R00002 - 12/4/2023 Technical Review

1.0 Document Purpose

This document serves as a review for management review, engineering changes, or design reviews for things pertaining to the QMS.

2.0 Document Scope

This document applies to the COSMIIC research organization and the review of all COSMIIC QMS activity. All reviews will be dictated by the *SOP0003 - Design Control Procedure* and *SOP0001 - Quality Manual*. Text that is not applicable to the review type selected can be omitted.

3.0 Review Form

Review Date: 12/12/2023

Review Type: *mark one*	**[ ]** Design Review *(Independent Reviewer required)* **[X]** Technical Review **[ ]** Phase Review for <phase name> **[ ]** Risk Analysis Review **[ ]** Management Review **[ ]** Other:
Review Purpose or Title:	Technical review of each of the nests in the development process
Item(s) under Review (Scope):	Review Slides from each nest review
Agenda:	Wing Nest Review Swarm Nest Review Hive Nest Review Nectar Nest Review

Participants, Function or Title
Kevin Kilgore, Review Chair
Michael Fu, Nest Lead
Tina Vrabec , Nest Lead
Cindy Chestek, Nest Lead
Nathan Makowski, Nest Lead

Instructions to Reviewers

General items:

Assess the design and the design results

Provide feedback to designers on opportunities and existing or emerging problems

Assess design progress and maturity and suggest recommendations and follow-up activities

Have the appropriate tasks and expected results, outputs, or products been established for the design(s) or activity under review at this phase / life cycle?

Do the tasks and expected results, outputs, or products of the design(s) or activity under review comply with the relevant requirements of other designs or projects in terms of correctness, completeness, consistency, and accuracy?

Do the tasks and expected results, outputs, or products of the design(s) or activity under review satisfy the standards, practices, and conventions for the design or activity?

Do the tasks and expected results, outputs, or products of the design(s) or activity under review establish a proper basis for initiating tasks for the next activity for the design under review?

Design Input (requirements specifications):

Do the requirements address the intended use of the device, including the needs of the user and/or patient?

Do the requirements adequately address the relevant safety and performance standards?

Do the requirements adequately address hazards/hazardous situations and risk controls?

Do the requirements adequately address human factors/usability?

Education and skill level (healthcare professional, lay person)

Type and diversity of users (age, gender, comorbidities, etc.)

Users' limitations: visual, auditory, acuity, dexterity, strength?

What type of training will the user receive?

How busy is the user and potential distractions?

Use environment(s): indoor/outdoor, complexity & other equipment, etc.

Hazards associated with use errors?

Are there incomplete, ambiguous, or conflicting requirements? Is the means to resolve any such issues understood?

Are the requirements verifiable through objective inspection, analysis, demonstration and/or test methods?

Design Output (drawings, code, labeling content, etc.):

Does the design output adequately address the relevant design inputs?

Do test results demonstrate that the design output conforms with the relevant design inputs?

Are the design outputs essential to the safe and proper functioning of the device identified; e.g., critical/inspection dimensions, inspection criteria, test criteria?

Attachments *Attach items to this record that are not separately released, such as draft documents*

WING Slides [COSMIIC WING design review Jan 2023 (Y1Q1).pdf]

SWARM Slides [SWARM Design Review 1.17.23.pdf]

HIVE Slides [HIVEPresentation.pdf]

NECTAR Slides [20230321 Design Review- notes.pdf]

WING- Wearable Interoperable Neuroprosthetic Gear

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"WING" – Wearable Interoperable Neuroprosthetic Gear

Aims:

- Aim 1: Develop a wearable Wireless Link for PCs, mobile devices, and sensors.
  - This Wireless Link will facilitate wired or wireless communication between the COSMIIC implanted modules and PCs used to program the modules, external sensors (EKG, PPG, inertial, etc.), external stimulators (developed in Aim 2) or actuators (assistive devices, connected appliances, wheelchairs, etc.) using common wired (USB, I2C, SPI, CAN) and wireless (WiFi, ZigBee, ANT) protocols. This Wireless Link can also become wearable by configuring a battery to power sensors and facilitate closed-loop stimulation in response to physiological signals or smartphone app visualization. The Wireless Link allows an existing implanted COSMIIC System to be enhanced with external components for research exploration and evaluation.
- Aim 2) Develop an expandable wearable Surface Stimulation module.
  - This battery-powered, four-channel stimulator will receive stimulation commands wirelessly from other COSMIIC modules and apply electrical stimulation to the skin surface, which is a low-risk and convenient way to prototype new stimulation functions. Multiple Surface Stimulation modules can be linked together wirelessly to increase the number of channels.

“WING” – Wearable Interoperable Neuroprosthetic Gear

Aims:

- Aim 3) Develop circuit board Evaluation Kit for COSMIIC modules.
  - These devices allow COSMIIC modules to function without implant-grade titanium enclosures or implant-grade connectivity to facilitate benchtop development. Electronic frames will be developed that house bare COSMIIC module circuit boards, supply network and power, and provide access to useful debugging connections.
- Aim 4) Develop a closed-loop rapid inductive battery charger.
  - The COSMIIC charger will be able to reduce charging time over the existing NNP charger by optimizing cooling and current flow based on battery status.

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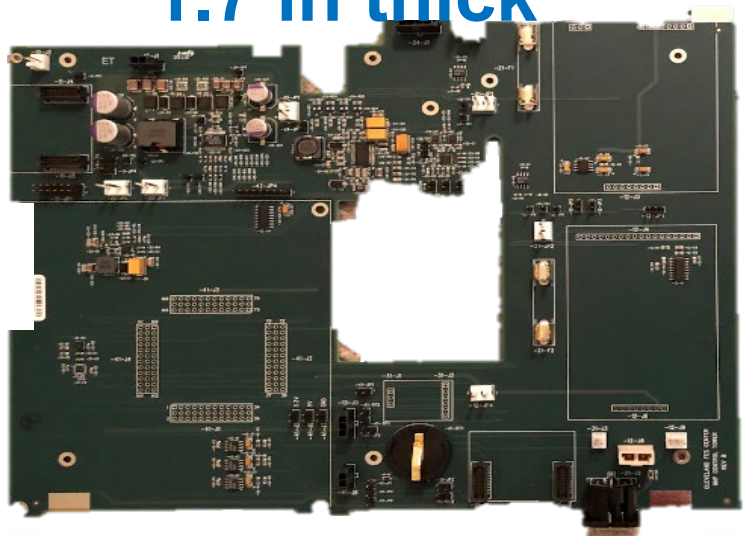
Existing External Devices

Control Tower (CT)

1.7 in thick



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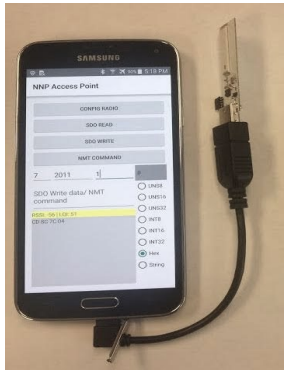
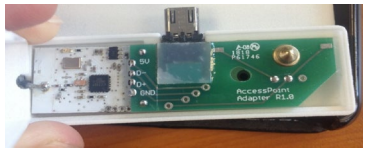
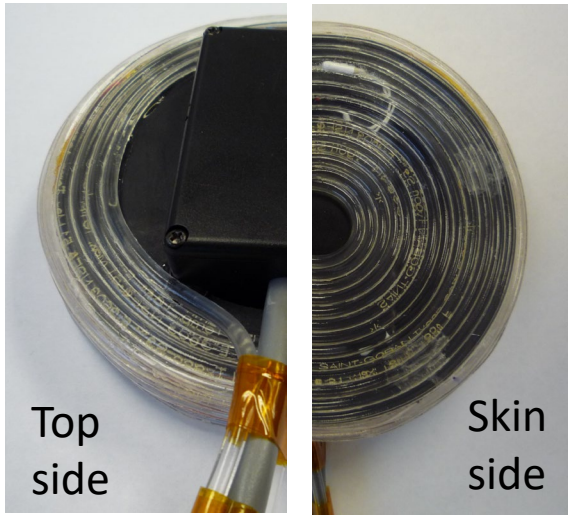




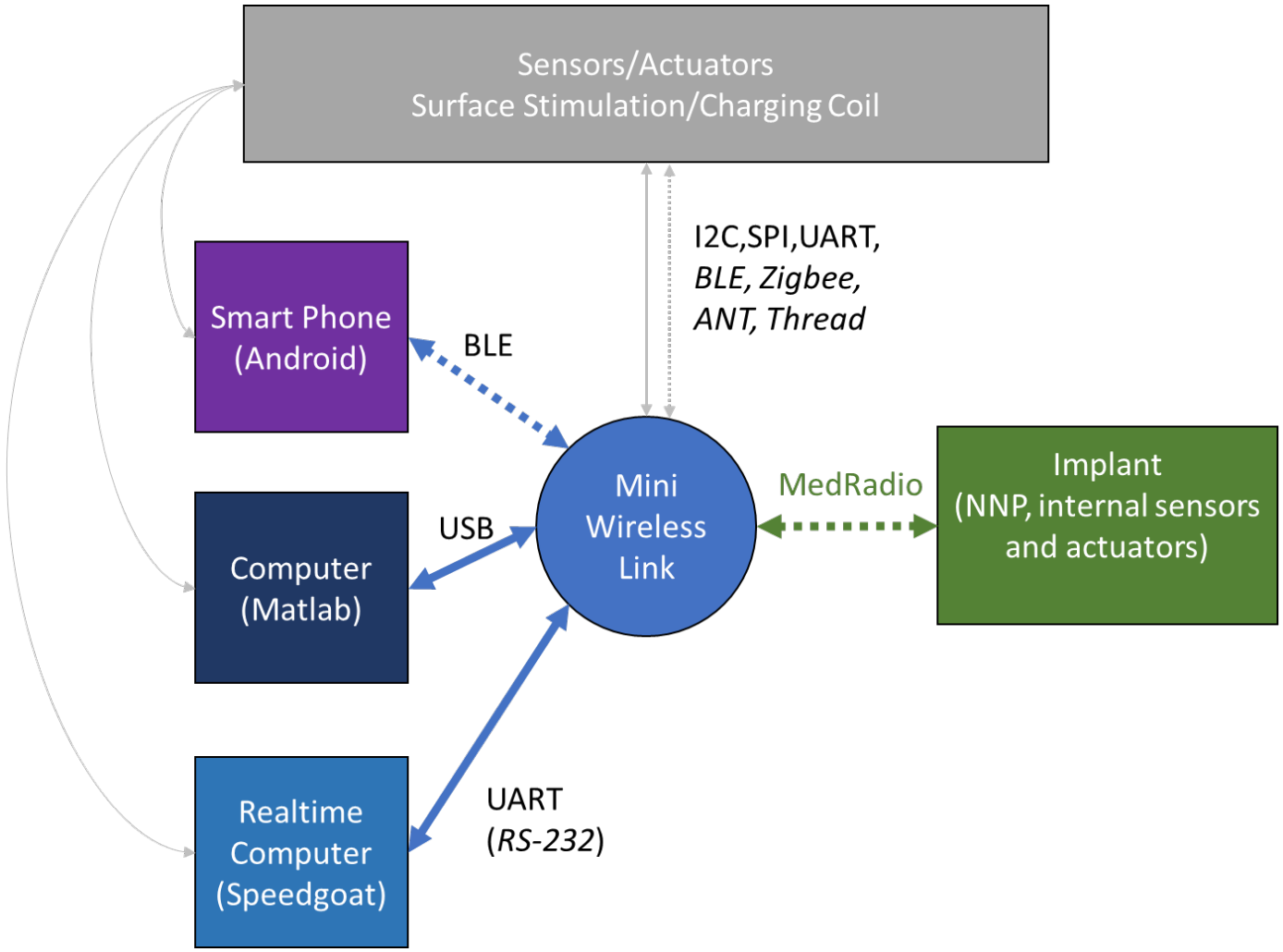
External Coil



"WING" – Wearable Interoperable Neuroprosthetic Gear

Wireless Link:

- Communicates between implanted modules and external components
- Wired or wireless communication to PCs, smartphones, sensors
- Enables module programing, visualization
- Battery power for mobile use
- Common wired (USB, I2C, SPI, CAN) and wireless (Bluetooth, MedRadio) protocols



