Bio/Nanotechnology, Sensors and Brain Research Programs at NSF

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Chenzhong Li, CBET
Kurt Thoroughman, SBE/BCS
Kenneth Whang, CISE/IIS
Wendy Nilsen, CISE/IIS

ECCS (Electrical, Communication and Cyber Systems) From Devices to Systems: Three Core Program Clusters

- **EPMD: Electronics, Photonics, and Magnetic Devices**
  - Nanoelectronic, Novel Semiconductor, and μWave-THz Devices
  - Nanophotonic, Optical Imaging, and Single-Photon Quantum Devices
  - Biomagnetic, Nanomagnetic and Spin Electronic Devices
- **CCSS: Communications, Circuits, and Sensing Systems**
  - RF Circuits and Antennas for Communications and Sensing
  - Communication Systems and Signal Processing
  - Dynamic Bio-Sensing Systems
- **EPCN: Energy, Power, Control, and Networks**
  - Control Systems
  - Energy and Power Systems
  - Power Electronics Systems
  - Learning and Adaptive Systems

Trends in Program Focus (FY19-21)

Dynamic Bio Systems (Shubhra Gangopadhyay)

- Growing interest in dynamic and reconfigurable systems with real-time learning, for example:
  - self-powered or wirelessly powered wearable and implantable dynamic systems for continuous health monitoring

- Increasing interest in continuous monitoring systems with multiple networked sensors integrated with real-time learning, signal processing, feedback and control, and data analytics

Stretchable Planar Antenna Modulated by Integrated Circuit (SPAMIC) for the Near Field Communication (NFC) of Epidermal Electrophysiological Sensors (EEPS)

1509767 – Nanshu Lu, Nan Sun – ut Austin

I. Recent Outcomes & Accomplishments:

We have demonstrated that stretchable planar antenna can be fabricated on ultrathin, ultrasoft wearable e-tattoos to enable NFC-based wireless power and data transmission even under severe skin deformation.

Outcomes:

- Cut-solder-paste manufacturing process has been developed for the rapid prototyping of NFC-enabled battery-free, wireless e-tattoo (*EMBC'17*)
- Stretchable planar antenna can be optimized to be almost insensitive to mechanical deformation (to be submitted)
- Multilayer e-tattoo exploring the modular concept allows the NFC and functional layers to be reusable (to be submitted)
- Low-power, low-noise IC amplifier has been designed, taped out and validated (*IEEE Journal of Solid-State Circuits* 53, 896-905, 2018)

III. Broader Impact:

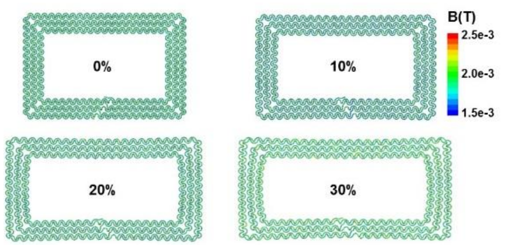
Intellectual, Industrial and Societal:

- Battery-free, wireless skin-like noninvasive e-tattoos are unobstructive to wear for days and disposable after use, which is ideal sensing modality for mobile health
- The rapid prototyping method has significantly lowered the barrier to manufacturing skin-like e-tattoos
- Wireless charging and low power amplifier are transformative because they can also benefit implantable devices
- Three female undergrads and one Africa American undergrad were trained to manufacture NFC-enabled wireless e-tattoos
- The wireless e-tattoos have been demonstrated in multiple outreach events including Explore UT, WE@UT, and Girls Day
- A school-level graduate course for interdisciplinary research is under discussion with UT Cockrell School of Engineering

II. Basic Principles:

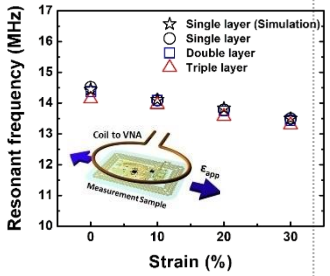
- Stretchable planar antenna is susceptible to mechanical deformation but can be optimized to be less sensitive to mechanical strain

a



a, finite element modeling (FEM) to unveil the coupled mechanical and electromagnetic behavior of the stretchable planar antenna

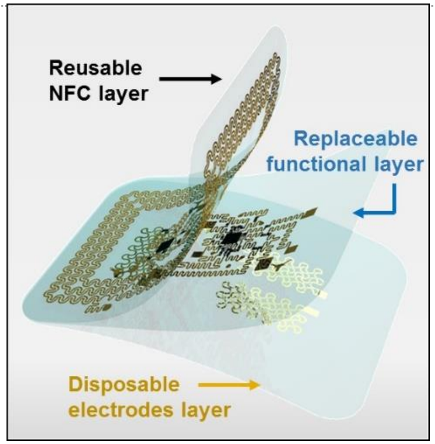
b



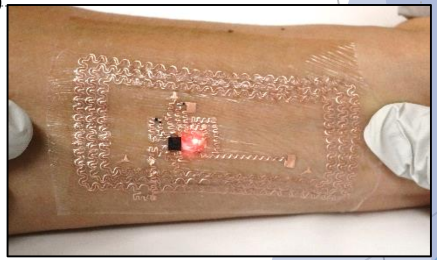
b, modeling and experimental results of resonant frequency shift with mechanical strain

- By stacking inverters and splitting the capacitor feedback network, the designed amplifier achieves six-time current reuse, thereby significantly boosting the transconductance and lowering noise without increasing the current consumption

a



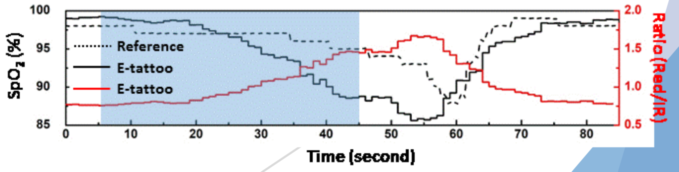
b



b, the e-tattoo on human skin under stretch. The LED is wirelessly turned on via inductive coupling from a primary coil concealed under the arm

a, modularized e-tattoo concept in which the NFC and functional layers are stackable and reusable.

c



c, SpO_2 wirelessly measured by the e-tattoo (solid curves) compared with conventional oximeter (dashed curve).

