N^3 Proposer's Day

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Next generation approach to brain interfaces

DOD Problem: Able-bodied military personnel cannot use current neural interfaces

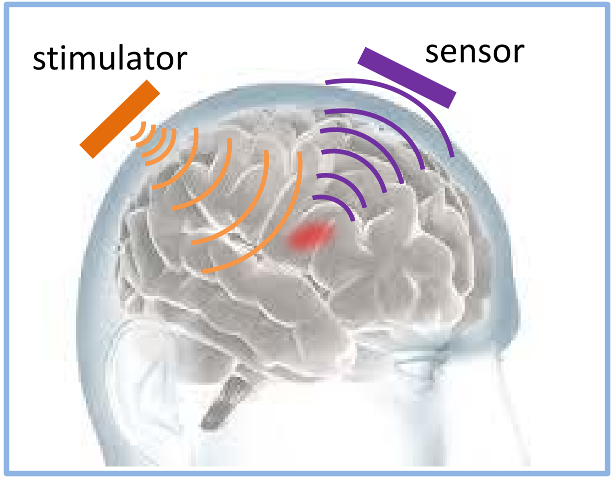
Goal:
Create reliable neural interfaces without the need for surgery or implanted electrodes

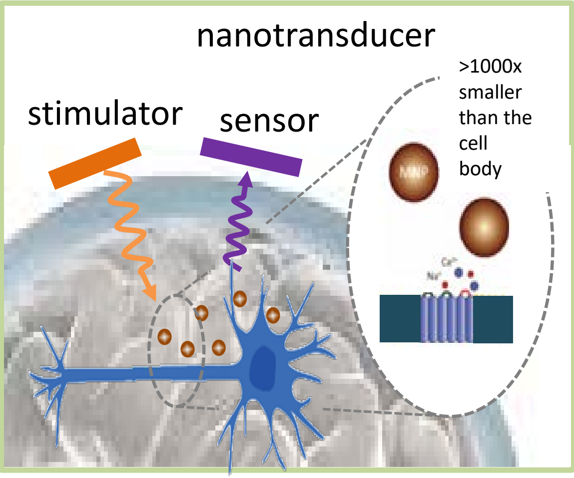
Facilitate multitasking at the speed of thought

Interface with smart decision aids

Two Technical Areas

	TA1: Noninvasive		TA2: Minutely Invasive
Invasiveness	External device	→	Injectable/ingestible/intranasal
Example Technology	Ultrasound, light, RF, magnetic fields	→	Nanotechnology, membrane modifications, molecular assembly
Signal Quality	Neural ensemble activity		Single neuron activity





TA1: Completely Noninvasive Neural Interfaces

Objective: Create a noninvasive read/write system

PHASE I
Develop subcomponent technology

Develop systems level design
link margin power budgets, channelization approaches

Fabricate subcomponents
circuits, sensor, emitter, hardware

Characterize subcomponents
resolution and latency performance

Assess scattering and attenuation
compare to systems level design parameters

Demonstrate read and write
through ”skull and tissue like” mediums

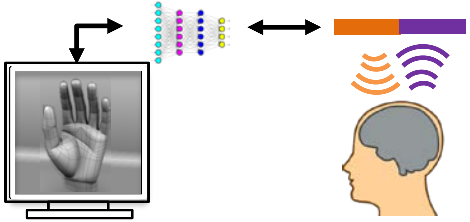
Bench top demo

PHASE II
Integrate and validate *in vivo*

Integrate subcomponents
combine multiple read and write subcomponents into one device

Evaluate physical properties
crosstalk, SNR, and safety parameters of integrated device *in vivo*

Develop algorithms
decode neural ensemble activity and encode sensory feedback to the brain



In vivo proof of concept

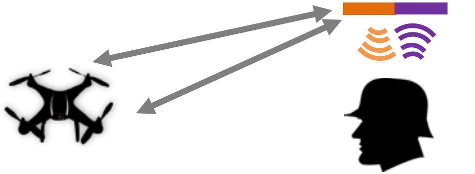
PHASE III
Refine and demonstrate

Characterize refined system
meet metrics for bidirectional system

Refine algorithms
achieve lower system latency

Demonstrate system capabilities
decode motor and cognitive signals, and encode sensory feedback

Design DoD relevant final demo
ex. simultaneously perform multiple tasks



In field proof of concept

Deliverable: Human demonstration of closed loop prototype system in a DoD relevant task

