US-JAPAN WORKSHOP ON BIO-INSPIRED ENGINEERING OF NEXT-GENERATION SENSORS AND ACTUATORS

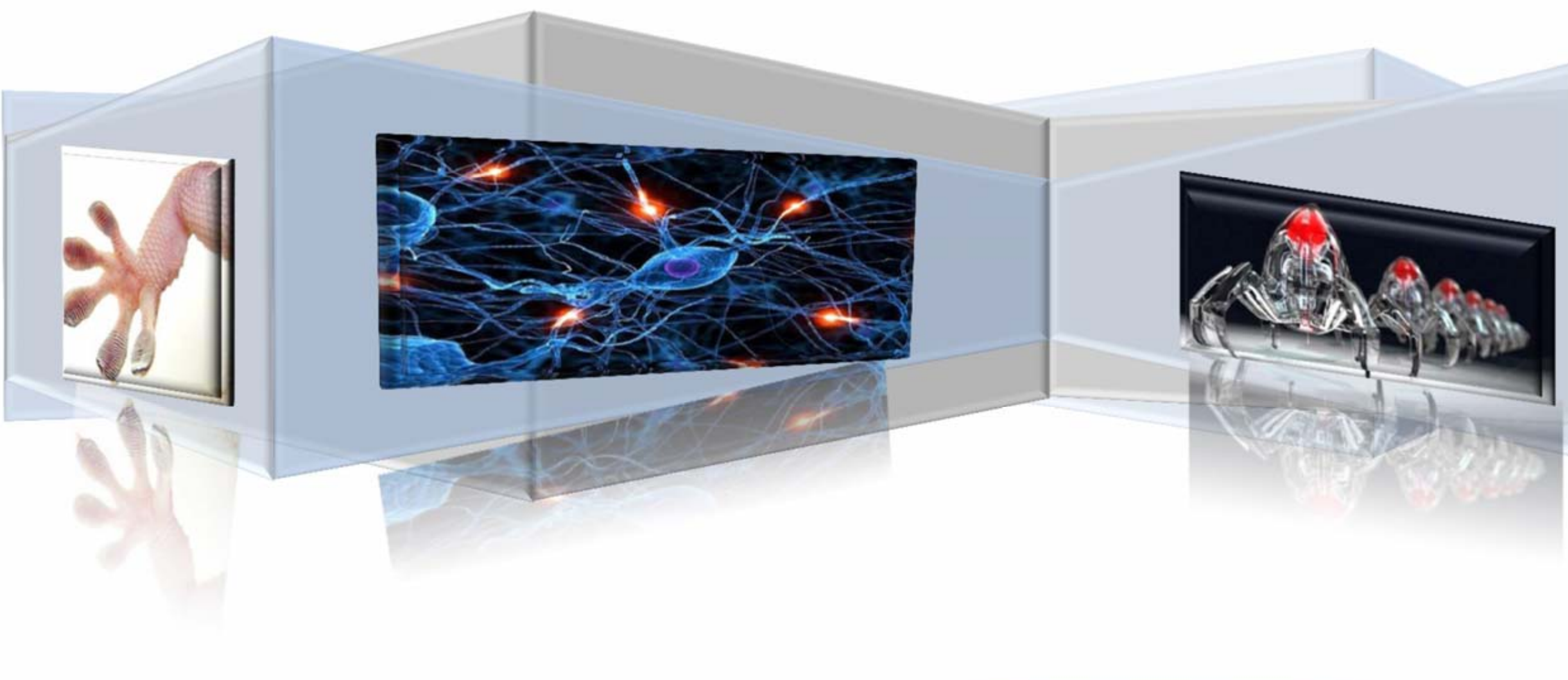
November 12-13, 2011

Berkeley, CA, USA

Sponsors:

National Science Foundation (NSF)

Japan Science and Technology Agency (JST)



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The National Science Foundation
4201 Wilson Boulevard
Arlington, Virginia 22230, USA

October 1, 2011

Dear US-Japan Workshop Participant,

I would like to extend my personal welcome to Berkeley and to the *U.S.-Japan Workshop on Bio-inspired Engineering of Next-Generation Sensors and Actuators*. You have been specially selected to participate in the workshop due to your leadership position in the biology and engineering fields and because of your distinguished record of unyielding commitment to international collaborations. The workshop chairs, Professor Takehiko Kitamori, University of Tokyo (Japan), Professor Yoshinobu Baba, University of Nagoya (Japan), Professor Masayoshi Tomizuka, University of California Berkeley (U.S.), and Professor Jerome P. Lynch, University of Michigan (U.S.) have done an excellent job planning our workshop activities. I am personally excited by the intellectual challenges we will explore together. Undoubtedly, the detailed U.S.-Japan research agenda that you will craft during the workshop will result in the creation of an empowered U.S.-Japan research community engaged in the advancement of bio-inspired technologies.

The most successful workshops are the ones that produce outcomes of high intellectual value and broad societal impacts. Undoubtedly, the organizers of this workshop have worked hard toward ensuring you collectively achieve a set of workshop outcomes distinguished by the highest level of quality. Towards this end, follow-up actions are already planned to ensure the workshop outcomes have broad-based impacts on the scientific community specifically, and societies across the Pacific in general. But clearly, whether this workshop will be considered a big success or failure will all depend upon three critical elements: 1) how serious you are about promoting an open discussion on the future challenges of BSBA technologies, 2) the level of preparation you diligently provide before the workshop, and 3) the concentrated focus you offer during all workshop deliberations which do not strictly represent your own individual R&D interests. I am confident that you will provide a level of commitment that not only meets the workshop objectives but that far exceeds them.

The workshop objectives are clearly identified and work plans are delineated in these workshop proceedings. In particular, the success of the workshop depends upon you being completely engaged in the discussions planned for the break-out sessions. I ask that you provide the break-out session chairs and recorders with assistance in preparing presentation materials and content for a paper each working group is being asked to prepare. In addition, each working group will be requested to formulate one (but not more than two) grand challenge problem/opportunity statements upon which future U.S.-Japan bio-inspired research initiatives can be built to advance technology innovation for the improvement of our large societies.

Again thank you for your participation and contributions - I am very much looking forward to working with you and engaging in exciting dialogue with you in the coming days.

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US-JAPAN WORKSHOP ON BIO-INSPIRED ENGINEERING OF NEXT-GENERATION SENSORS AND ACTUATORS

Bechtel Engineering Center, University of California, Berkeley
November 12-13, 2011

WORKSHOP AGENDA

Friday, November 11:

6:00 pm	Welcome Reception Hotel Durant

Saturday, November 12:

7:30 am	Registration (Bechtel Engineering Center, UC Berkeley) Continental Breakfast
8:15 – 8:30 am	Welcome & Introductions (Sibley Auditorium) *Dr. Hideo Nakajima, Deputy Director, JST* *Dr. S. C. Liu, Program Director, NSF* *Prof. M. Tomizuka, Associate Dean, University of California Berkeley* *Prof. T. Kitamori, Dean, University of Tokyo*
8:30 - 9:00 am	Keynote Presentation #1 *Prof. Takehiko Kitamori, University of Tokyo* *"Creation of fluid engineering in extended-nano space and development of novel devices using its unique properties"*
9:00 - 9:30 am	Keynote Presentation #2 *Prof. Morteza Gharib, California Institute of Technology* *"Lessons for bio-inspired design: morpho-dynamics of the embryonic heart"*
9:30 – 10:00 am	Keynote Presentation #3 *Prof. Akira Mita, Keio University* *"From smart building to biofied building"*
10:00 - 10:30 am	Coffee Break
10:30 - 11:00 am	Keynote Presentation #4 *Prof. Mark Nelson, University of Illinois Urbana Champaign* *"Biological sensory acquisition strategies in electric fish"*
11:00 - 11:30 am	Keynote Presentation #5 *Prof. Yoshinobu Baba, University of Nagoya* *"Grand challenge: nanobiodevice for future personalized medicine and evidence based healthcare"*

11:30 – 12:00 pm	Keynote Presentation #6 *Prof. Gerard Marriott, University of California Berkeley* *"Design and optimisation of synthetic and genetically-encoded optical switches for high-contrast imaging and reversible manipulation of biological system"*
12:00 – 1:00 pm	Lunch (Box lunch) and Student Poster Session (Lounge area)
1:00 – 1:30 pm	Keynote Presentation #7 *Prof. Tomokazu Matsue, Tohoku University* *"Highly-sensitive electrochemical imaging for biosensing"*
1:30 – 2:00 pm	Keynote Presentation #8 *Prof. Robert Full, University of California* *"Cautions on extracting principles from nature to inspire the design of sensors and actuators"*
2:00 – 3:00 pm	Break-out Session #1 (Sibley /Rm 205A/Rm240) *Participants - 3-minute Introduction*
3:00 - 3:30 pm	Coffee Break
3:30 – 5:30 pm	Break-out Session #2 (Sibley/Rm 205A/Rm240) *Initiation of Discussions*
6:30 – 9:00 pm	Banquet (Seaborg Room, Faculty Club)

Sunday, November 13:

7:30	Continental Breakfast
8:15 – 8:30 am	Welcome & Introductions (Sibley) *Prof. Y. Baba, Professor, University of Tokyo* *Prof. J. P. Lynch, Associate Professor, University of Michigan*
8:30 - 9:00 am	Keynote Presentation #9 *Prof. Yasuteru Urano, University of Tokyo* *"Rational development of activatable fluorescence probes for in vivo medical imaging"*
9:00 - 9:30 am	Keynote Presentation #10 *Prof. Edward Yeung, DOE Ames Laboratory / Iowa State University* *"Biosensing based on single nanoparticles and nanorods"*

9:30 – 10:00 am	Keynote Presentation #11 *Prof. Toshio Fukuda, University of Nagoya* *"Micro and nano devices for single cell nano surgery"*
10:00 - 10:30 am	Coffee Break
10:30 – 12:00 pm	Break-out Session #2 (Sibley/Rm 205A/Rm240) *Discussions Continue*
12:00 – 1:00 pm	Lunch (Box Lunch)
1:00 – 3:00 pm	Break-out Session #3 (Sibley/Rm 205A/Rm240) *Grand Challenges Finalized* *Preparation of Slides for Closing Session*
3:00 - 3:30 pm	Coffee Break
3:30 – 4:50 pm	Reports from Working Groups (Sibley) *Working Group #1* *Working Group #2* *Working Group #3*
4:50 – 5:00 pm	Closing Remarks *Prof. M. Tomizuka, Associate Dean, University of California Berkeley* *Prof. T. Kitamori, Dean, University of Tokyo*

STUDENT POSTER LISTING

Name	Affiliation	Poster Title
Daniel Ebert	Ohio State University	Durable Lotus-effect surfaces with hierarchical structure using micro- and nanosized hydrophobic silica particles
Courtney Peckens	University of Michigan	Cochlea-based spectral decomposition of signals in resource constrained sensor networks
Donghyeon Ryu	UC Davis	Self-sensing poly(3-hexylthiophene)-based structural coatings inspired by photosynthesis
Evan Chang-Siu	UC Berkeley	Active Tail for Improved Robotic Terrestrial Locomotion Inspired by Lizards
William Stewart	UC Irvine	The kinematics of predator evasion by zebrafish larvae
Xiaofang Gao	The University of Tokyo	Creation of a cell-based separation microdevice using renal tubule cells
Tadahiro Yamashita	The University of Tokyo	Development of a separable microchip toward in vitro construction of a small artery
Takao Yasui	Nagoya University	Label-free biomolecular sensing by combining nanowall array and laser diffraction

WORKSHOP INTRODUCTION

Organizing Committee:

Professor Yoshinobu Baba	Nagoya University
Professor Takehiko Kitamori	The University of Tokyo
Professor Jerome P. Lynch	University of Michigan
Professor Masayoshi Tomizuka	University of California at Berkeley

I. Introduction

Sensor and actuation technologies play a critical role in the design and construction of modern engineered systems spanning from industrial machines to large-scale civil infrastructure systems. Sensors platforms include the sensing transducer and often signal processing and sensor networking capabilities. Actuation technologies include actuators, processing units (*e.g.*, controllers) and sensors integrated within a closed-loop feedback system. Sensors and monitoring systems are widely used to monitor civil infrastructure systems (*e.g.*, bridges, pipelines, buildings), industrial machines (*e.g.*, manufacturing equipment), transportation vehicles (*e.g.*, aircraft, cars, ships), human health (*e.g.*, blood pressure, biomarker), among many others. Similarly, actuation systems are used to operate manufacturing equipment, aircraft, among many other important systems. The past two decades has witnessed an explosion in enabling technologies such as embedded electronics, wireless communications, miniaturization technology, nanotechnology and information technology. In particular, the convergence of many of these technologies into a single platform has had a profound impact on sensing and actuation technology. While sensing and control technologies continue to improve in many engineering disciplines, there is a dire need to accelerate the development of sensing and actuation technologies for the sustainable performance and functional enhancement of many engineered systems. While physics and chemistry have historically driven the major advances in sensing and actuation in the 20th century, comparatively less focus has been paid on biology. *This workshop aims to establish a comprehensive U.S.-Japan collaborative research program that aims to fundamentally explore how recent advances in the biological fields can be leveraged to engineer the next-generation of sensors and actuators.*

2. Biology-Engineering Reinforcing Loop of Discovery

The field of biology has witnessed unprecedented advances in the past decade due in large part to the field of engineering which has offered new and powerful means of observing (*i.e.*, sensing) and manipulating (*i.e.*, actuation) biological systems at all length-scales spanning from the sub-cellular to the ecosystem scale. For example, powerful microscopic tools have rapidly evolved to a point where cells can be observed, stimulated and manipulated. Microelectromechanical systems (MEMS) technology has allowed for the sorting and manipulation of individual cells using microfluidics. Furthermore, parallel computing platforms and cyberinfrastructure have facilitated the field's efforts aimed towards the decoding of the human genome. All of these technological advances have uniquely positioned biology to ambitiously tackle some of the major challenges facing society in the 21st century. The National Research Council

(NRC) recently concluded that the field of biology is currently at a major inflection point. Specifically, new found knowledge of biological systems and processes hold the key to resolving long-standing issues in food availability, affordable public health services, sustainable stewardship of the environment, and the creation of renewal energy sources.[1] One way biology is addressing these grand societal challenges is by empowering engineers with new concepts for bio-inspired and bio-mimicked design of engineered systems. Another way is through the intentional re-design of biological systems to produce engineering materials and products; such an approach is often termed synthetic biology.

Biological systems have been proposed for the inspiration of a new generation of sensors and actuators with performance attributes far surpassing current technologies. The field of biology offers engineers endless opportunities to devise engineered systems that are mimicked from and inspired by biological systems. Specifically, nature exhibits a diverse suite of sensing and actuation mechanisms used to regulate and control biological systems. Over the past decade, interest in mimicking biological sensing and actuation mechanisms has grown within many of the engineering disciplines (*e.g.*, mechanical engineering, civil engineering, electrical engineering, aerospace engineering, chemical engineering, computer science and material science). Many early examples exist of engineers and biologists working in close partnership on the design of new sensing and actuation technologies. For example, new multifunctional materials with self-sensing and self-healing attributes have been proposed based on biological materials that naturally sensing and heal. The spatial-temporal processing of information naturally handled by neurological networks is being explored to create new approaches to data compression and information extraction in monitoring and control systems.

The increasingly cohesive partnership between engineers and biologists has resulted in the formation of a feedback loop of discovery as shown in Figure 1. Engineering has created new approaches to sensing and control at all length-scales that have fundamentally advanced the state-of-knowledge in the biology fields by creating technologies such as high-resolution microscopy, nano- and micro-fluidic systems, man-made bio-interfaces, and large-scale computational resources, just to name a few. In turn, the resulting advances in biology are leading to revolutionary advances in understanding the secrets of biological systems; this new found knowledge makes bio-inspired and bio-mimicked design possible. Improved sensing and actuation technologies based on bio-inspiration will ultimately translate into improved technologies for fundamental biology research. Hence, the feedback loop of discovery between engineering and biology is self-reinforced.
This workshop aims to bring together experts from the domains of biology and engineering to identify how this emerging loop of discovery can be utilized to develop the next generation of sensors and actuators.

[1] Board of Life Sciences (2009). *A New Biology for the 21st Century*. National Academies Press, Washington DC.

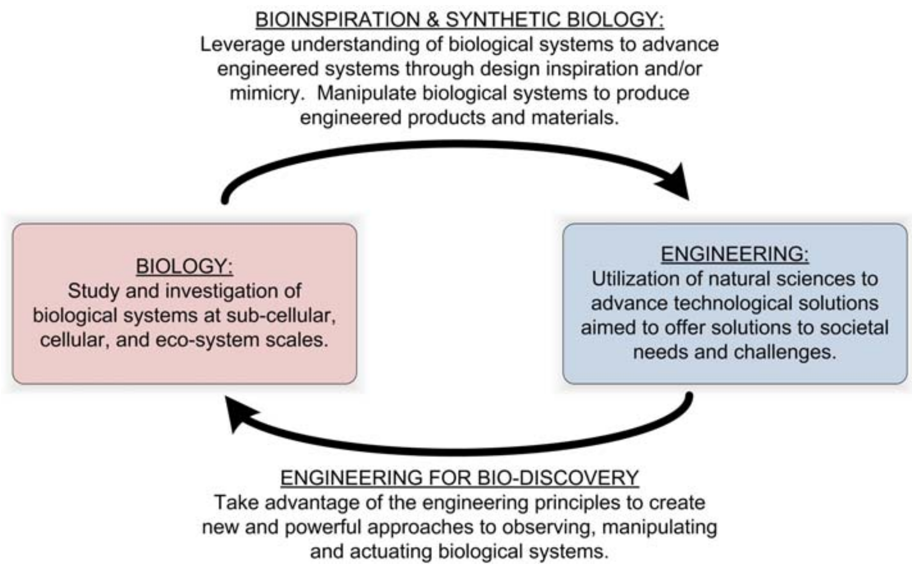

Figure 1. Self-reinforcing loop of discovery between engineering and biology to have emerged in the past decade.

