NIST's Perspective on Bioelectronics

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Agenda

- NIST
  - Innovation
  - Bioscience and Health
- Bioelectronics: A New Frontier
- Summary

NIST Mission

- To promote U.S. **innovation** and industrial **competitiveness** by advancing
  - measurement science,
  - standards, and
  - technology

What

How

- in ways that enhance *economic security* and improve our *quality of life*

Why

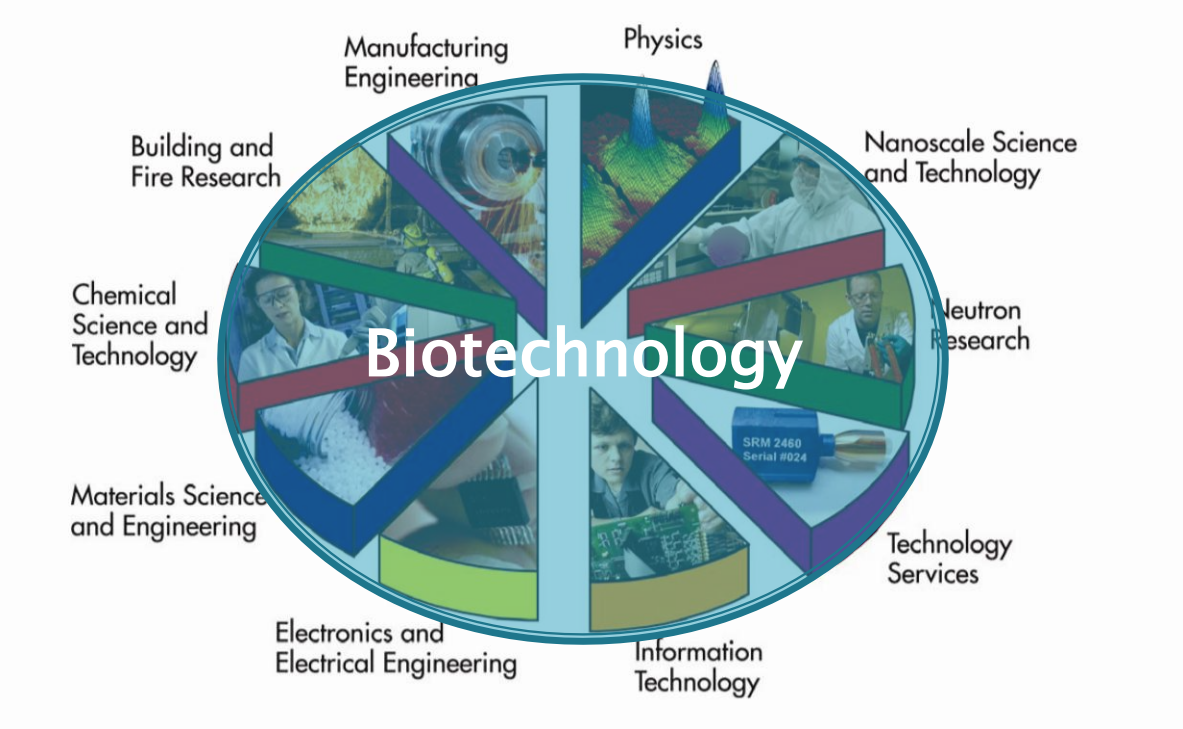
From E. Steel, “The Innovation Ecosystem,” June 2008.

Innovation & Competitiveness

- Complex capabilities, relationships, and interactions lead to innovation
  - Requires the right knowledge in the right place, at the right time, among the right people, with the right resources
  - An innovation "ecosystem"
- Can the Government enable faster/more innovation and help make the US more competitive?
  - What does NIST do to enable innovation?
    - Knowledge creation, transfer and use
  - How does NIST leverage its resources to maximize its impact on innovation.

From E. Steel, "The Innovation Ecosystem," June 2008.