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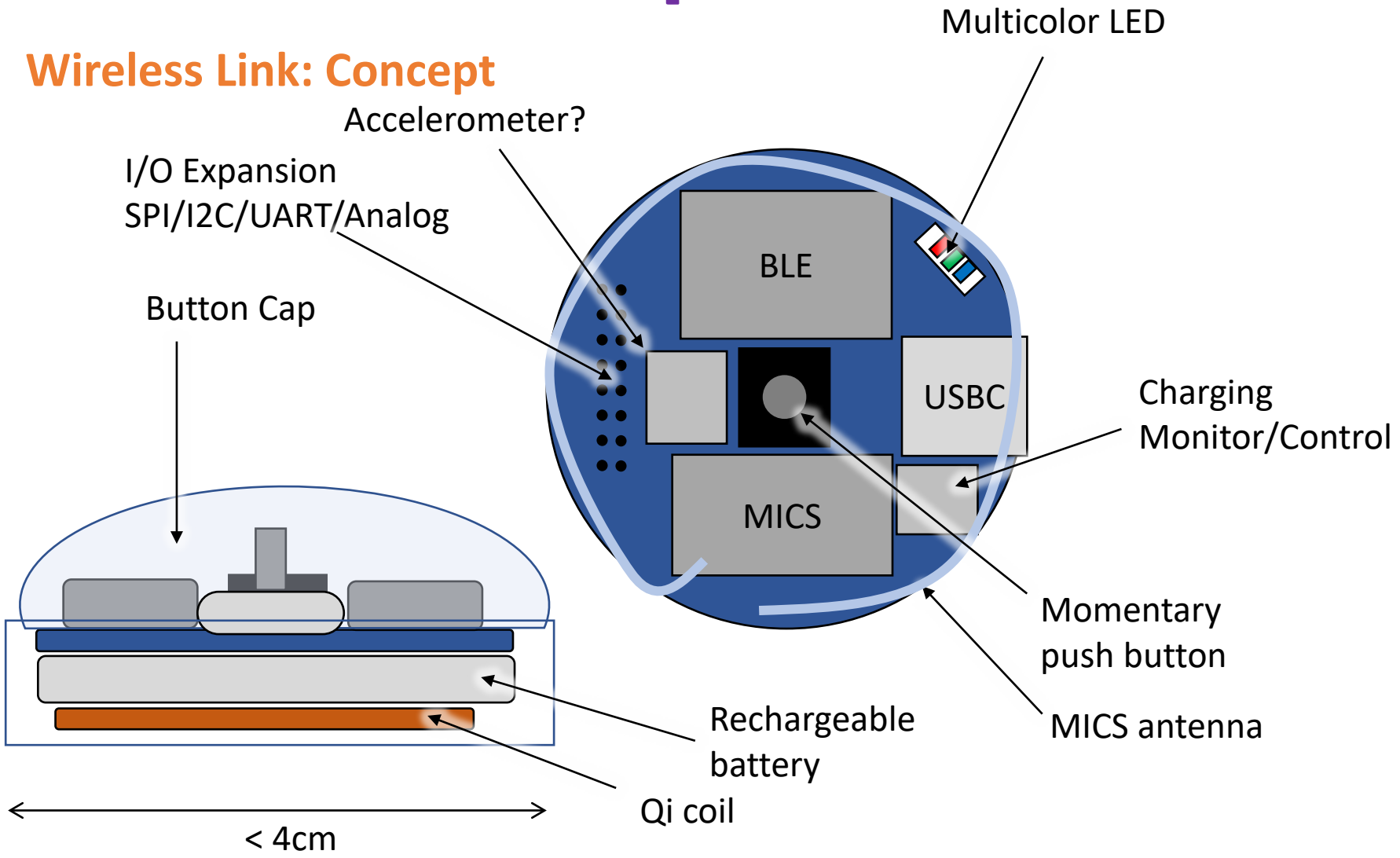
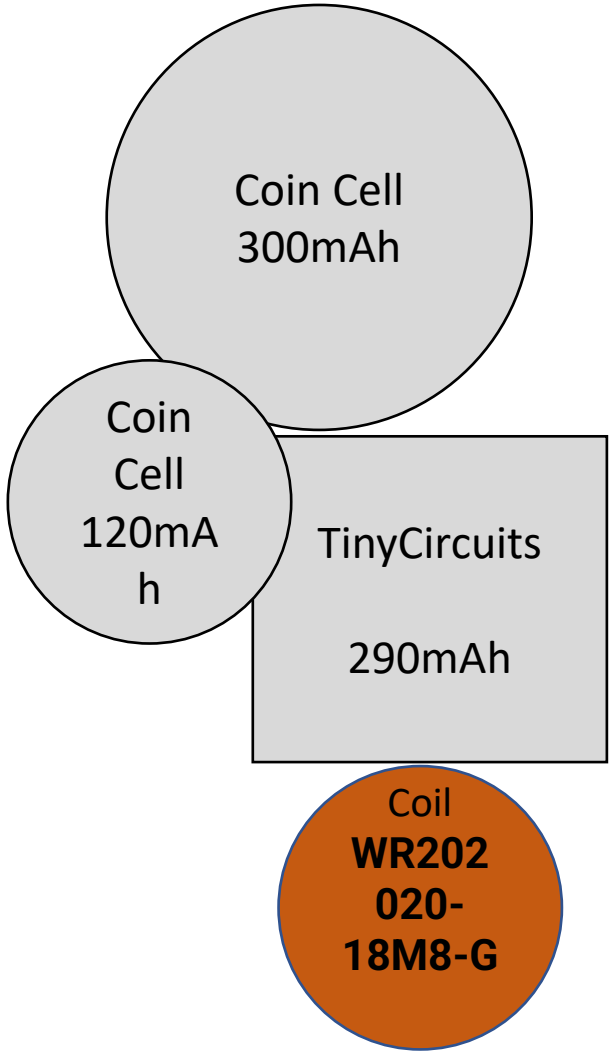
Wireless Link: Concept





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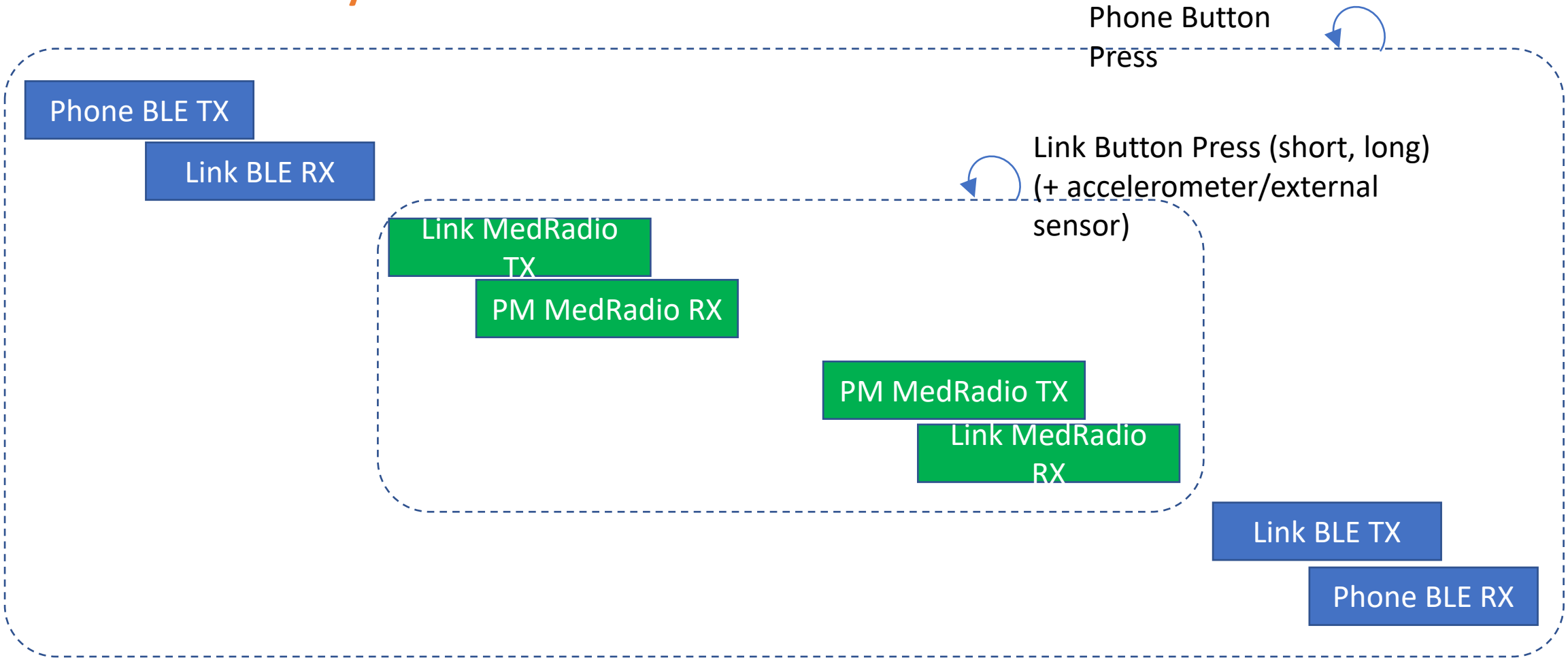
Wireless Link: Primary Function



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Wireless Link: Requirements

•Device Power Supply Requirements

- The device shall have the ability to be powered by an alternating current (AC) adapter.
- The device shall have the ability to be powered by a USB power supply.
- The device shall have the ability to be powered by a [rechargeable] battery.
- The device shall have the ability to recharge [its] battery.
- The device’s power supply interface should be accessible by people with disabilities by using inductive power delivery (Qi standard) or magnetic connectors for AC adapter or USB power.
- The device shall supply power to wired electronic components or sensors.

•Device Enclosure Requirements

- The device enclosure shall have at least one user interface switch.
- The device enclosure shall have at least one visual indicator.
- The device enclosure should have a wired sensor interface port.

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Wireless Link: Requirements

•Device System Board Requirements

- The device’s system board shall support wireless radio communications over Bluetooth (2.4 GHz) and implant-compatible communications over Medical Device Radiocommunications Service (MedRadio, 402-405 MHz).
- The device system board shall support wired communications over SPI, I2C, and UART protocols.
- The device system board shall support analog input from wired electronic components or sensors.
- The device system board shall have an expansion port to interface with wired electronic components or sensors.
- The device system board shall have a USB interface for firmware or software programming and computer control of device functions.

•Device Software Requirements

- The device shall have a software application programming interface (API)
- The software API shall define how to control the device and use it to issue commands to and acquire data from implanted devices, electronic components, and/or sensors that it communicates with.
- The device API shall be compatible with mobile computing devices for the purposes of data visualization or device control via wired or wireless communication.
- The device shall have firmware that is able to execute software programs in a stand-alone mode without being connected to a computer.

The device API shall have a method to restrict pairing to authorized devices.

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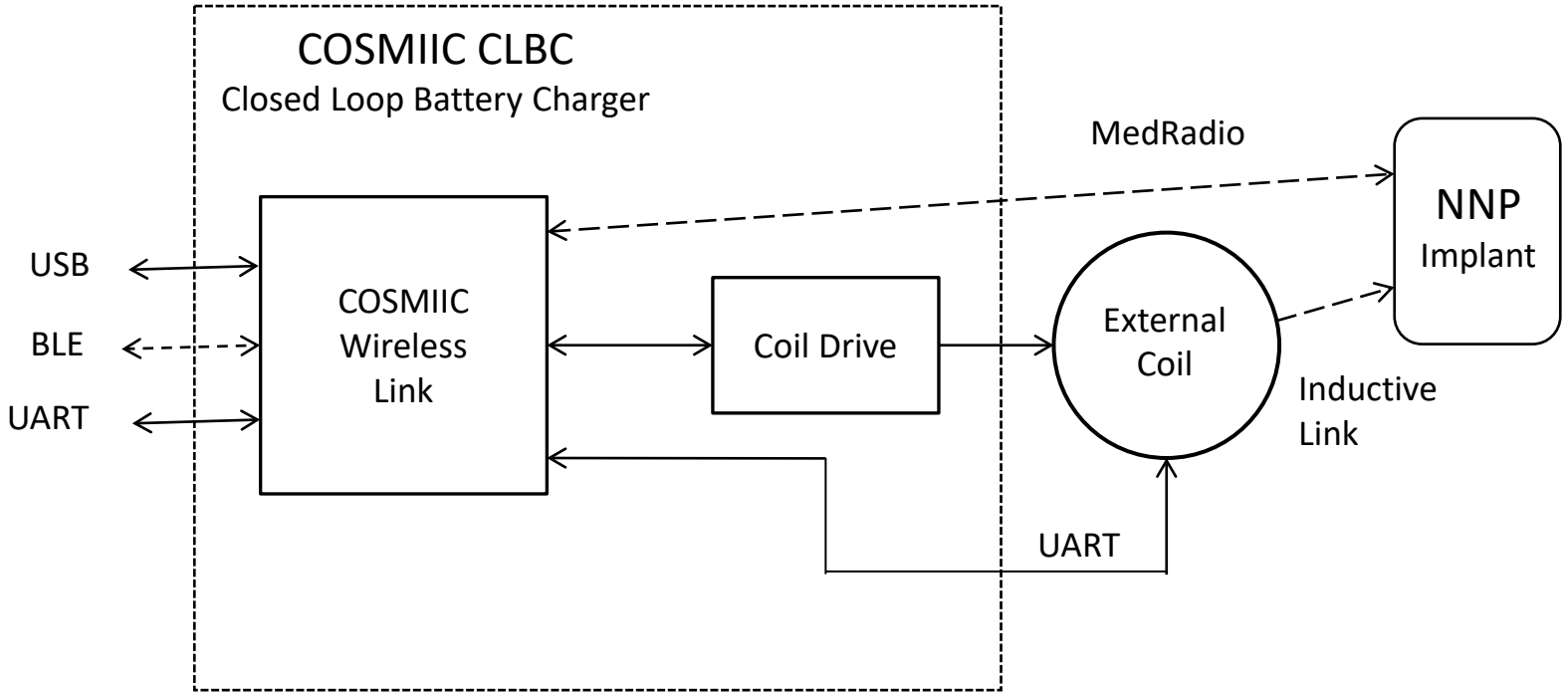
Closed Loop Battery Charger:

- Closed-loop charging based on real-time monitoring of battery capacity, temperatures, and current
- Active liquid cooling channels integrated with inductive charging coil