3. Broader Context for the Workshop

The *U.S.-Japan Workshop on Bio-inspired Engineering of Next-Generation Sensors and Actuators* builds on the momentum that has been growing internationally in bio-inspired engineering design. The global development of BSBA research communities can be summarized as follows:

- *United States:* The U.S. has already taken a bold step forward in cultivating BSBA research aimed at addressing the growing needs of civil and mechanical engineering systems. For example, the National Science Foundation's 2009 Emerging Frontier in Research and Innovation (EFRI) was focused on the development of BSBA technology for many application areas. In FY09, NSF funded 12 projects in Bio-inspired Sensing and Bio-inspired Actuation topic area through the EFRI Program. Since that time, NSF's Sensors and Sensing Systems Program (Director: Dr. S. C. Liu) has devoted significant resources aimed toward developing international collaboration in BSBA technology in other regions of the world. For more information, please visit the following website: http://www.nsf.gov/eng/efri/fy09awards_BSBA.jsp
- *Taiwan*: In April 2009, an International Workshop in BSBA Technology was held in Taipei, Taiwan to identify ways U.S. and Taiwan could partner in BSBA research and education initiatives. A key outcome of that workshop was the establishment of a US-Taiwan research program that was supported as supplemental funding to a number of NSF grantees engaged in BSBA research with a collaborator in Taiwan. Another key outcome of the workshop was the establishment of a Summer Institute in BSBA Technology for graduate students from the US and Taiwan; this is a 5 year institute funded by NSF and the National Science Council (NSC) of Taiwan.
- *China:* The US-Sino Workshop on Advanced Sensors and Bio-inspired

Technologies was held in November 2010. The workshop resulted in a detailed research agenda that resulted in a formal joint call for proposals organized by NSF and the National Science Foundation of China (NSFC) in the early 2011. It is anticipated that US-Sino research teams will make revolutionary advances in BSBA technologies aimed to solve societal issues of common interest to the US and China.

- *Europe:* In addition to Asia, NSF is closely coordinating with the European Science Foundation (ESF) in the establishment of formal collaborations in the BSBA research area. For example, ESF has recently announced an FY10 EUROCORE program, "EuroBioSAS: Bio-inspired Engineering of Sensors, Actuators & Systems" which aims to establish a cohesive European research community in BSBA research. As the EuroBioSAS program gets underway, an increased level of coordination is anticipated between NSF and ESF.
- *Transworld BSBA Forum*: With significant momentum building in BSBA research across the US, Asia and Europe, a Transworld BSBA Forum is being planned by Professor Adnan Akay, Vice President of Bilkent University, Ankara, Turkey, and Professor Rahmat Shoureshi, Dean of the School of Engineering and Computer Science, University of Denver, to bring together BSBA researchers from the US, Europe, and Asia and their respective national funding agencies including NSF, NSFC, NSC, JST and ESF. Another key goal of the forum is to develop a roadmap and/or handbook for BSBA education of students. The forum is being planned for 2011 in Istanbul, Turkey.

JST has partnered with NSF in the past to explore opportunities to collaborate and establish joint research projects in the field of sensors and actuators. For example, from FY2007 to FY2009, the JST has partnered with NSF to offer funding to U.S.-Japan research teams through a targeted solicitation in "Advanced Integrated Sensor Technologies." This program was born out of the *U.S.-Japan Workshop on Advanced Integrated Sensor Technologies for Safe and Secure Societies and Better Quality of Life* which was held in Tokyo in 2007 through support offered by NSF and JSPS (Japan Society for Promotion of Science). For more information regarding this workshop, please check: http://www.jst.go.jp/inter/english/project/country/usa.html. Two common threads evident in the discussions of that workshop was the need to leverage sensing technologies to improve the quality of life while enhancing the security and safety of both societies. Similar to the success of the *U.S.-Japan Workshop on Advanced Integrated Sensor Technologies for Safe and Secure Societies and Better Quality of Life*, the *U.S.-Japan Workshop on Bio-inspired Engineering of Next-Generation Sensors and Actuators* is intended to lead to coordinated activities between NSF and JST that support the new modes of U.S.-Japan collaborations within the BSBA field.

4. Workshop Goals:

The *U.S.-Japan Workshop on Bio-inspired Engineering of Next-Generation Sensors and Actuators* is expected to produce a comprehensive vision statement on how the biology-engineering loop of discovery can be leveraged to create a new generation of sensors and actuators designed and fabricated by bio-inspired, bio-mimicked, and synthetic biology principles. Broadly termed bio-inspired sensors and bio-inspired actuators (BSBA), this new generation of sensors and actuators are intended to translate the revolutionary advances in biology into solutions that are aimed at addressing societal grand challenges including, but not limited to:

- Design of sensors and actuators that emulate biological sensors including ultra-compact devices that operate on minimal power yet provide superior levels of resolution and sensitivity. Such sensors could be used to monitor civil infrastructure while actuators can be used in the feedback control of various mechanical systems including machines and aircraft.
- Creation of new multifunction materials which are more durable and sustainable for civil infrastructure systems and engineered commercial products. Such materials would not only have superior mechanical attributes, but also possess self-sensing and self-healing capabilities.
- Development of low-cost biological sensors that can be deployed in public health systems to ensure the general population can access affordable but high quality medicine.
- Advancement of collective intelligence principles found in biological ecosystems to create new paradigms for the processing of distributed sets of data collected by monitoring systems.
- The creation of bio-medical devices that can be implanted in and attached to human beings for sensing and control of organs and internal systems that prolong life and improve human quality of life. External actuators and feedback control systems can be used to enhance physical therapy of injured patients.

To tackle these grand challenges, the workshop has invited delegates working at the forefront of discovery in Japan and the U.S. The interdisciplinary complexity of bio-inspired sensing and bio-inspired actuation (BSBA) requires a large and diverse team of researchers to tackle. Hence, the workshop participants have been selected from many different fields of specialization including evolutionary biology, molecular biology, biochemistry, chemistry, civil engineering, electrical engineering, mechanical engineering, bioengineering, mathematics, medicine and architecture. The participants of the two-day workshop are given the following four overarching goals to work towards:

- To understand the current state of research and educational activities in the multidisciplinary field of BSBA technologies in the U.S. and Japan, in particular, from the viewpoint of applying them to enhance the performance and resiliency of civil and mechanical systems, improve public health, and to generally improve the quality of life of both nations.
- Identify and define critical technological bottlenecks associated with current sensing and actuation technologies that would benefit from the paradigm-shift associated with BSBA approaches to technology development.
- Identify joint research projects and multidisciplinary, trans-Pacific research teams for collaborative research in the development and use of BSBA technology to specifically address the critical bottlenecks identified by the workshop participants.
- Formulate a strategy for securing funding in the U.S. and Japan to sustain the existence and further growth of nascent U.S.-Japan research teams.

5. Workshop Activities:

The two-day workshop will begin the first day with 12 keynote presentations given by the Japanese and U.S. experts in the thematic areas of the workshop. Each keynote presentation will be 30 minutes long. In the late afternoon of the first day, the workshop will be devoted to deep discussion and dialogue between the U.S. and Japanese researchers to identify the current state of research and knowledge in the two countries as well as to facilitate direct trans-Pacific exchange of information on research and/or educational activities in the BSBA field. The invited workshop participants (including students and early career researchers) and invited international observers will be divided into three working groups with each group given the direction to discuss, deliberate and formulate research and educational plans to address the workshop objectives. Each working group will have multi-disciplinary representations from chemistry, material sciences, biology, aerospace, civil and mechanical engineering and will have two co-chairs (one from Japan and the other from the U.S.) and one reporter. On the second day of the workshop, each group will continue discussion and prepare a summary, and the reporter of each group will present the summary at the final plenary session. Findings of the three working groups will be consolidated into a single resolution. This resolution will include plans for follow-up activities to be jointly overseen by JST and NSF.

Each breakout sessions will address the following questions over two days:

1. *Assessment of the Current State-of-the-Art [Day 1]*: Before the groups can discuss a specific research agenda, an inventory of biological knowledge and technological bottlenecks must first be created. These questions seek to identify societal problems for which current sensors and actuators fail yet are ripe for the adoption of BSBA solutions.
    a. What sensing and actuation principles of biological systems exceed the performance of engineered sensors and actuators? Are these biological systems able to be mimicked or leveraged to achieve a new generation of sensors and actuators?
    b. What are the current technological bottlenecks in sensing and actuation that current technologies do not currently overcome? Can biological principles be adopted to overcome these limitations?
    c. How do these technological bottlenecks impact the quality of life in society? Which technological bottlenecks can most benefit from the adoption of BSBA technology?

2. *BSBA Research Roadmap Development [Day 1/2]*: What is the next step? Given the identified limitations associated with current technologies, how do we capitalize on the tremendous untapped potential of bio-inspired technologies to revolutionize our approach to technology advancement?
    a. What are the grand challenges for research in BSBA technology?
    b. Identify examples of fundamental research issues and general research areas that will benefit from BSBA research collaboration. Provide specific examples of proposed bio-inspired research topics.
    c. In overcoming the identified grand challenges, what is the anticipate impact on society, quality of life and the future of the engineering field?

d. What are the institutional barriers and field biases that exist which currently limit the cross-fertilization of ideas between engineering and the natural science? What can both fields do to reduce or outright eliminate such barriers?

3. *Development of a Structured JST-NSF Collaboration [Day 2]:* How can NSF and JST create a collaborative research and education program that seeks to accelerate the development of BSBA technology in the U.S and Japan?
   a. What factors warrant international collaboration in BSBA technologies?
   b. What are realistic expectations for a trans-Pacific multi-disciplinary collaborative program in BSBA technologies?
   c. Are there barriers in place that prevent successful long-term collaboration?
   d. What high risk-high reward areas in BSBA should funding agencies emphasize in future funding opportunities?
   e. How can a jointly funded BSBA program build and connect (link) a strong and resilient BSBA R&D community on each side of the Pacific for the creation of mutually profitable advanced bio-sensor technology enterprises?
   f. Are the U.S. and Japanese educational systems well equipped to generate a work force of the 21st century well equipped for BSBA research and industrial implementation?
   g. How can NSF-JST jointly fund BSBA education programs that enhance the education of future undergraduate and graduate students?

WORKSHOP PARTICIPANTS

U.S. Delegates

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WORKSHOP RESOLUTIONS

The US-Japan Workshop on Bio-inspired Engineering of Next-Generation Sensors and Actuators was held on November 12 and 13, 2011 at the Bechtel Engineering Center on the University of California Berkeley campus. The workshop was supported by the National Science Foundation (NSF) and the Japan Science and Technology (JST) Agency. A total of 54 participants attended the workshop representing a multidisciplinary group of researchers from the fields of biology, chemistry, material science, and engineering (civil, mechanical, electrical and chemical). The workshop participants were focused on the development of a detailed roadmap for a trans-Pacific research program in bio-inspired engineering of common interest to the US and Japanese research communities. A particular emphasis was placed on the identification of research problems that would have the highest level of impact on societal quality of life. Toward that end, the workshop began with a series of keynote presentations from both Japanese and US participants followed by extensive breakout group discussions. A total of three breakout groups were formed with an equal number of participants from the US and Japan. The three breakout groups were given the same goal: define one or two grand challenge problems upon which future US-Japan research collaborations can be formed.

Working group participants identified five major interdisciplinary research themes that exemplify the spirit of the US-Japan Workshop. The multi-disciplinary grand challenge themes in the bio-inspired sensing and bio-inspired actuation (BSBA) area are summarized as follows:

- **Design of Multi-Level and Multi-Length Hierarchical Systems Inspired by Biology**: Biological systems employ hierarchical structures to achieve multifunctional system performance that far exceed the performance of current engineered systems. The grand challenge is to synthesize new fabrication methods that utilize and achieve hierarchical systems, utilize reverse engineering techniques to develop new tools, and integrate sensing and actuation technologies into those structures. The research challenges include integration and scalability of top-town and bottom-up fabrication methodologies, multi-dimensional fabrication principles that encode desirable properties at drastically different length scales, self-assembly methods for attaining precise spatial structures, arrangements, and functionalities, and comprehensive and realistic mathematical models and representations of biological systems and functionalities.

- **Teaching Bio-inspired Engineering:** To support the next-generation of BSBA researcher, the community should create education programs geared toward teaching engineers, biologists, chemists, and material scientists the principles and applications of bio-inspired design. For example, a 5-week summer program should be created for graduate students and post-doctorate researchers consisting of lessons, on-hand experiments and an extensive bio-inspired design project.

- **Bio-inspired Biochemical Engineering of Systems for Energy, Water, Food, Communications, and Medical Applications**: Biological systems thrive by inherent biochemical processes capable of controlling energy, material, and information interactions between components in the system. The grand challenge is to design robust, durable, self-regulating, and self-healing engineered systems with built-in artificial homeostasis, metabolic and enzymatic mechanisms. The research challenges include the incorporation of a heterogeneous network of evolving, adjustable, and adaptive multifunctional nodes capable of direct energy transduction, storage, and utilization. Accomplishing this grand challenge will result in sustainable food, energy, and water supply.

- **Biologically-inspired Robustness: Self-sustaining Sensors and Actuators**: The grand challenge is to understand the mechanisms of self-renewal and self-repair in biological systems and to translate the knowledge towards designing a new generation of self-sustaining sensors and actuators. The vision is that the developed sensors will maintain its performance under uncontrolled and harsh environments. The research challenges include: developing techniques for recognizing damage in sensors and actuators that could then be used for self-repair and self-renewal; incorporating redundancy in the sensor and actuator design; developing new functional materials with feedback for diagnostics and prognostics; and developing sensors with energy sustainability.

- **BICEP: Biologically Inspired Control, Enhancement and Processing:** The grand challenge is to understand biological mechanisms of amplification, sensitivity, and selectivity in sensing and actuation and to translate these principles into developing integrated sensory and actuation systems with local feedback control. The research challenges include: identification and distinguishing between local and global sensory information under resource constraints (size, energy, speed, *etc*); incorporation of amplification and feedback in sensors and actuators using biomimetic processes, such as avalanche, cascade, *etc*; understanding and exploiting the role of noise and nonlinearity in biological sensory systems; and design of novel systems based on these bio-inspired principles. Fundamental research aimed towards the design of actuators based of ATP-inspired chemical energy processes, such as those found in sarcomere, is also proposed. Key technical challenges includes energy management in self-generation and delivery of energy, the formation of sarcomere-actuators based on self-assembly methods.

These grand challenge problems have the potential to build on the historical legacy of US-Japan collaboration to pioneer new sensing and actuation technologies based on inspiration of natural processes. Undoubtedly, a formal US-Japan research and education program based on these grand challenge problems would pay major dividends including improved public health, the development of cost-efficient manufacturing processes, the creation of green energy sources, and enhanced safety of civil infrastructure systems. Given this abundance of potential impact, the participants of the workshop unanimously make the following recommendations to NSF and JST:

- A self-reinforcing loop of discovery must be promoted by NSF and JST to form explicit linkages of intellectual discovery between biologists/chemists and engineers in both the US and Japan. Engineers have the potential to provide tools and processes that can drive new and paradigm-shifting discovery in the biological and chemical fields through sensors and actuators defined at biological length-scales. Similarly, biologists/chemists can provide the fundamental understanding of natural sensors and actuators that can lead to the formation of bio-inspired sensors and actuators that solve engineering problems.
- To establish a vibrant bio-inspired engineering research community working in close collaboration, NSF and JST should place a particular emphasis on a jointly-funded bilateral US-Japan cooperative research program centered on bio-inspired sensing and actuation. A priority should be given to BSBA research aimed toward rendering society resilient to natural and man-made disasters and to the betterment of human life.
- Given the high potential for broad-based impact, NSF and JST should prioritize university-industry collaborations that accelerate the transfer of bio-inspired sensing and actuation technologies from the laboratory to implementation in society.
- To address critical research needs and tackle the grand challenges in the BSBA area, high priority should be placed on training the next generation of high quality, interdisciplinary researchers who are equally knowledgeable in engineering (including sensing and actuation technologies) and biology/chemistry. The United States and Japan are strongly urged to create a paradigm-shift in academic programs to produce future students with cross-disciplinary bio-sensing and bio-actuation knowledge and skills. In particular, a Summer Student/Early-Career Faculty Research Institute program, jointly organized and held in Japan and the US in annual rotation, should be carefully planned and implemented.