NIST Has Traditionally Focused on the Physical Science and Engineering Disciplines



Bioscience and Health Is Identified as an Area for Significant Growth at NIST

Adapted from W. May, "Overview of Partnerships with The Hollings Marine Laboratory and The University of Maryland Biotechnology Institute," June 10, 2008.

Why NIST and the Biosciences?

It is **congruent with our mission, and indeed our mandate**, to support U.S. industry and other stakeholders in overcoming measurement and standards-related challenges in the biosciences

by leveraging our vast multidisciplinary expertise in the quantitative physical and informational sciences, to:

- provide the measurement infrastructure to provide confidence in the results from measurements of complex biological systems

Which will

- enable and facilitate realization of optimal economic and broad societal benefits from new innovations

Current NIST Plans for Biosciences Program Growth

- FY07 Budget Increase — Calibration and IT standards for MRI, CT, PET and cellular imaging
- FY09 Budget Request — Technology and standards for individual and multiplex measurements of biochemical health status markers
- Under Discussion — Support for development of advanced tools for visualization of structural and biochemical changes associated with disease

	FY07 **+ $3M**	**FY09** **+ $10M**	**Under Discussion**
Medical Imaging	➢ **Standards for MRI contrast agents** ➢ **Phantoms for PET/CT**		➢ **Standards tools to enable enhanced image analysis, data comparison and feature extraction**
Cellular and Biomolecular Measurements	➢ **Standards and techniques to enable quantitative fluorescence microscopy and cellular imaging.**	➢ **Quantifiable measurements of individual biomolecules and biomarkers** ➢ **Development of multiplexed measurement platforms**	➢ **Technologies and standards for quantitative protein measurements,** ➢ **structure function analysis,** ➢ **manufacturing and process monitoring**
Computational Tools	➢ **Software validation for image analysis and extraction**	➢ **Uncertainty analysis** ➢ **Collection and exchange of data** ➢ **Validation of modeling tools**	

Why Bioelectronics at NIST?

- Bioelectronics is an emerging discipline where semiconductor nanofabrication, biology, and electronics is creating an interdisciplinary research field that includes chemistry, biology, physics, electronics, and materials

- Bioelectronics is an emerging interdisciplinary field that requires the application of core NIST competencies such as rigorous measurement, characterization and detection techniques.

- New semiconductor-based structures will need to be developed and tested to meet the rigorous conditions of a biological system. The continuing advances in nanofabrication positions NIST to explore these new structures.

EEEL Bioscience Vision

- EEEL's vision in the biosciences is to leverage our vast expertise in the quantitative electromagnetic and condensed matter sciences to provide the measurement infrastructure to underpin increased innovation in the biosciences and healthcare.
  - Includes three core competencies
    - Measurement science and technology from DC to lightwaves with rigorous traceability including uncertainty measurements;
    - Quantum-based electronics and photonics expertise for developing primary standards;
    - Fabrication and characterization of micro- and nano-scale devices.

EEEL Has Strong Strategic Focus on Bioelectronics

- World-class leadership in bioelectronics is already in place in EEEL's Semiconductor Electronics Division. Division's strategic plan in 2008 recommends strengthening bioelectronics efforts further.

