

Advanced Research
and Technology
Symposium

2018

Revolutions in Biotechnology

Warfighter Health and Performance

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Mr. Edward Wack
MIT Lincoln Laboratory
6 March 2018

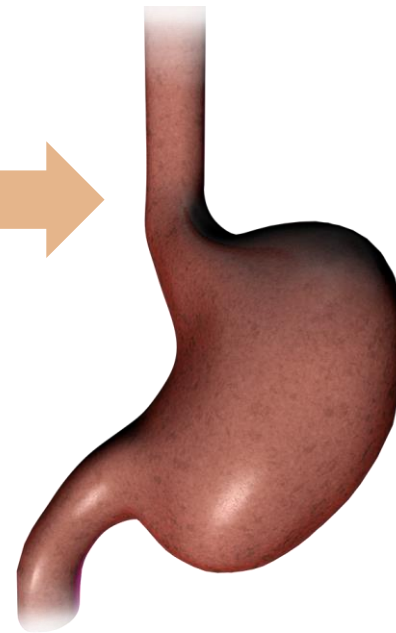
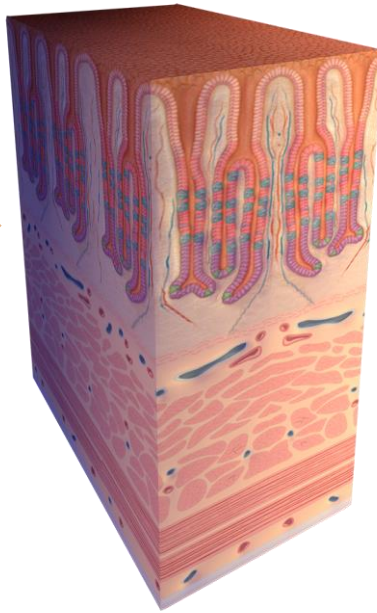
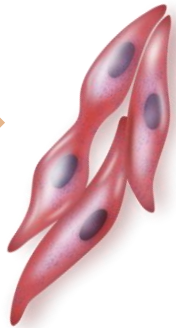
Select Revolutions in Biotechnology

