SPARC Workshop

Human Use - Cross-Cutting Technologies – Part II

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Nerve Block/Modulation

- **Temporary Block**: reversible (within seconds to minutes) arrest conduction of action potential along a neuron
- **Modulation**: increase or decrease the excitability of a neuron (or group of neurons)

- **These features are particularly relevant to SPARC applications, because down-regulation is often as important as up-regulation (in contrast to most neuromuscular applications)**

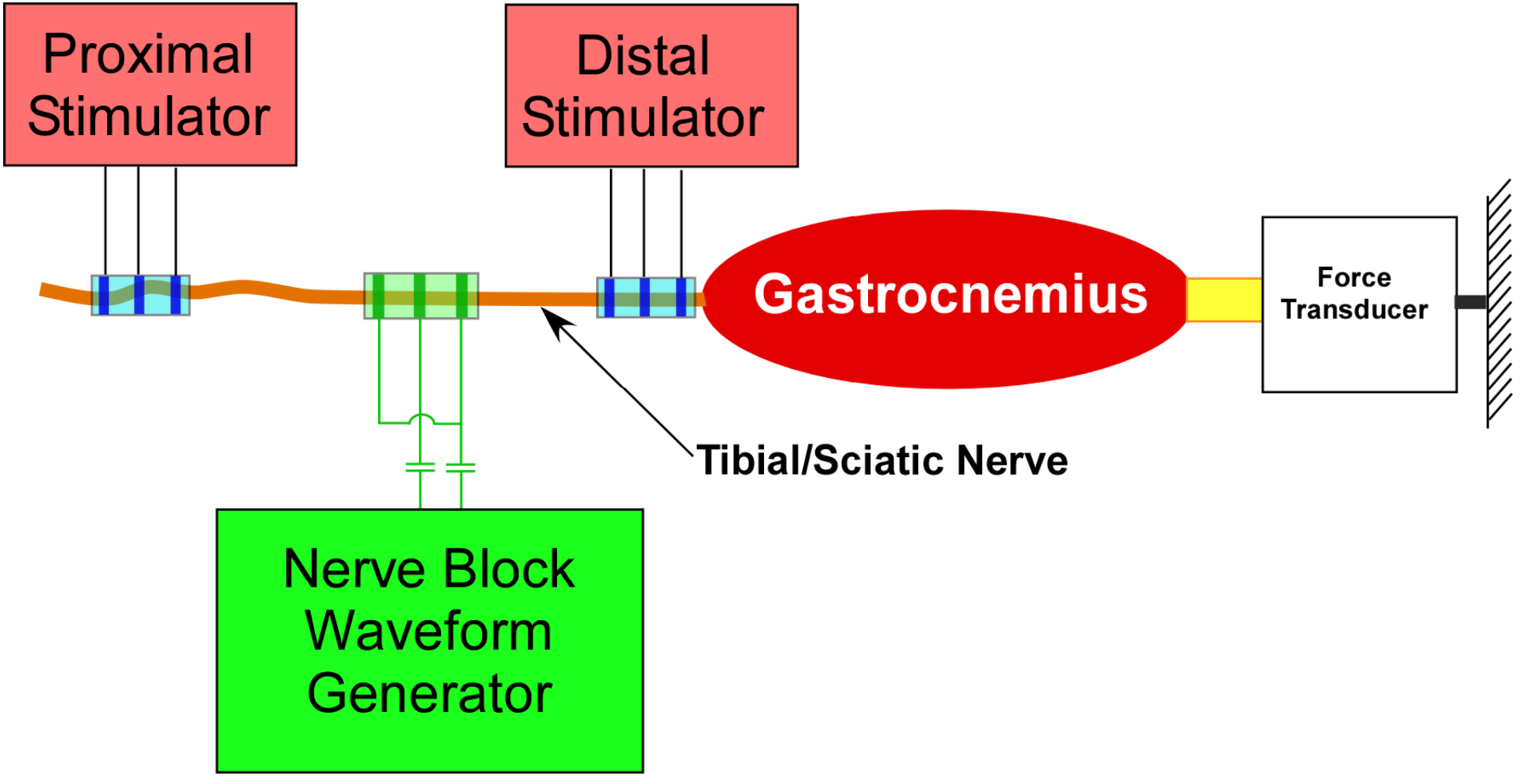
Nerve Block/Modulation

- **Technologies available**
  - Kilohertz Frequency Alternating Current (KHFAC)
  - Direct Current
  - Infrared (thermal) block
  - Optogenetics
  - Magnetic
  - Others…?