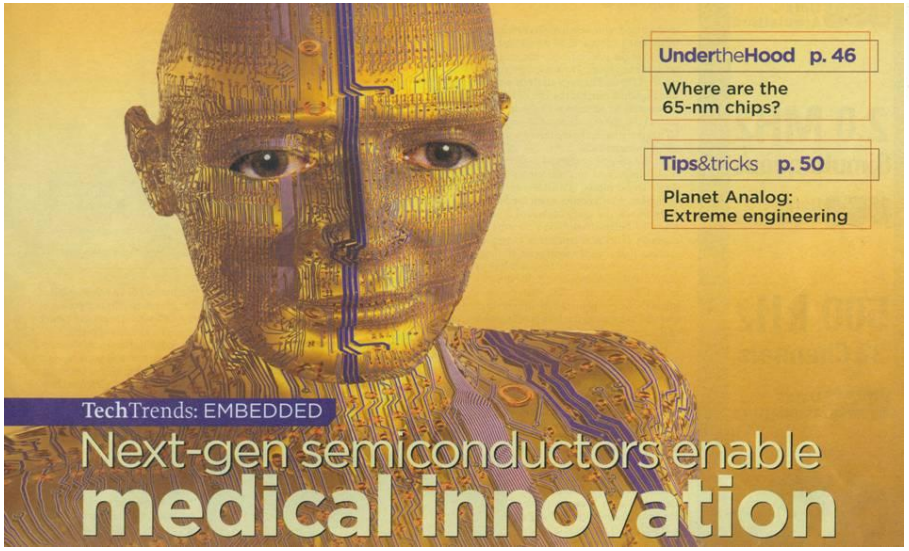
- EEEL made a strategic decision to concentrate on bioelectronics in May 2008.

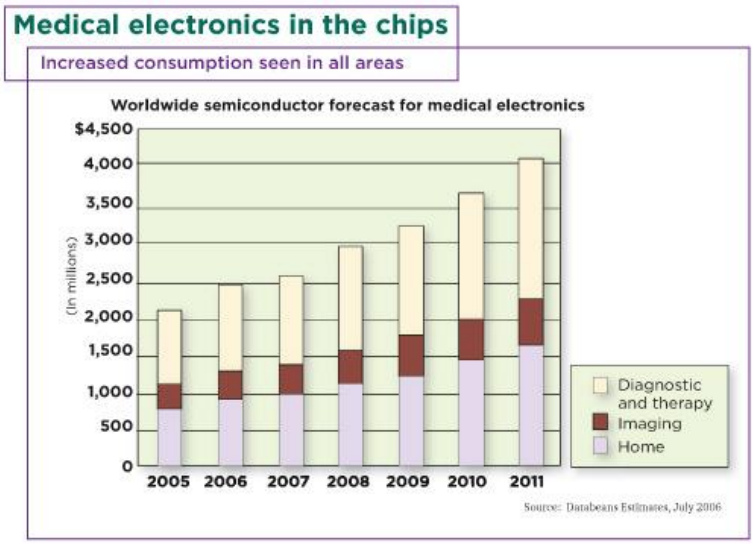
- Agreement in place to carry out a study, evaluation, and report on the emerging field of bioelectronics as related to the semiconductor industry
  - Produce Collaborative Research Plan for NIST and the Semiconductor Industry for Bioelectronics
  - Hold Bioelectronics Roundtable, Nov. 4, 2008

Potential Impact of Report Far Reaching

- First felt in research community, assuming the implementation results in programs to address the needs identified in the plan
- Training of outstanding graduate students in nano-electronics and bio-sciences
- Better understanding of biological systems that could be translated into improved methods and tools used in medical instrumentation, test, and therapy
- Large scale applications of this research could promote the growth of future industries, thereby stimulating the economy

Bioelectronics: Opportunity For Innovation





- "Biomedical research is making huge strides in unlocking the secrets of human physiology and identifying potential new therapeutic and diagnostic instruments."
- "… advances in electronics are enabling those new devices to be realized.
- "…medical applications make up one of the fastest-growing segments for semiconductors.
- "The growing convergence of electronics and medicine can also be seen in trends common to both disciplines."

From S. Kennelly, "Next-gen semiconductors enable medical innovation," Electronic Engineering Times, Nov. 6, 2006.

