Human Performance and Biosystems

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Spring Review

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Integrity ★ Service ★ Excellence
Human Performance and Biosystems Program

- Investigates scientific challenges of Bioenergy from cells
- Develops a mechanistic understanding of microbes, nanowires and their energy transfer processes
- Studies electrical transfer capabilities between biotic and abiotic surfaces

Air Force Relevance

Sensors: mapping of Brain/neural activity for cognitive enhancement

: Early detection of cell product and pathway processes

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Areas of Emphasis

Biofilms/Nanowires – microbe communication, extracellular electron transfer, cyborg cell

Trans cranial direct current stimulation – neuronal pathways, biochemical/electrophysiological changes

Biomarkers – breath based, sweat based, odor based
Program Trends

• Enzymatic/Microbial Fuel Cells
• Artificial Photosynthesis
• Algal oil generation
• Biofilm, Nanowires, Cyborg Cell
• tDCS
• Biomarkers
Program Interactions

- tDCS/Cyborg cell
- Microbes/nanowires
- Biomarkers
- BRI magnetic navigation
- Synthetic Biology
Biofilms and Nanowires Challenges

Channel electronic signals between synthetic devices and the electron transport chains of live cells

Develop solid-state and molecular (electrode-free) interfaces to bacterial nanowires, for control of cellular bioenergetics

Channel photo-excited states into donating electrons to multiheme cytochromes instead of fluorescence
Physiological switch: Developed methodology to physiologically induce bacterial nanowires in microfluidic devices as shown here by switching to extracellular respiration conditions.

Can we achieve a genetic switch? Long-term goal: Synthetic biology approach for transferring the extracellular electron transport function naturally existing in microbes to other cell types.

Can we “plug” cells directly to synthetic devices using this same methodology? Long-term goal: Connecting and powering a synthetic device using cellular metabolic activity.

Next-generation sequencing
Discover the **nanoscale** spatial organization of electron transport proteins in bacterial nanowires

**Goal** - channel electronic signals between synthetic devices and the electron transport chains of live cells.
Interfacing to the Electron Transport Chain of Living Cells

Develop both **solid-state and molecular (electrode-free) interfaces to bacterial nanowires**, to control cell bioenergetics

**Solid-state interfaces:**

Nanowires membrane = lipid-based. Does a phospholipid-coated metallooxide electrode increase connectivity?

**Molecular “Stealth” interfaces:**

Basic idea: channel photo-excited states into donating electrons to multiheme cytochromes instead of fluorescence.

Electrode

GFP

MtrC/F
Can bacterial extracellular electron transport and bacterial nanowire functionality be relevant to mitochondria?

Adapt a technology developed for bacterial electron transport, while studying the feasibility of expressing bacterial ET components in mitochondria (high risk):

Manipulation and ET measurements of individual microbes on microscale “landing pad” electrodes

Single-cell electron transfer rates → 300 fA
Nanoelectronic Structures for Single Cell to Cell-Network Interfaces – Cyborg Cell

Charles M. Lieber
Harvard University

Distribution A: Approved for public release; distribution is unlimited.
“Blur the distinction between electronic devices, circuits, living cells & tissue!”

Future: Interfaces to Cells, Tissue & Organs

ENIAC 30 tons, 150 kW, 100-5000 instructions/sec

“Blur the distinction between electronic devices, circuits, living cells & tissue!”

New Materials!

Novel Tools!

grams, <100 W, 50×10^9 instructions/sec
Challenges:

- Finding external energy source
- Determining how to manipulate and measure organelle changes
- How to deliver this to the system

Charles M. Lieber

*Harvard University*
Macroporous 3D Nanoelectronics: Cyborg Tissue

** 3D addressable nanodevices **
3D Macroporous Nanoelectronic Scaffolds

- 3D nanoelectronic scaffolds matrix prepared from 2D structures that are fully released from substrate.
- 3D scaffolds can exceed thickness $>>1$mm and maintain all key feature on micron-to-nanometer scale similar to natural biological scaffolds
‘Cyborg’ Neural Tissue

3D neural tissue ‘innervated’ with 3D nanoelectronic circuitry – future is only limited by our imagination!
Neurobiological effects of direct current stimulation

Goal: provide protection and enhanced performance to the warfighter
Transcranial Direct Current Stimulation (tDCS)

- Non-invasive, portable, well-tolerated neuromodulation.
- Low-intensity (1-2mA) current passed between scalp electrodes.
- Clinically used for: Depression, pain, migraine, epilepsy, PTSD, schizophrenia, tinnitus, rehabilitation, TBI, attention deficit, autism
- In laboratory setting used for: accelerated learning (reading, motor skills, threat detection), memory…etc.

QUESTION - Does a “simple” directed current modulate brain function? If so, how does it work, what does it change, what parameters are associated with the changes, are they repeatable, why do changes take place…?

“Cellular Mechanisms of Transcranial Direct Current Stimulation”, PI - Marom Bikson, CUNY
Transcranial Direct Current Stimulation

Two pad electrodes placed on head and connected to DC current stimulator.

Current passed between ANODE(+) and CATHODE(-)

DC CURRENT FLOW across cortex.

Current is INWARD under ANODE and OUTWARD under CATHODE
Introduction

- Intervention/Treatment for neurological Disorders: Parkinson’s, Psychiatric Disease & Stroke
- Cognitive improvements reported in both Disease and Control Populations
- Increased Cerebral Oxygen Saturation
- Improved Target Detection

Andy McKinley, PhD - AFRL
Hypothesis

Purpose of study: Identify biological pathways thought responsible for enhanced cognitive performance after tDCS

• Objective 1: Identify pathways recruited by single bout of tDCS.

• Objective 2: Determine effects of repeated tDCS when coupled with training.
tDCS Research at CUNY

Computational Models

Animal DCS

Tissue/Brain Slice tDCS
Immunohistochemistry
Immunohistochemistry

SSC

CA1

DG
tDCS Summary

• Molecular, anatomical and genetic approach to studying changes associated with tDCS.
• Anecdotal evidence prevalent not much hard science to support claims
• 2 studies on going in Air Force Research Laboratory, one currently underway in academic setting looking at mechanisms.

• Potential benefit if positive results – decrease neurological fatigue, increased awareness, shortened learning time to task, focused attention
Biomarkers

- Interested in discovering new biomarkers from sweat, breath and odor associated with sweat and breath
- F22 grounding may have been prevented if O2 system was monitored and sensor development was available
  - Current new study looking at breath biomarker to determine early stage of hypoxia.
- Additional study for FY14 funding looking at the analytical identification of stress odors from human breath
- Potential benefit – if we can find a problem before it happens we can avoid costly mistakes
Summary

• Molecular, anatomical and genetic approach to studying microbe physiology and electron transfer.

• Microbial mechanisms led to communication capabilities and cyborg cell development idea.

• Cyborg cell and 3D nanoelectric scaffold enables cellular communication from outside cell and ability to “program” individual cell as well as “correct”, change, direct cell to target.

• Transcranial Direct Current Stimulation studies are underway to determine the efficacy of this modality.