Bio-artificial Neuromorphic System Based on Synaptic Devices

[CAREER-1752241] – Duygu Kuzum – University of California, san diego

I. Recent Outcomes & Accomplishments:

The aim is to develop a neuromorphic interface, which will serve as a translator adapting time, amplitude and shape characteristics of the electrical stimuli transmitted to/from the brain.

Challenges that will be addressed during the course of the project include:

- Poor signal transduction between electronics and the tissue
- Limited information transfer capacity of microelectrode arrays
- Severe foreign body response induced by these invasive inorganic devices

II. Basic Principles:

This CAREER proposal pioneers a new effort to develop a neuromorphic tissue made of biological neurons dynamically connected with synthetic synaptic devices, combining our expertise in neuromorphic devices and neural interfaces. Bio-artificial neuromorphic tissue will deliver several revolutionary features including (1) Biocompatible plastic synaptic devices engineered for dynamically connecting biological neurons, (2) Gaphene-based approaches for enhanced synaptic device-cell coupling and effective signal transduction, (3) Geometrical design of neural cultures for well-defined connectivity, (4) Pattern recognition capability, and last but not least (5) Potential for natural synaptic integration with the tissue to prevent chronic immune response.

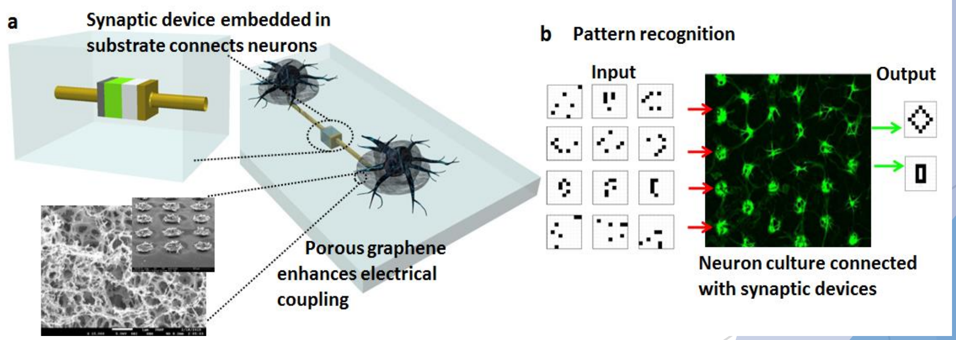
III. Broader Impact:

Intellectual, Industrial and Societal:

The aim of the proposed research is to develop a neuromorphic interface made of synthetic synaptic devices to form a stable, long-term input/output interface to the brain.

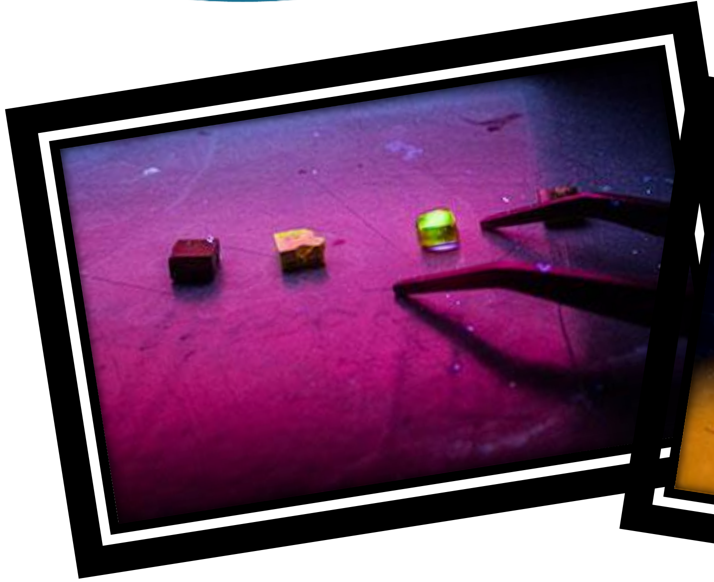
Such a technology can help development of targeted and selective neuromodulation therapies for various neurological disorders (epilepsy, depression, memory disorders, etc) affecting one billion people worldwide.

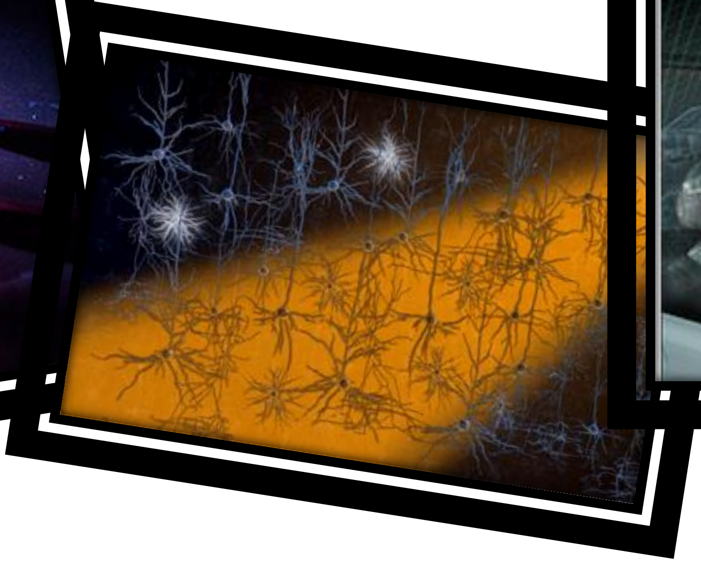
Long-term chronic studies enabled by this technology can revolutionize the speed of progress in brain activity mapping.