Workshop Co-chairs:

Prof. Masayoshi Tomizuka
University of California, Berkeley

Prof. Takehiko Kitamori
University of Tokyo

Prof. Yoshinobu Baba
Nagoya University

Prof. Jerome P. Lynch
University of Michigan

Grand Challenges

Design Multi-Level and Multi-Length Scale Hierarchical Systems Inspired by Biology

Objectives

- Synthesize new fabrication methods suitable for creating multi-level hierarchical systems that possess desirable material properties and functionalities at specified length scales
- Reverse engineer biological systems and develop new tools/approaches for identifying their fundamental operating principles and design
- Integrate sensing/actuation for synergistically performing specific engineering functionalities

Multi-hierarchical design in gecko feet

Integrated sensing and actuation in the wings of fruit flies

Technological Challenges

- Integration and scalability of top-town and bottom-up fabrication methodologies
- Multi-dimensional fabrication principles that encode desirable properties at drastically different length scales
- Self-assembly methods for attaining precise spatial structures, arrangements, and functionalities
- Comprehensive and realistic mathematical models and representations of biological systems and functionalities
- Fusion of multiple sensing modalities, linear versus logarithmic processing, and digital versus analog data

Broader Impacts

- New self-assembly and fabrication methods
- New sensing/actuation functionalities
- Efficient structural systems
- Military applications of new technologies
- Medical breakthroughs in diagnostics, monitoring, therapeutics, and prosthetics
- Understanding the central nervous system and immune system (and biological systems)

Design of Multi-Level and Multi-Length Scale Hierarchical Systems Inspired by Biology

Summary: Biological systems employ hierarchical structures to achieve multifunctional system performance that far exceed the performance of current engineered systems. The grand challenge is to synthesize new fabrication methods that utilize and achieve hierarchical systems, utilize reverse engineer techniques to develop new tools, and integrate sensing and actuation technologies. The research challenges include integration and scalability of top-town and bottom-up fabrication methodologies, multi-dimensional fabrication principles that encode desirable properties at drastically different length scales, self-assembly methods for attaining precise spatial structures, arrangements, and functionalities, and comprehensive and realistic mathematical models and representations of biological systems and functionalities. Accomplishing this grand challenge will yield a new generation of leaders adept in bio-inspired sensing and actuation systems.

Teaching Biologically-Inspired Design

Objectives

- Support intensive courses for graduate and postdoctoral students in bio-inspired design.
- Courses must include participation of both students and instructors from biology and engineering.
- Organizers are encouraged to combine practical training and independent research project as components of the course.

Technological Challenges

- There are no technological hurdles to be overcome by such a course. However, course organizers will face a number of logistical challenges. These include recruiting top instructors and guest lecturer from both disciplines, the setup of laboratory equipment for use in student projects and attracting promising students.

Broader Impacts

- This program will foster a cross-disciplinary exchange that generally does not currently exist in the training of either engineers or biologists.
- Engineering students will be exposed to biological concepts that could lead to the development of revolutionary devices or engineering approaches.
- Biology students will be exposed to cutting-edge techniques and rigorous analytical approaches to greatly enhance biological research.

Grand Challenge Summary

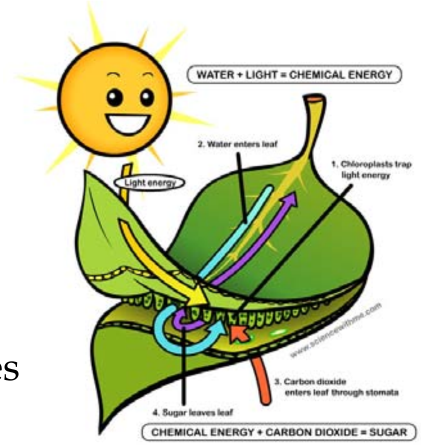
Teaching Biologically-Inspired Design

Summary: While there are numerous examples of revolutionary advances in engineering that have been inspired from biology, the education of engineers in the US and Japan generally does not expose students to biological concepts. The training of biologists in these countries similarly does not generally include education on the state-of-the art techniques and quantitative approaches offered by engineering. We propose that program that supports intensive training in biological-inspired engineering for graduate and postdoctoral students of engineering and biology. These courses are intended of offer a multidisciplinary training in techniques as well as an exposure to research in both engineering and biology.

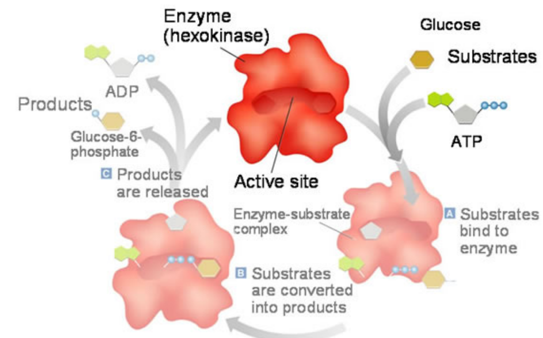
Bio-inspired Biochemical Engineering of Systems for Energy, Water, Food, Communications, and Medical Applications

Objectives

- Design robust, durable, self-regulating, and homeostasis engineered systems with inherent failure tolerance, monitoring, and self-repair
- Control energy, material, and information interaction among networked nodes using homeostasis, metabolic, and enzymatic processes
- Enable self-diagnosing sensors/actuators that self-regulate and self-control while reducing system complexity with improved performance



Plant photosynthesis



Enzyme reaction process

Technological Challenges

- Incorporate a heterogeneous network of evolving, adjustable, and adaptable multifunctional nodes
- Cradle-to-grave sustainable design approaches
- Artificial enzymatic systems for material generation, operation, and digestion/decomposition
- Direct energy transduction, storage, and utilization
- Achieve efficient energy use and production that's complimentary to environmental resources
- Active and responsive nanomaterials for medical diagnostics and therapeutics

Broader Impacts

- Intelligent and self-diagnosing infrastructures and artificial/engineered systems
- New media for energy, materials, and information exchange and broadcasting
- Biocompatible and implantable active devices
- Fault-tolerant, self-corrective devices/networks
- Early warning systems and disaster prevention
- Sustainable food, energy, and water supply

Grand Challenge Summary

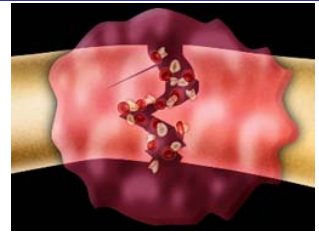
Bio-inspired Biochemical Engineering of Systems for Energy, Water, Food, Communications, and Medical Applications

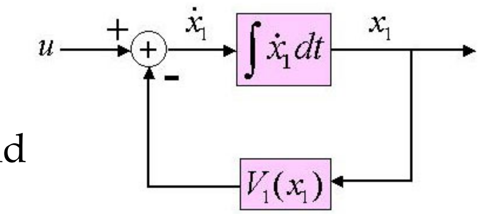
Summary: Biological systems thrive by inherent biochemical processes capable of controlling energy, material, and information interactions between components in the system. The grand challenge is to design robust, durable, self-regulating, and self-healing engineered systems with built-in artificial homeostasis, metabolic and enzymatic mechanisms. The research challenges include the incorporation of a heterogeneous network of evolving, adjustable, and adaptive multifunctional nodes capable of direct energy transduction, storage, and utilization. Accomplishing this grand challenge will result in sustainable food, energy, and water supply.

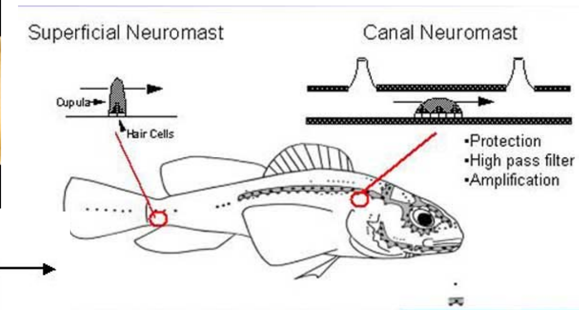
Biologically Inspired Robustness: Self-sustaining sensors and actuators

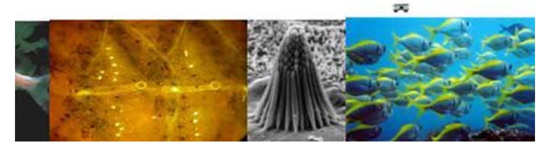
Objectives

- To understand the mechanisms for self renewal and self repair in biological systems
- Identify physical, chemical, and mechanical principles that perform similar functions
- Design and build new generation of sensors and actuators that incorporate self-renewal and self-sustaining characteristics
- Maintain performance in uncontrolled and harsh environments









Technological Challenges

- Develop sensors for recognizing damage in sensor and actuation systems
- Develop sensors and actuators that have ability to be repaired and renewed
- Incorporate redundancy in sensor and actuator design.
- Developing new functional materials with feedback for diagnostics and prognostics
- Sensors and actuators with energy sustainability

Broader Impacts

- Lower cost in sensor and actuator replacement
- Environmentally sensitive engineering and manufacturing
- Increased safety in harsh environments and critical applications
- Self-sustaining sensors for implants in patients and synthetic organs
- Novel sensing and actuation
- Training of students in cross-disciplinary field.
- Self-healing mechanisms

Grand Challenge Summary

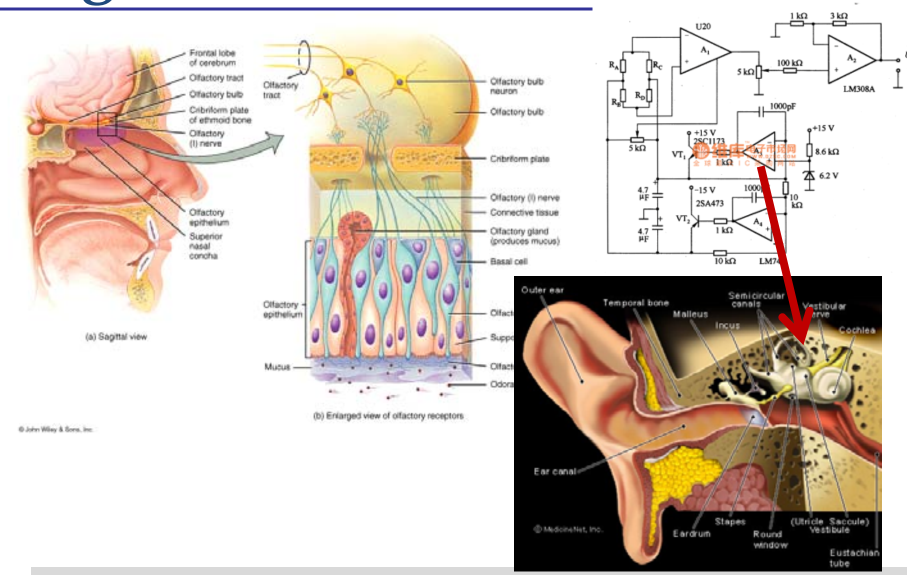
Biologically Inspired Robustness: Self-Sustaining Sensors and Actuators

- ***Summary:*** Biologically Inspired Robustness: Self-sustaining sensors and actuators. The grand challenge is to understand the mechanisms of self renewal and self repair in biological systems and to translate the knowledge towards designing a new generation of self-sustaining sensors and actuators. The vision is that the developed sensors will maintain its performance under uncontrolled and harsh environments. The research challenges include: developing techniques for recognizing damage in sensors and actuators that could then be used for self-repair and self-renewal; incorporating redundancy in the sensor and actuator design; developing new functional materials with feedback for diagnostics and prognostics; and developing sensors with energy sustainability.

BICEP: Biologically-Inspired Control, Enhancement and Processing

Objectives

- Understand biological mechanisms of amplification, sensitivity, and selectivity in sensing and actuation
- Identify local sensing and processing in biological actuation systems
- Translate biological principles for developing integrated sensory and actuation systems with local feedback control
- Development of paradigms in education integrating computer science, engineering, and biology



Technological Challenges

- Identification and distinguishing between local and global information under resource constraints (size, energy, speed, etc)
- Incorporate amplification and feedback in sensors and actuators using biomimetic processes, such as avalanche, cascade, etc.
- Understanding role of noise and nonlinearity in biological sensory systems
- New system design and control based upon above

Broader Impacts

- Computational reduction in central processing of complex systems
- Next generation of intelligent robotics
- Smart house/factory/office
- Smart grid
- Increased sensor sensitivity, selectivity, and signal to noise ratio
- Training next generation of students in multi-disciplinary research

Grand Challenge Summary

BICEP: Biologically-Inspired Control, Enhancement and Processing

- *Summary:* BICEP: Biologically Inspired control, enhancement and processing. The grand challenge is to understand biological mechanisms of amplification, sensitivity, and selectivity in sensing and actuation and to translate these principles into developing integrated sensory and actuation systems with local feedback control. The research challenges include: identification and distinguishing between local and global sensory information under resource constraints (size, energy, speed, etc); incorporation of amplification and feedback in sensors and actuators using biomimetic processes, such as avalanche, cascade, etc; understanding and exploiting the role of noise and nonlinearity in biological sensory systems; and design of novel systems based on these bio-inspired principles.

Keynote Presentations

From smart building to biofied building

Akira Mita

Professor,
Department of System Design Engineering
Keio University

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Ever lasting dream for building

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Tokyo U TRON Intelligent House
http://www.monotsukuri.net/mirai98/tron/tron.htm


Waseda WABOT-HOUSE http://www.wabot-house.waseda.ac.jp/index.html
WABOT-HOUSE LABORATORY


GIT AWARE HOME
http://www.cc.gatech.edu/fce/house/house.html
Center


Aware Home

Smart buildings require thousands of sensors to be embedded.

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Kisho Kurokawa

Metabolism

Capsules have never been replaced.

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Metabolism of living things involves transfer of:

- ✓ Materials
- ✓ Information
- ✓ Energy

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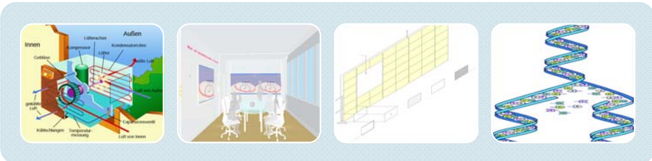
Biofied building



Sensory adaption
- Sensors trigger necessary action based on the prescribed scenario.

Adaption by learning
- Several appliances already have this adaption mechanism. However, the application of this adaption in buildings is still in a preliminary stage.

Physiological adaption
- This adaption mechanism deal with unexpected events that had not been considered in the design stage. The use of this adaption mechanism is promising to make the control system more flexible, robust and simple.

Evolutionary adaption
- Any events occurred during the life of a building are recorded so that the necessary evolution can be identified. The information embedded in DNA is different from that provided in drawings.

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Elements needed for adaption

Sensors
- Acquisition of environmental information
- Sensory adaption

Brain
- Centralized control system
- Adaption by learning

Immune and homeostasis
- Distributed intelligence
- Physiological adaption

DNA
- Creation of next generation
- Evolutionary adaption

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What kind of paradigm shift?

- The building will talk to its residents and adapt to them.
- The building will detect changes of physical and mental ability of the residents from implicit signs of their daily life and reorganize the building system to help them.
- Any events will be recorded and they will be used for creating next generations. Evolution of building systems will become much faster.
- Many controllers for TV, air conditioners, water supply systems, lights and other appliances will disappear. The sensor agent robots will take care of these tasks.

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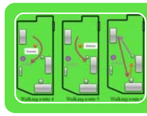
First phase research projects

Sensor agent robots
- e-bio with many sensors
- Biomimetic ears and servo accelerometers



Recognition of emotion and flow line
- Emotion detection using walking patterns
- Flow line detection using laser range finder

Homeostasis control
- Homeostasis control of living space
- Data model for the server

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Sensor agent robots

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First generation: e-bio

320(L) x 320(W) x 180(H) mm, 5kg

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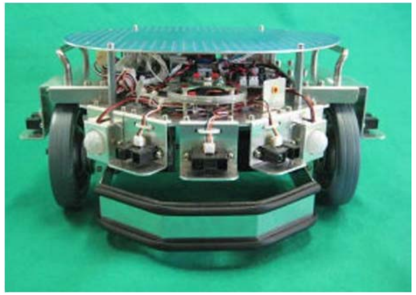
Second generation: e-bio Q



400(L) x 320(W) x 180(H) mm, 5kg
5km/h

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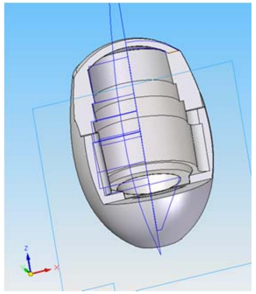
Ear learnt from rabbit and bat



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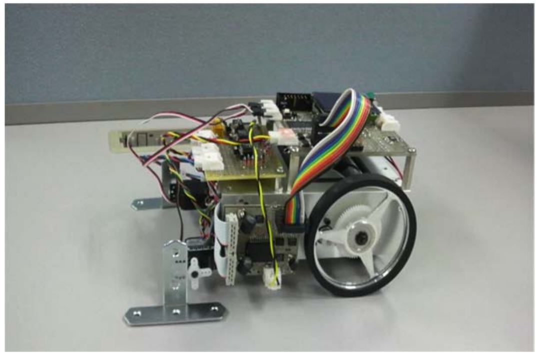
Robot for SHM and security



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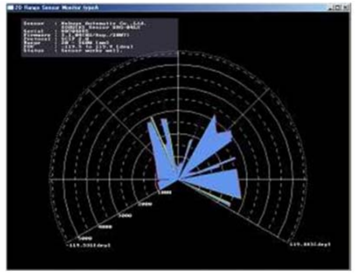
Laser range finder



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Biomimetic ears for a sensor agent robot to localize sound sources

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Sensors

- A large variety of sensors

Camera

Microphone

CO2 sensor

- Analogy with human : ears

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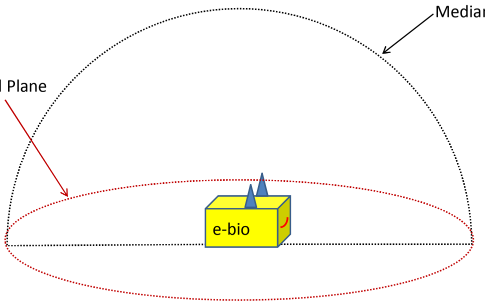
Goal

Build **only 2 ears** for the e-bio to get as much information as possible from sound, especially, sound localization information.