Prescription Chips

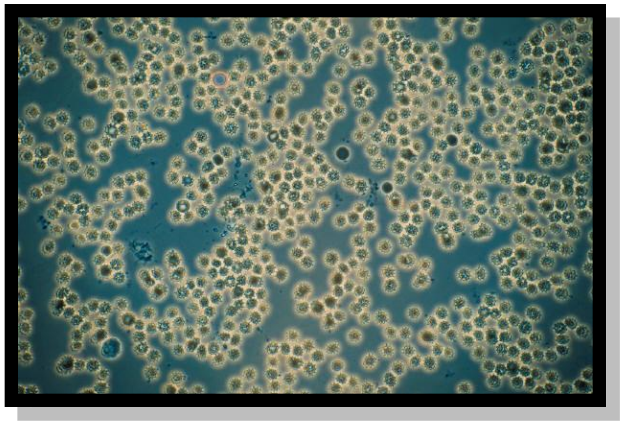
- "Biochips or other biosensing devices are among the most powerful tools for research in modern biotechnology. They are good examples of how the combination of biotechnology and microelectronic or semiconductor techniques may become the backbone of a new bioelectronics industry. The future of diagnosis, pharmaceuticals, and medical care for the post-genomic era may heavily rely on the application of semiconductor chips. Succeeding its glory days in informational technology and electronics, the next triumph of the semiconductor may be associated with biotechnology."

- "The fusion of biotechnology with the semiconductor and microelectronic industry has great potential for generating advanced technology and novel devices to solve a variety of biological problems. With further miniaturization and integration, enzyme chips will be used not only to monitor biochemical reactions but also to record ongoing biological processes, analyze complex biological reactions, and respond to abnormal biochemical reaction for disease treatment."

- "The information provided by functional genomics and proteomics may be considered as a map for "treasure hunting" in many different applications. One of the most efficient experimental tools for discovering nature's treasure may be the semiconductor biochip."

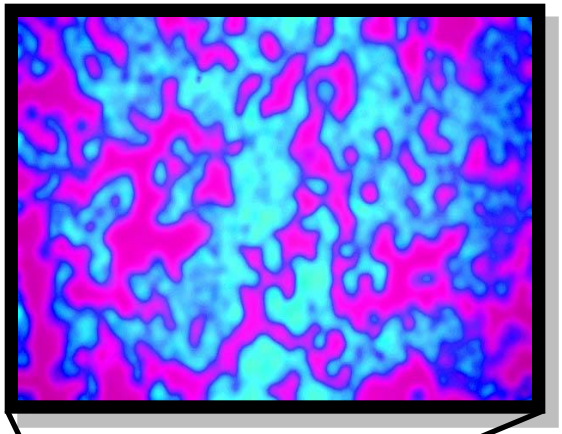
From B.Y-S. Yang, U. Lu, and B.C.P. Hu, "Prescription Chips," IEEE Circuits & Devices Magazine, pp. 8-16 (September 2002)

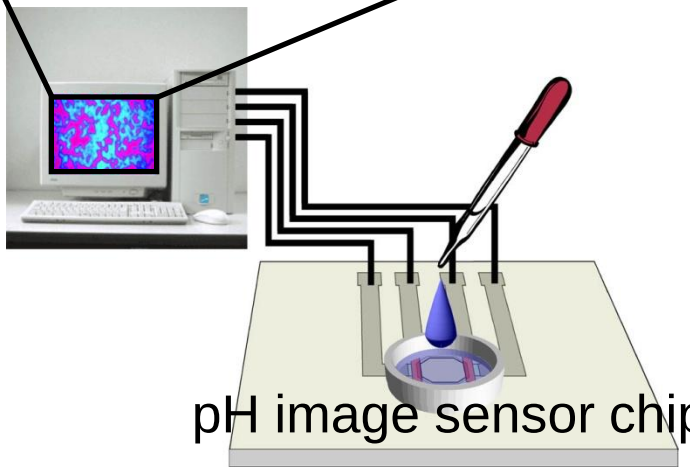
Smart micro chip for pH imaging



Microorganism with microscope

- Based on CMOS Technology
- Using Charge Transfer Technique





Novel pH Sensor (pH Imaging Sensor)