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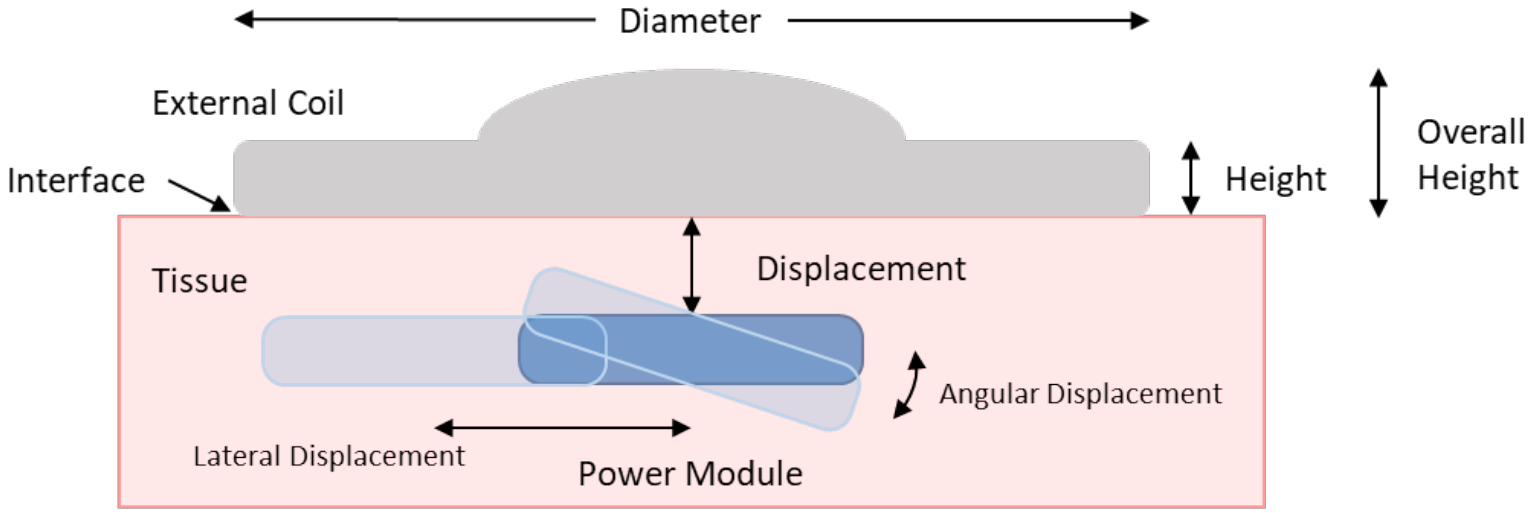
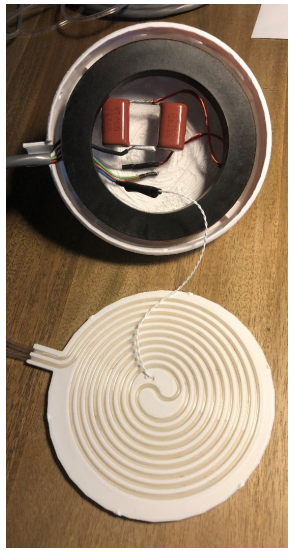
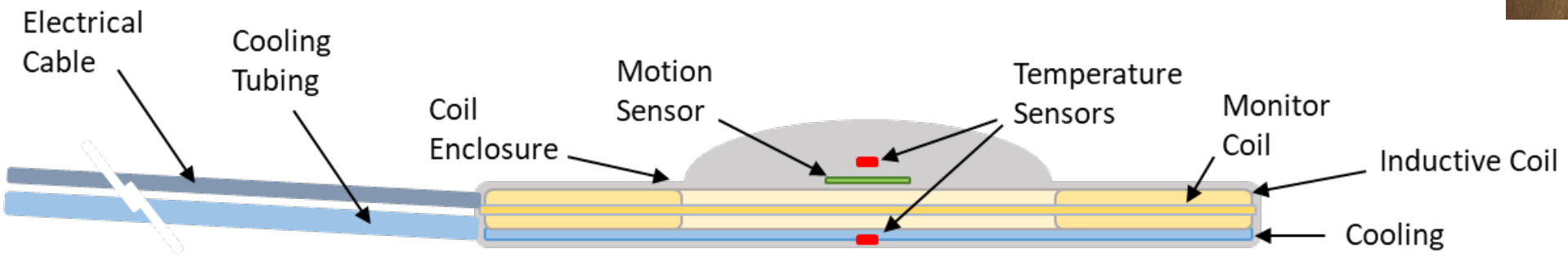
Closed Loop Battery Charger:



Charger Coil Prototypes





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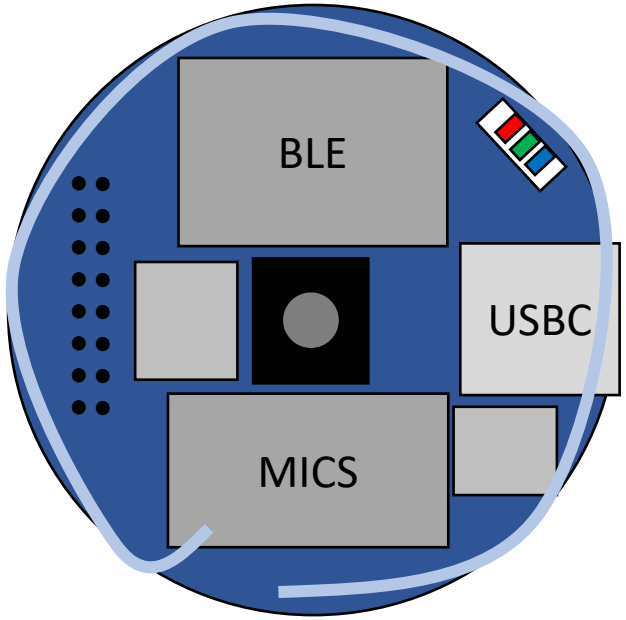
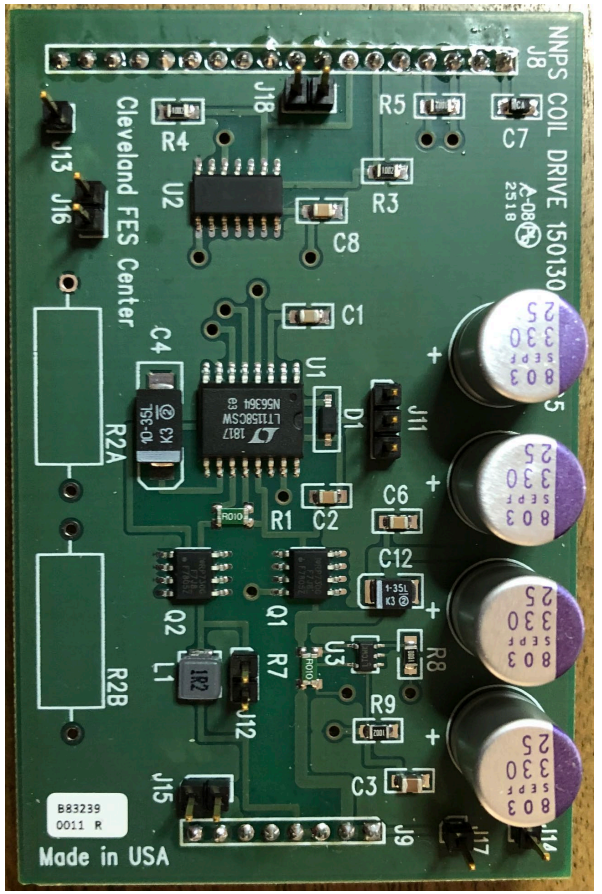
Closed Loop Battery Charger: Concept

Wireless Link + Coil Drive Power System





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Closed Loop Battery Charger: Requirements

•Battery Charging Control Algorithm

- This device's control algorithm should adjust coil voltage based on transmitting coil enclosure motion, coil enclosure temperatures, transmitting coil current, battery voltage, battery temperature, implant temperature, and receiving coil voltage at the implant.
- This device's control algorithm shall maintain charging at up to 100 mA per battery cell.
- This device's control algorithm shall maintain skin and implant temperatures per FDA regulations.
- This device's control algorithm shall supply inductive power transfer up to a maximum of at least 1.7 W over a displacement of at least 1 inch.

•External Coil Enclosure

- This device's coil enclosure shall be skin contact safe at the interface between skin and the external coil.
- This device's external enclosure shall have integrated active cooling of the interface between skin and the external coil.
- This device's external enclosure shall sense temperatures at the interfaces between skin and the external coil enclosure.
- This device's external enclosure should have motion or orientation sensing of the external coil enclosure.

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Closed Loop Battery Charger: Requirements

•Coil Drive Power System

- The device's coil drive power system shall have an enclosure.
- The device's coil drive power system shall control voltage to the coil based on the Battery Charging Control Algorithm.
- The device's coil drive power system shall communicate with the implant using wireless communication.
- The device's coil drive power system shall have a real time clock and date.
- The device's coil drive power system shall log charging activity, time, and date.
- The device's coil drive power system shall have an audio transducer to indicate charging status.
- The device's coil drive power system shall provide visual indicator of charging status.
- The device's coil drive power system shall have at least one user input switch.
- The device's coil drive power system shall have a USB interface for firmware programing and control.
- The device's coil drive power system shall have the ability to be powered by [an] alternating current (AC) power adapter.
- The device's coil drive power system shall have the ability to be powered by a direct current (DC) supply.

•Electrical Cable and Cooling Tubing

- The device's electrical cable should have ergonomics, flexibility, and durability that is suitable for daily community use.
- The device's electrical cable and cooling tube [shall] use skin-safe material construction.

"WING" – Wearable Interoperable Neuroprosthetic Gear

Closed Loop Battery Charger: Requirements

•Cooling Device

- The device's active cooling shall supply chilled liquid to the external coil enclosure near the interface between skin per FDA specifications.
- The device's active cooling shall have the ability to be powered by AC power adapter.
- The device's active cooling shall have the ability to be powered by a DC supply.

•Battery Charger Software

- The device shall have a software application programming interface (API)
- The software API shall define how to control the device and use it to issue commands to and acquire data from implanted devices and/or sensors that it communicates with.
- The device API shall be compatible with mobile computing devices for the purposes of data visualization or device control via wired or wireless communication.
- The device shall have firmware that is able to execute software programs in a stand-alone mode without being connected to a computer.

[The device firmware shall be updated through a standard protocol]

“WING” – Wearable Interoperable Neuroprosthetic Gear

Proof of Concept

- Microcontroller functions inside charging coil
  - Microcontroller board needs to be oriented perpendicular to coil
    - Due to inductive link magnetic field
  - Enables sensors and buttons to be placed at coil enclosure
    - Temperature sensors
    - Magnetic field monitor
    - coil motion sensing (inertial measurements)
- Bluetooth Low Energy communicates in proximity with MedRadio
  - Enables both Bluetooth and MedRadio circuits to be placed within the same enclosure for Wireless Link and Battery Charger

"WING" – Wearable Interoperable Neuroprosthetic Gear

Feature Summary Table

Item	Feature	CT	CAP	LAP	LAB	LAB2	KickStart	MWL	CLBC
1	Coil Drive	X			X	X	X		X
2	Coil Frequency Control	X [1]			X	X	X		X
3	Coil Power Control	X			X [2]	X [2, 5]			X
4	Requires Bench Supply				X	X			
5	Coil Mag Field Monitor								X
6	Coil Temperature	X			X	X			X
7	Coil Cooling	X [3]							X [3]
8	Coil Motion Sensing								X
9	MedRadio	X	X	X	X	X		X	X
10	BLE					X		X	X
11	Requires USB [4]		X	X	X	X			
12	Battery	X					X	X	
13	AC Adapter	X							X
14	User Input	X					X	X	X
15	User Output Visual	X					X	X	X
16	Audio					X	X		X
17	Clock / Calendar	X				X			X
18	Enclosure Accelerometer	X				X			
19	Small Size		X					X	

CT - Control Tower

CAP - Chronos Access Point

LAP - LaunchPad Access Point

LAB - LaunchPad Adapter Board

LAB2 - LaunchPad Adapter Board 2

KickStart - LAB2 Based KickStart Coil

MWL - Mini Wireless Link

CLBC - Proposed Closed Loop Battery Charger

Notes:

1 - Manually adjustable

2 - Manually adjustable via bench supply

3 - Separate device

4 - All devices include USB

5 - Fixed 5V optional

SWARM- Sensor Withdrawn from a Remote Module

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"SWARM" – Sensor Withdrawn from a Remote Module

Aims:

- Aim 1: *Develop SWARM Host circuitry for communication with outlying sensors and integrate into a full module.*
  - Our team will develop the SWARM Host circuits, including those for enabling switching communication protocols and power output levels as well as a method for detecting failures between the Sensor and the Host. The Host module will be produced for testing in Aim 3.
- Aim 2: *Design and fabricate a SWARM IMU Sensor as a proof-of-concept*.
  - The team will generate the necessary circuitry for the IMU sensor and the necessary packaging, feedthroughs, and header for communication with the SWARM Host. The SWARM Sensor will be produced for testing in Aim 3.
- Aim 3: *Complete bench-top testing for a full SWARM System to generate data for an early feasibility study IDE submission.*
  - The Host and Sensor developed in Aims 1 and 2 will be tested to support research teams' IDE submissions for incorporating these components into their own implementations as well as their development of additional sensors for the SWARM within the COSMIIC ecosystem. Tests will include electromagnetic compatibility, current leakage during failure modes, and hermeticity tests.