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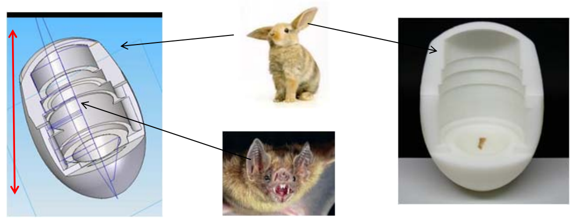
Ears

Bioinspired ears to reproduce human/animal ear functions



CAD model of the ear / Ear prototype

A prototype without inside for comparison

A microphone is then inserted into each ear (left and right)

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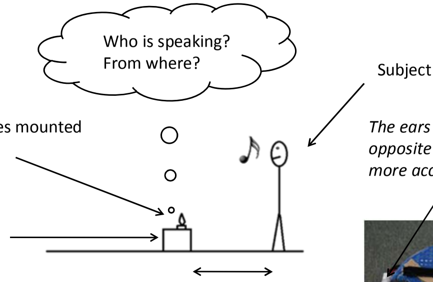
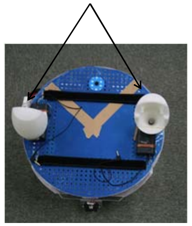
Experiment Settings



The ears are heading in opposite directions to get more accurate results



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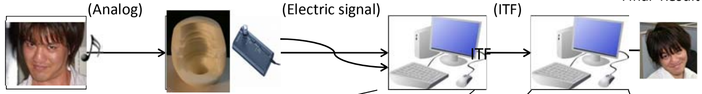
Experiment Flow



- Fourier Transform
- Computation of the Interaural Transfer Function

$$ITF = \frac{\text{Sound reaching the left ear (L)}}{\text{Sound reaching the right ear (R)}}$$

- Training Data
- Principal Component Analysis
- Pattern recognition

K-nearest neighbor algorithm

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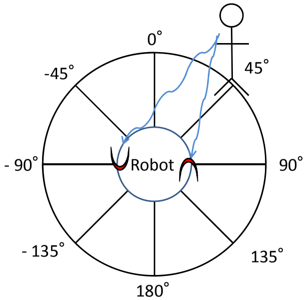
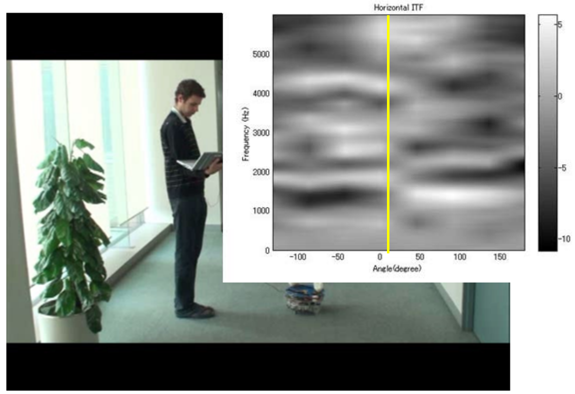
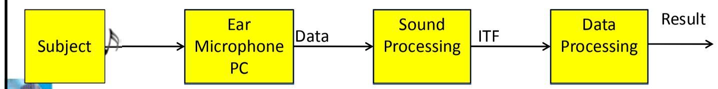
Horizontal Localization

- First results where obtained in the horizontal plane to test and experiment the system

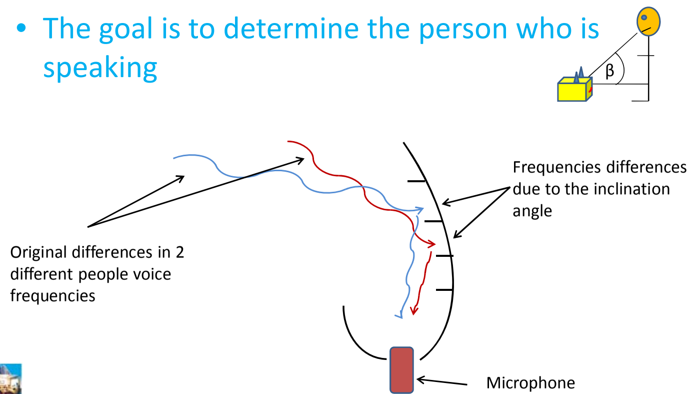


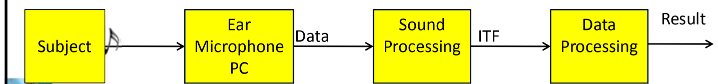




Vertical localization

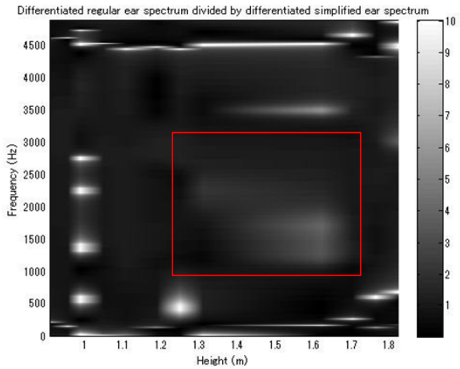
- The goal is to determine the person who is speaking





Ears comparison

$$\frac{\frac{\partial Amp_{regular}}{\partial Height}}{\frac{\partial Amp_{simplified}}{\partial Height}}$$



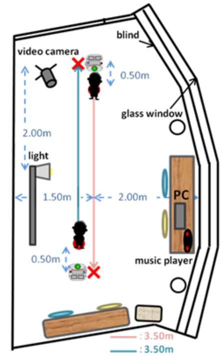
Remarks on biomimetic ears

- 2 biomimetic ears were built and mounted on the e-bio sensor agent robot
- Sound localization was achieved in the median and horizontal plane
- Influences of the inside of the ear were proved
- The programs and the shapes may still be improved to get a better adaption to the residents

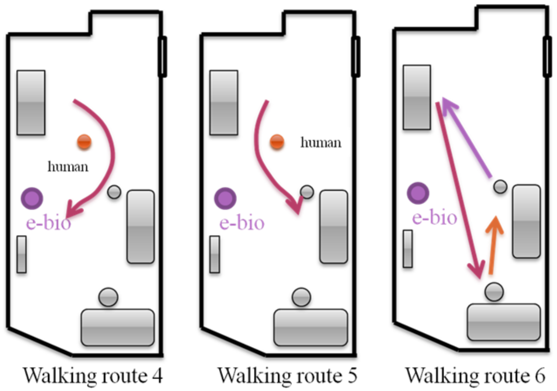
Recognition of emotion and activities

Experimental setup for measuring human emotion using walking pattern

- e-bio follows the resident using proximity sensor and/or laser range finder
- The walking patterns of the resident as well as e-bio will be used to recognizing emotion.



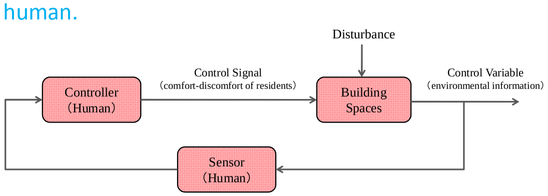
Walking routes detection



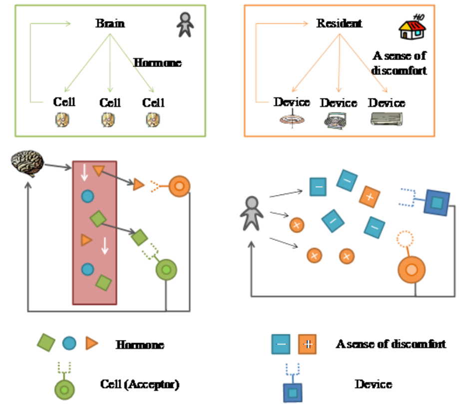
Homeostasis control

What is homeostasis control?

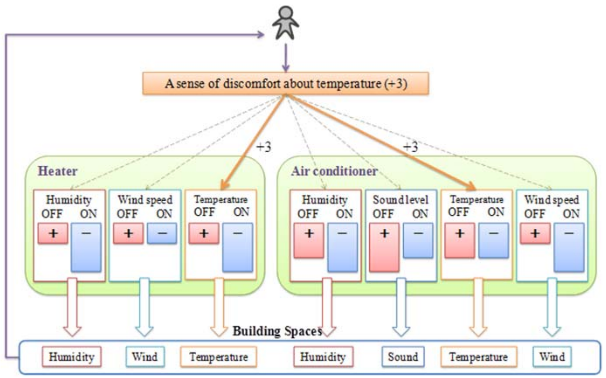
- Broadcast communication by hormone is used.
- Each device has own receptors (or acceptors) to respond the hormone.
- Human is the sensors and controllers.
- The building space is controlled based on inherent intension of human.



Homeostasis control



Broadcast communication by hormone



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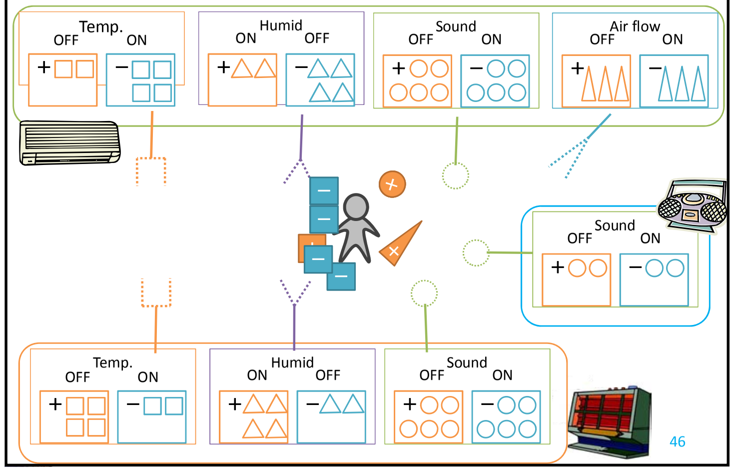
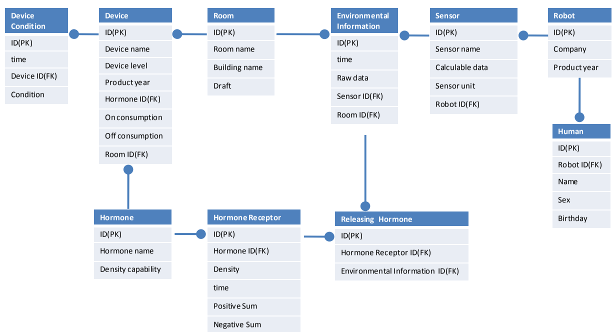
Homeostasis control



46

Data model for homeostasis control



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Conclusions

- Biofied buildings that have four adaption mechanisms are the future of buildings.
- Among four adaptions, physiological adaption and evolutionary adaption mechanisms are being explored.
- Sensor agent robots interface building and residents.
- Sensing systems to detect emotion and implicit intension are the key.
- Success of homeostasis control relies on such sensors.

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ILLINOIS
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

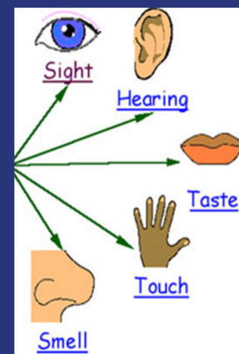
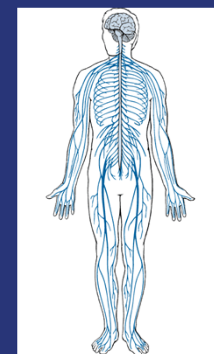
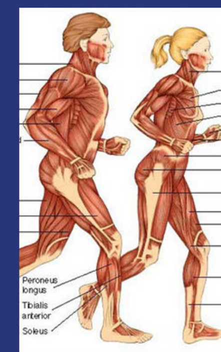
Prof. Mark E Nelson
Beckman Institute

Biological Sensory Acquisition Strategies in Electric Fish

US-Japan Workshop on Bio-inspired Engineering of Next-Generation Sensors and Actuators

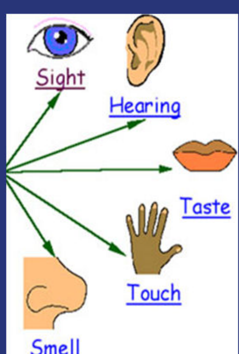
Nov 12-13, 2011
Berkeley, CA, USA

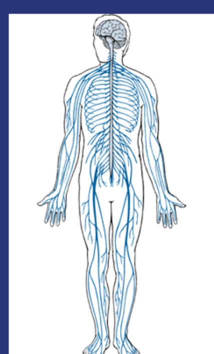
Nervous System Organization

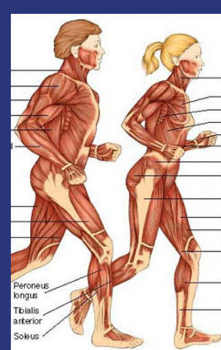
Bio-Sensing	Information Processing	Bio-Actuation
		
~10^8 photoreceptors ~10^7 chemoreceptors ~10^6 mechanoreceptors	~10^{11} neurons	~640 muscles

Bio-inspired Information Processing (BIP)

BS ⟷ BIP ⟷ BA





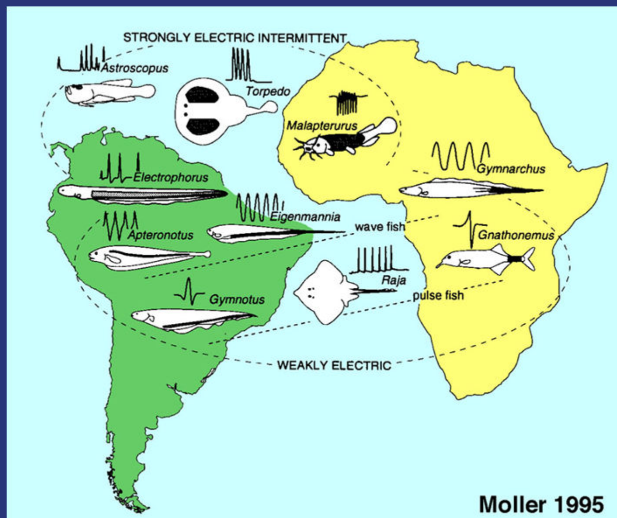


Electric Fish as a Model System for

Bio-inspired Information Processing

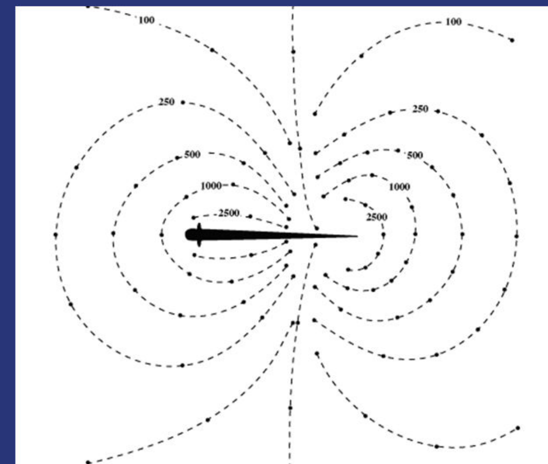
BS ⟷ BIP ⟷ BA

The World of Electric Fish

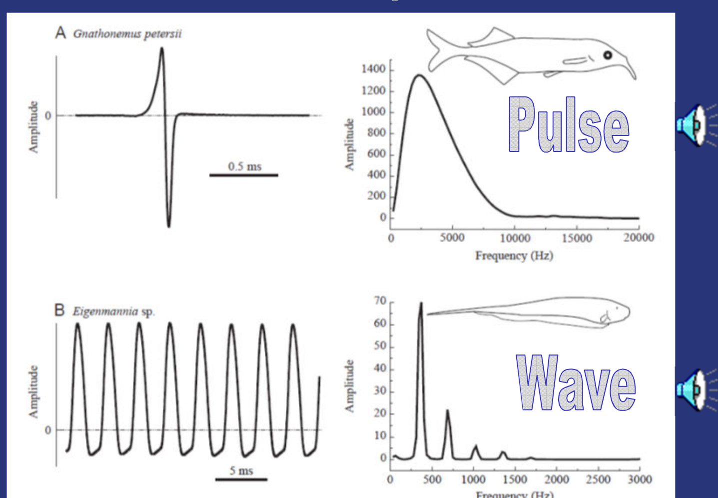


Moller 1995

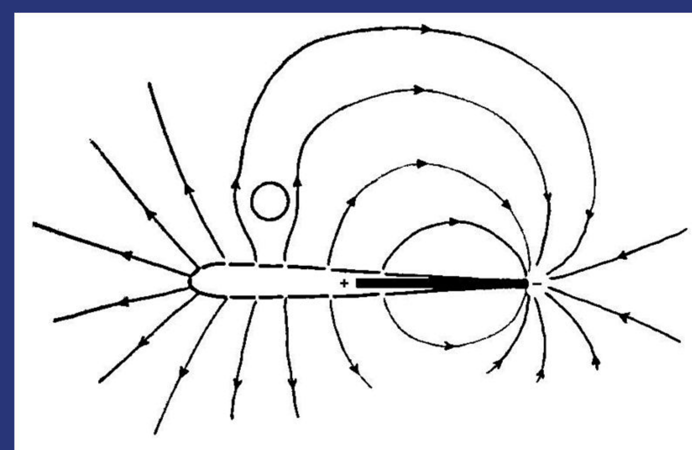
Electric Organ Discharge (EOD) - Spatial