pH Imaging Model

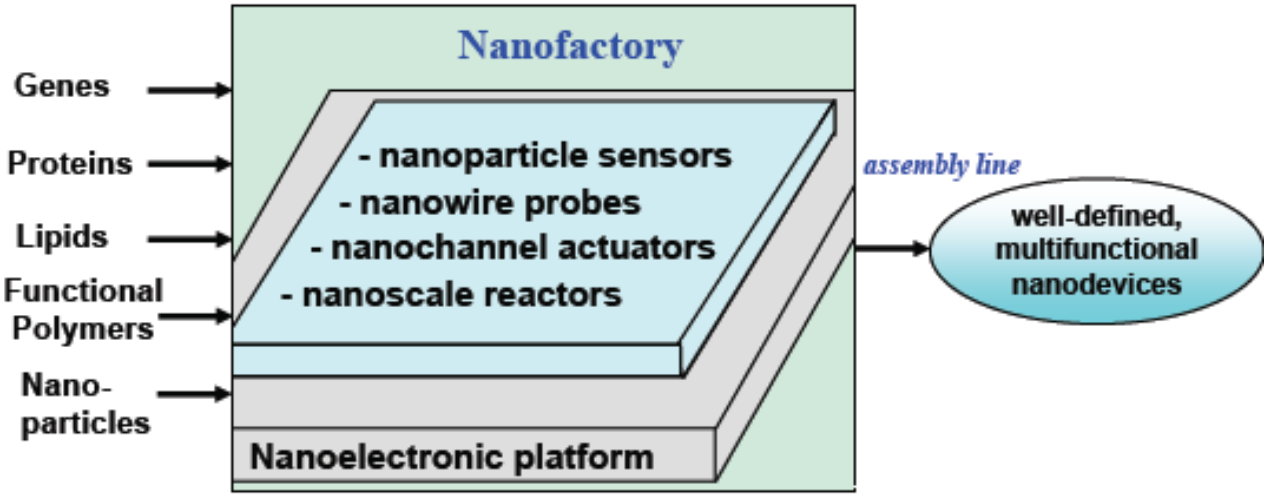
From M. Ishida, "Bio-Medical Si Microchips with Sensors and IC," Summary More Than Moore: Bridge to Bio, April 2008.

Bioelectronics Research can be found at universities, industry, government

NANOSCALE SCIENCE AND ENGINEERING CENTER
Center for Affordable Nanoengineering of Polymeric Biomedical Devices
THE OHIO STATE UNIVERSITY

The Ohio State University
Purdue
Florida State
MIT
UCSF
UCB
University of Missouri-KC
University of Michigan
Duke University
VCU
University of Akron

Nanofactory Concept



Potential Applications:

- Artificial virus and chromosomes for gene therapy
- Nanomachines for *in vivo* cell repair
- Artificial live systems, e.g. cells

From "Atomic Force Microscopy for Nanotechnology," G. Agarwal, Biomedical Engineering Center, Center for Affordable Nanoengineering of Polymer Biomedical Devices (NSEC), the Ohio State University

MS in Bioelectronics – Proposed New Graduate Degree in Fall 2008

- In the fall of 2008, pending approval, NJIT will offer a new master's degree in Bioelectronics. In this interview, Atam Dhawan, chairman of the Electrical and Computer Engineering Department, discusses the new degree.
- **Can you define Bioelectronics? It sounds like a combination of biology and sophisticated electronics.** Right. It is a novel combination of high-tech electronics, such as micro-electronics or nano-electronic technology, merged with the biological sciences.
- **What in your view is most exciting about bioelectronics?** There are a number of exciting bioelectronic applications in cellular, molecular and functional imaging used in the medical and life sciences. A combination of neuroscience and bio-nano-electronics has led to the development of neural prosthetic devices. Such devices allow researchers to better study organs and neural systems and develop therapies that help treat neurological disorders such as spinal-cord injuries, Parkinson's and Alzheimer's diseases.
- **Will they one day conduct important research?** The bioelectronics industry is evolving fast and developing new products that are playing a major role in the life sciences. Our graduates, whether they work in industry or in research, will work to quickly develop new devices that will revolutionize biology and medicine and improve the quality of life for many people.