"SWARM" – Sensor Withdrawn from a Remote Module

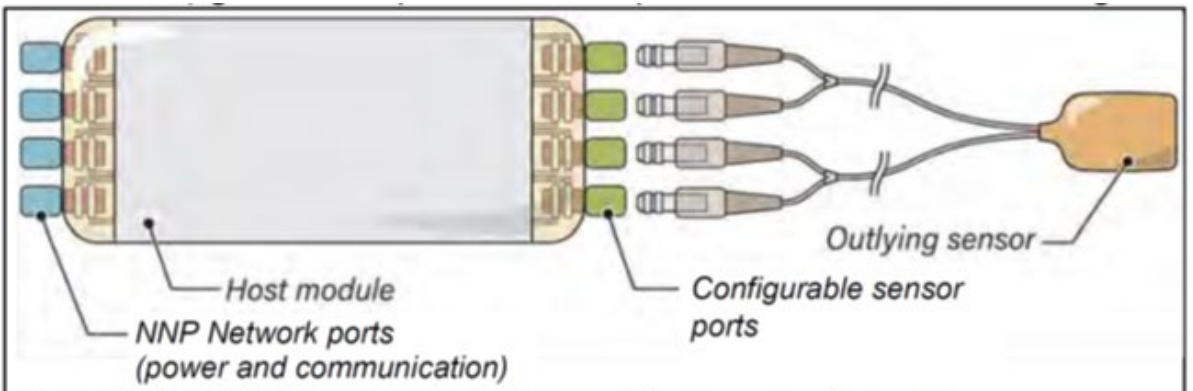


Figure SW-3: SWARM concept art with an outlying sensor with 8 cables

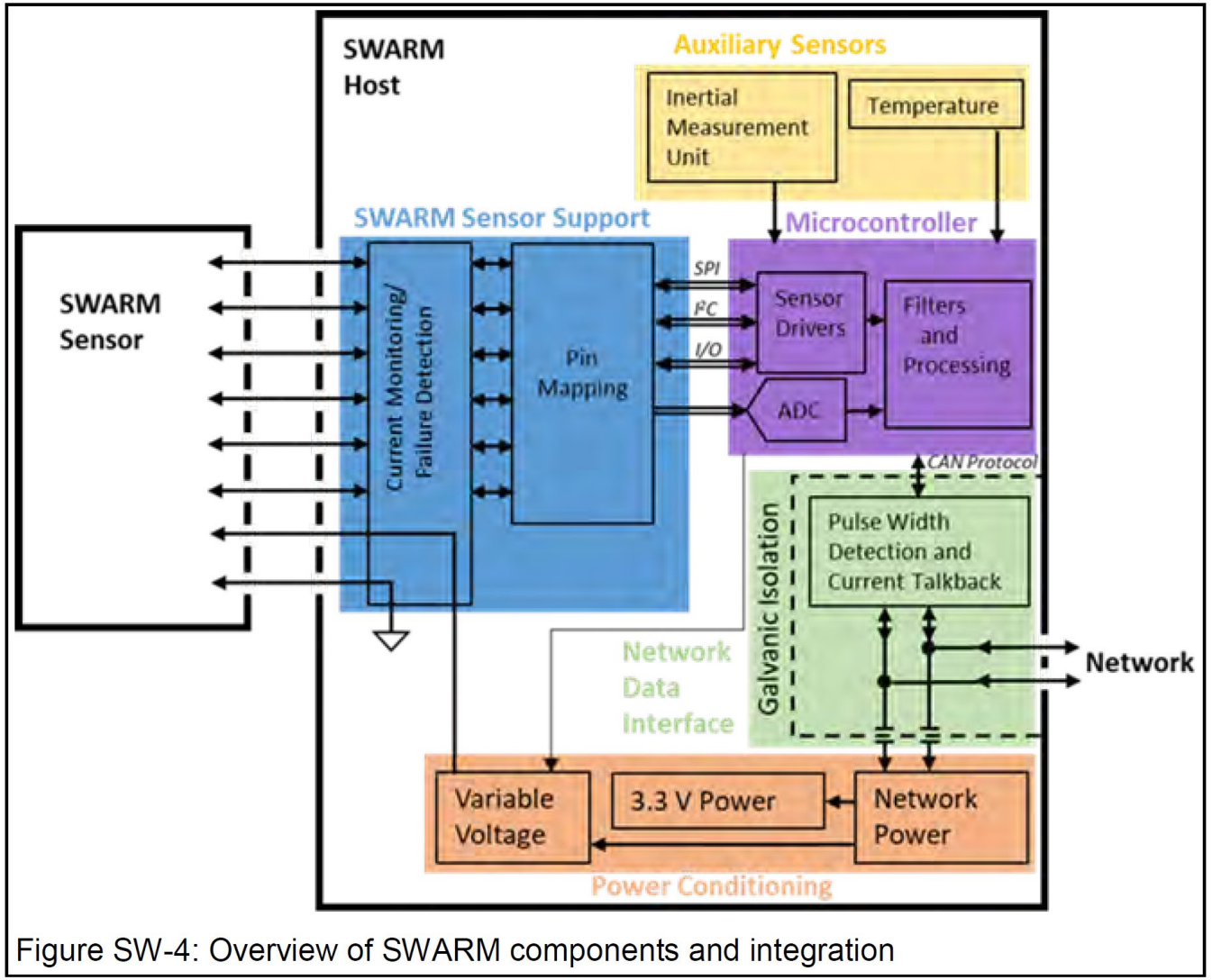


Figure SW-4: Overview of SWARM components and integration

“SWARM” – Sensor Withdrawn from a Remote Module

Specifications:

- Communication – shall support I2C, SPI, UART, analog sampling from outlying module
- Power - shall support up to 5V output
  - We haven’t defined current requirements
- Sampling – shall sample at at least 100Hz (IMU)
- ADC and filtering – requirements have not been defined
- Leakage current
  - Shall have leakage current less than 1uA
  - Shall have a method to detect if failure occurs and the cease current output
  - Outlying sensor can shall NOT be grounded and must be floating when the device is unpowered
- Pin mapping
  - Shall have configurable pin mapping
  - Should have programmable pin mapping
- Auxiliary Sensors
  - Shall have onboard IMU

"SWARM" – Sensor Withdrawn from a Remote Module

Plan:

- Evaluate whether the existing connector design supports DC powering safely
- Develop circuit for detecting failure modes
- Implement microcontroller and develop circuit for supporting two sensor modalities
  - IMU
  - Analog with a strain gauge (Steve Majerus work) – it is feasible and we have received responses
- Leave space on the circuit layout for other potential options

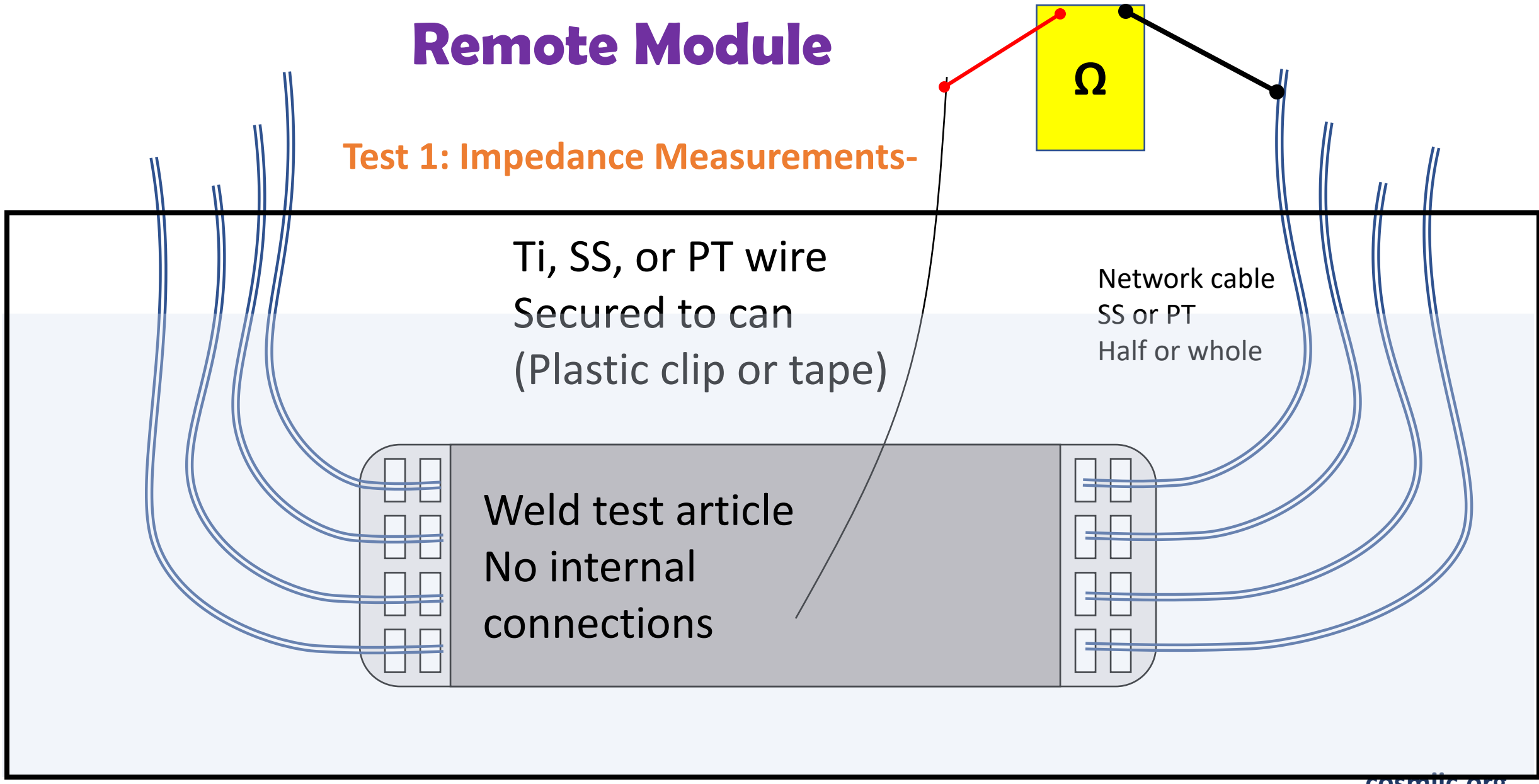
“SWARM” – Sensor Withdrawn from a Remote Module

Test 1: Impedance Measurements-Does the existing connector method provide safe DC Powering

- There may be current leakage through the connector ports
- Can we safely use the existing connector method or do we need to consider a redesign
- Additional tests will be done to evaluate potential current leakage
- This was NOT in the proposal, but necessary to verify we have something usable

"SWARM" – Sensor Withdrawn from a Remote Module

Test 1: Impedance Measurements-



“SWARM” – Sensor Withdrawn from a Remote Module

Test 1: Impedance Measurements-Results interpretation

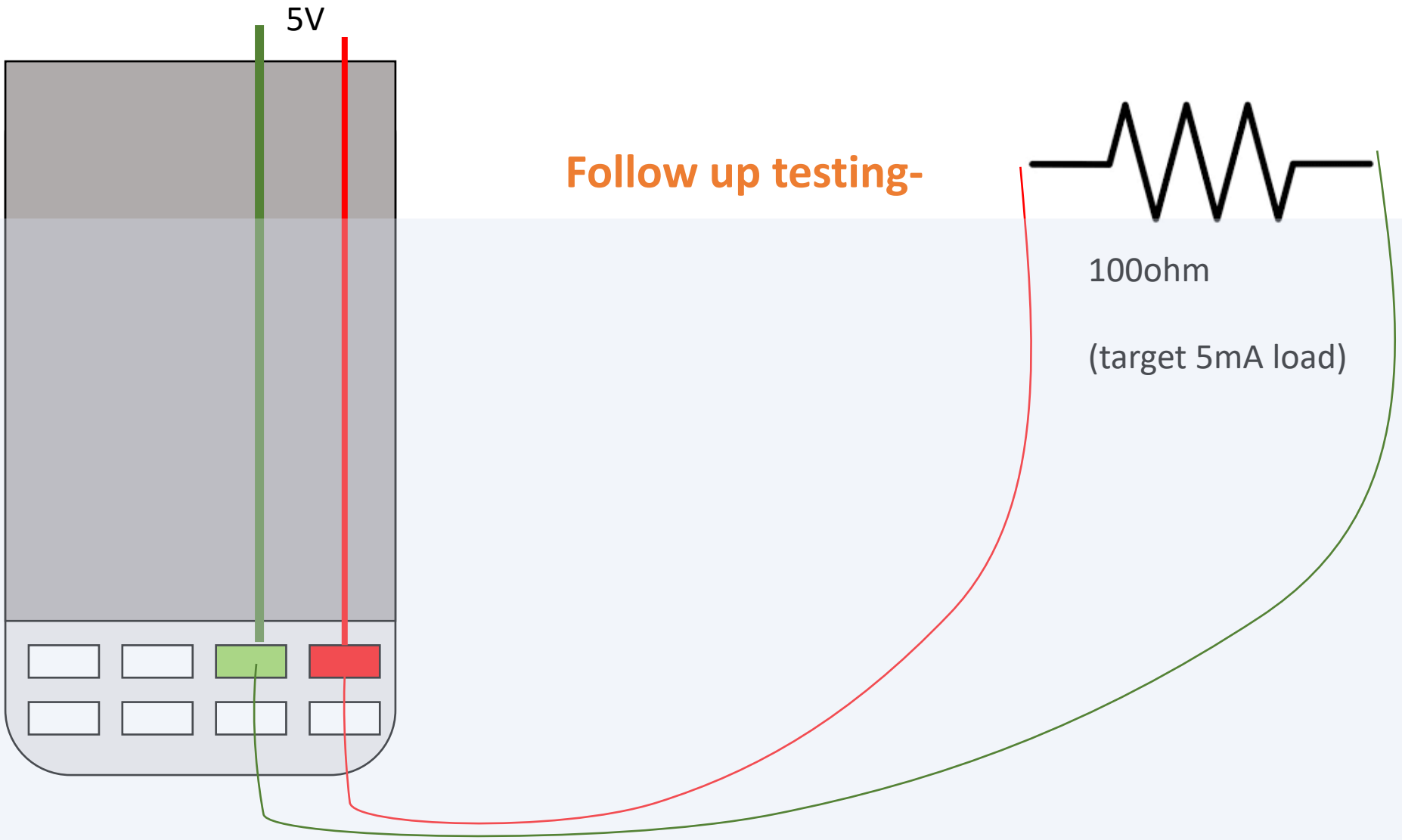
- If measured resistances are <5Mohm, the seals are not sufficient to guarantee DC leakage < 1uA at 5V
- If measured resistances are <3.3Mohm, the seals are not sufficient to guarantee DC leakage < 1uA at 3.3V
- If measured resistances are <1.8Mohm, the seals are not sufficient to guarantee DC leakage < 1uA at 1.8V.
    - This is the required supply voltage for the ICM-20948 IMU we are planning to support as a first SWARM sensor