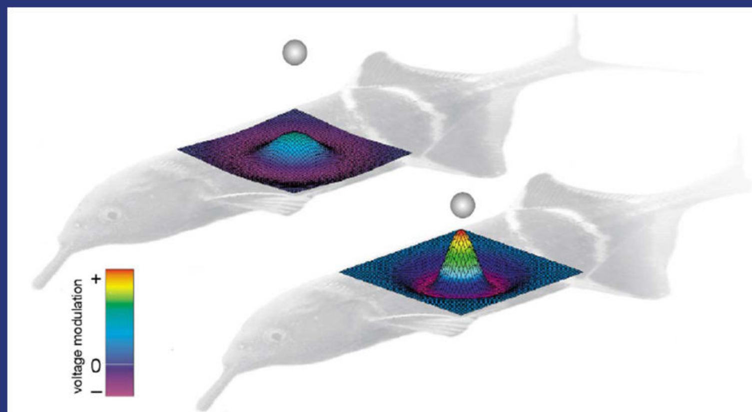
EOD - Temporal



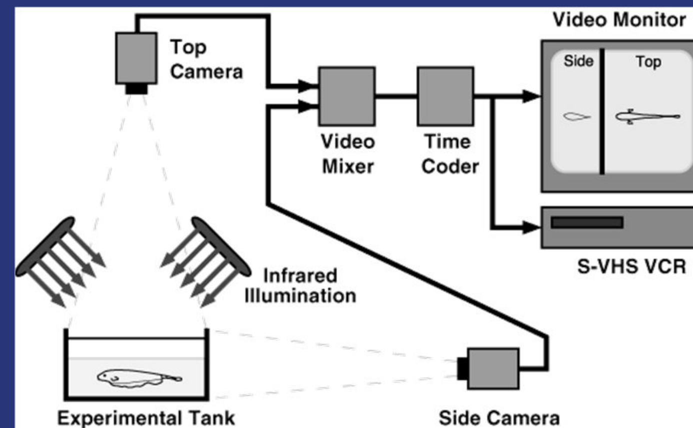
Principle of active electrolocation



Electrosensory Image Formation

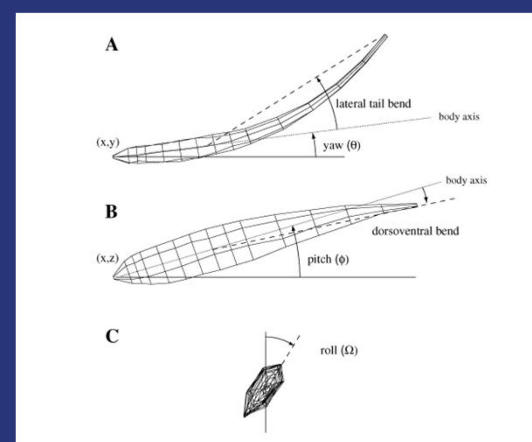


Prey-capture video analysis

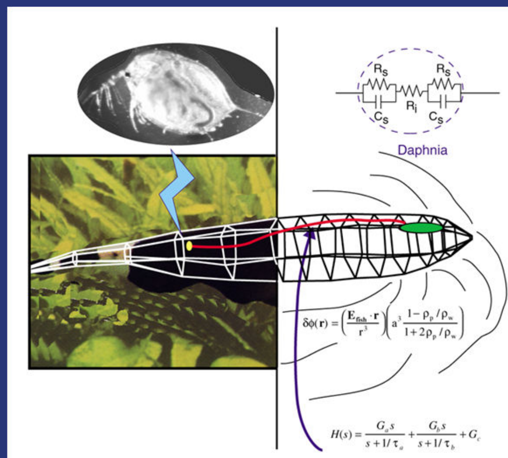


Prey capture behavior

Fish Body Model



Electrosensory Image Reconstruction



Estimating *Daphnia* signal strength

- Voltage perturbation at skin $\Delta\phi$:

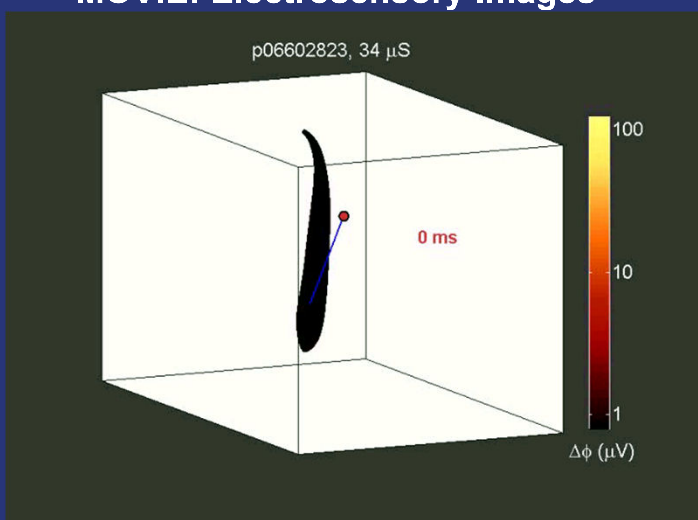
fish E-field at prey — prey volume — electrical contrast

$$\Delta\phi = \frac{\vec{E}_{fish} \cdot \vec{r}}{r^3}\left(a^3 \frac{1-\rho_{prey}/\rho_{water}}{1+2\rho_{prey}/\rho_{water}}\right)$$

distance from prey to receptor

THIS FORMULA CAN BE USED TO COMPUTE THE SIGNAL AT EVERY POINT ON THE BODY SURFACE

MOVIE: Electrosensory Images

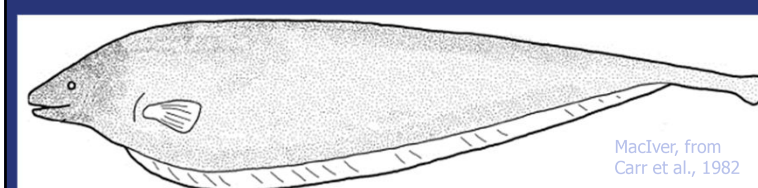


Electroreceptors

~15,000 sensors distributed over body surface

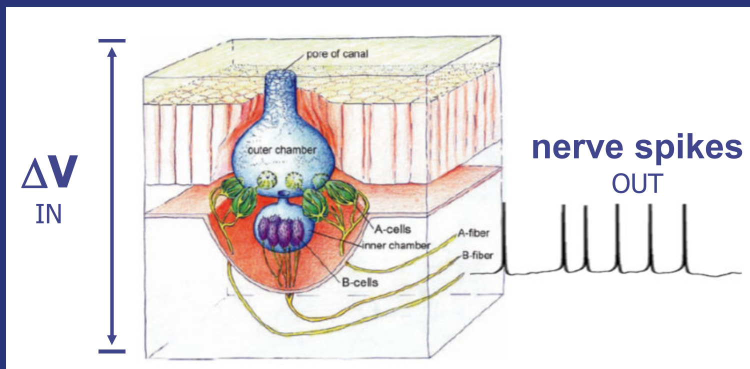
Much higher spatial density than is necessary to reconstruct spatial image properties

Dense array of "cheap" low-resolution sensors

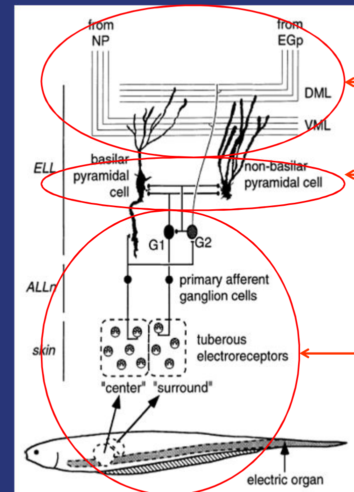


MacIver, from Carr et al., 1982

Individual Sensors (Electroreceptors)



Data Acquisition Strategies



2) Global feedback for contextual processing

3) Output neurons act as task-specific feature detectors; they have much lower data rate than input

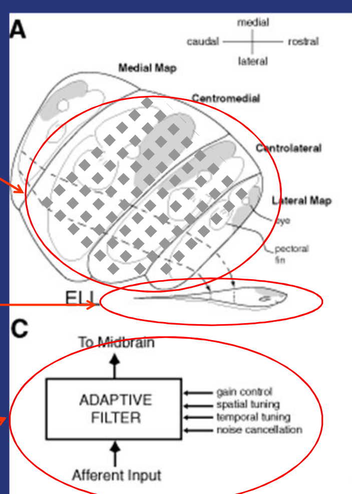
1) Local differencing for contrast enhancement

Data Acquisition Strategies

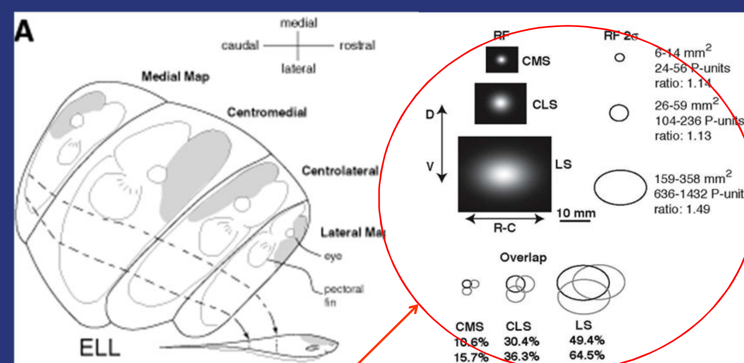
5) Virtual sensor arrays, many fewer virtual sensors than physical sensors

4) Topographic mapping, multiple maps for parallel processing

6) Adaptive filtering, adjustable gain, spatio-temporal filtering props.



Data Acquisition Strategies



7) Multiscale processing across a range of spatial and temporal scales.

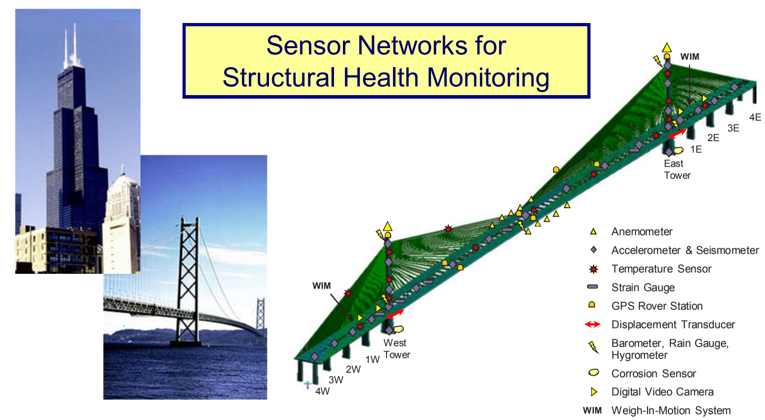
Data Acquisition Strategies - Summary

- real-time monitoring
- dense arrays of cheap, low-resolution sensors

- **Smart sensing strategies**
  1. Local contrast enhancement
  2. Global contextual processing
  3. Task-dependent feature detection
  4. Topographic mapping
  5. Parallel virtual sensor arrays
  6. Adaptive filtering
  7. Multiscale processing

Applications / Bio-Inspired Information Processing

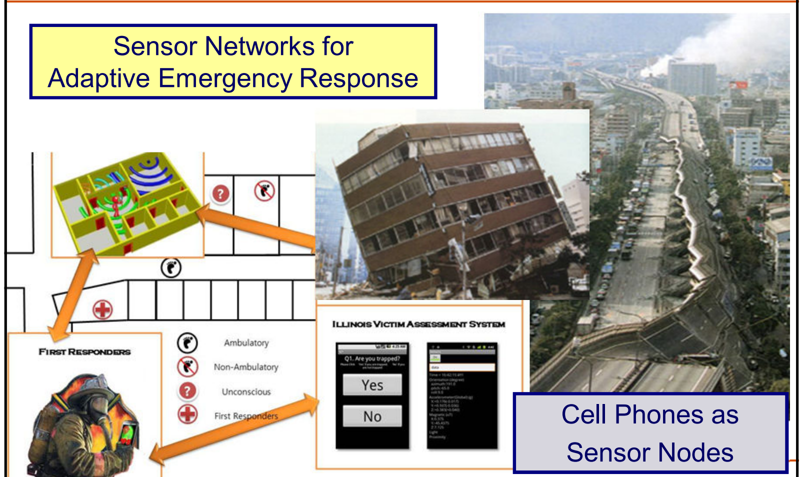
Sensor Networks for
Structural Health Monitoring



SSTL

Applications / Bio-Inspired Information Processing

Sensor Networks for
Adaptive Emergency Response

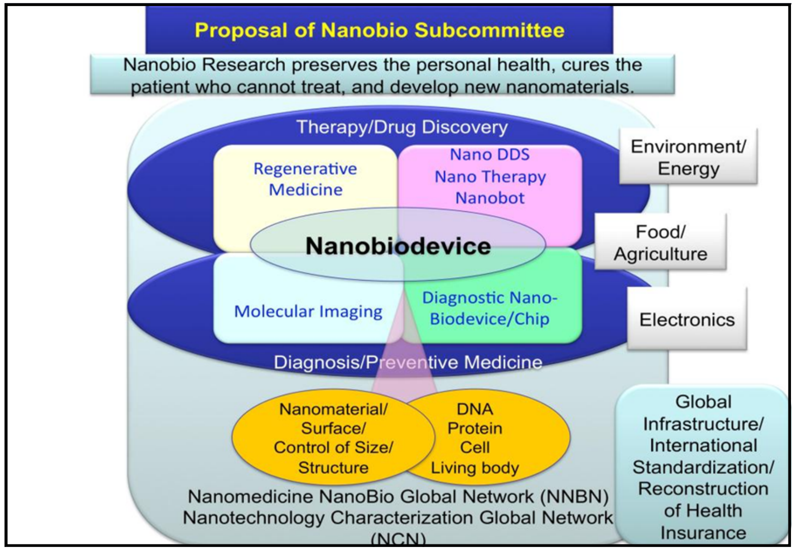


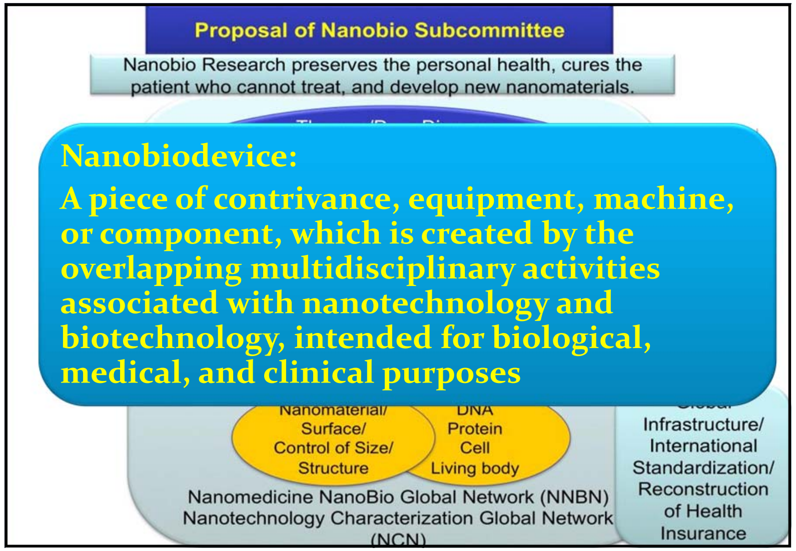
Cell Phones as
Sensor Nodes

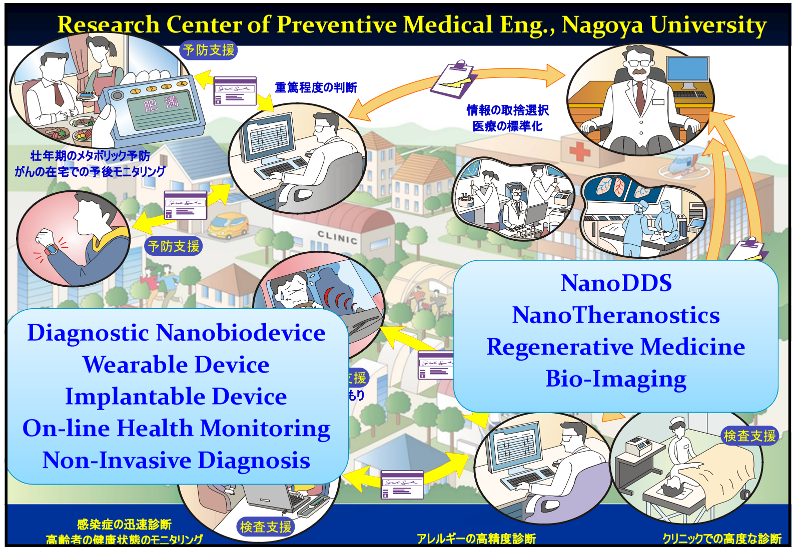
Supported by NSF Grants
0422073 Scale-Dependent Processing of Clustered Sensory Signals
1030454 EAGER: Bio-inspired Smart Sensor Networks for Adaptive Emergency Response

Questions / Discussion ?