DNA read, writing,
editing

Stem cell
reprogramming

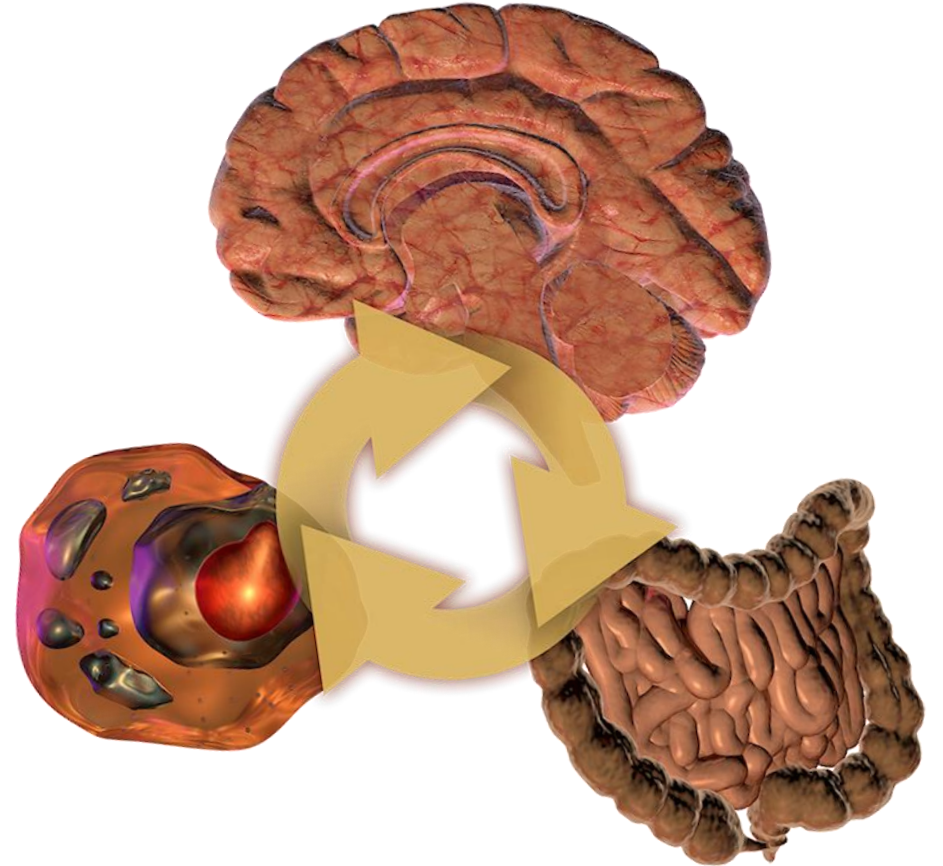
Organs-on-a-chip

Structural
and functional
measurements/models

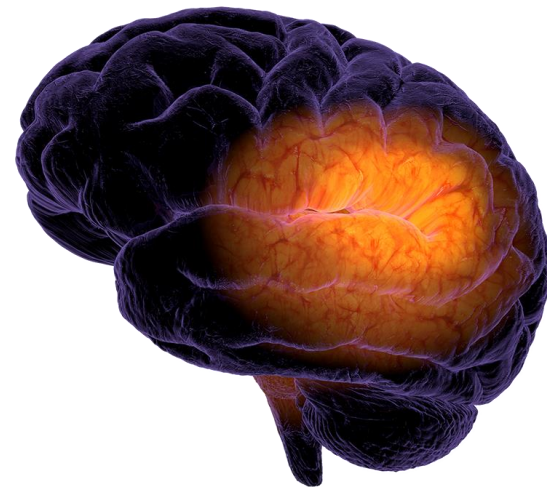
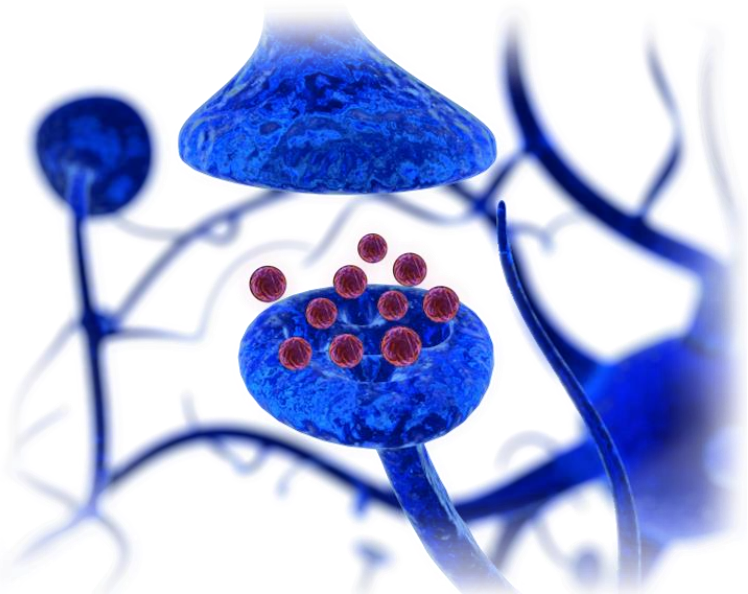


Complex Biological System Interactions

- Understanding complex systems, like the microbiome and its affect in the gut, immune system, and brain
- Modulating the body through these routes to improve health and performance



Complex Biological System Interactions



Operational Threats to Our Warfighters

- Environmental extremes (heat, cold, altitude)
- Physical and cognitive load
- CBRN
- Ballistic/kinetic
- Directed energy
- Psychological trauma
- Trauma care in austere environments