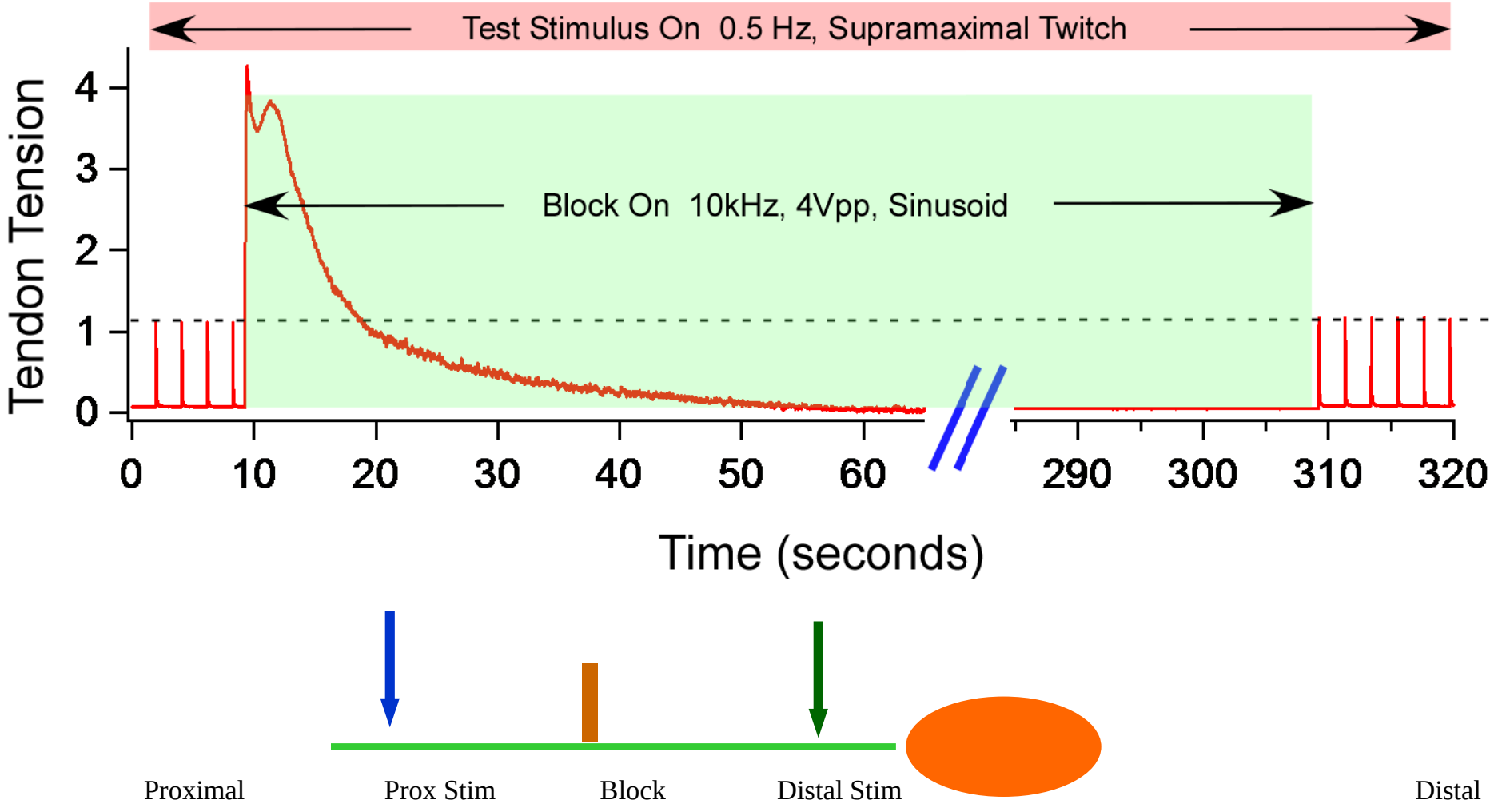
KHFAC – Brief Tutorial

- **Illustrates the difficulties that we face in applying “new” technologies to “not fully characterized” physiology**
  - In contrast to motorneuron->skeletal muscle
- **Illustrates the critical need for clinicians and engineers to work directly together if SPARC initiatives are to be successful**