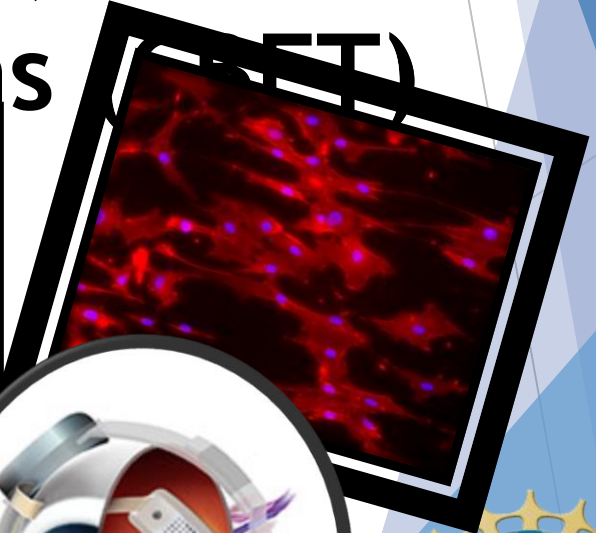


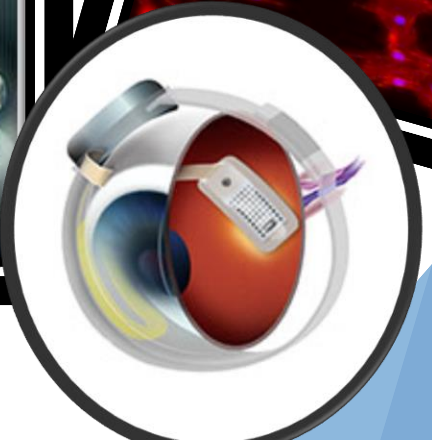
a. Plastic synaptic devices connecting biological neurons. Porous graphene enhances electrical coupling. **b.** Conceptual schematic shows geometrical cultures forming neuromorphic networks with pattern classification capability.

Division of Chemical, Bioengineering, Environmental, and Transport Systems









National Science Foundation

ENGINEERING BIOLOGY & HEALTH

Chenzhong Li

Biosensing
- Multi-purpose sensor platforms
- Novel transduction principles, mechanisms and sensor designs
- Nano-biosensors for biomolecular interactions
- Intracellular biosensing

Alex Simonium

Engineering Biomedical Systems
- Models for tissues and organ systems
- Advanced biomanufacturing of 3-D tissues and organs
- New tools to study physiological processes

Disability and Rehabilitation Engineering
- Neuroengineering
- Rehabilitation robotics

Leon Esterowitz

Biophotonics
- Macromolecule Markers
- Micro- & Nano-photonics; Low-Coherence Sensing @ Nanoscale
- Neurophotonics and Optogenetics

Steve Peretti

Cellular & Biochemical Engineering
- Biomanufacturing: Metabolic eng, “omics”, single cell dynamics and synthetic biology
- Quantitative systems biotechnology
- Cell culture technologies
- Protein and enzyme engineering

PROGRAMS SUPPORTING RESEARCH WITH BIOMEDICAL & HEALTH APPLICATIONS

October 2018

ENGINEERING DIRECTORATE

Chemical, Bioengineering, Environmental, & Transport Systems
- Biophotonics
- Biosensing
- Cellular & Biochemical Engineering
- Disability & Rehabilitation Engineering
- Engineering of Biomedical Systems
- Fluid Dynamics

Civil, Mechanical, & Manufacturing Innovation
- Advanced Manufacturing
- Biomechanics & Mechanobiology
- Dynamics, Controls, & Systems Diagnostics
- Mind, Machine, & Motor Nexus
- Operations Engineering

Electrical, Communications & Cyber Systems
- Communications, Circuits, & Sensing Systems
- Electronics, Photonics, & Magnetic Devices

Industrial Innovation & Partnerships
- All IIP programs will consider projects related to biomedical & health applications

Emerging Frontiers & Multidisciplinary Activities
- Chromatin & Epigenetic Engineering
- Continuum, Compliant, & Configurable Soft Robotics Engineering

MATHEMATICS & PHYSICAL SCIENCES DIRECTORATE

Division of Materials Research
- Biomaterials

Division of Physics
- Physics of Living Systems

COMPUTING & INFORMATION SCIENCE & ENGINEERING DIRECTORATE

Information & Intelligent Systems
- Cyber Human Systems

CROSS-AGENCY, CROSS-DIRECTORATE, & SPECIAL SOLICITATIONS

- Smart & Connected Health
- Cyber-Physical Systems
- National Robotics Initiative 2.0
- NSF/FDA Scholar-in-Residence at FDA
- Computational & Data-Enabled Science & Engineering
- Leading Engineering for America's Prosperity, Health, & Infrastructure (LEAP HI)
- Collaborative Research in Computational Neuroscience
- Integrative Strategies for Neural & Cognitive Systems
- NSF/CASIS Collaboration on Tissue Engineering and Mechanobiology on the ISS to Benefit Life on