“SWARM” – Sensor Withdrawn from a Remote Module

Test 1: Impedance Measurements-Results discussion

- The DC resistance test is not sufficient to demonstrate longevity of the system, so it is just a preliminary test
  - If it fails to show >1.8Mohm for even the tip connectors, then we will have to use a different interconnect system or avoid DC
  - If it passes, then we need to do a long term test to demonstrate that maintained DC current is not degrading interconnect points
    - This likely requires a different setup with access to the internals of the RM can

“SWARM” – Sensor Withdrawn from a Remote Module



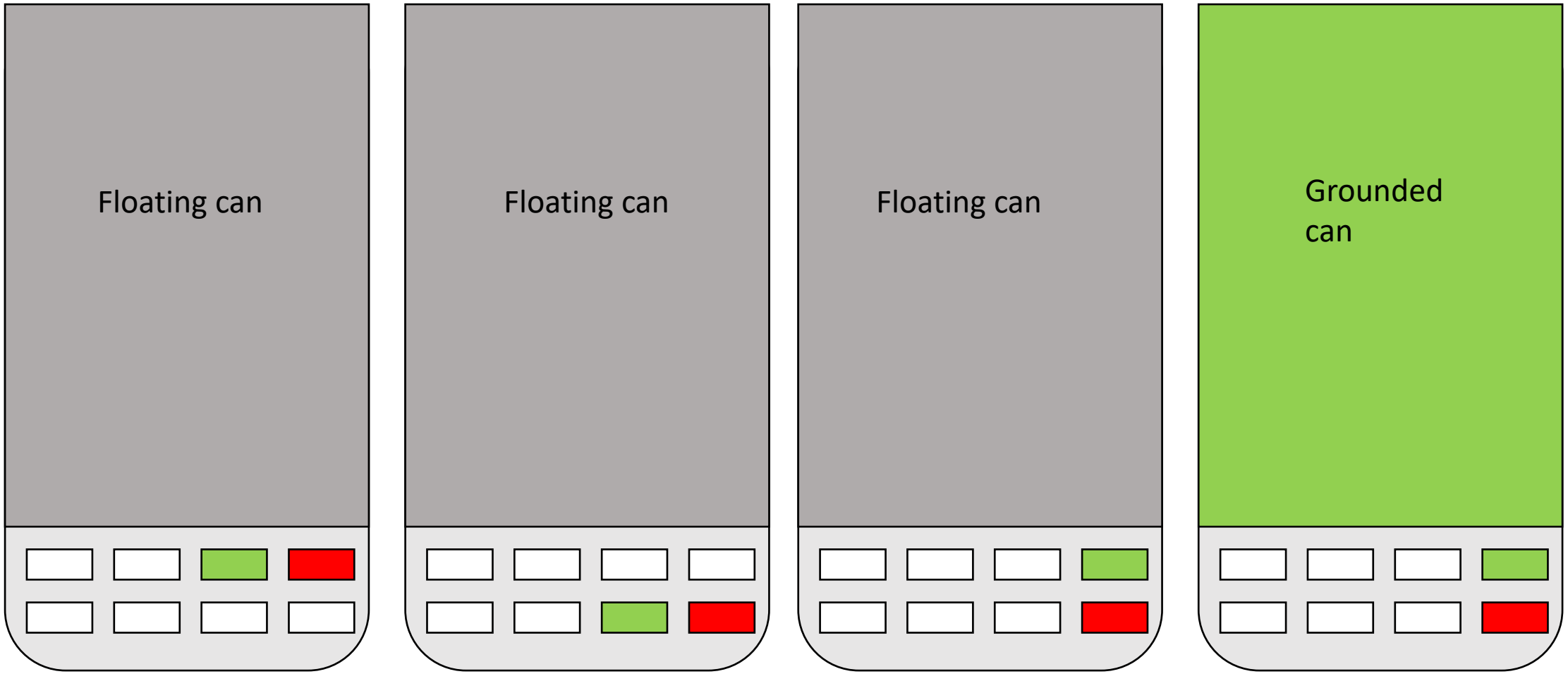
“SWARM” – Sensor Withdrawn from a Remote Module

Follow up testing-

- Active test continuously driving 5V, 5mA across connectors
- Monitor source current
  - Optional: monitor load current
- Look for discoloration and other visual signs of change
- Test different combinations of (ideally in parallel, not on same unit)
  - Inner,inner
  - Outer,outer
  - Inner,Outer (same port)
  - Outer,Inner with grounded can
- Should be done with Pt-Ir network cables, MP35N BalSeal housings
- Is there anything available?
  - Unlike weld test article, needs connection within module

“SWARM” – Sensor Withdrawn from a Remote Module

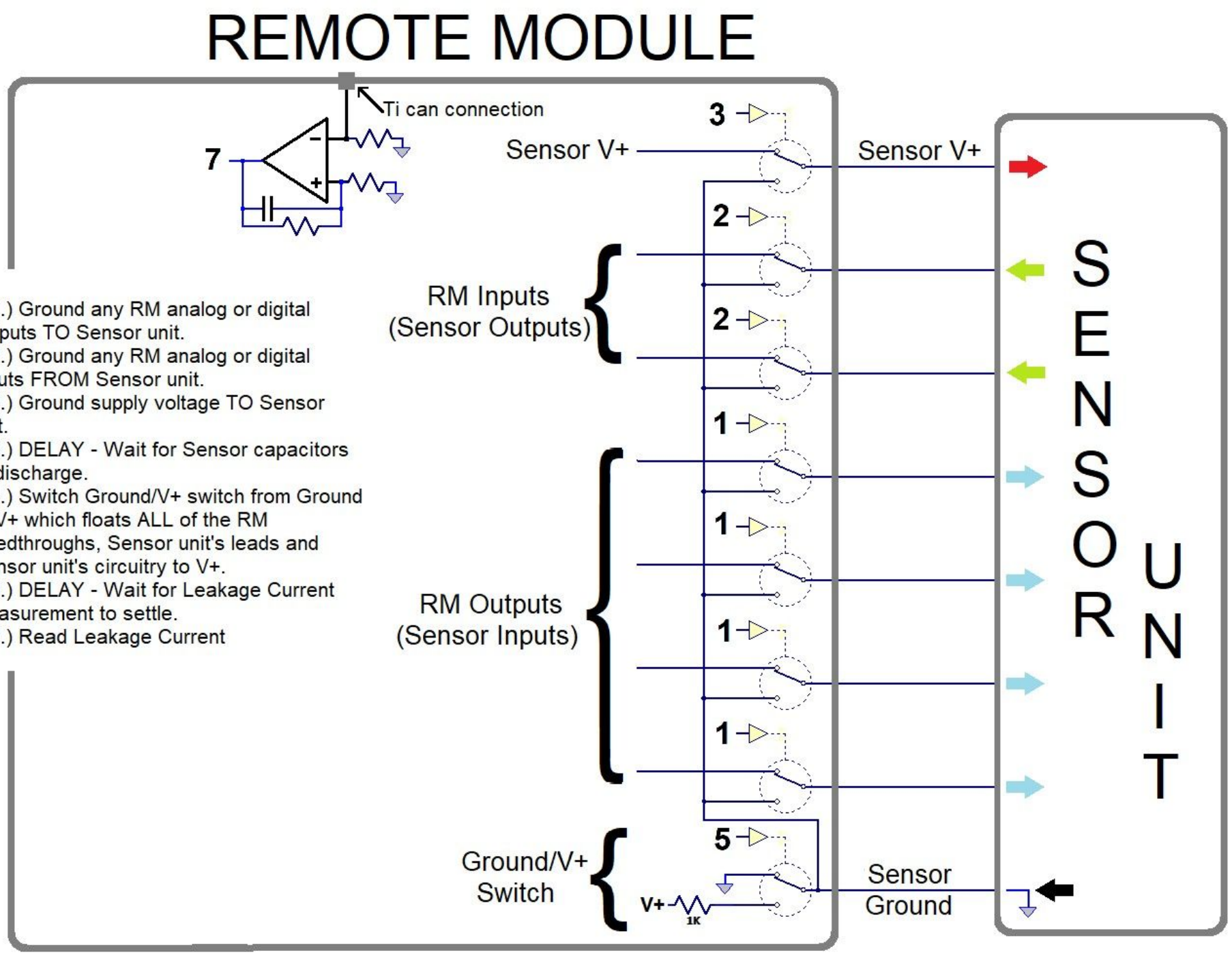
Follow up testing-



"SWARM" – Sensor Withdrawn from a Remote Module

Failure Detection

- Goal is to determine whether there is a failure that could result in current leakage
- Then the module would be turned off
- Goal is NOT to determine what the exact problem is and where it is
- Digital switching approach proposed by Fred to identify current back through the enclosure



- Turn everything high to determine if current leakage through the body back to the can
- Does NOT identify wire breakage
- Requires pause in functional use of outlying sensor

“SWARM” – Sensor Withdrawn from a Remote Module

Sensing Implementation

- Microcontroller communicating with two IMUs
- To determine what is needed to support Steve Majerus strain gauge approach

“SWARM” – Sensor Withdrawn from a Remote Module

Open Questions

- Proposed diagnostic approach tells us IF there is a problem that causes risk to the user, not where it is or other potential problems – any objections to this approach?
- Outlying sensor enclosure cannot be grounded
- Are there other sensors we should definitely approach
- Is it alright to support up to 8 feedthroughs even if we don’t intend to support them all?
- How often does the test protocol need to be run?
- How important is it to support more than one sensor from a single host sensor?

HIVE (High-density Interconnect with Variable Electronics)

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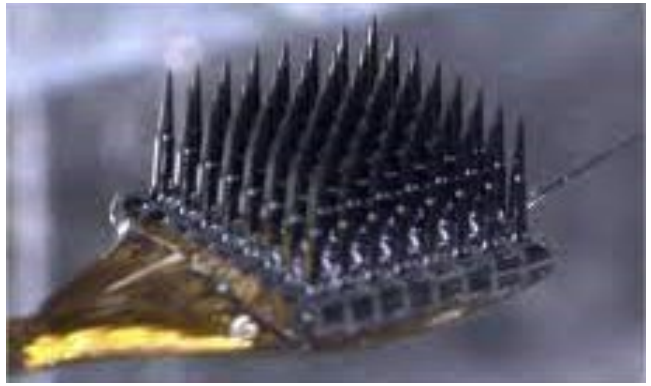
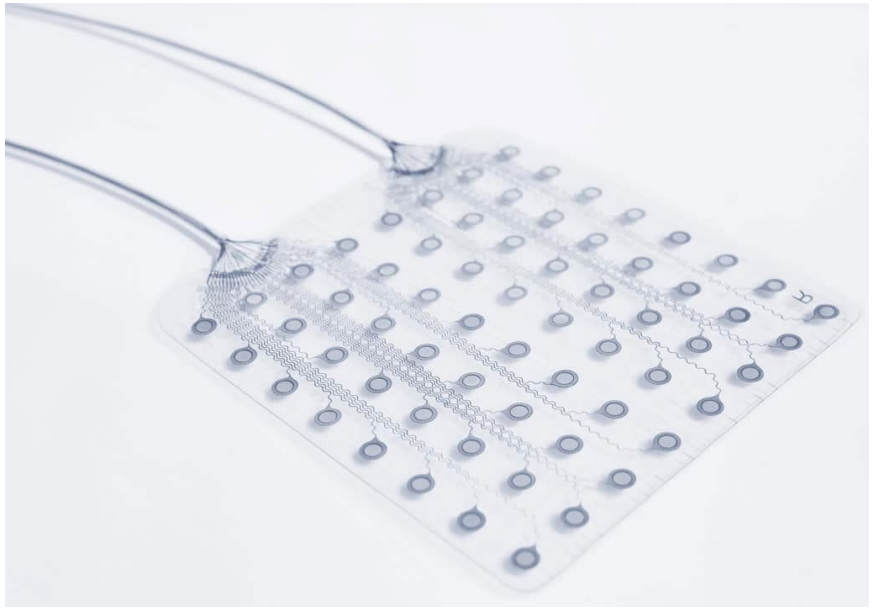
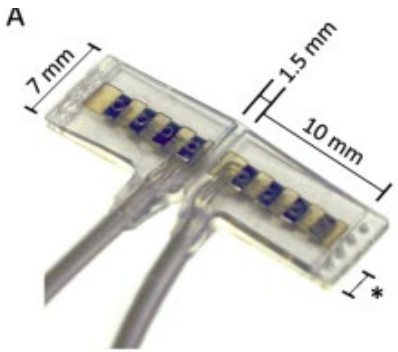
Aims