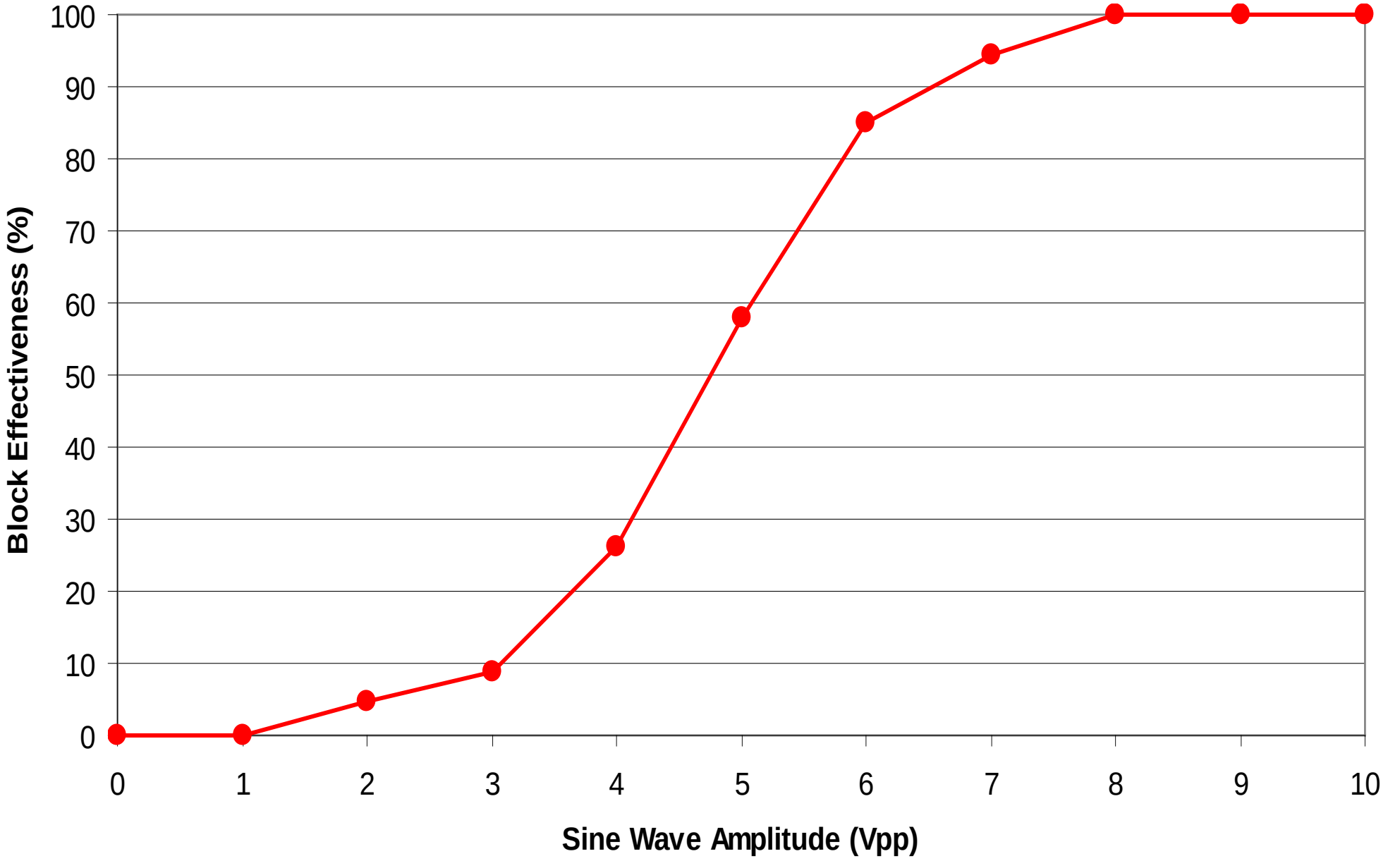
Nerve Conduction Block Experimental Setup