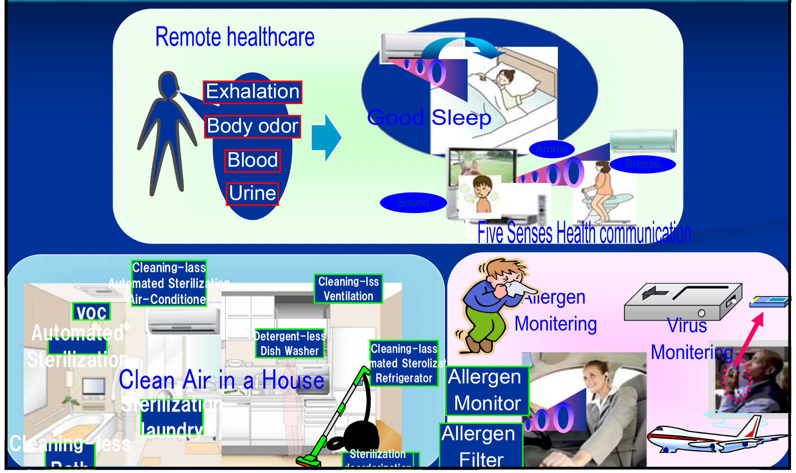

Nanobiodevice for Future Personalized Medicine and Evidence Based Healthcare
Yoshinobu BABA
Department of Applied Chemistry, Graduate School of Engineering
FIRST Research Center for Innovative Nanobiodevices
Synchrotron Radiation Research Center
Department of Advanced Medical Science, Graduate School of Medicine
Nagoya University
Health Research Institute
National Institute of Advanced Industrial Science and Technology
Nagoya University
AIST
US-Japan Workshop on Bio-inspired Engineering of Next-generation Sensors and Actuators
Berkeley, Nov. 12, 2011


Proposal of Nanobio Subcommittee
Nanobio Research preserves the personal health, cures the patient who cannot treat, and develop new nanomaterials.
Therapy/Drug Discovery
Regenerative Medicine
Nano DDS
Nano Therapy
Nanobot
Nanobiodevice
Molecular Imaging
Diagnostic Nano-Biodevice/Chip
Diagnosis/Preventive Medicine
Environment/ Energy
Food/ Agriculture
Electronics
Nanomaterial/ Surface/ Control of Size/ Structure
DNA
Protein
Cell
Living body
Nanomedicine NanoBio Global Network (NNBN)
Nanotechnology Characterization Global Network (NCN)
Global Infrastructure/ International Standardization/ Reconstruction of Health Insurance


Proposal of Nanobio Subcommittee
Nanobio Research preserves the personal health, cures the patient who cannot treat, and develop new nanomaterials.
Nanobiodevice:
A piece of contrivance, equipment, machine, or component, which is created by the overlapping multidisciplinary activities associated with nanotechnology and biotechnology, intended for biological, medical, and clinical purposes
Nanomaterial/ Surface/ Control of Size/ Structure
DNA
Protein
Cell
Living body
Nanomedicine NanoBio Global Network (NNBN)
Nanotechnology Characterization Global Network (NCN)
Infrastructure/ International Standardization/ Reconstruction of Health Insurance


Research Center of Preventive Medical Eng., Nagoya University
予防支援
重篤程度の判断
情報の取捨選択
医療の標準化
壮年期のメタボリック予防
がんの在宅での予後モニタリング
予防支援
CLINIC
Diagnostic Nanobiodevice
Wearable Device
Implantable Device
On-line Health Monitoring
Non-Invasive Diagnosis
NanoDDS
NanoTheranostics
Regenerative Medicine
Bio-Imaging
検査支援
検査支援
感染症の迅速診断
高齢者の健康状態のモニタリング
アレルギーの高精度診断
クリニックでの高度な診断

Healthcare Nanodevices with Electronics and Home Electrical Appliance



International Study of the Long-term Impacts and Future Opportunities for Nanoscale Science and Engineering

Organized by National Science Foundation

Chicago (for US), March 9-10, 2010 Hamburg (for EU), June 23-24

Tokyo (for Japan, Korea and Taiwan), July 26-27 Singapore (for China, India), July 29-30

NSF, Washington DC, Sep. 30, 2010

Nanotechnology Goals for the next 10 years

Goal 1: Multifunctional **Theranostic nanobiodevices**

Goal 2: **Ultra-high sensitive**, highly specific, **low invasive** and reliable (robust) **multiplexed detection technologies.**

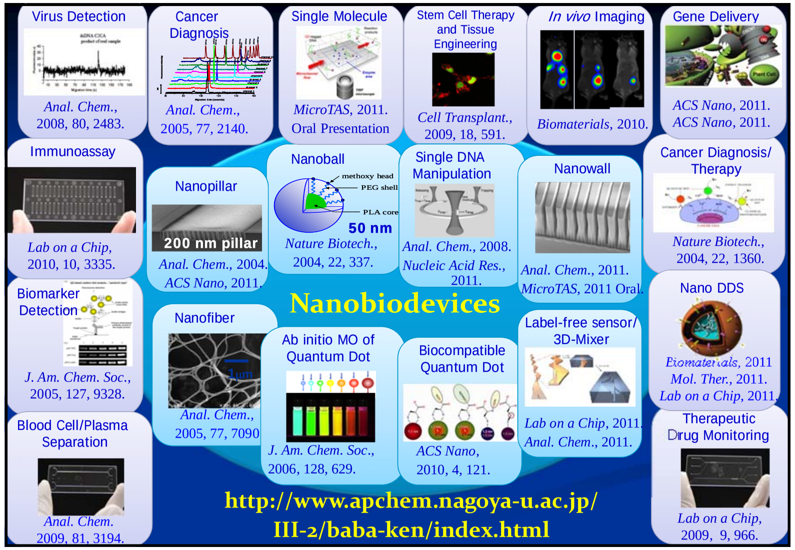
Goal 3: **Remote disease monitoring** on-line nanosensing.

Goal 4: Tissue-growth facilitating **nanostructured cell sheets.**

Goal 5: Biological nanostructures in bioelectronics.

Goal 6: **Single cell** interventions and **diagnostics.**

Goal 7: **Stem cell** differentiation and site-specific delivery



Contents

- **Nanobiodevices for Ultrafast Analysis of DNA and Nanopore Single DNA Molecule Sequencing:**

Nanopillar, Nanowall, Nanowire for Milli-Second DNA Separation and Single DNA Molecule Manipulation for Nanopore Sequencing

Nature Biotech., 2004; *ACS Nano*, 2011; *Anal. Chem.*, 2011.

Kawai, et al., *Nature Nanotech.*, 2010.

- **Single Cancer Cell Diagnosis and Single Molecular Epigenetic Analysis for Cancer Metastasis Diagnosis :**

Microfluidics with Euglena for CTC (Circulating Tumor Cell) Separation Towards Liquid Biopsy and Single Molecular DNA Methylation Detection

ACS Nano, 2010; *Nucleic Acids Res.*, 2011; *Lab on a Chip*, 2011.

- **High-Speed, High-Sensitive Immunoassay for Cancer Diagnosis:**

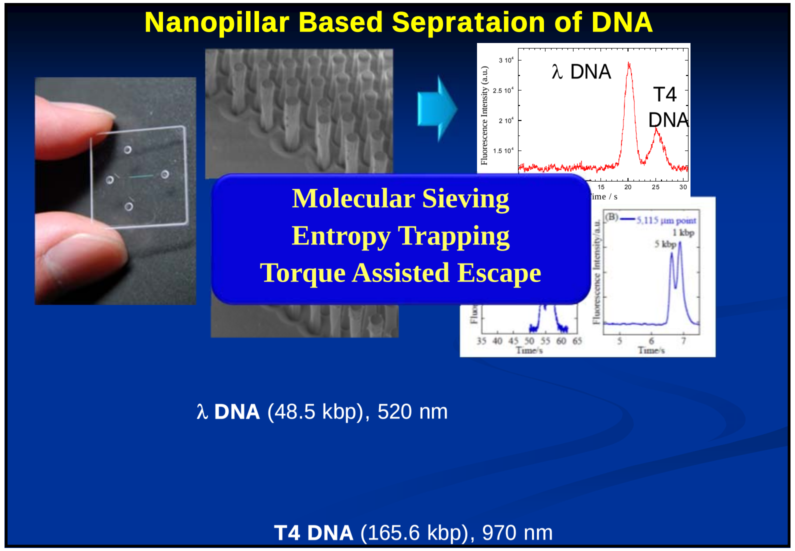
Immuno-Pillar Chip for 5-min Immunoassay From a Drop of Blood

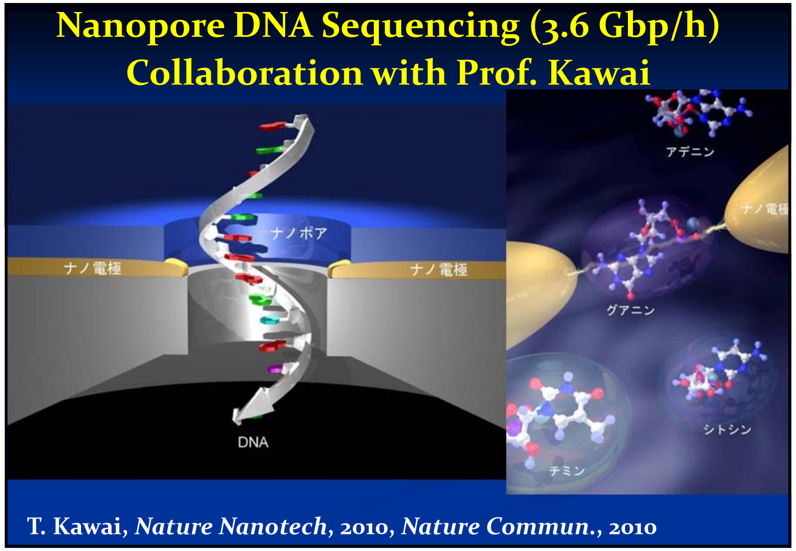
Lab on a Chip, 2010; *PLoS ONE*, 2011; *Anal. Chem.*, 2011.

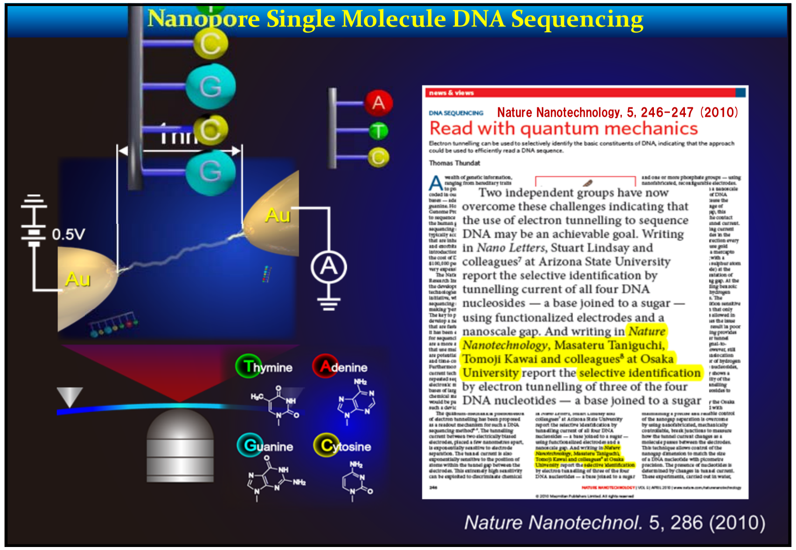
- **Theranostic Nanobiodevice for Stem Cell Therapy:**

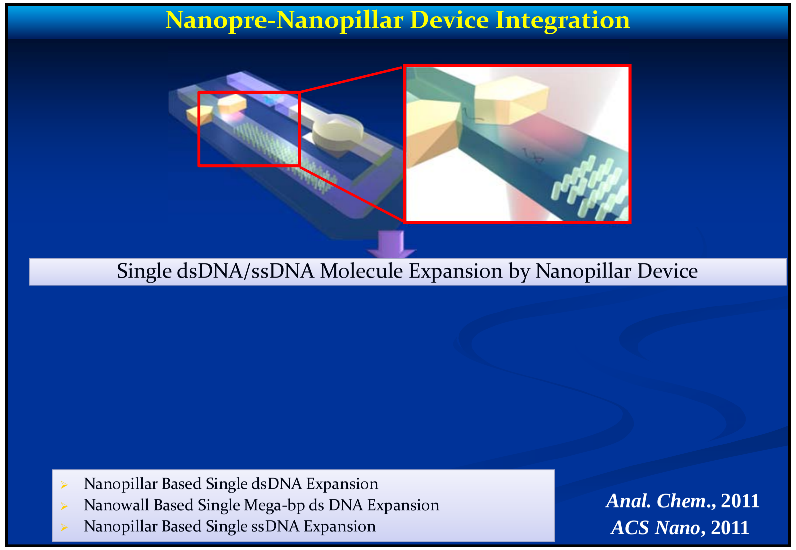
Quantum dots for Stem Cell Therapy, *in vivo* Imaging, and optical/MRI bi-modal Imaging

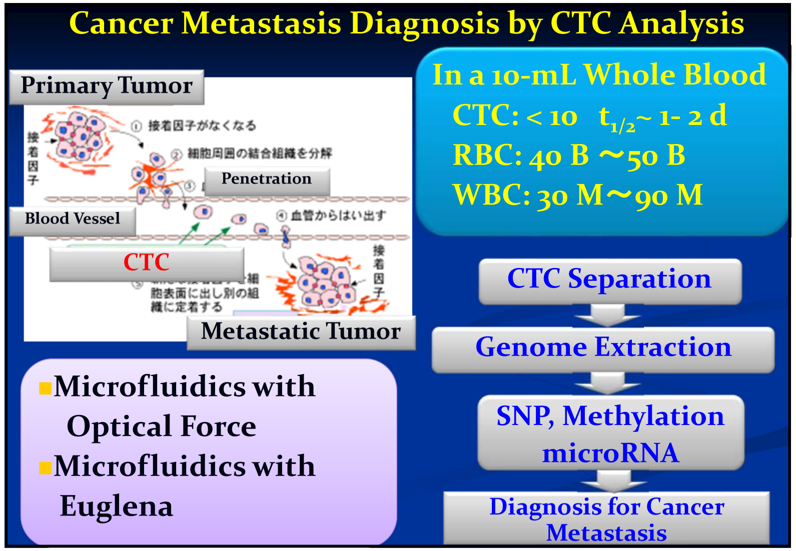
Nature Biotech., 2004; *Biomaterials*, 2010; *ACS Nano*, 2010; *Biomaterials*, 2011; *ACS Nano*, 2011; *ACS Nano*, 2011; *Mol. Therapy*, 2011.

