364/OL.40.002553

Collaboration with Prof. Diego Restrepo, Department of Cell and Developmental Biology, Director Center of Neuroscience

SPARC4 – Funding Opportunity

SPARC Data and Resource Center: Data Coordination, Map Synthesis, and Simulation Cores

- RFA-RM-16-008 (OT3)
- **Letter of intent (LOI) is required** and is due by April 7, 2017
- LOIs will be reviewed for programmatic relevance by April 21, 2017. A subset of applicants will be **invited** to submit a written application (due June 2, 2017).
- A subset of applicants who submit a written application will be **invited** to present their applications to an interactive review panel (July 21, 2017), after which awardees will be selected.

SPARC Data and Resource Center

- Serve as SPARC's **central sharing hub**, continuing to exist beyond the end of the SPARC program as a critical resource for neuromodulation target development.
- Host an **interactive atlas** of human and selected animal peripheral nervous systems.
- Allow users to design and place nerve stimuli and observe predictions of their effects at multiple organs, while accounting for user-defined anatomical and physiological parameters.
- Offer a readout of which input uncertainties drive the output uncertainty, providing guidance for where repeated measurements and new experiments are needed.

Data and Resource Center (DRC) Cores

The SPARC DRC will serve as a hub for the research, engineering, and clinical communities, disseminating knowledge and tools to advance neuromodulation of target organs.

The DRC is composed of three Cores:

Data Coordination Core	Store, organize, manage, and track access to data and resources generated by SPARC
Map Synthesis Core	Build interactive, modular, continually updated visualizations of nerve-organ anatomy and function
Modeling and Simulation Core	Develop an online framework capable of hosting and connecting simulations to create predictive, multiscale, multiphysics models spanning from modulation sources acting at feasible access points to organ functional responses

Data Coordination Core (DAT-CORE)

Store, organize, manage, and track access to data and resources generated by SPARC.

- Sample objectives (*see funding announcement for full list*)
  - Store and facilitate access to anatomical and physiological data sets, metadata, protocols, simulation tools, etc.
  - Develop a web portal front-end that provides clear and easy management and retrieval of data and tools from SPARC.
  - Define data standards and implement a process to validate submitted data prior to release.

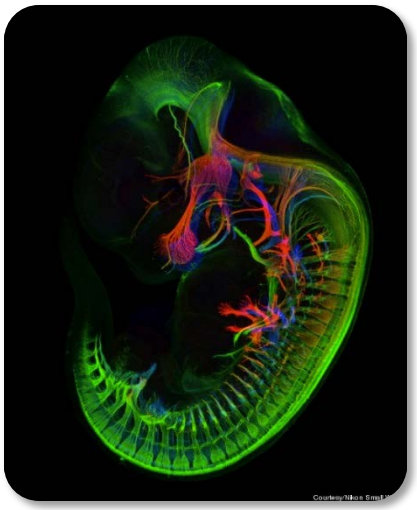
- Applicants should have experience with coordination of large, multi-dimensional, multi-modality data sets; a cloud-first mentality; and openness regarding new models of data management.

upload.wikimedia.org/wikipedia/commons/5/5d/BalticServers_data_center.jpg

Map Synthesis Core (MAP-CORE)

Build interactive, modular, continually updated visualizations of nerve-organ anatomy and function.

- Sample objectives (*see funding announcement for full list*)
  - Develop detailed, functional, and anatomical neural circuit maps of the autonomic and sensory innervation of multiple organs.
  - Produce interactive, multilayered visualizations that span organizational levels from gross organ anatomy to circuit anatomy to cell physiology to gene expression, as appropriate.
- Applicants should have experience in analysis and 3D/4D visualization of heterogeneous data sets, as well as experience developing or adapting ontology and provenance tools.



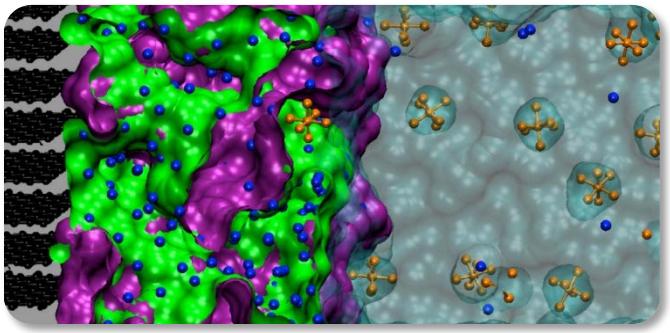
flickr.com/photos/126011099@N05/14809820807/

Modeling and Simulation Core (SIM-CORE)

Develop an online framework capable of hosting and connecting simulations to create predictive, multiscale, multiphysics models spanning from modulation sources acting at feasible access points to organ functional responses.