NSF'S TEN BIG IDEAS RELATED TO BIOMEDICAL & HEALTH APPLICATIONS

- Future of Work at the Human- Technology Frontier
- Understanding the Rules of Life: Predicting Phenotype
- Harnessing Data for 21st Century Science & Engineering
- Growing Convergence Research at the National Science Foundation

(Keep an Eye Open for Dear Colleague Letters & Solicitations)

Engineering of Biomedical Systems

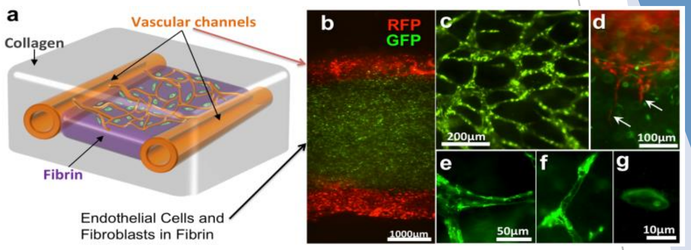
Biomedical & Health Applications

Program Objectives:

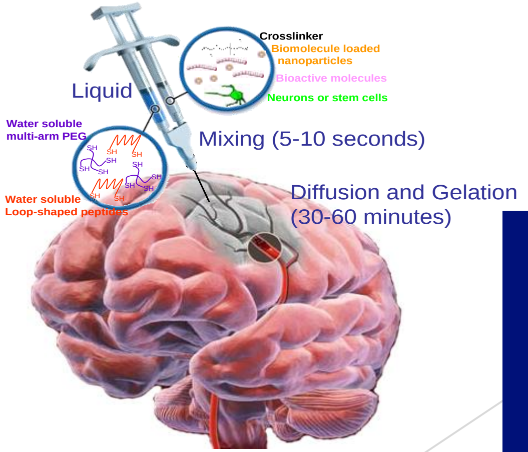
- Develop novel ideas into transformative solutions for biomedical problems
- Advance engineering and biomedical sciences, integrating the two disciplines

Key Components :

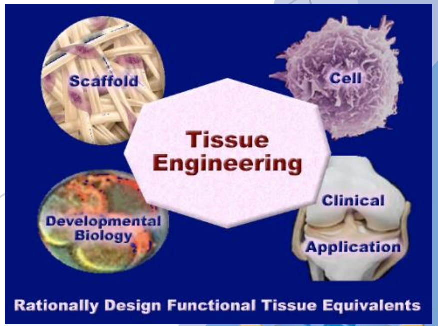
- Development of validated models of normal and pathological tissues and organ systems
- Design of systems that integrate living and non-living components for improved diagnosis, monitoring, and treatment of disease or injury
- Advanced biomanufacturing of 3D tissues and organs
- Design and subsequent application of technologies and tools to investigate fundamental physiological and pathophysiological processes



***In vitro* vascularization**



CNS regeneration



National Science Foundation

Disability & Rehabilitation Engineering (DARE)

Biomedical & Health Applications

Program Objectives:

- Develop understanding, interventions, & technologies to improve the quality of life of persons with disabilities
- Support research directed to the characterization, restoration, and/or substitution of human functional ability or cognition
- Novel engineering approaches to understanding human motion
- Understanding injury at the tissue or system-level

Key Components:

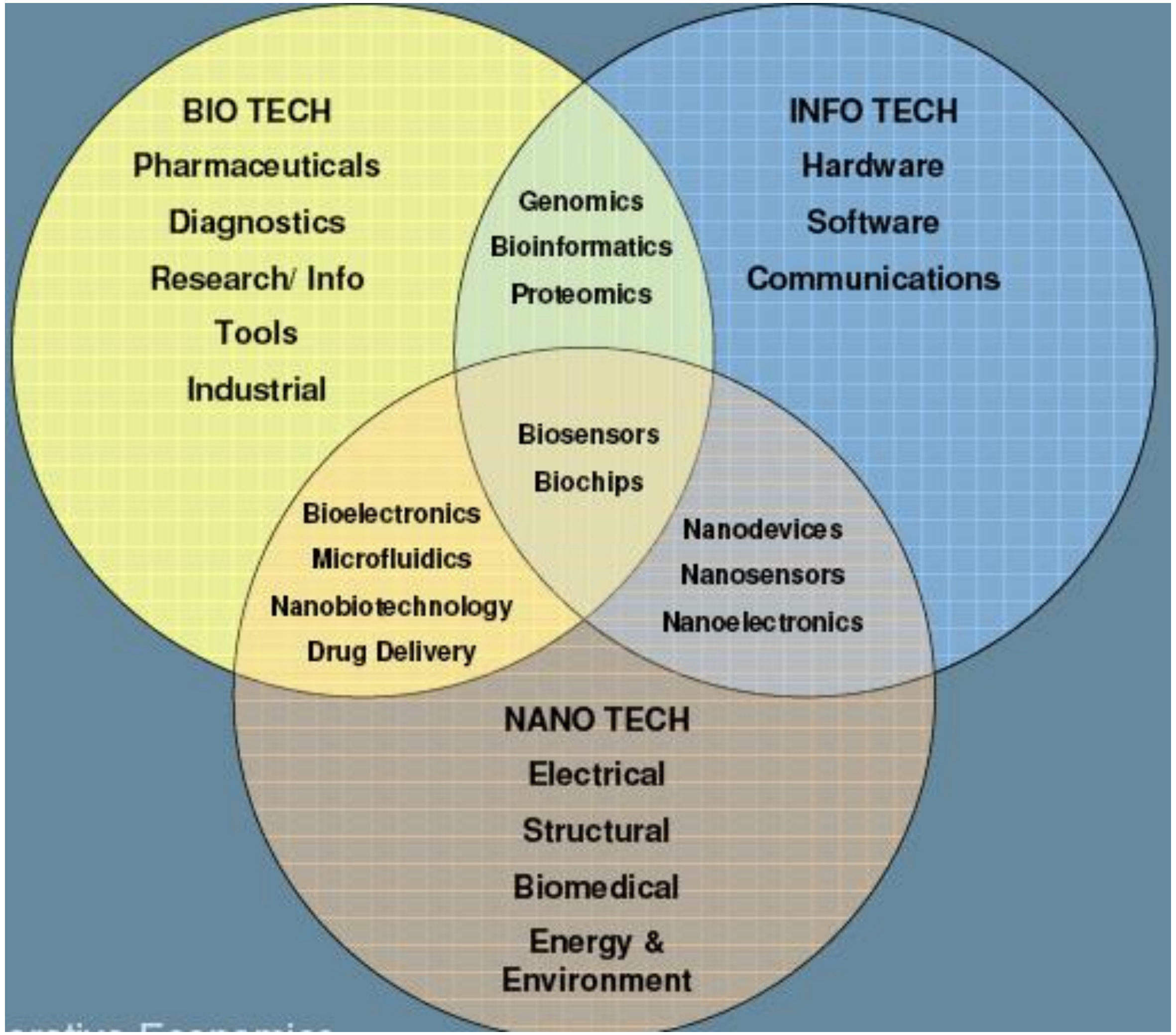
- Fundamental engineering research
- Transformative outcomes
- Focus on a single disability if addressing objective #1