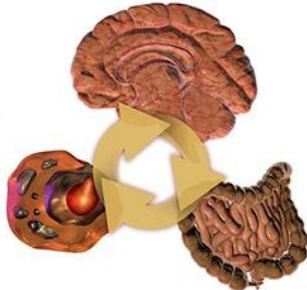


Revolutions in Biotechnology – The Speaker Session

Keynote Speaker for Revolutions in Biotechnology

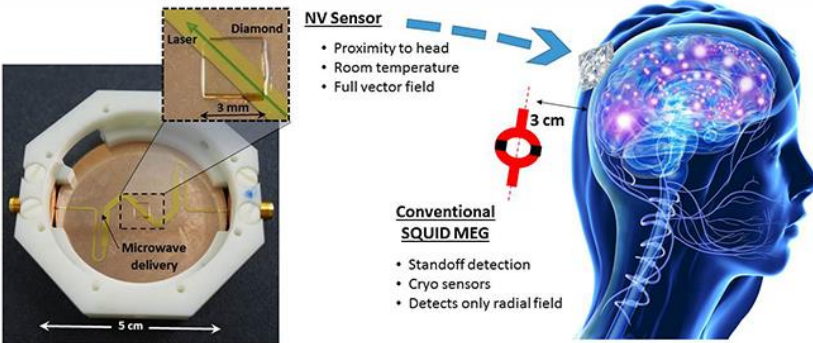
The Brain-Immune-Gut Super System
and the Emergence of Human Chronic Disease

- Understanding complex systems, like the microbiome and its affect in the gut, immune system, and brain
- Modulating the body through these routes to improve health and performance



ARTS Warfighter Health and Wellness - 6
ECW 03/06/18 LINCOLN LABORATORY
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

NV Sensor Advantages over Conventional MEG



NV Sensor

- Proximity to head
- Room temperature
- Full vector field

Conventional SQUID MEG

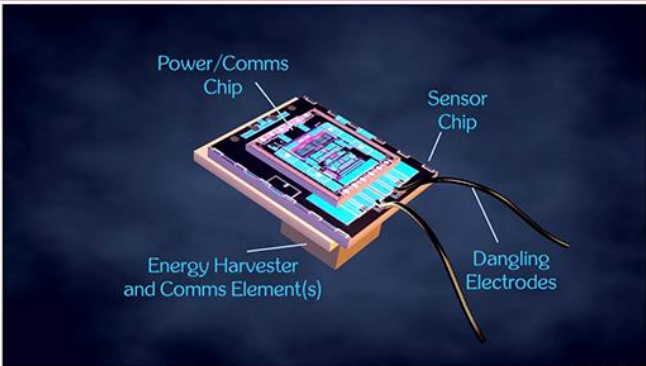
- Standoff detection
- Cryo sensors
- Detects only radial field

ARTS Quantum Sensing - 8
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Diamond Sensors for Brain Imaging

Microelectronics Interfacing Neural Devices (MIND)

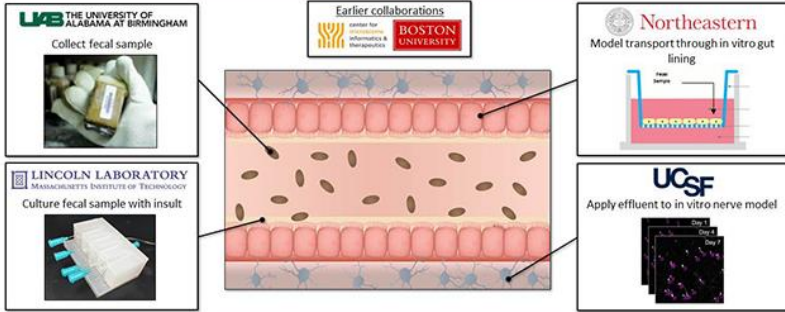
The Vision



Power/Comms Chip
Sensor Chip
Energy Harvester and Comms Element(s)
Dangling Electrodes

ARTS MIND - 1
AT 03/06/18 LINCOLN LABORATORY
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FY18 ArtGut Project



Earlier collaborations

- THE UNIVERSITY OF ALABAMA AT BIRMINGHAM: Collect fecal sample
- LINCOLN LABORATORY: Culture fecal sample with insult
- BOSTON UNIVERSITY: Model transport through in vitro gut lining
- UCsf: Apply effluent to in vitro nerve model

Meaningful collaborations shepherded by LL
create an integrated strategy to study Parkinson's

ARTS The Microbiome & M2 Movement - 14
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Microbiome

ARTS

The diagram illustrates the CLARITY/Map Intact Brain Imaging workflow and its associated data management components.