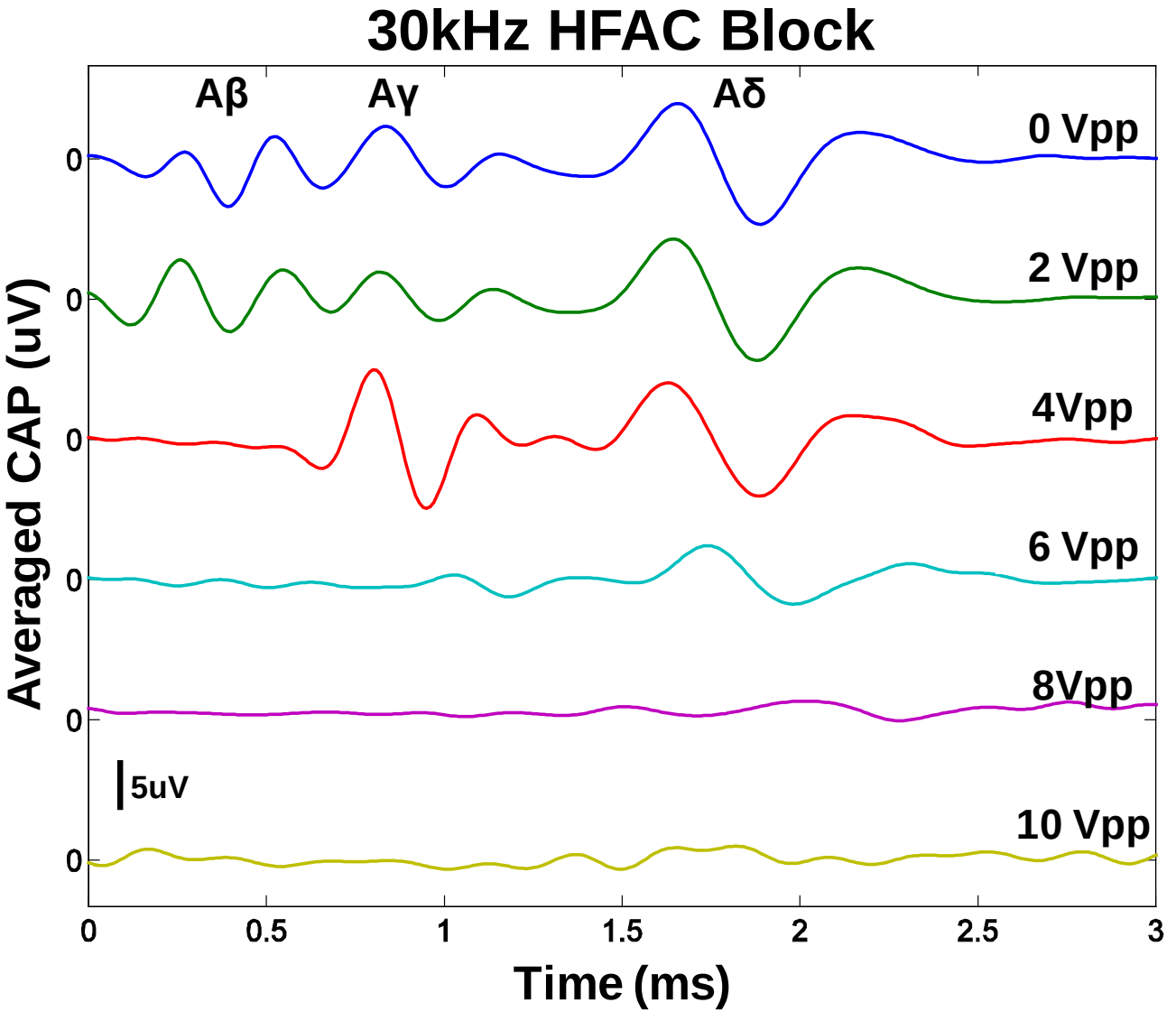
KHFAC Instant Reversibility



KHFAC Graded Block



Block in Sensory Nerve

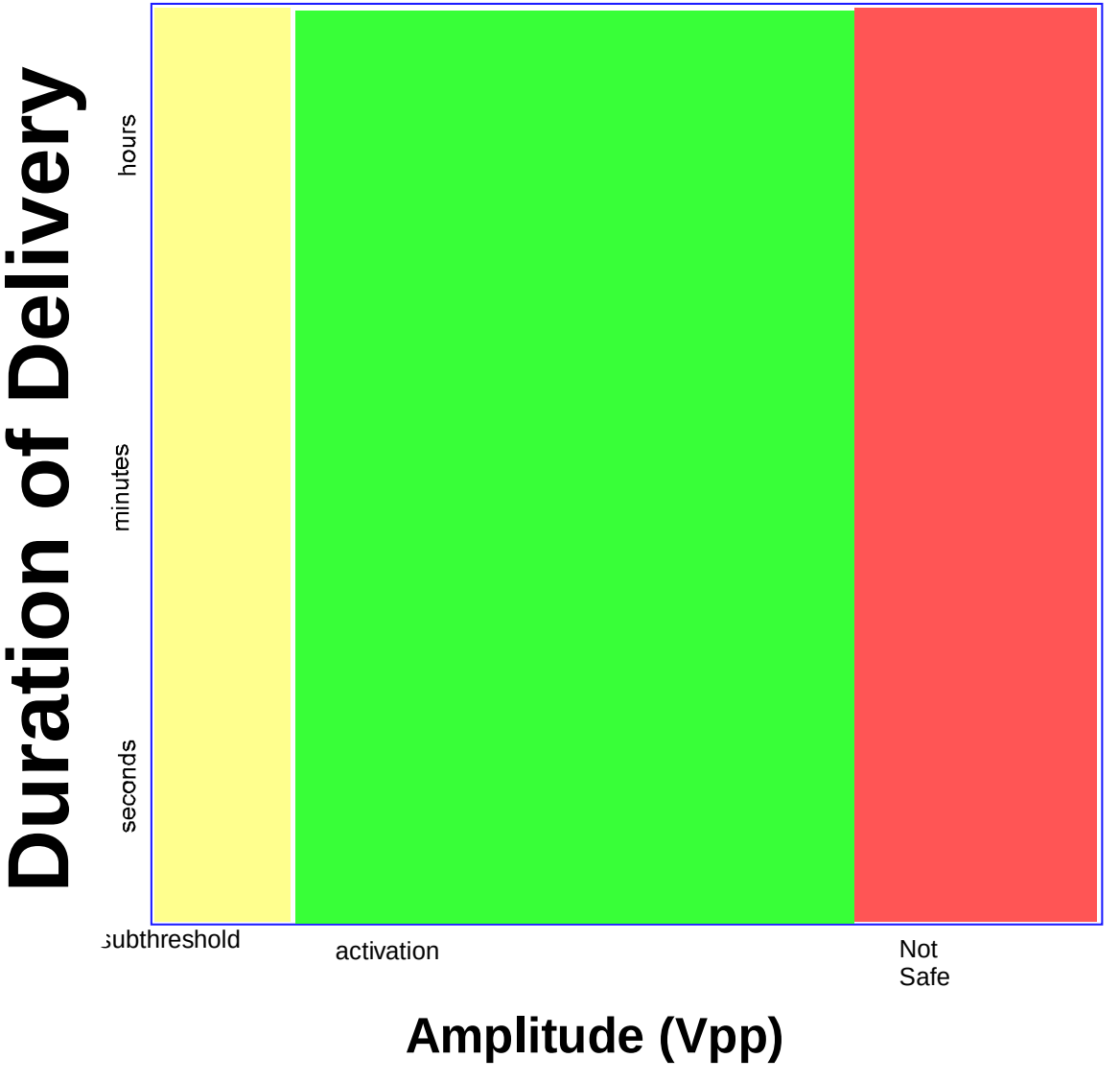


Direct Effect of KHFAC on Neural Structures

- KHFAC can block conduction of action potentials (within 10ms in some cases)
- KHFAC block can be quickly reversible (within 1s)
- Block effect is strongly dependent on amplitude
- At block threshold and above, activation *always* occurs at startup (“onset response”)
- *There is a lot of unexplored territory in this field*
- *Neural response to KHFAC is complex*
- *Almost all of the basic work to date is in myelinated nerves*