Exoskeleton optimization

Brain computer interface for prosthetic and robotic control

Biosensors- Miniaturized Analytical Tools

Device that detects, records, and transmits information regarding a physiological change or process



- **Rapid**
- **Specific**
- **Sensitive and able to detect small amounts of target within a high background matrix**

- **Easy to use: portable, disposable, stable, etc.**
- **Multiplex assay**
- **Low cost**
- **Fast response**

Biosensor Applications

Biosensors are not just for quantitate analysis, also for characterization-function, structure, properties, etc.

National Science Foundation

biosensing

Program Scope

- **Support engineering research on biosensor design and fabrication for novel biological analysis.**
- **Examples of biosensors include, but are not limited to, electrochemical/electrical biosensors, optical biosensors, plasmonic biosensors, wearable biosensors, paper-based and nanopore-based biosensors**
- **Biosensor-based technologies to address critical needs for biomedical research, public health, food safety, agriculture, forensics, environmental protection, and homeland security are highly encouraged**
- **Miniaturization of biosensors for lab-on-a-chip and cell/organ-on-a-chip applications to enable measurement of biological properties and functions of cell/tissues in vitro.**
- **Biosensors that enable measurement of biomolecular interactions in their native states, transmembrane transport, intracellular transport and reactions, and other biological phenomena**
- **Integration of AI and machine learning to biosensing technology is encouraged**

Program Director: Dr. Chenzhong Li, Email:chli@nsf.gov

The Biosensors Program does not encourage proposals addressing

- **Surface functionalization and modulation of bio-recognition molecules**
- **Development of basic chemical mechanisms for biosensing applications**
- **Circuit design for signal processing and amplification, computational modeling, and microfluidics for sample separation and filtration.**
- **Medical imaging-based measurements are out of the scope of the program interests.**
- **Proposals for optimizing and/or utilizing established methods for specific applications should be directed to programs focused on the application.**

Integrative Strategies for Understanding Neural and Cognitive Systems

http://www.nsf.gov/ncs/ (CISE, EHR, ENG, SBE)

Emphasis on ***transformative, integrative approaches*** to tackle previously intractable challenges. Integrative themes represent emerging foci where novel integrative strategies are expected to have significant impact:

- ***Neuroengineering and Brain-Inspired Concepts and Designs***
- ***Individuality and Variation***
- ***Data-Intensive Neuroscience and Cognitive Science***
- ***Cognitive and Neural Processes in Realistic, Complex Environments***

Due Dates (due by 5 p.m. submitter's local time)

FOUNDATIONS:

LOI January 8, 2020

Full Proposal February 26, 2020

FRONTIERS (large projects); **FOUNDATIONS** (500K-1M, 2-4 yrs); **CORE+ SUPPLEMENTS** (CISE, EHR, ENG) to connect new or existing projects to neural and cognitive systems

Questions? e-mail NCS@nsf.gov

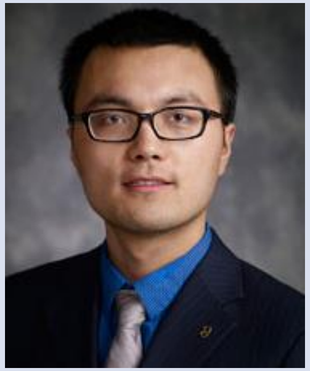
Integrative Strategies for Understanding Neural and Cognitive Systems (NCS)

Program Goals

- The complexities of brain and behavior pose fundamental questions in many areas of science and engineering, drawing intense interest across a broad spectrum of disciplinary perspectives while eluding explanation by any one of them.
- NCS calls for innovative, integrative, boundary-crossing proposals that can best address these questions and map out new research frontiers. NSF seeks proposals that are bold and risky, and transcend the perspectives and approaches typical of disciplinary research efforts.

NCS is supported by CISE, EHR, ENG, and SBE.