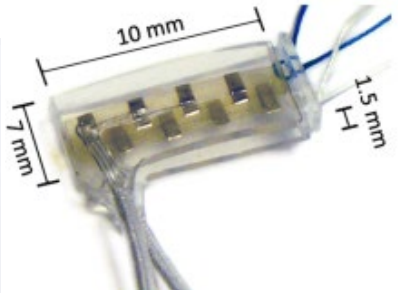
- Aim 1) Create and validate an electronics module for 64 channel recording.
  - We will design and validate modular circuitry for 64-channel recording, based on our previous published NNP module (Bullard et al. 2019). We will have multiple modes of operation available, including for spiking data by using low bandwidth features, within the constraints of the existing NNP power system. This aim will include establishing a supply chain for all items, documenting all electrical safety tests, providing test hardware, and obtaining FDA feedback through a pre-submission inquiry.
- Aim 2) Create and validate a general purpose 64-channel package.
  - We will create a general purpose 64-channel package compatible with the NNP network, only slightly larger than existing modules. We will utilize a suite of leading-edge vendors from the medical device packaging industry to implement a hermetic feedthrough flange that will be laser-welded to a titanium enclosure, which in turn will be laser-sealed after installing the internal electronics of Aim 1. We will also optimize current high-density in-line connector designs for use with the 32/64-channel systems to enable attaching connectors during surgery. We will establish an open-source, academically accessible supply chain. By the end of the project we will provide data on hermeticity testing, electrical and mechanical testing of these modules.
- Aim 3) Create and validate a module for 32 channel stimulation and recording.
  - There are many applications that would benefit from higher channel count stimulation as well as simultaneous recording and stimulation on the same electrodes. Therefore, we will design and validate modular circuitry for a 32-channel bidirectional module. Again, we will establish a supply chain and complete safety data dossier for this design.

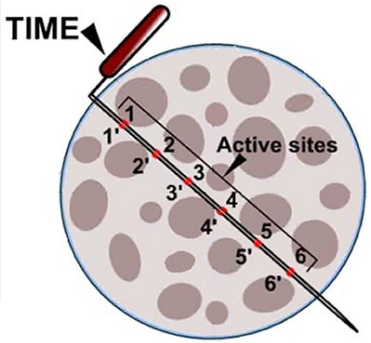
Introduction











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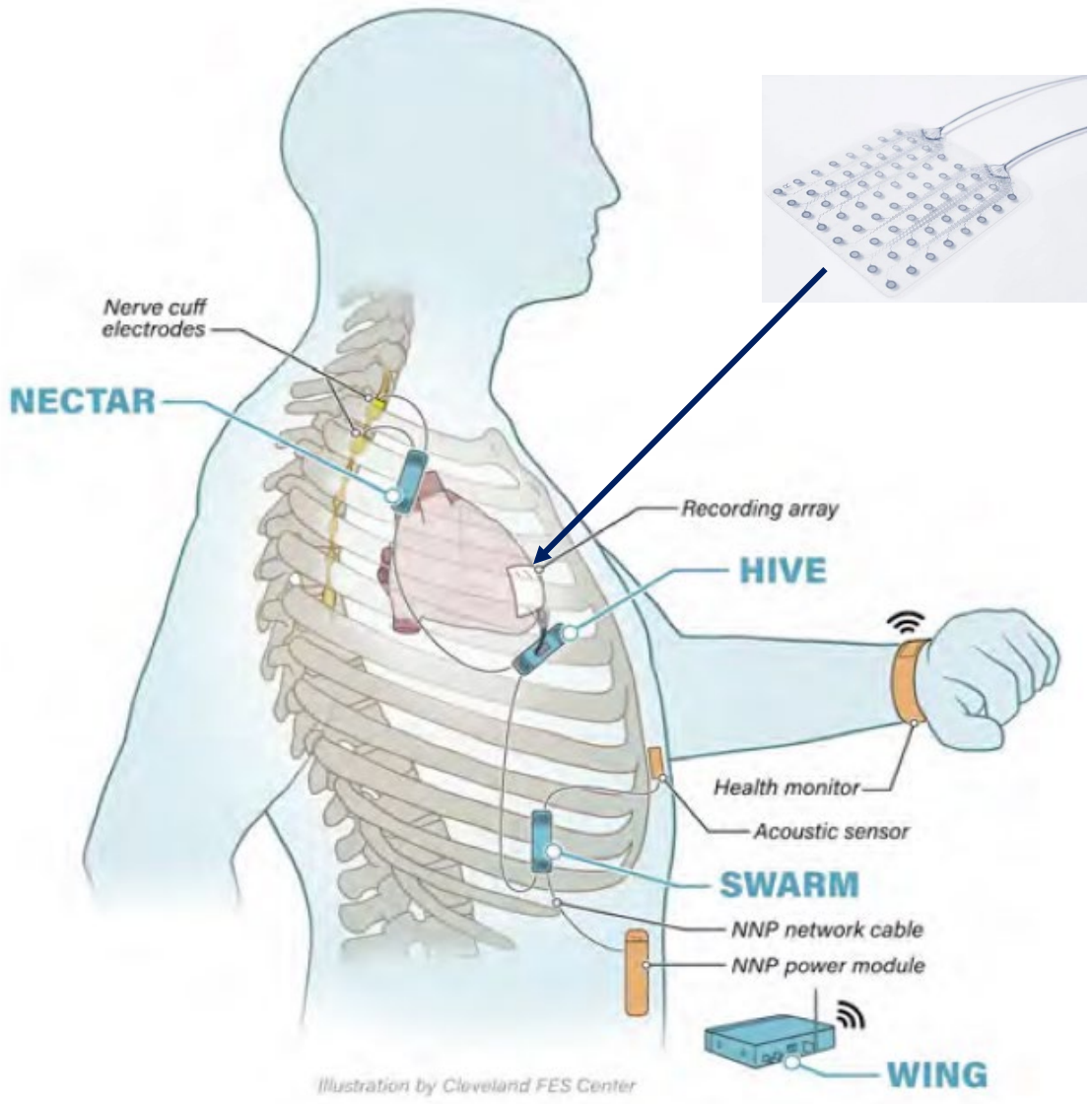
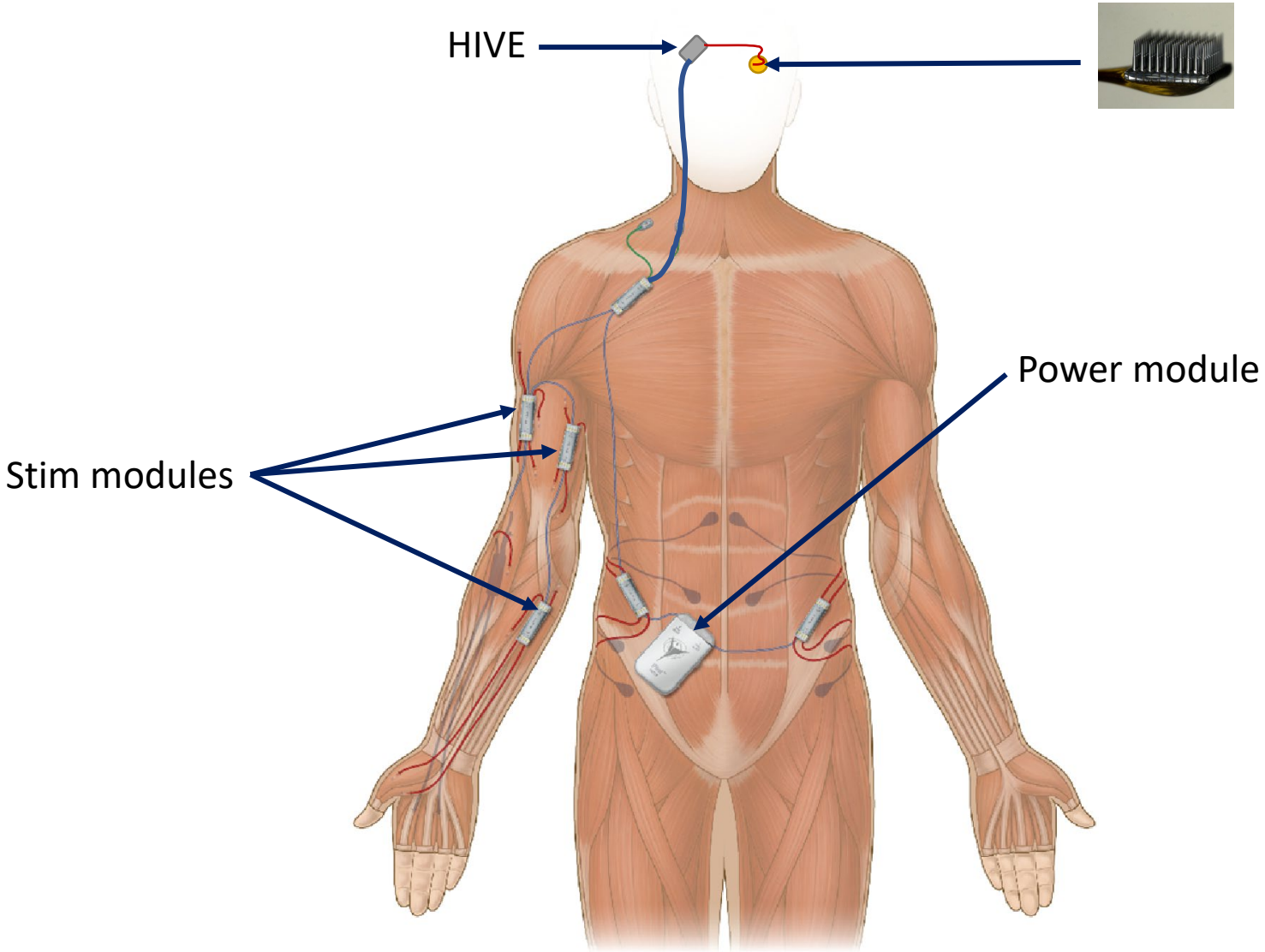
HIVE Use Cases



- High density electrode grid for cardiac monitoring

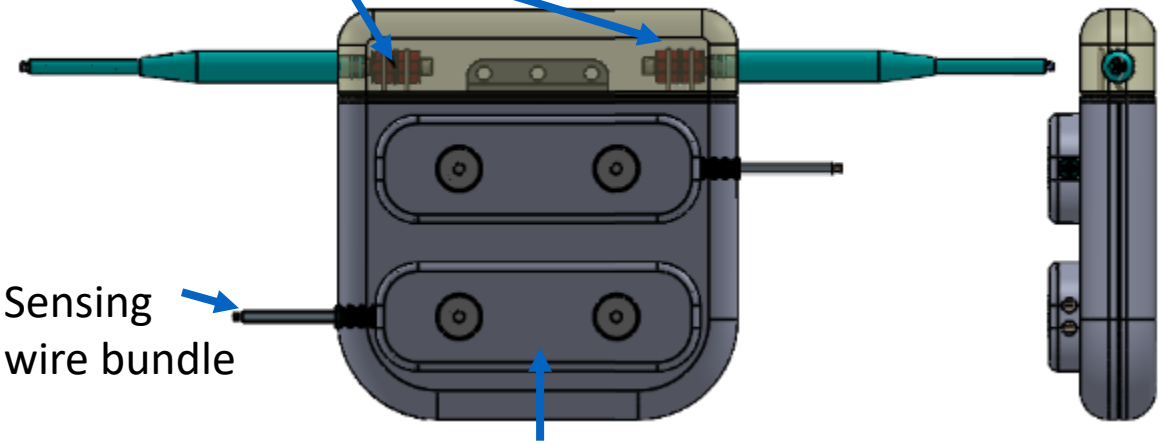
Hive Use Cases



- Intracortical array for high fidelity Functional Electrical Stimulation

64 Channel Recording Module

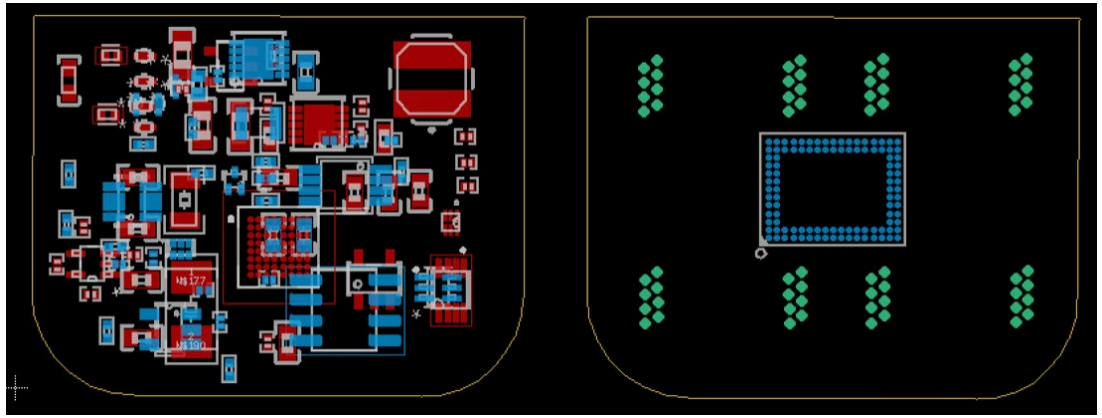
COSMIIC network connections



Sensing wire bundle

Configurable feedthrough covers (2x32 shown)