- Sample objectives (*see funding announcement for full list*)
  - Develop a technical framework to host and connect simulations developed by other SPARC teams.
  - Users should be able to run composite models by specifying a neuromodulation pattern and receiving a predicted organ readout, or by specifying a desired organ readout and intervention point and receiving a neuromodulation pattern.

- Applicants should *not* propose to develop models for individual organs.



Cross-Cutting Responsibilities

All three Cores must:

Coordinate with the other DRC Cores, components 1-3 of the SPARC program, other SPARC Consortium members, and SPARC program partners and collaborators

Support SPARC program data upload and release, as governed by consortia agreements pertaining to sharing and confidentiality and the SPARC Material Sharing Policy

Interact closely with informatics and data science experts from other SPARC-funded teams

Upon completion or termination of the funded work, make all study materials, data, and procedures available to SPARC program staff and to the public

Data and Resource Sharing

Before applying, read the **Material Sharing Policy**
https://go.usa.gov/xX8Hh

Funded projects will be **required** to make SPARC-developed data and technologies available to other projects in the SPARC Consortium, and more broadly to the research community

Application Process

Discuss

- Optional, but encouraged discussion with SPARC program staff.

LOI

- Email letter of intent by **April 7, 2017**
- Must propose to address at least one of the three DRC Cores

Invitation to Submit

- Within two weeks, a subset of LOI applicants will be invited to submit a full OT3 application

OT3 App

- Full OT3 applications are due by **June 2, 2017**
- These applications are invite-only

Invitation to Present

- Within four weeks, a subset of OT3 applicants will be invited to present their applications to an interactive review panel

Present

- By **July 21, 2017**, at least one member from each invited team will give a presentation in Bethesda, MD

Negotiate

- SPARC will negotiate budget, benchmarks, and deliverables with selected applicants

Award

- NIH will award an Other Transaction Award (OT3) after successful negotiation

OT3 Letter of Intent

The LOI is **required** but is not binding

Number and title of funding opportunity

Descriptive title of proposed activity

Core(s) for which application is intended

For each Core:

- Contact information for project lead and affiliation of all key personnel
- Description of **relevant expertise** for key personnel (up to 100 words per person)
- Description of **planned activity** to address the Core objectives (up to 800 words)
- Description of **resources available** to accomplish the activity (up to 500 words)
- If intent is to apply for more than one Core, a description of how the Cores will interact (up to 500 words)

Email to SPARC_Data@mail.nih.gov by **April 7, 2017**

OT3 Full Application

This is not a typical NIH grant application

Cover page (up to 1 page)

Summary vision statement (up to 500 words)

Detailed activity plan (up to 4000 words and 2 figures per Core)

- Applicants encouraged to provide links to videos, demos, and simulations

Letter of institutional support

Letters of support from SPARC Consortium members (optional)

Bibliography (up to 1 page)

Major tasks and milestones (up to 1 page per Core)

Budget (custom format provided in the FOA; not using SF424)

Budget justification

Other Considerations

Budget

- The SPARC DRC budget is currently planned for $10 million over a 5-year period; however, Common Fund procedures and OT mechanisms allow for significant flexibilities to make adjustments that may be needed to pursue catalytic and transformative initiatives.
- Award levels and total budget may increase or decrease over time based on programmatic needs, funding availability and awardee performance.

Period of performance

- Project duration is anticipated to be **5 years**

Evaluation

SPARC uses objective review

Applications will be evaluated for the following:

- Plan for accomplishing the specific objectives of the relevant Core(s)
- Past performance and expertise of the team members and complementarity with other awardees
- Plan for addressing cross-cutting responsibilities

Advice

Read the funding opportunity

Read the funding opportunity

Read the funding opportunity

Clear tasks and milestones

Be specific

Don’t distort reality

Don’t waste pages

Don’t be late

Justify

ASK!

Talk to NIH staff before applying

- Use proper channels
- Visit http://nihsparc.setmore.com to sign up for virtual office hours
- We strongly encourage applicants to discuss concepts with the SPARC team
- We will provide feedback on program fit and suggestions on your concepts

SPARC Contacts and Resources

Office of the NIH Director Team

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