What are the products of the awards? Example 1



Zhenpeng Qin (Mech Eng, UTDallas), with collaborators:

Jonathan Ploski, Beh & Brain Science

Sven Kroener, Mol and Cell Bio

3 team members, from 2 disciplines

All three team members are ***first time NSF awardees****!*

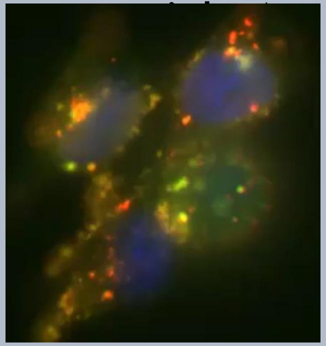
Wrote a proposal to NCS

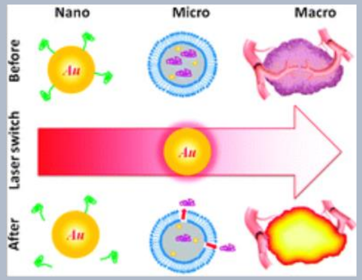
NCS-FO: Sub-millisecond Optically-triggered Compound Release to Study Real-time Brain Activity and Behavior

2016

Funding resulted in

- 2 publications
- 4 conference publications
- 1 science outreach highlight by NSF
- 1 invention (mechanosensitive





Leading to these impacts

- Papers released in late 2017, patent application in 2018 – so we don't know the wider impacts yet!

- New ways to study neurotransmitters?

- Real time study of brain+behavior?

NSF-NIH-BMBF-ANR-BSF-NICT-AEI-ISCIII Joint Program

Collaborative Research in Computational Neuroscience

http://www.nsf.gov/crcns

- Computational neuroscience, inclusively defined

  encompassing many approaches and goals; related to biological processes; disease and normal function; theory, modeling, and analysis; implications for biological and engineered systems

- ***Innovative, collaborative, and interdisciplinary***

  to make significant advances on important hard problems, and to develop new research capabilities

The program considers **Research Proposals** describing collaborative projects that bring together complementary expertise on interdisciplinary challenges; and **Data Sharing Proposals** to support preparation and deployment of data and other resources, in a manner that responds to the needs of a broad community.

US domestic and international collaborations are welcome. Opportunities for ***parallel international funding*** (Germany, France, Israel, Japan, Spain, and multilateral). Next deadline: November 25, 2019

Smart & Connected Health (SCH)

Inter-Agency Program
National Science Foundation
National Institutes of Health

NSF Solicitation NSF 18-541

Wendy Nilsen, PhD
Program Director, Smart and Connected Health
Computer and Information Sciences and Engineering, NSF

Scope of SCH Program

***Goal:** To accelerate the development and integration of innovative computer and information science and engineering approaches to transform health and medicine.*

- **Funded** work must address:
  - ✓ Existing research gaps in science & technology
  - ✓ A key health problem
  - ✓ Include a research team with appropriate expertise in the major areas involved in the work

- SCH projects connect data, systems and people. The goal is not to create one-off projects, but sustainable change.

- Activities should **complement** rather than duplicate core programs of NSF & NIH as well as those of other agencies (ex. Agency for Healthcare Research and Quality / Veteran's Administration)

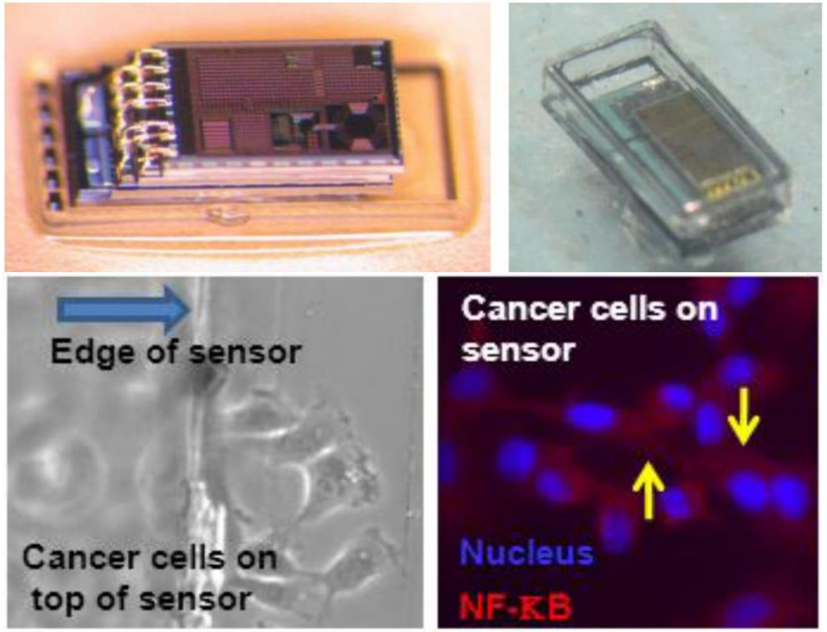
NSF

NIH National Institutes of Health
Turning Discovery Into Health

NSF

Wireless Implantable Electronic Biosensors for Tumor Monitoring

David Blaauw, University of Michigan NSF Grant #1418472



Motivation:

- Ability to quantitatively analyze biochemistry and physiology continuously in intact organs and tissues has the potential to revolutionize medical research and clinical care
- Current technologies, such as biomedical imaging and tissue analysis, give only snapshots of in vivo structure and provide poor temporal granularity

Transformative:

- A new generation of ultra-low power, wireless, implantable, and miniaturized biosensors for real-time, continuous monitoring of key biochemical parameters
- Determine response to therapy within days, ability to optimize chemotherapy protocols for individuals

Broader Impacts:

•Ultra-low power ≈ 1 mm^3 scale sensors are a major contribution with widespread applications in many areas of medicine and other scientific disciplines

•Ambitious educational program including curriculum development and K-12 outreach using the proposed sensor nodes.