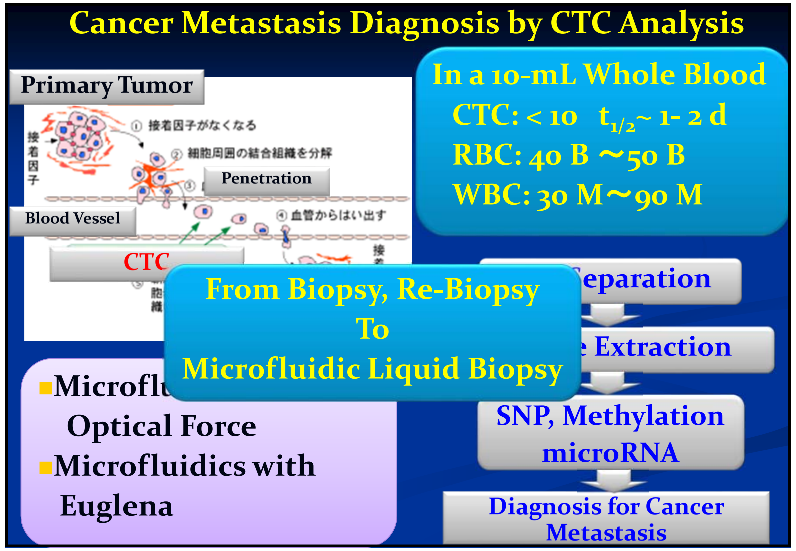

Nanopillar Based Seprataion of DNA
λ DNA
T4 DNA
Molecular Sieving
Entropy Trapping
Torque Assisted Escape
λ DNA (48.5 kbp), 520 nm
T4 DNA (165.6 kbp), 970 nm

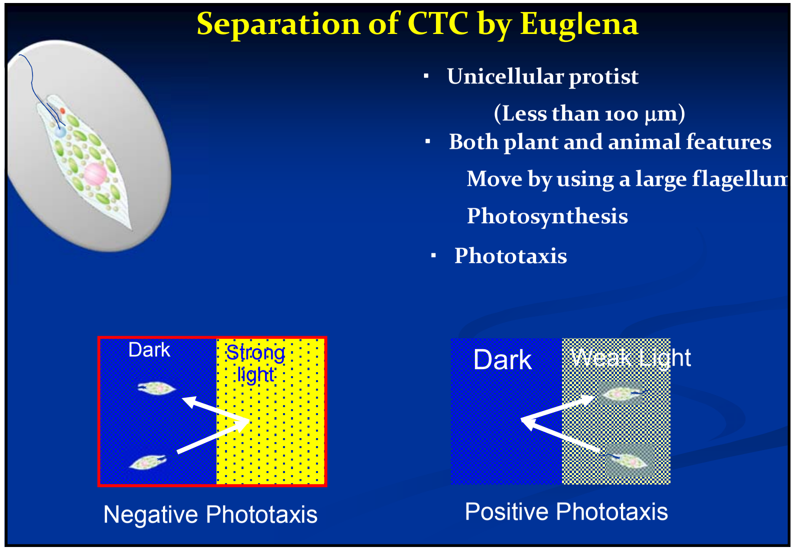

Nanopore DNA Sequencing (3.6 Gbp/h)
Collaboration with Prof. Kawai
ナノポア
ナノ電極
ナノ電極
DNA
アデニン
グアニン
シトシン
チミン
T. Kawai, Nature Nanotech, 2010, Nature Commun., 2010

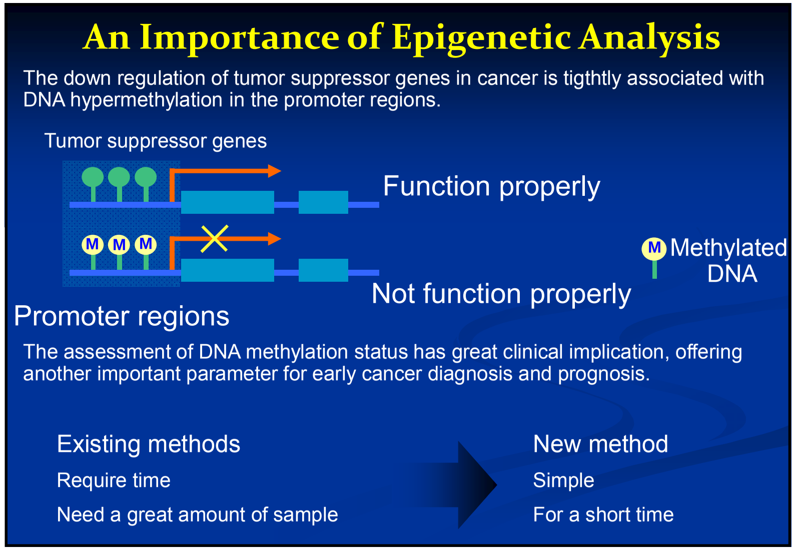

Nanopore Single Molecule DNA Sequencing
0.5V
Au
Au
A
Thymine
Adenine
Guanine
Cytosine
Nature Nanotechnology. 5, 246–247 (2010)
Read with quantum mechanics
Two independent groups have now overcome these challenges indicating that the use of electron tunnelling to sequence DNA may be an achievable goal. Writing in Nano Letters, Stuart Lindsay and colleagues at Arizona State University report the selective identification by tunnelling current of all four DNA nucleosides — a base joined to a sugar — using functionalized electrodes and a nanoscale gap. And writing in Nature Nanotechnology, Masateru Taniguchi, Tomoji Kawai and colleagues at Osaka University report the selective identification by electron tunnelling of three of the four DNA nucleotides — a base joined to a sugar
Nature Nanotechnol. 5, 286 (2010)

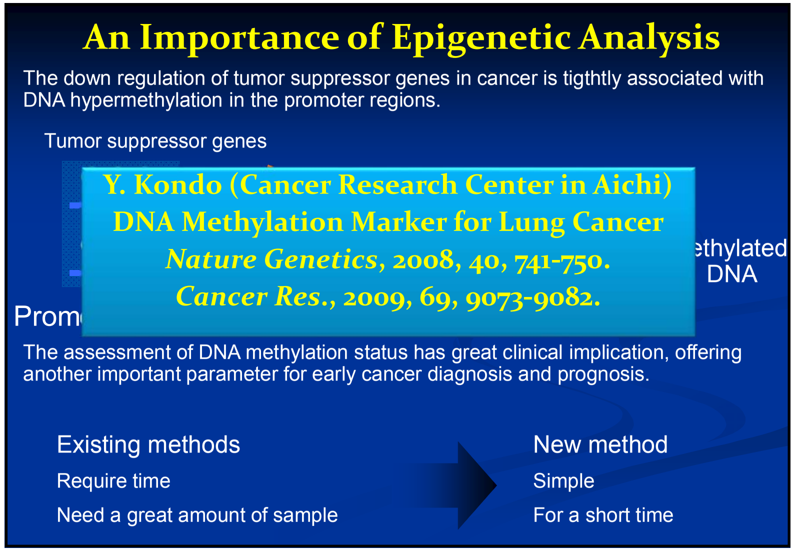

Nanopre-Nanopillar Device Integration
Single dsDNA/ssDNA Molecule Expansion by Nanopillar Device
Nanopillar Based Single dsDNA Expansion
Nanowall Based Single Mega-bp ds DNA Expansion
Nanopillar Based Single ssDNA Expansion
Anal. Chem., 2011
ACS Nano, 2011


Cancer Metastasis Diagnosis by CTC Analysis
Primary Tumor
Penetration
Blood Vessel
CTC
Metastatic Tumor
In a 10-mL Whole Blood
CTC: < 10 t1/2 ~ 1- 2 d
RBC: 40 B ~50 B
WBC: 30 M~90 M
CTC Separation
Genome Extraction
SNP, Methylation microRNA
Diagnosis for Cancer Metastasis
Microfluidics with Optical Force
Microfluidics with Euglena


Cancer Metastasis Diagnosis by CTC Analysis
Primary Tumor
Penetration
Blood Vessel
CTC
In a 10-mL Whole Blood
CTC: < 10 t1/2 ~ 1- 2 d
RBC: 40 B ~50 B
WBC: 30 M~90 M
From Biopsy, Re-Biopsy
To
Microfluidic Liquid Biopsy
SNP, Methylation microRNA
Diagnosis for Cancer Metastasis
Optical Force
Microfluidics with Euglena


Separation of CTC by Euglena
・ Unicellular protist
(Less than 100 μm)
・ Both plant and animal features
Move by using a large flagellum
Photosynthesis
・ Phototaxis
Dark
Strong light
Negative Phototaxis
Dark
Weak Light
Positive Phototaxis


An Importance of Epigenetic Analysis
The down regulation of tumor suppressor genes in cancer is tigthtly associated with DNA hypermethylation in the promoter regions.
Tumor suppressor genes
Function properly
Methylated DNA
Not function properly
Promoter regions
The assessment of DNA methylation status has great clinical implication, offering another important parameter for early cancer diagnosis and prognosis.
Existing methods
Require time
Need a great amount of sample
New method
Simple
For a short time


An Importance of Epigenetic Analysis
The down regulation of tumor suppressor genes in cancer is tigthtly associated with DNA hypermethylation in the promoter regions.
Tumor suppressor genes
Y. Kondo (Cancer Research Center in Aichi)
DNA Methylation Marker for Lung Cancer
Nature Genetics, 2008, 40, 741-750.
Cancer Res., 2009, 69, 9073-9082.
ethylated DNA
Prom
The assessment of DNA methylation status has great clinical implication, offering another important parameter for early cancer diagnosis and prognosis.
Existing methods
Require time
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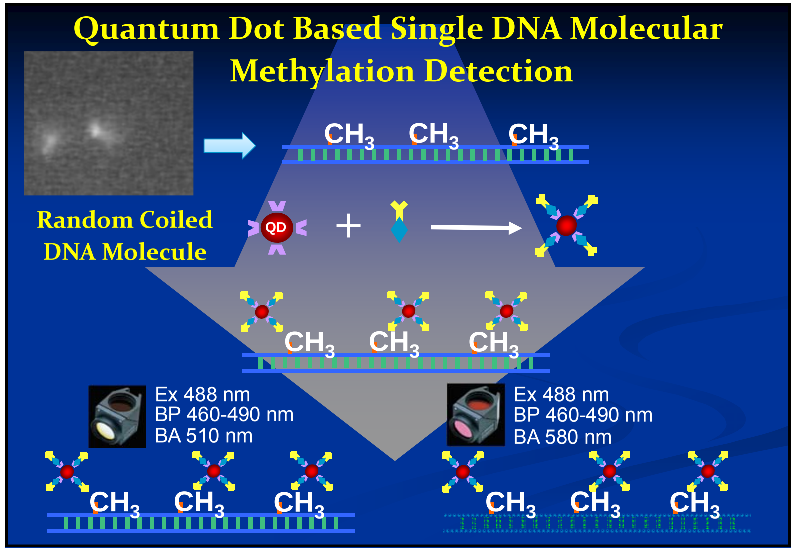
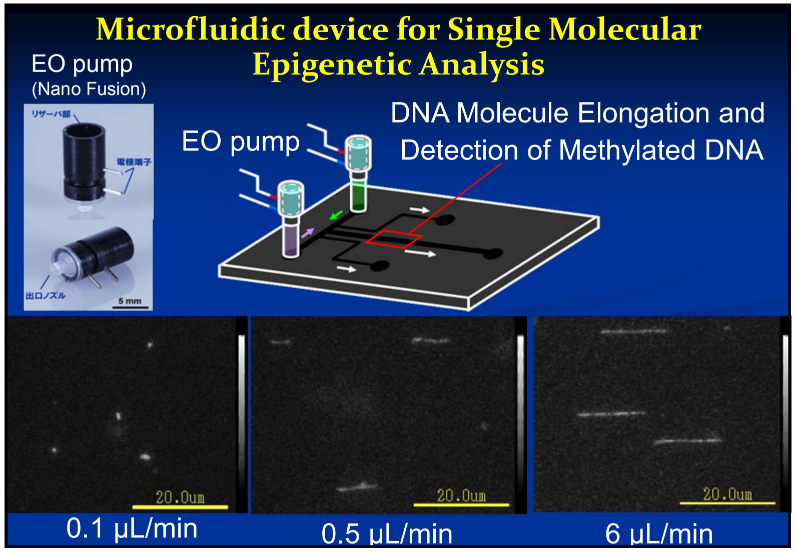
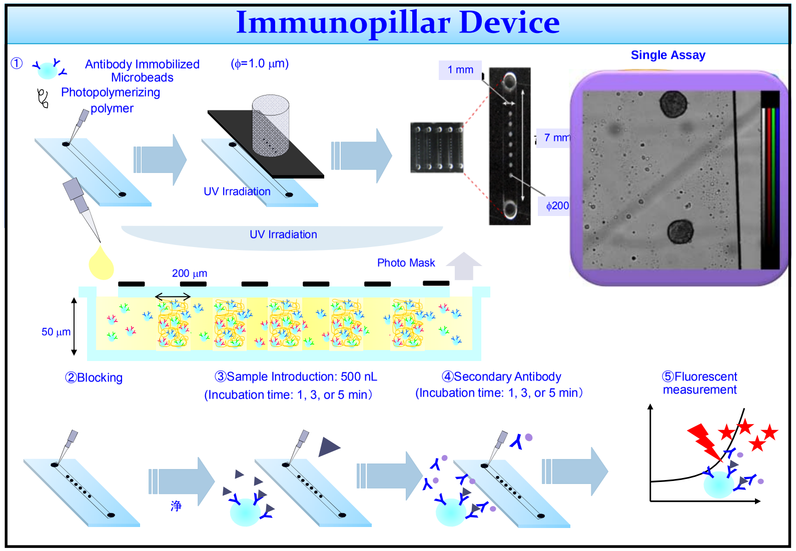
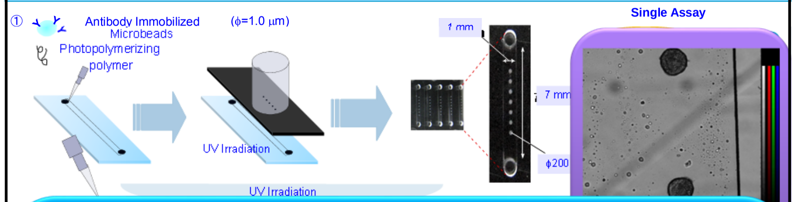

Quantum Dot Based Single DNA Molecular Methylation Detection
Random Coiled DNA Molecule
QD
CH3 CH3 CH3
Ex 488 nm
BP 460-490 nm
BA 510 nm
Ex 488 nm
BP 460-490 nm
BA 580 nm


Microfluidic device for Single Molecular Epigenetic Analysis
EO pump
(Nano Fusion)
EO pump
DNA Molecule Elongation and Detection of Methylated DNA
20.0um
0.1 μL/min
0.5 μL/min
6 μL/min

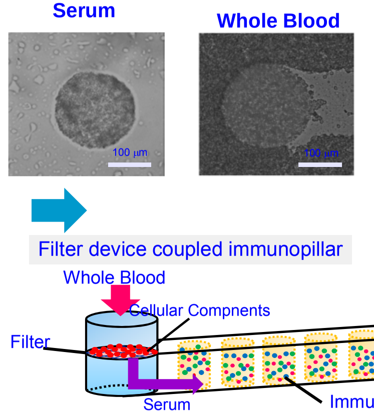

Immunopillar Device
① Antibody Immobilized Microbeads
Photopolymerizing polymer
(ϕ=1.0 μm)
UV Irradiation
1 mm
7 mm
ϕ200
Single Assay
UV Irradiation
Photo Mask
200 μm
50 μm
②Blocking
③Sample Introduction: 500 nL
(Incubation time: 1, 3, or 5 min)
④Secondary Antibody
(Incubation time: 1, 3, or 5 min)
⑤Fluorescent measurement

Immunopillar Device



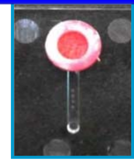
- 30,000 particles in a single immunopillar
- 200 nm pore size for photopolymerized polymer
- 50 times larger surface-to-volume ratio
- Less than μm distance between antibody
- 500 nL Whole Blood Analysis
- 3-8 min Total Analysis Time
- Sub pM (pg/mL) Detection limit

Immunopillar device for whole blood assay



Components of blood

- ○Plaque (血小板)：1~4 μm
- ○White blood cells (白血球)
  - small lymphoeyte (小リンパ球)：6~9 μm
  - large lymphoeyte (大リンパ球)：9~15 μm
  - neutrophil (好中球)：10~12 μm
  - one of granulated leukocyte (顆粒球の一種:好酸球) :10~15 μm
- ○Red blood cells (赤血球)：7~8 μm

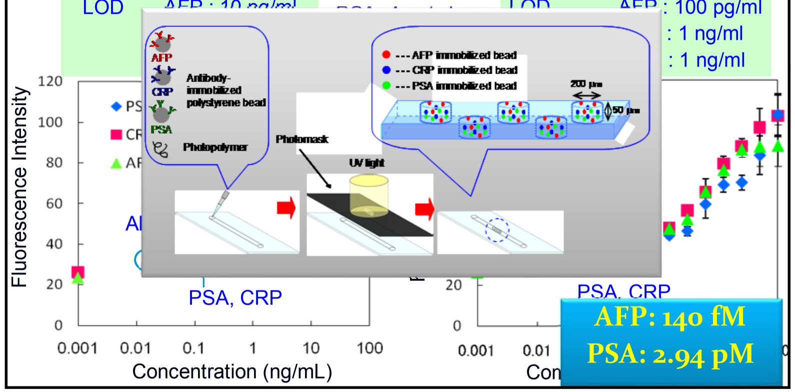


Simultaneous Immunoassay for AFP(liver cancer), PSA (Prostate cancer), CRP(Inflammation and infection) from 1-μL Whole Blood

Incubation time :3 min
Total Assay Time : 8 min
LOD AFP : 10 pg/ml

Cut Off Value
AFP: 10 ng/ml

Incubation time : 1 min
Total Assay Time : 4min
LOD AFP : 100 pg/ml
: 1 ng/ml
: 1 ng/ml