TA1: Noninvasive metrics

Phase I

Read and Write Subcomponents

Spatial resolution
<1 mm^3

Temporal resolution
<10 ms

Stability
continuous operation for ≥ 2 hrs

Accuracy (read/write)
correlation to ground truth accuracy ≥ 95%

Phase II

Integrated Device

Safety
≤ 1°C rise in tissue volume being read from/written to

Closed loop system latency
< 100 ms

Control signals
≥ 3 DOF

Sensory signals
≥ 3 categories
(ex: detection, alarm)

Integrated device size
≤ 125 cm^3

Channel count
read channels/volume (≥16/16mm^3)
write channels/volume (≥16/16mm^3)

Phase III

Final System

Closed loop system latency
< 50 ms

Control signals
≥ 6 DOF

Sensory signals
≥ 6 categories

Multifocal capability
≥ 4 read/write locations without crosstalk

TA2: Minutely Invasive Neural Interfaces

Objective: Create a minutely invasive read/write system

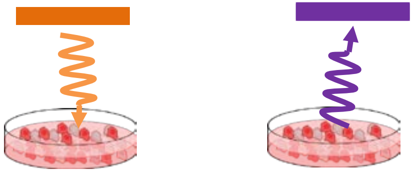
PHASE I
Develop subcomponents and nanotransducers

Develop system level design
nanotransducer and sensor/stimulator

Fabricate subcomponents
circuits, hardware and nanotransducer
(particle, genetic component, encapsulation material)

Characterize nanotransducer
cell type specificity at single neuron resolution

Demonstrate system interaction
sensor/stimulator ↔ nanotransducer



In vitro demo

PHASE II
Integrate and validate *in vivo*

Integrate subcomponents
combine multiple read and write subcomponents into one device

Evaluate physical properties
crosstalk, SNR, specificity of sensor/stimulator
toxicity and stability of nanotransducer

Develop algorithms
decode and encode from/to single neurons

Identify patient population
prepare for clinical proof of concept

Optimize peripheral delivery route
cross the BBB targeting specific neurons

Preclinical proof of concept

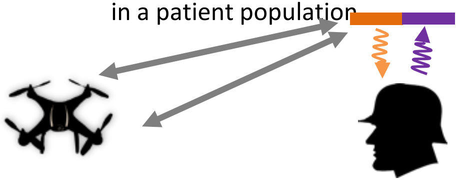
PHASE III
Refine and demonstrate

Characterize refined system
bidirectional system and interaction with nanotransducer

Refine algorithms
achieve lower system latency

Demonstrate system capabilities
decode motor and cognitive signals, and encode sensory feedback

Design DoD relevant final demo
in a patient population



Clinical proof of concept

Deliverable: High spatiotemporal resolution bidirectional system demonstrated in animal and human.

TA2: Minutely Invasive Metrics

Phase I
Subcomponents and Transducers

Spatial resolution
<50 µm^3

Temporal resolution
<10 ms

Stability
Continuous operation for ≥ 2 hrs

Accuracy (read/write)
Correlation to ground truth accuracy ≥ 95%

Cell type specificity
Excitatory/inhibitory control for stimulation

Delivery
Viable strategy identified

Phase II
Integrated Device

Safety
≤ 1°C rise in tissue volume being read from/written to

Closed loop system latency
< 100 ms

Control signals
≥ 5 DOF

Sensory signals
≥ 5 categories
(ex: detection, alarm)

Integrated device size
≤ 125 cm^3

Channel count
read channels/volume (≥16/16mm^3)
write channels/volume (≥16/16mm^3)