Contacts:

- PI: David Blaauw (EECS), University of Michigan
- Yoonmyung Lee (EECS), Gary Luker (Radiology), Kathryn Luker (Radiology), Joanna Millunchick (Mat. Sci.), Jamie Phillips (EECS), and Dennis Sylvester (EECS)

Technical Approach:

- Develop low-power mm-scale sensor nodes capable of through-tissue infrared energy harvesting and robust analog to digital conversion for pressure and pH sensing
- Compare results using biosensors to assess response of living mice to therapy with F18-fluorodeoxyglucose (FDG) PET/CT

PATHS-UP NSF ERC
THRUST 4: REMOTE BIO-BEHAVIORAL INFERENCE FOR PERSONALIZED PATIENT SUPPORT SYSTEMS

I. Anticipated Outcomes & Accomplishments:

- The ability to identify early signs of long-term complications by combining biomarker data from novel lab-on-a-wrist (LoaW) and lab-in-your-palm (LiyP) systems with population data (including electronic medical records)
- The ability to identify moments of food intake and predict the nutritional value of those foods
- An understanding of the primary barriers to healthy behavior and effective reinforcements to encourage healthy behaviors
- An understanding of the barriers to technology adoption and reduction of these barriers through participatory design and stakeholder engagement across the ERC

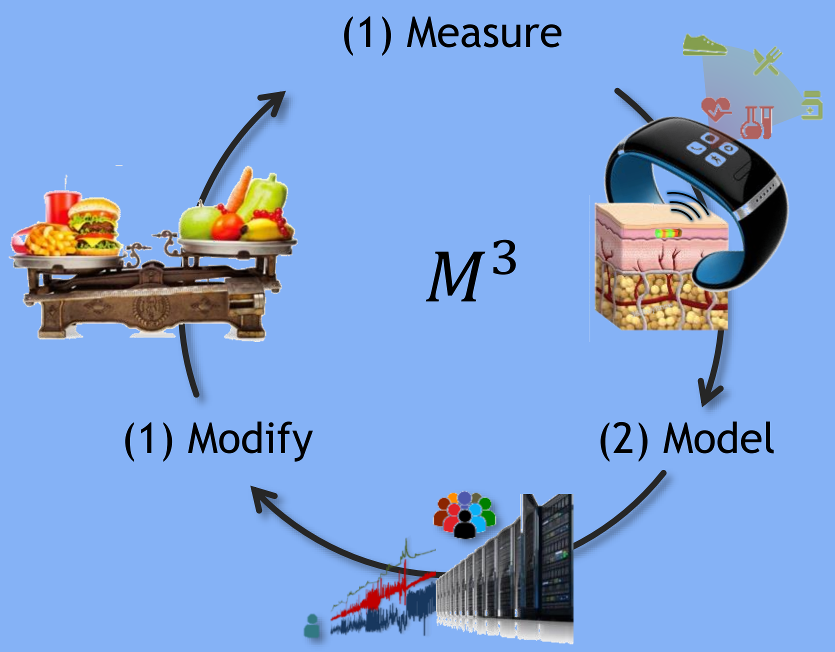
II. Basic Principles:

Thrust 4 of NSF PATHS-UP is driven by the goal of converting innovative biomarker measurements (thrust 1-3) into breakthrough patient support systems. To achieve the goal we will follow a comprehensive framework cyclical model (M^3) that consists of three basic principles:

- **Measure:** Infer key behaviors (food intake, medication adherence, exercise) from and chemical, physiological biomarkers measured with the innovative LoaW and LiyP engineered systems
- **Model:** Predict the risk of long-term complications and identify early signs in biomarker data
- **Modify:** Design technology-based interventions for behavior change via participatory design and stakeholder engagement in the communities and across the ERC

III. Broader Impact:

- Increased adherence with medical treatments by developing personalized reinforcers
- Personalized nutrition programs for metabolic diseases beyond diabetes and cardiovascular disease
- Reduced healthcare costs by anticipating long-term complications and acute episodes with a focus on diabetes and cardiovascular disease
- Recruit and educate the next generation of diverse innovation leaders who are ready to impact the future in developing transformative technologies to significantly improve health in underserved communities including for thrust 4 student training opportunities in data analytics, participatory design and stakeholder engagement across the ERC