2 panel rigid-flex PCB



Signal processing, communication, power

Feedthroughs + amplifier

64 Channel Recording Module

Specifications

Package Dimensions	35.8 x 36.6 x 9.4 mm
Package material	Titanium
Electrode connection methods	Hard-wired or in-line connector
Bioamplifier	Intan RHD2164
	Sampling rates up to 30KSps
	Lower cutoff frequency 0.1-500Hz
	Upper cutoff frequency 100-20KHz
Microcontroller	STM32L433RCI6
Power and communication	FESCAN

Performance Goals

Input referred noise	2.4μV_{rms}
Power consumption	30mW sampling at 2KSps

32 Channel Record + Stim Module

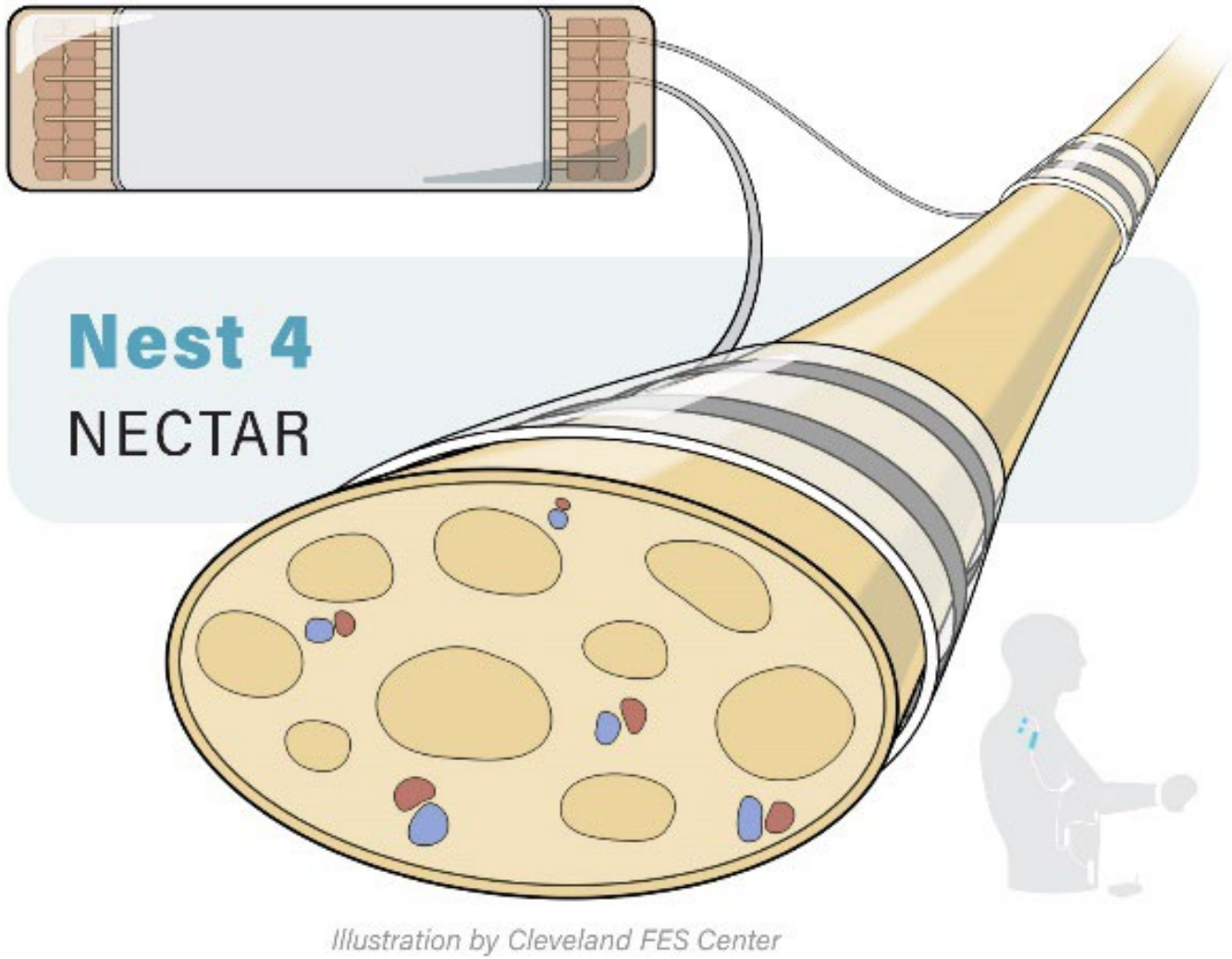
Features

Package	Similar to 64 channel recording module
Electrode connection methods	Hard-wired or in-line connector
Bioamplifier+stimulator	2x Intan RHS2116
	Programmable current controlled stim
	10nA to 2.55mA over 14V range per contact
	Amplifier fast settle feature
	Sampling rates up to 40KSps
	Lower cutoff frequency 0.1Hz-1KHz
	Upper cutoff frequency 100Hz-20KHz
Microcontroller	STM32 same or similar to 64 channel recording module
Power and communication	FESCAN

Nerve Excitation Control Through AC Regulation

cosmiic.org

“NECTAR” – Electrical Nerve Block Module



- Aim 1) Develop an open source NECTAR module capable of both upregulation (stimulation) and downregulation (block) for complete closed-loop control
- Aim 2) Fully characterize the therapeutic window of the NECTAR System and provide the complete procedures and data under an open source license.

“NECTAR” – Electrical Nerve Block Module

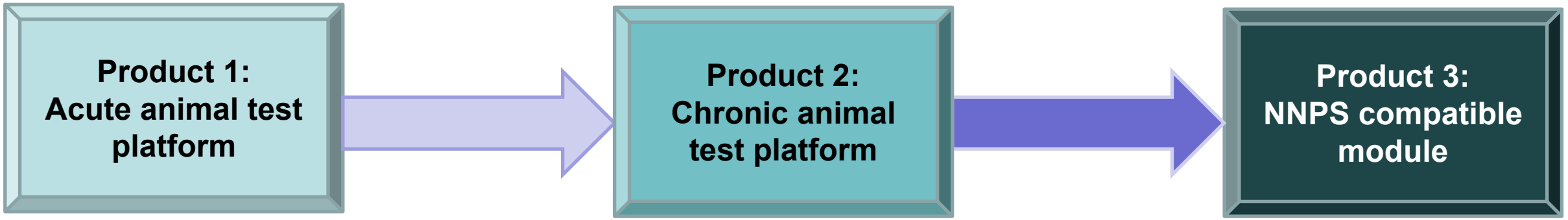
- **Features:**
  - **Functionality:** Frequencies to apply both stimulation and block to both **upregulate** and **downregulate** the nervous system
  - **Full waveform adjustment:** The waveform can be adjusted in both amplitude and frequency
  - Voltage and current control will both be supported
  - Electrode evaluation capability
- **Performance Considerations:**
  - Ensure amplitude accuracy across all frequencies and realistic load conditions
  - Charge balanced output
  - DC mitigation

NECTAR Module Specifications

	Range	Resolution
Frequency - KHFAC	1KHz - 20KHz	1KHz
Frequency - Stimulation	1-20Hz	1Hz
Amplitude - KHFAC	0-30Vpp	0.1Vpp
Amplitude - Stimulation	0-20mA	0.1mA
KHFAC vs Stimulation	Selectable	
KHFAC Freq Modulation	0-10KHz/sec	
KHFAC Amp Modulation	0-5mA/sec	
KHFAC Charge Balance	<1uA	

"NECTAR" – Electrical Nerve Block Module

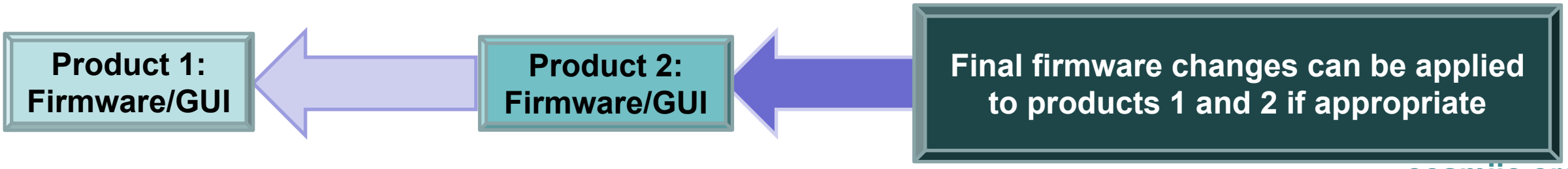
- **Development Strategy**



- **Benchtop form**
- Full frequency and amplitude range
- CIC measurements
- Tethered possibly
- Basic GUI for control
- Preliminary quality testing

- **Chronic small animal form**
- Standalone run mode
- Enhanced firmware for wireless communication
- Preliminary quality testing

- **NNPS form factor**
- CAN interface
- Complete waveform control
- Finalize CIC algorithm
- Formal verification



“NECTAR” – Electrical Nerve Block Module

- **KHFAC Block Features:**
  - **Frequency/Amplitude range:** As the frequency of KHFAC increases, the block threshold increases but the onset decreases . It is the intent of this device to provide a range of values that allows the use to determine the appropriate compromise for their application.
  - **Square waveform-continuous:** Electrical nerve block using alternating waveforms has been demonstrated in the 10-30 KHz range using several different types of waveforms. Square wave waveforms have the lowest block thresholds. Onset response is larger for lower frequencies, but is unaffected by waveform shape. Therefore, the waveform shape will be constrained to square waveforms.
  - **Current and Voltage Control:** Initial KHFAC experiments used voltage control mode which is easier to implement from a DC mitigation perspective. However, current control limits the amount of charge delivered which is safer for the tissue. Both will be provided to accommodate a range of experimental needs

“NECTAR” – Electrical Nerve Block Module

- **Module Output Specifications:**
  - The NECTAR device shall provide four independent bipolar channels

- **KHFAC Block Specifications:**
  - The KHFAC device shall provide continuous square waveforms
  - The KHFAC device shall provide current as well as voltage control
  - The KHFAC device shall provide frequencies 10KHz-30KHz in 100 Hz increments
  - The KHFAC device **may** provide frequencies up to 40KHz in 100 Hz increments
  - The KHFAC device shall provide amplitudes up to 20 mApp in 0.1 mA increments
  - The KHFAC device **may** provide amplitudes up to 30 mApp in 0.1 mA increments
  - The KHFAC device shall provide amplitudes up to 20 Vpp in 0.1 V increments
  - The KHFAC device **may** provide amplitudes up to 30 Vpp in 0.1 V increments

“NECTAR” – Electrical Nerve Block Module

- **Stimulation Features:**
  - **Frequency/Amplitude range:** The ability to use electrical waveforms to both upregulate and downregulate the nervous system creates the possibility of developing closed loop control strategies that can accurately control a measured physiological parameter to mitigate a disease state.
  - **Square waveform-discontinuous:** At lower frequencies that are typically used for stimulation, a continuous waveform would cause the waveform to exceed the safe charge/cycle limit. A discontinuous waveform will be used for these lower frequencies.
  - **Charge limited waveform :** To prevent the device from operating the electrode outside the water window, the user will be able to specify a maximum charge/cycle. This value would typically be determined from the CIC testing but could be adjusted by the user to test electrode limits in vitro or in pre-clinical testing

“NECTAR” – Electrical Nerve Block Module

- **Stimulation Specifications:**
  - The Stimulation device shall provide discontinuous square waveforms
  - The Stimulation device shall provide frequencies 1Hz-40Hz in 0.1 Hz increments
  - The Stimulation device **may** provide frequencies up to 1 KHz in 0.1Hz increments
  - The Stimulation device shall provide amplitudes up to 20 mApp in 0.1 mA increments
  - The Stimulation device **may** provide amplitudes up to 30 mApp in 0.1 mA increments
  - The Stimulation device shall provide amplitudes up to 20 V in 0.1 V increments
  - The Stimulation device **may** provide amplitudes up to 30 V in 0.1 V increments
  - The Stimulation device shall provide pulse widths 20usec-2 msec in 1 usec increments

“NECTAR” – Electrical Nerve Block Module

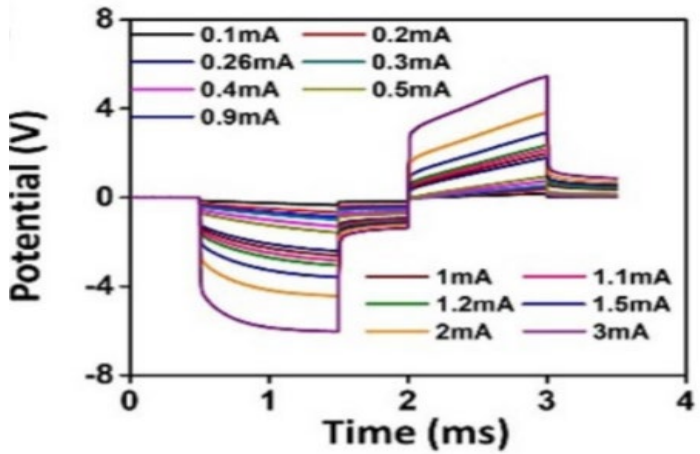
- **Performance Considerations:**
  - **Amplitude accuracy at all frequencies:** Most standard benchtop laboratory stimulators cannot achieve 5kHz or higher, and most commercial stimulators that claim specifications of 5kHz or higher do not achieve their rated frequencies without significant attenuation and distortion. These issues are critical for successful KHFAC block. Therefore, the output of the NECTAR module will be validated across multiple loading conditions and reported as a peak to peak value.
  - **True charge balancing/DC removal:** For KHFAC, the charge imbalance between the cathodic and anodic phases can result in Net DC current, which is defined as the average DC current that occurs over the course of many pulse cycles. Depending on the electrode material, surface area, and target nerve tissue, acceptable levels can be 10-100 nA.