20 Hz Stimulation

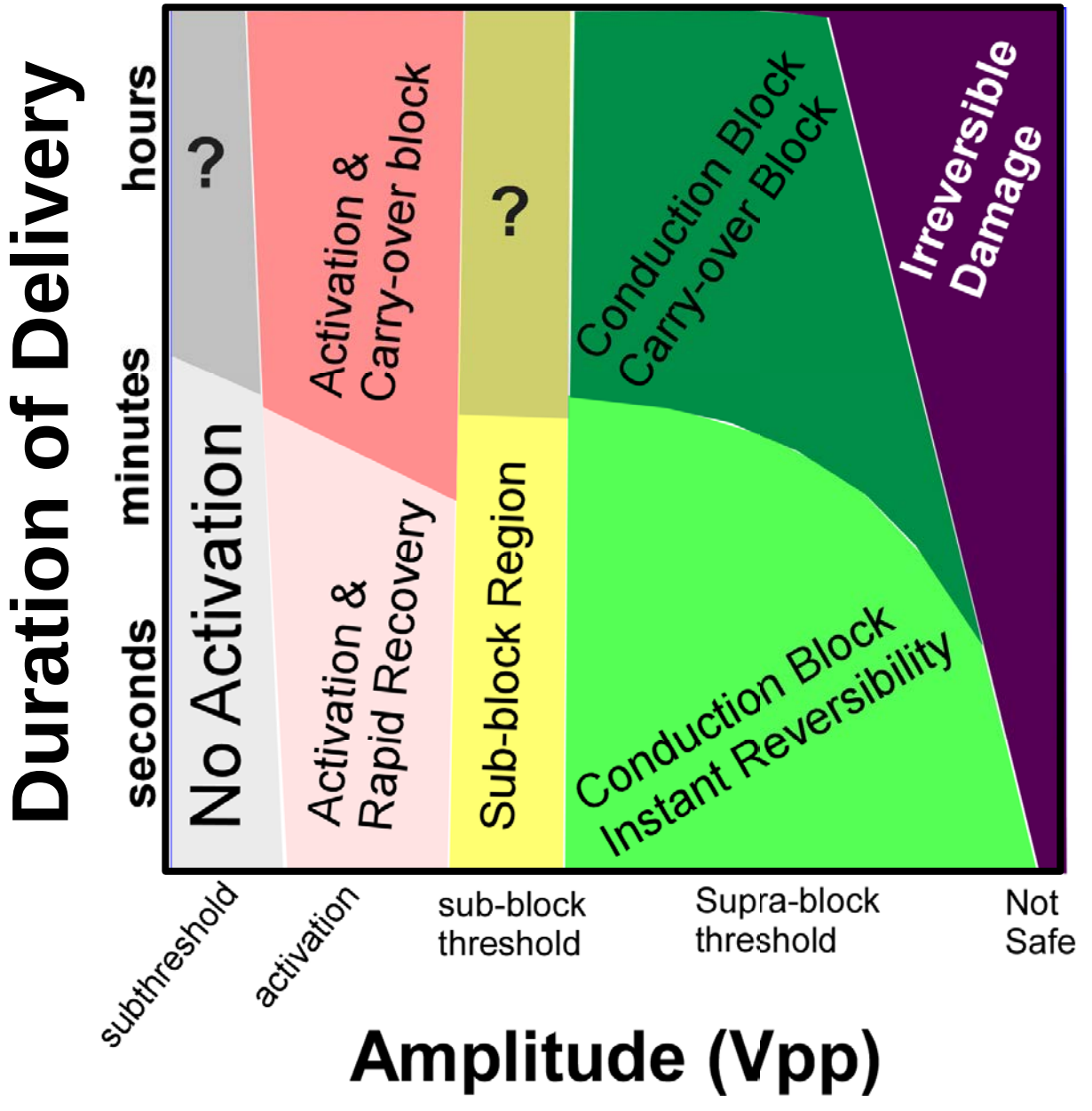
Typical stimulation frequency – neural response is simple and **very well characterized**



Neural Response at ~5kHz and higher

The neural response to KHFAC is extremely complex.

This map only considers the amplitude-time domain!