Advanced Self-Powered Systems of Integrated Sensors and Technologies

SSIST

NSF NANOSYSTEMS ENGINEERING RESEARCH CENTER FOR

ADVANCED SELF-POWERED SYSTEMS OF INTEGRATED SENSORS AND TECHNOLOGIES

NC STATE UNIVERSITY

FIU FLORIDA INTERNATIONAL UNIVERSITY

PennState

UNIVERSITY of VIRGINIA SCHOOL OF ENGINEERING

UNIVERSITY OF NOTRE DAME

UNC SCHOOL OF MEDICINE

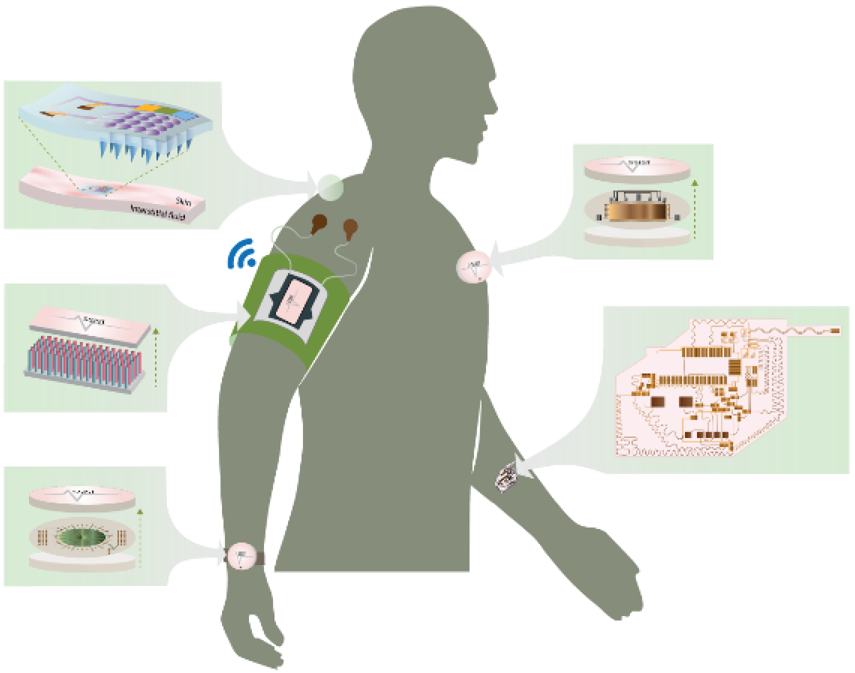
UNIVERSITY OF MICHIGAN

THE UNIVERSITY OF UTAH

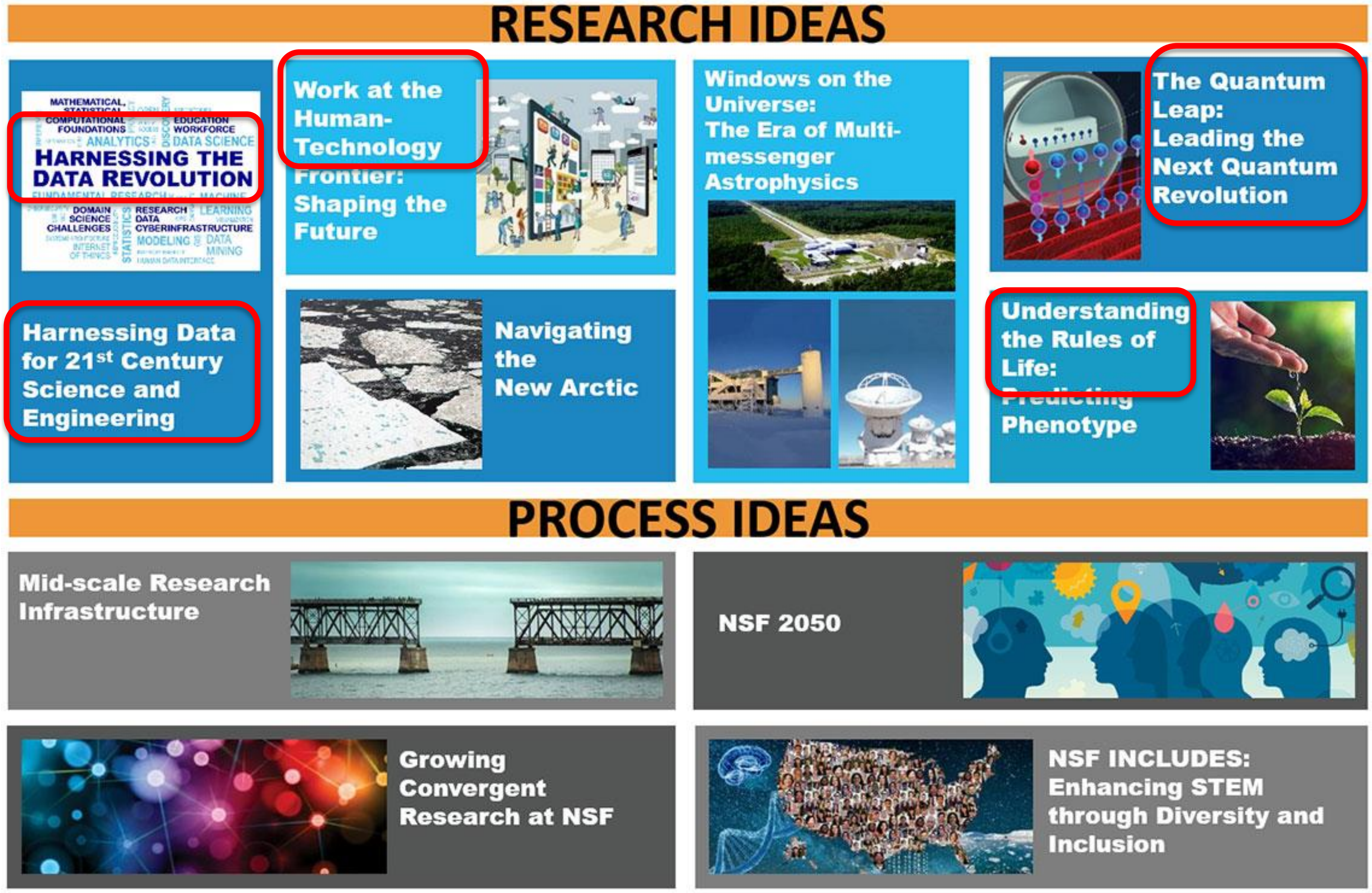
ASSIST's Always-on Wearable Platforms

Long Term Monitoring of health and environment
Correlation of multiple sensors signals
Clinical studies in various health domains

- ***Long term operation via self-powering***
- ***Physiological, biochemical*** *and* ***environmental*** *sensor*
- ***Wearable, wireless*** *and* ***comfortable***
- *Informative and* ***continuous data***



NSF's Big Ideas for Future Investment



Thank you!