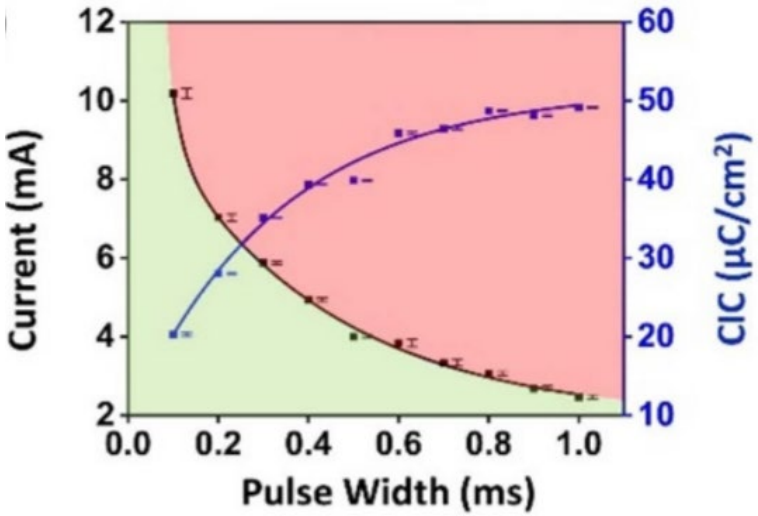
“NECTAR” – Electrical Nerve Block Module

- **Performance Specifications:**
  - The device shall be tested to ISO 14708-3 standards for DC leakage
  - The device shall provide charge balancing to 0.1 uC
  - The device **may** provide DC removal to 0.01 uC
  - The device shall provide amplitude accuracy to 0.05 mA
  - The device shall provide amplitude accuracy to 0.05 V
  - The device **may** provide amplitude accuracy to 0.01 mA
  - The device **may** provide amplitude accuracy to 0.01 V

"NECTAR" – Electrical Nerve Block Module

- **Electrode Evaluation Considerations:**
  - Use charge injection capacity (CIC) to determine charge delivery limits
  - Calibration table will be available for operational limit testing
  - Charge limit will be incorporated into the module to limit unsafe pulse widths regardless of frequency
  - Adaptable to different electrode chemistries
  - User would have the ability to develop new algorithms





“NECTAR” – Electrical Nerve Block Module

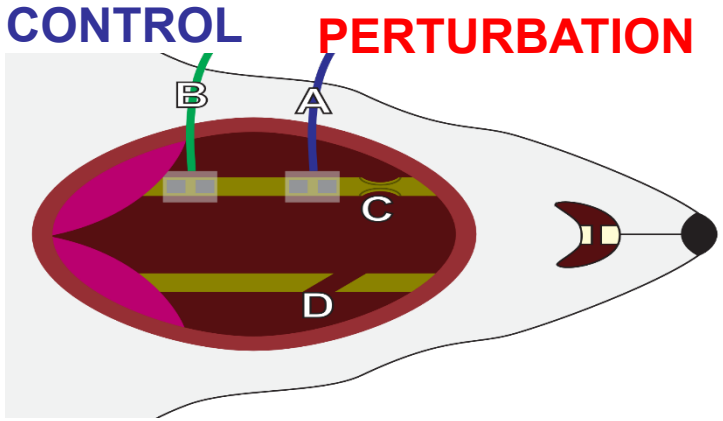
- **Electrode Evaluation Specifications:**
  - The device shall be able to measure the voltage of a stimulus pulse at a resolution of 0.05 mV
  - The device **may** be able to measure the voltage of a stimulus pulse at a resolution of 0.01 mV
  - The device shall provide an algorithm to determine the safe range for an electrode in terms of charge: **under development.**
  - The device shall provide the calibration curves to the user for evaluation
  - The device shall provide internal storage for calibration curves.

“NECTAR” – Electrical Nerve Block Module

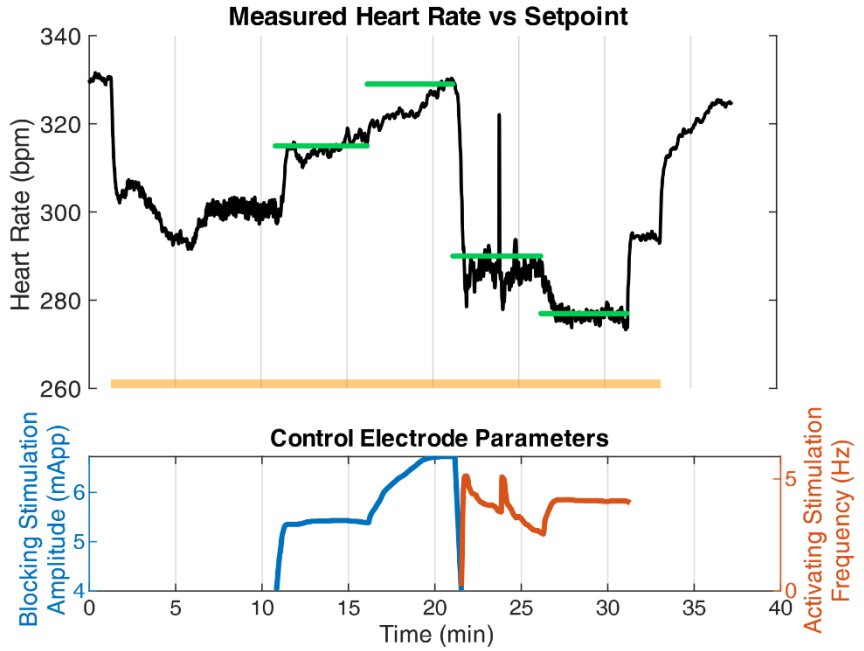
- **Programmability Specifications:**
  - The device shall provide amplitude ramping at 1 mA/S
  - The device **may** provide amplitude ramping at 0.1 mA/S
  - The device shall provide amplitude ramping at 1 V/S
  - The device **may** provide amplitude ramping at 0.1 V/S

"NECTAR" – Electrical Nerve Block Module

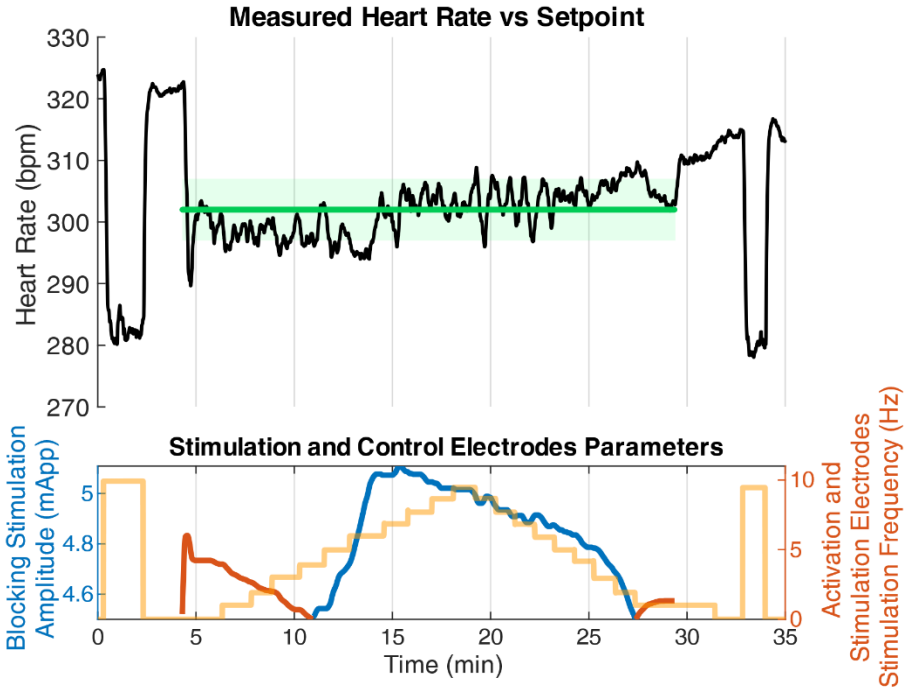
- **Closed Loop Control Example**
  - Bi-modal Neuromodulation
    - **KHFAC amplitude control**
    - **Stimulation frequency control**



Variable Setpoint /Constant Perturbation

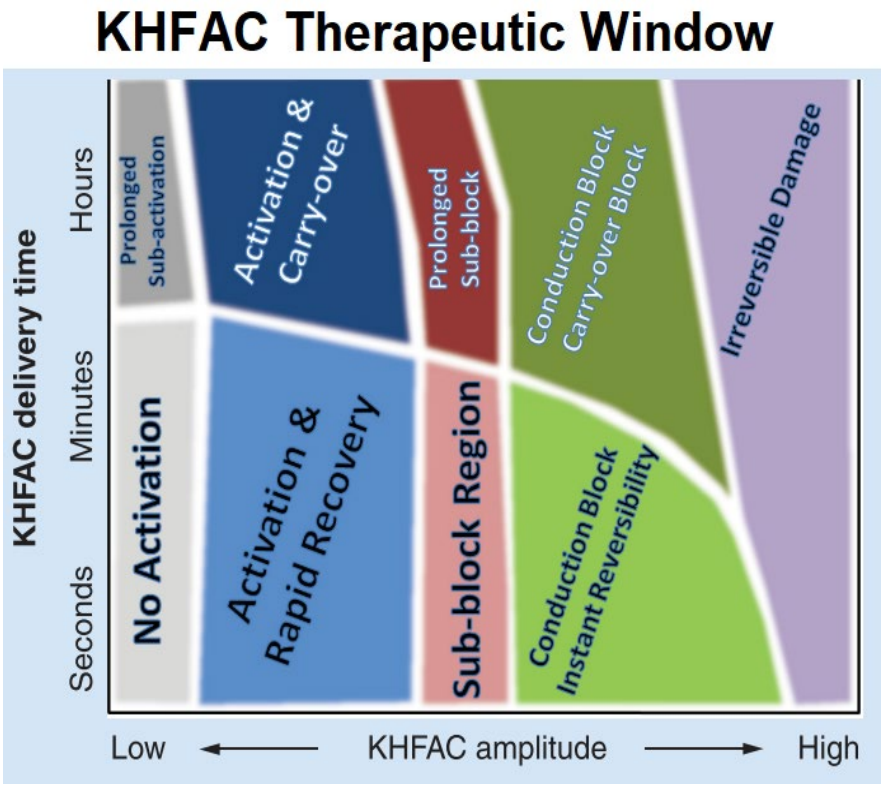


Constant Setpoint /Variable Perturbation



"NECTAR" – Electrical Nerve Block Module

- **KHFAC Therapeutic Window Considerations**
  - **Therapeutic effect of KHFAC is complex and multi-modal**
  - Perform chronic in vivo studies to provide data that establishes the therapeutic window for KHFAC block
  - Evaluate frequency, amplitude, charge delivery, and duty cycle.
  - Include both functional and histological metrics for safety and efficacy
  - FDA engagement to ensure that the results are acceptable as background data for any future IDE submissions using the NECTAR System.



Therapeutic Region	Timeframe	Application
Instant Reversibility	<= 2 seconds	Closed loop control, spasticity
Rapid Reversibility	< 5 minutes	Closed loop control, autonomic
Delayed Reversibility	Within 24 hours	Pain relief
Reversible Damage	More than 24 hours	Similar to neurapraxia, observable histological changes
Irreversible Damage	N/A	Requires nerve regrowth, obvious histological damage

KHFAC Therapeutic Window: Within the Amplitude-Duration space, KHFAC has at least nine possible "effect states", including activation, block, and many longer-term effects.

"NECTAR" – Electrical Nerve Block Module

- **KHFAC Acute Therapeutic Window Specifications:**
  - KHFAC testing shall be on the rat sciatic nerve
  - Testing of force output will be performed
  - **Static testing**
    - KHFAC shall be tested acutely in durations 5-30 minutes
    - KHFAC **may** be tested acutely in durations >30 minutes
    - KHFAC shall be tested acutely at block threshold amplitudes as well as 150% and 50% of the block threshold
  - **Duty cycle testing**
    - KHFAC shall be tested using repetitive on/off cycles where the "on" cycle duration is 1-30 minutes and the "off" cycle duration is varied between 50% and 250% of the "on" cycle for 5-20 repetitions
    - KHFAC shall be tested acutely at block threshold amplitudes as well as 150% and 50% of the block threshold

"NECTAR" – Electrical Nerve Block Module

- **KHFAC Chronic Therapeutic Window Specifications:**
  - KHFAC testing shall be on the rat sciatic nerve **or larger animal**
  - Both functional/behavioral and histological testing will be performed
  - **Static testing**
    - KHFAC shall be tested chronically in dosages 5-30 minutes 1-4 times/day
    - KHFAC **may** be tested chronically in durations >30 minutes
    - KHFAC shall be tested chronically at block threshold amplitudes as well as 150% and 50% of the block threshold
  - **Duty cycle testing**
    - KHFAC shall be tested using repetitive on/off cycles where the "on" cycle duration is 1-30 minutes and the "off" cycle duration is varied between 50% and 250% of the "on" cycle for 5-20 repetitions 1-4 times/day
    - KHFAC shall be tested chronically at block threshold amplitudes as well as 150% and 50% of the block threshold