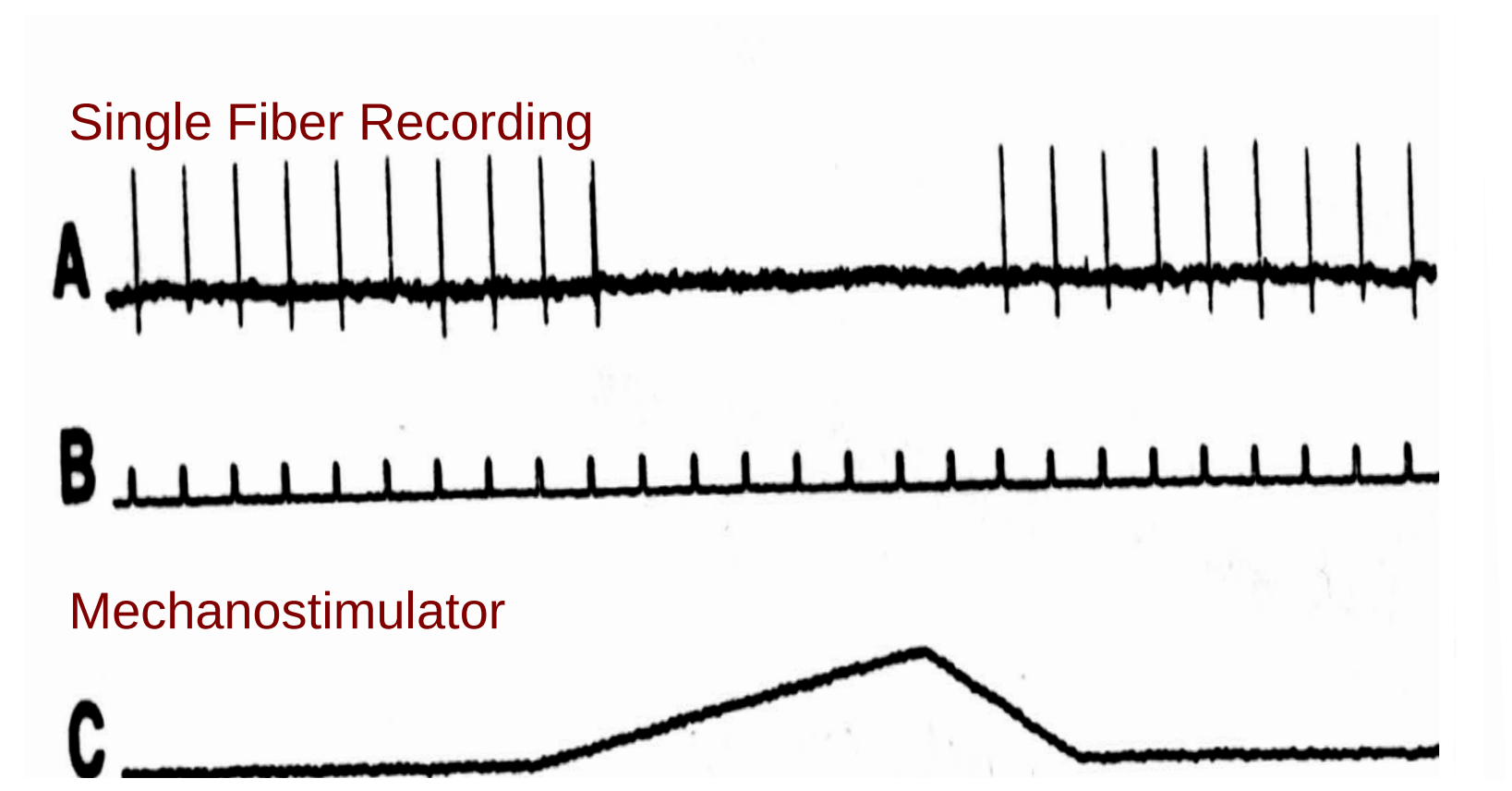


KHFAC Block

- You must know the dose you are delivering
  - *What is the **real** output of the generator?*
- *You must know what the KHFAC is doing to the nerve fibers*
  - *Activated? Blocked? Nothing? Cooked?*
- *Requires a methodical approach*
  - *See Canning/Kollarik approach – start with the simplest system possible and work up to the complete in-vivo system*