Bioelectronics Degrees offered in:
- New Jersey's Science & Technology University
- St. Louis University

Bioelectronic-focused research groups:
- University of California, Santa Cruz
- Clemson University
- Chien-Shiung Wu Laboratory, China
- Singapore Polytechnic
- Institute of Bio- and Nano Systems, Germany
- Laboratory of Biosensors and Bioelectronics, Switzerland

From www.njit.edu/features/sceneandheard/ms-bioelectronics.php

Diversity of Bioelectronics

Items in purple are projects already underway in EEEL.

Applications of biochip technology in relation to molecular diagnostics

Research applications
- Molecular epidemiology

Study of gene expression in diseases

Rapid DNA sequencing

Design and stratification of clinical trials

Drug safety applications pharmacogenetics and toxicogenomics

Genetic screening and detection of single nucleotide polymorphisms (SNPs)

Identification of pathogens and resistance in infections

Molecular oncology
- Cancer prognosis
- Cancer diagnosis
- Cancer typing

Forensic identification: PCR on a chip

Detection of biological and chemical warfare agents

Public health: testing of water supply for microorganisms

Pharmacogenomics
- Gene identification
- Genetic mapping
- Gene expression profiling

Integration of diagnosis and therapeutics

From K.K. Jain, Nanobiotechnology in Molecular Diagnostics: Current Technique and Applications, Horizon Bioscience, Table 1-4, page 26, 2006.

Diversity of Bioelectronics (cont.)

Items in purple are projects already underway in EEEL.

Applications of molecular diagnostics

- **Practice of medicine**
  - As an aid to clinical diagnosis of various diseases
  - Diagnosis of disease susceptibility
  - Tissue typing in organ transplantation
  - Screening of blood transfusion
  - Combination of diagnosis and therapeutics
  - Development of personalized medicines
- **Forensic medicine for identification**
- **Early and fast diagnosis of biowarfare agents**
- **Use in biopharmaceutical industry**
  - Use in drug discovery
  - Molecular toxicology
  - Pharmacogenomics
  - Pharmacogentics
  - Gene therapy
  - DNA tagging for control and tracing of drug distribution channels
  - Detection of microbial contamination in biopharmaceutical manufacturing
- **Public health**
  - Detection of food-borne pathogens
  - BSE detection
  - Testing for water supply safety
  - Molecular epidemiology

From K.K. Jain, Nanobiotechnology in Molecular Diagnostics: Current Technique and Applications, Horizon Bioscience, Table 1-5, page 30, 2006.

Diversity of Bioelectronics (cont.)

Items in purple are projects already underway in EEEL.

Molecular diagnostic technologies for drug discovery

Genotyping
- Mutation detection
- Identification of single nucleotide polymorphisms (SNPs)

High-throughput DNA sequencing

Gene expression profiles
- Biochips/ microarrays/ microfluidics
- Molecular imaging of gene expression

Proteomic technologies
- Mass spectrometry for target identification
- Protein-protein interactions analyses
- Protein chip
- Biosensors for detection of small molecule-protein interactions

From K.K. Jain, Nanobiotechnology in Molecular Diagnostics: Current Technique and Applications, Horizon Bioscience, Table 6-1, page 130, 2006.

Bio-Electronics Roundtable (BERT)

- Purpose
  - To bring experts from government, industry, and academic together to develop a framework to guide multidisciplinary research in semiconductor bioelectronics for the next decade.
  - BERT will focus on the development and use of semiconductor technology in biological and medical applications. Examples include:
    - lab-on-a-chip systems for medical diagnostics or bio agent detection
    - implantable devices for monitoring health
    - tools for dynamic characterization of biomolecular properties at nanoscale resolution
- Goals
  - To identify a number of critical research needs and opportunities in the broad area of bioelectronics
  - This meeting could be a preliminary step leading to a bioelectronics roadmap