Brain Imaging at Different Scales: The workflow starts with a whole mouse brain, which is sectioned into coronal, sagittal, and horizontal planes. These sections are then processed through a series of steps: Embedding, Sectioning, Clearing, and Imaging. The final output is a high-resolution 3D volume rendering of the brain, showing cellular structures and molecular information. The workflow is supported by a database and a web interface.

CLARITY/Map Intact Brain Imaging:

- CLARITY/Map: High throughput (~1 TB/hr) and high resolution (cellular)
- Challenges: Efficient and fast analysis of massive brain images

CLARITY

MAP

(Magnified Analysis of the Proteome)

Before

After

CLARITY

MAP

CLARITY/Map Intact Brain Imaging

- Enable volumetric imaging
- Track long-range projections
- Resolve cellular structures
- Perform molecular phenotyping
- Expand linearly by four-fold
- Preserve overall architecture
- Resolve subcellular structures

MIT Lincoln Laboratory Advancing Data Science

LLC Bio Drive

PostgreSQL

- Image metadata
- Cytological/histological metadata
- Biological metadata (tissue type, staining technique, etc.)

SciDB/TeDB

- 3D MAP/CLARITY image data
- Fiber tracks

Accumulo

- Graph data from fiber tracks
- Connectivity analysis

MIT Lincoln Laboratory Application Expertise

- Provides a Results backend using a hybrid of databases (text, image, graph, etc.)
- Utilizes a common user interface/API
- Facilitates data sharing and collaborations with campus and the neuroscience community worldwide

Adam Brenner¹, Mark Hernandez¹, Mihnea Buzughiu¹, Lawrence Thul², Brian Telfer³, Ayaz Majumdar¹, Siddharth Sankar¹, Tessa Ku¹, Huiyong Chen¹, Kanchan Choudhary^{1,4,5,6}, Laura A. Bortolus¹

MIT Lincoln Laboratory, Lexington, MA¹, Northeastern University, Department of Chemical Engineering², Department of Chemical Engineering³, Department of Chemical Engineering⁴, Department of Chemical Engineering⁵, Department of Chemical Engineering⁶

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MIT Lincoln Laboratory is pioneering this technique using *acoustically isolated mice* or *microsensors* that are **flexible** and **biocompatible** and **incorporate** into a **hearing enhancement system**.


MIT Lincoln Laboratory collaborators at **Columbia University** pioneered this technique using **invasive neural recordings** (Mangunatne and Cheng, 2010; Nerturk) and more recently using **EEG** (O'Sullivan, 2016; Crevier-Curtis).

MicroProbes

• Microfabricated arrays for **neural arrays**


• Microfabricated arrays for **neural arrays**

Christopher Smith – MIT Lincoln Laboratory



- 250,000 traced fibers in a 250 GB volume
- 50 hrs on LISC (as opposed to months if done manually)
- Total length ~34 m
- Longest fiber is ~2 mm

Most fNIRS techniques use a **continuous-wave** laser source and **single-photon detectors** to measure changes in **blood volume** and **hemoglobin oxygenation** in response to brain function.



Continuous-wave Near-Infrared Spectroscopy


Goals

- Build a **high-resolution** whole brain atlas
- Enable cell **typing** by morphology and **connectivity**
- Map the **structure** to **function**
- Compare **healthy** and **diseased** brains

Challenges

- Need novel algorithms for **large-scale cell detection**
- Need to **improve** the processing speed and **accuracy**
- Need novel **user interface** to support interactive analytics

By using a **train of long-coherence length** laser pulses and **gated single-photon detectors**, Lincoln Laboratory can **simultaneously** measure **blood volume**, **blood oxygenation**, and **blood flow**.



Time-Domain Diffuse Correlation Spectroscopy

[illegible]

Looking Towards the Future



- Biotechnologies are advancing at a rapid pace
- We will continue to develop and apply these biotechnologies to solve critical health and performance challenges
- This will lead to healthier and more effective servicemembers
 - Active duty and reintegrating into civilian life
- ... and healthier and happier civilians as military medical technologies transition to the commercial sector