DC Block with No Onset Response

Well known in the literature

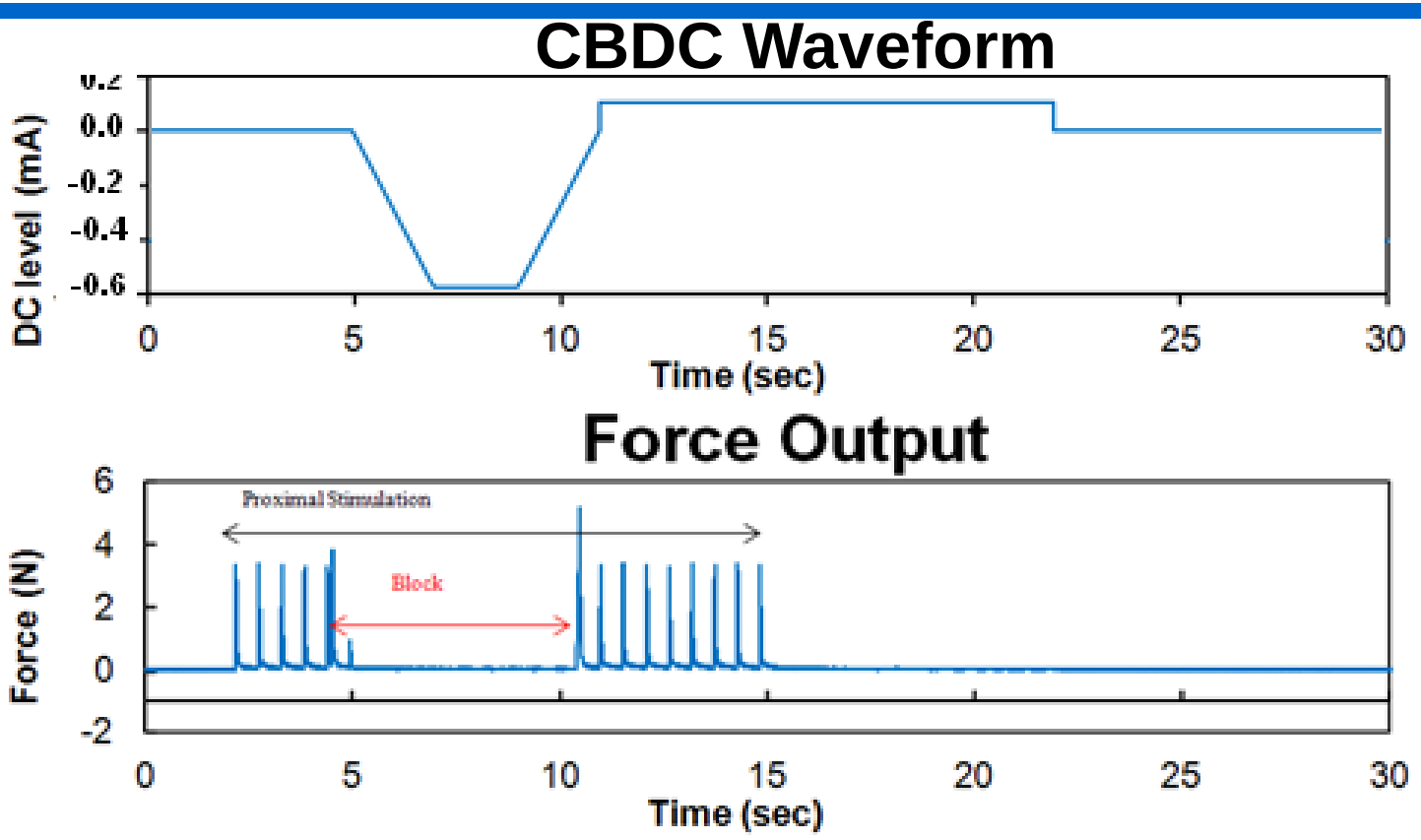


Blocking Stimulus

50μA Amplitude

Petruska, Hubscher, Johnson : Anodally focused polarization of peripheral nerve allows discrimination of myelinated and unmyelinated fiber input to brainstem nuclei. Exp Brain Res 1998.

Considering Direct Current Nerve Block



- ***The current controlled waveform is a charge-balanced direct current waveform (CBDC) consisting of a cathodic blocking phase followed by a anodic recharge phase.***
- ***The total charge delivered was less than the Q value for Pt-Black and IrO_2 electrodes.***
- ***The length of the recharge was selected to return 100% of the charge at a current level of 10% of the cathodic DC.***

Nerve Block and Neuromodulation

- Features Relevant to SPARC
  - Downregulation of neural activity
- Availability and Human Use Status
  - KHFAC – human use
  - Other modalities – animal only
- Areas for Research and Development
  - Consistent and repeatable block
  - Chronic safety
  - Small fiber block (esp. C-fiber)
  - Targeted block of small fibers

Nerve Cuff Electrodes

- **Features Relevant to SPARC**
  - Generally – activate whole nerve/fascicles
  - Generally >1mm diameter nerves
- **Availability and Human Use Status**
  - 10+ years of human use
  - Have been used on vagus
- **Areas for Research and Development**
  - Target <1mm diameter nerve branches
  - Activation of specific fibers sizes
  - Surgical techniques for electrode placement

Implanted Electrodes in Proximity to Nerve

- **Features Relevant to SPARC**
  - Can target nerves of any size
  - Easy to implant
  - Poorly controlled selectivity
- **Availability and Human Use Status**
  - Widely used in humans and widely available
- **Areas for Research and Development**
  - Usefulness and practicality for targeting small nerve branches

Optrodes for Neural Activation

- Features Relevant to SPARC
  - High degree of specificity
- Availability and Human Use Status
  - Not yet available for human use
- Areas for Research and Development
  - Use as tool in animal models?
  - Groundwork for human use (safety, practical designs)
  - Possible unique features, such as activation and block; fiber type selectivity

Non-invasive Neural Activation

- Features Relevant to SPARC
  - Non-invasive
  - Poor specificity
- Availability and Human Use Status
  - Low threshold for human use
- Areas for Research and Development
  - Possibility of activating autonomic neural structures from skin surface