Phase III
Final System

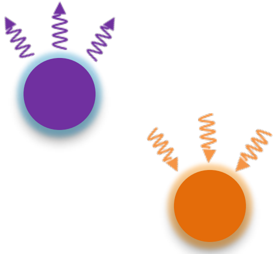
Closed loop system latency
< 50 ms

Control signals
≥ 10 DOF

Sensory signals
≥ 10 categories

Multifocal capability
≥ 4 read/write locations without crosstalk

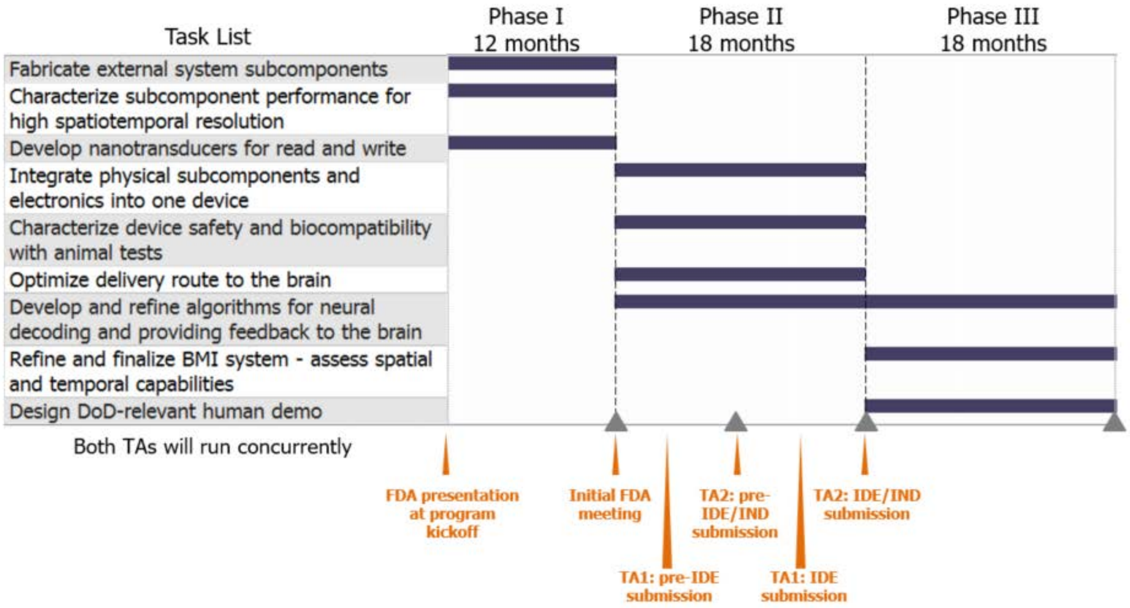
N³ Notional System



	Nanotransducer (TA2 only)	Integrated Device	Processing Unit
Read	Transduce neural activity into sensor input modality →	• Acquire signal • Amplify, filter, sort, multiplex signal • Transmit to external processing unit →	• Receive incoming signal • Decode signal • Provide signal to DoD application
Write	• Transduce stimulation modality into neural activity	← • Receive stimulation parameters from external processing unit • Broadcast stimulation waveform	← • Receive signal from DoD application • Encode signal • Transmit signal to integrated device

internal (Nanotransducer) | external (Integrated Device, Processing Unit)

N³ program structure and milestones



FDA milestones

21 Mo. Pre-IDE submission for TA1

24 Mo. Pre-IDE/IND submission for TA2

27 Mo. IDE submission for TA1

30 Mo. IDE/IND submission for TA2

Program demos ▲

12 Mo. Benchtop independent read and write capabilities

21 Mo. *In vivo* (animals, humans) open loop read and write capabilities

30 Mo. Demo: *In vivo* (animals, humans) closed-loop of integrated read and write capabilities

48 Mo. Demo: DoD relevant task with closed-loop control and feedback in humans

Technical Descriptions to Include in the Proposal

1. **Fabrication description for subcomponents (TA1 and TA2) and nanotransducer (TA2)**
   - Provide a detailed development timeline that describes relevant microfabrication or nanofabrication processes
2. **System-level design descriptions**
   - Describe the components, and a strategy for identifying system parameters
   - Describe the underlying physics, how to overcome scattering/attenuation challenges
3. **Phase I, II, III demonstration descriptions**
   - Describe demonstration ideas, justify the chosen method and why it is DoD relevant
4. **System integration description**
   - Identify a system integrator, and describe how to integrate read/write subcomponents
5. **Safety and histology description**
   - Describe procedures to collect the appropriate safety and histology data for FDA approval and to meet N^3 metrics
6. **Security Measures**
   - Describe approaches to ensure confidentiality, integrity, and availability to prevent spoofing, tampering, or denial of system
7. **Ethical, Legal, and Societal Implications (ELSI)**
   - Address the potential ELSI implications of the proposed technology

Teaming

To fully address the BAA you will likely need to team with other entities

- You must find your collaborators on your own
- Your team should submit a unified proposal under a single PI
- This BAA is open to educational institutions, government labs, and/or private companies
- Foreign entities may join a team or submit as the PI
- If you are a member of a team, you may join any number of other teams or form your own and submit a proposal as PI
- Note that the cost volume for each team member must be at the same level of details as for the PI

Additional Advice

- Read the BAA and follow all instructions carefully
- A successful proposal addresses all aspects of the BAA
- Pay attention to “must” and “should” language in the BAA
- Do not submit work that is not applicable to the BAA
- Do not propose to do anything that is not directly relevant to the BAA
- Do not propose incremental improvements to existing technology
- Do not submit an irrelevant or incomplete proposal in the hope we’ll fund it anyway
- Submitting a proposal abstract is **highly recommended**

Final Bits of Advice

Teaming is very important!

Use today to network and team