Sensor Modalities

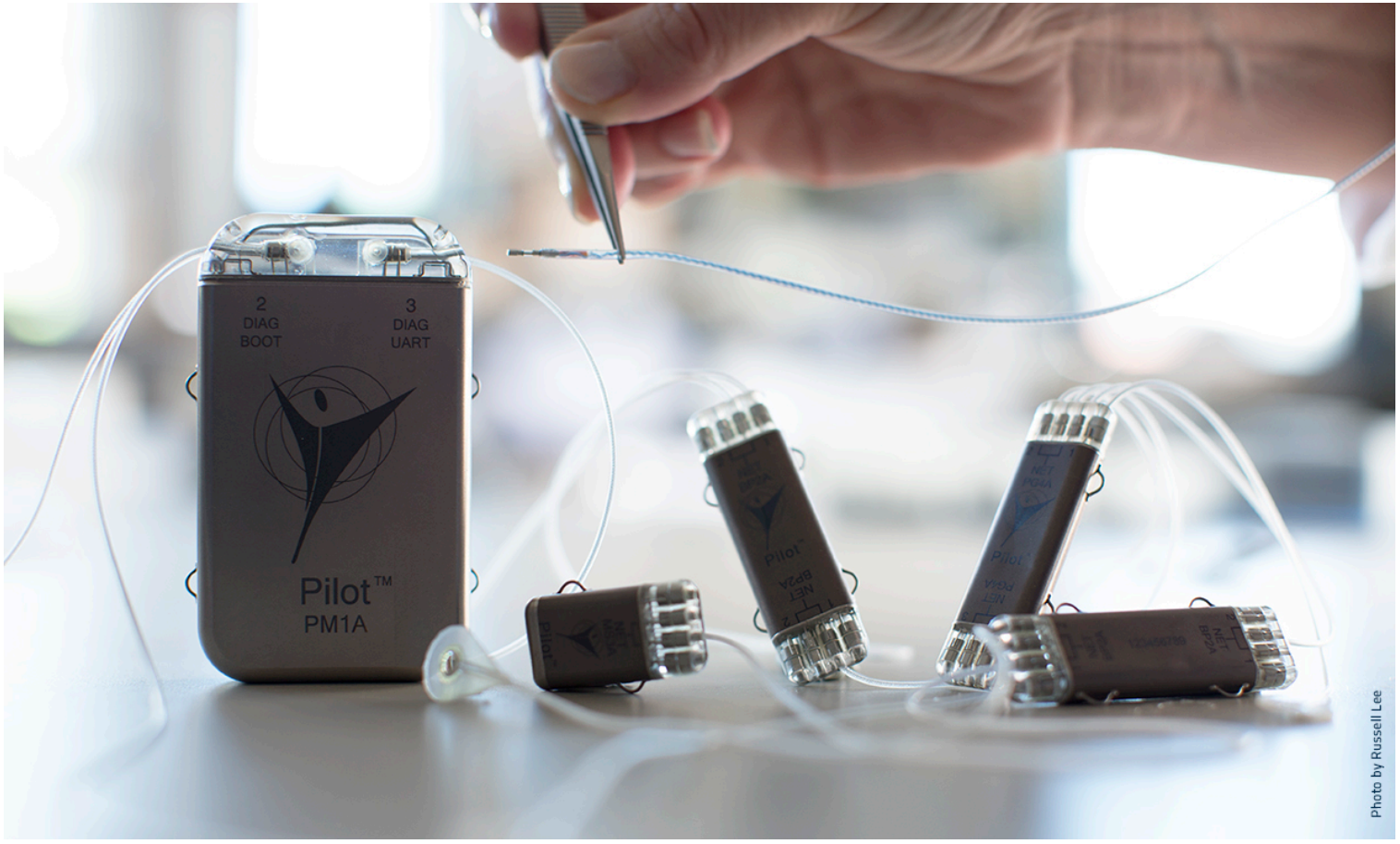
- **Blood Pressure/Bladder Pressure**
- **Biomarkers of various sorts**
- **pH**
- **Ions**
- **Cardiac output**
- **Airway resistance**
- **Glucose**
- ***More to come…***

Sensor Systems

- Features Relevant to SPARC
  - Most systems will require regulation to a mean, not to an extreme
- Availability and Human Use Status
  - Few have extensive human use
- Areas for Research and Development
  - Identify important modalities
  - Chronic efficacy of sensors
  - Accuracy of sensor data
  - Incorporation into complete system

Implant Systems

- **Stimulators**
- ***Stimulator/sensor systems***
- ***Modular systems***



Implant Systems

- Features Relevant to SPARC
  - In many cases, will require stimulation, block, sensing, and signal processing
- Availability and Human Use Status
  - Some have extensive human use
- Areas for Research and Development
  - Identify system requirements
  - Regulatory requirements

Cross-Cutting Technology Summary

- Technologies for Activation
- Technologies for Block/Modulation
- Sensor Technologies
- System Technologies
- Signal Processing
- Computational Modeling