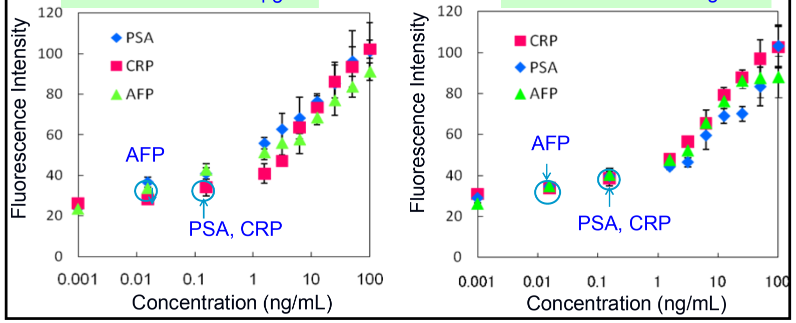
AFP: 140 fM
PSA: 2.94 pM

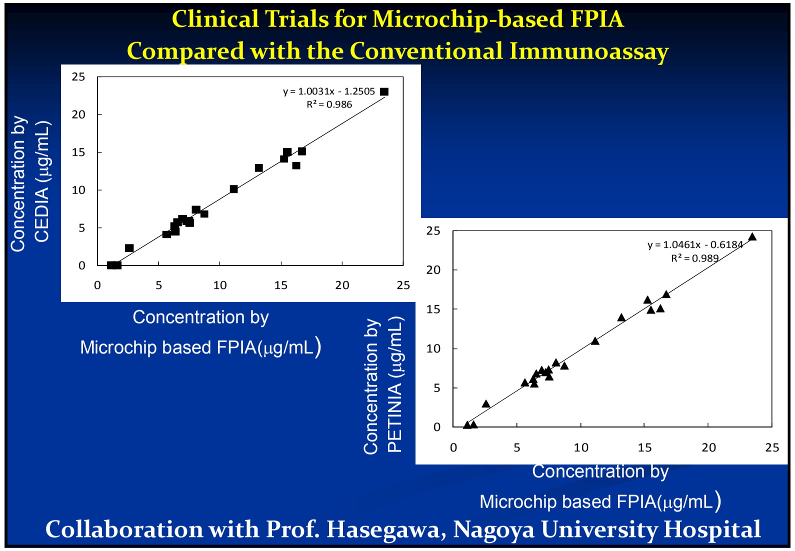
Simultaneous Immunoassay for AFP(liver cancer), PSA (Prostate cancer), CRP(Inflammation and infection) from 1-μL Whole Blood

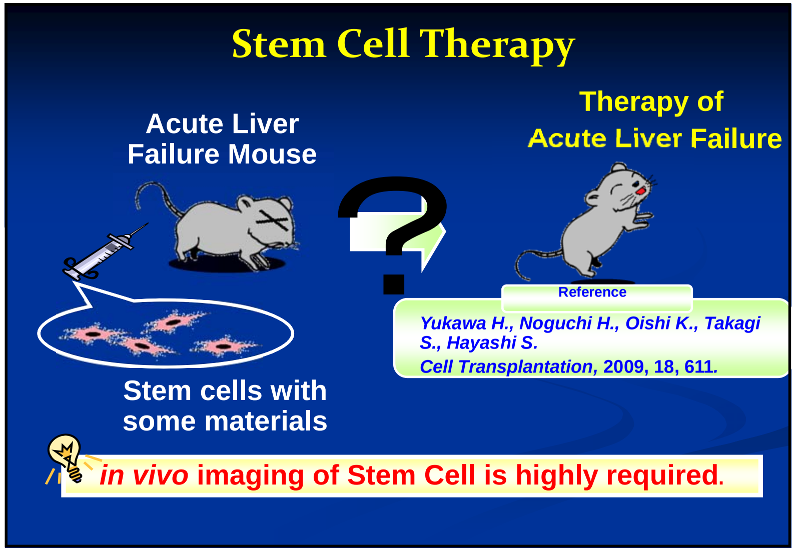
Incubation time :3 min
Total Assay Time : 8 min
LOD AFP : 10 pg/ml
PSA : 100 pg/ml
CRP : 100 pg/ml

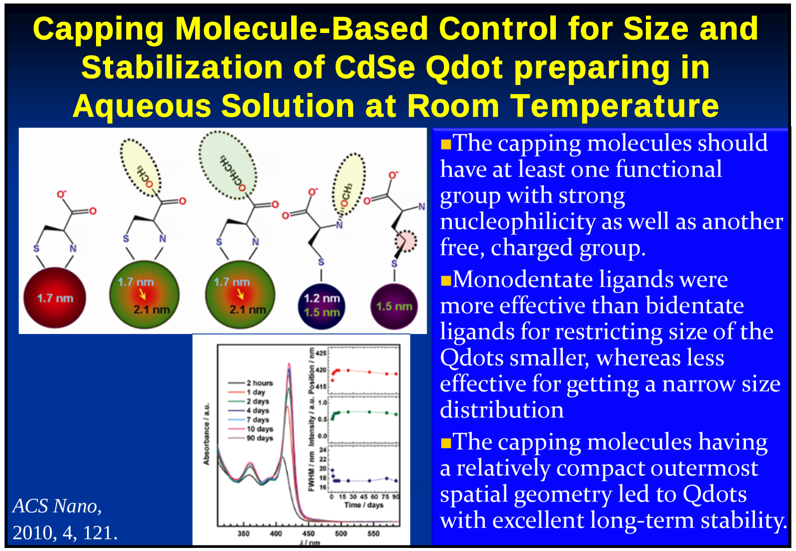
Cut Off Value
AFP: 10 ng/ml
PSA: 4 ng/ml
CRP: 1.9 μg/ml

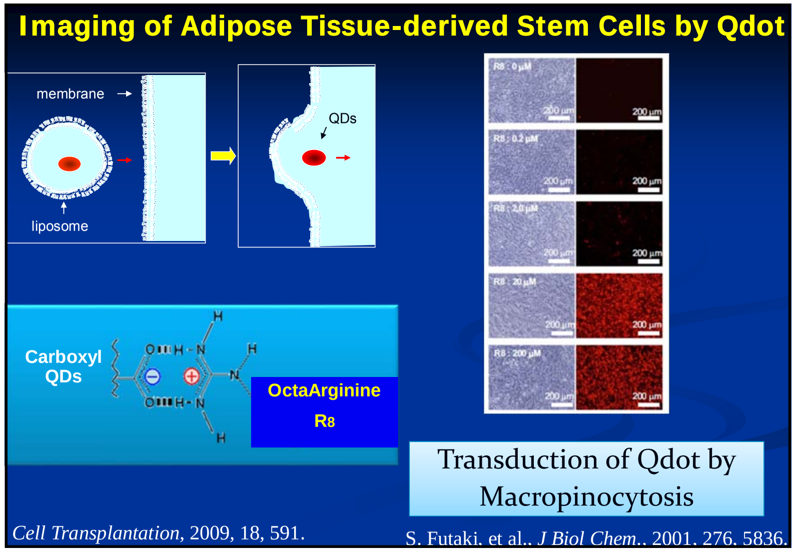
Incubation time : 1 min
Total Assay Time : 4min
LOD AFP : 100 pg/ml
PSA : 1 ng/ml
CRP : 1 ng/ml

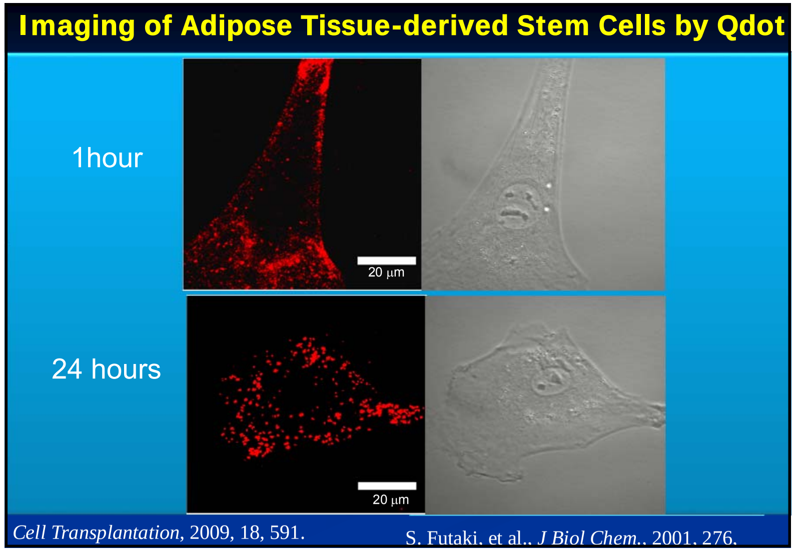


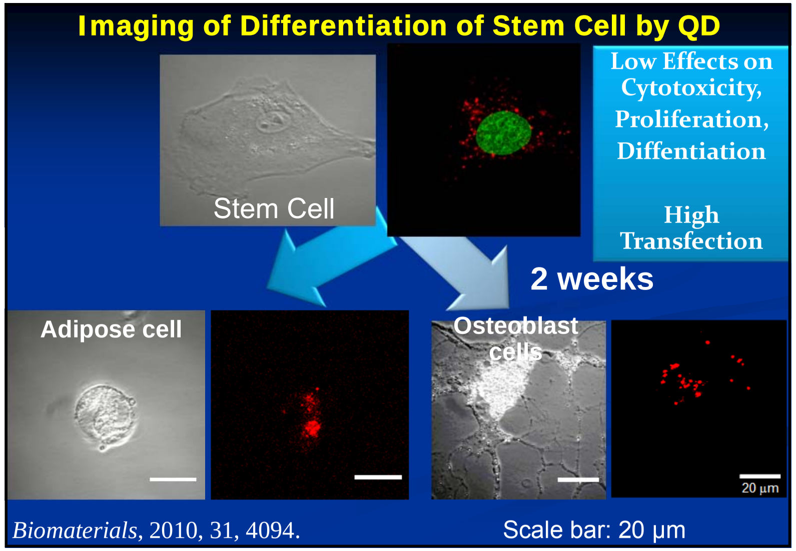

Clinical Trials for Microchip-based FPIA
Compared with the Conventional Immunoassay
Concentration by CEDIA (μg/mL)
y = 1.0031x - 1.2505
R² = 0.986
Concentration by
Microchip based FPIA(μg/mL)
Concentration by PETINIA (μg/mL)
y = 1.0461x - 0.6184
R² = 0.989
Concentration by
Microchip based FPIA(μg/mL)
Collaboration with Prof. Hasegawa, Nagoya University Hospital

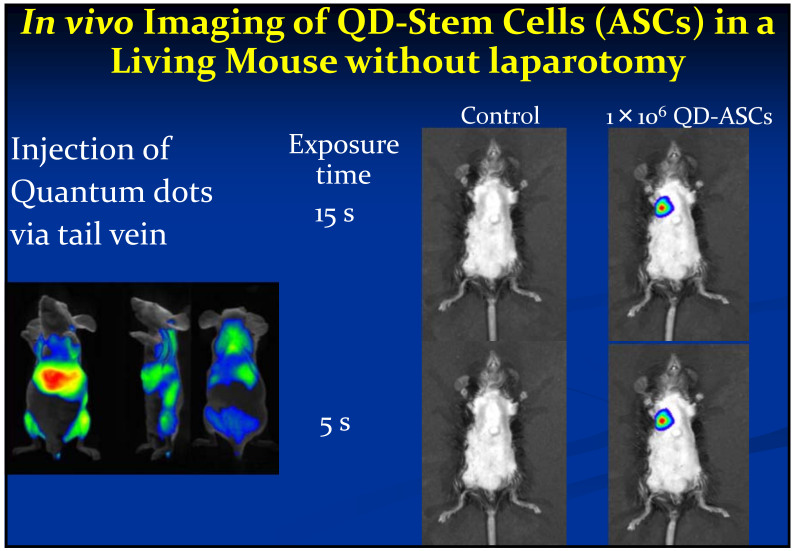

Stem Cell Therapy
Acute Liver
Failure Mouse
Therapy of
Acute Liver Failure
Reference
Yukawa H., Noguchi H., Oishi K., Takagi S., Hayashi S.
Cell Transplantation, 2009, 18, 611.
Stem cells with
some materials
in vivo imaging of Stem Cell is highly required.

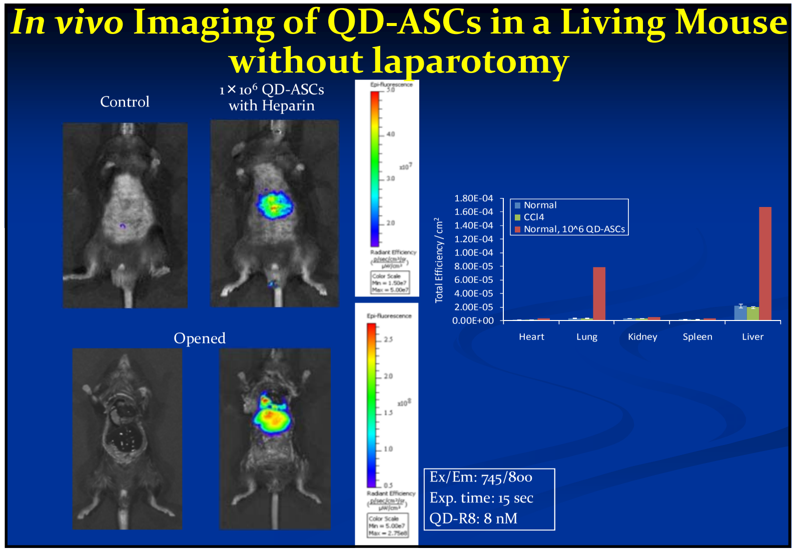

Capping Molecule-Based Control for Size and Stabilization of CdSe Qdot preparing in Aqueous Solution at Room Temperature
1.7 nm
1.7 nm 2.1 nm
1.2 nm 1.5 nm
1.5 nm
The capping molecules should have at least one functional group with strong nucleophilicity as well as another free, charged group.
Monodentate ligands were more effective than bidentate ligands for restricting size of the Qdots smaller, whereas less effective for getting a narrow size distribution
The capping molecules having a relatively compact outermost spatial geometry led to Qdots with excellent long-term stability.
ACS Nano, 2010, 4, 121.


Imaging of Adipose Tissue-derived Stem Cells by Qdot
membrane
liposome
QDs
Carboxyl QDs
OctaArginine R8
Transduction of Qdot by Macropinocytosis
Cell Transplantation, 2009, 18, 591.
S. Futaki, et al., J Biol Chem., 2001, 276, 5836.


Imaging of Adipose Tissue-derived Stem Cells by Qdot
1hour
24 hours
20 μm
20 μm
Cell Transplantation, 2009, 18, 591.
S. Futaki. et al.. J Biol Chem.. 2001. 276.


Imaging of Differentiation of Stem Cell by QD
Stem Cell
Low Effects on Cytotoxicity, Proliferation, Diffentiation
High Transfection
2 weeks
Adipose cell
Osteoblast cells
20 μm
Biomaterials, 2010, 31, 4094.
Scale bar: 20 μm


In vivo Imaging of QD-Stem Cells (ASCs) in a Living Mouse without laparotomy
Injection of Quantum dots via tail vein
Exposure time
15 s
5 s
Control
1 × 10⁶ QD-ASCs


In vivo Imaging of QD-ASCs in a Living Mouse without laparotomy
Control
1 × 10⁶ QD-ASCs with Heparin
Opened
Normal
CCl4
Normal, 10^6 QD-ASCs
Total Efficiency / cm²
Heart
Lung
Kidney
Spleen
Liver
Ex/Em: 745/800
Exp. time: 15 sec
QD-R8: 8 nM

Grand Challenge Towards 2020

Nanotechnology Goals for the next 10 years

Goal 1: Multifunctional **Theranostic nanobiodevices**

Goal 2: **Ultra-high sensitive**, highly specific, **low invasive** and reliable (robust) **multiplexed detection technologies.**

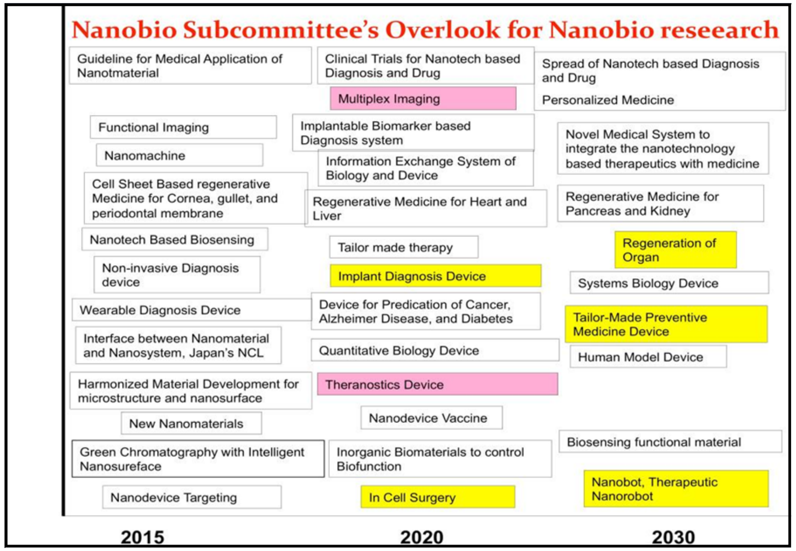
Goal 3: **Remote disease monitoring** on-line nanosensing.

Goal 4: Tissue-growth facilitating **nanostructured cell sheets.**

Goal 5: Biological nanostructures in bioelectronics.

Goal 6: **Single cell** interventions and **diagnostics.**

Goal 7: **Stem cell** differentiation and site-specific delivery



Team Leader Takahiro Hirotsu
Team Leader Toshihiko Ooie
Team Leader Shinichi Wakida
Team Leader Masatoshi Kataoka
Team Leader Kenichi Nakayama
6 Research Assistants

Funding
JSPS FIRST Program
MEXT, JST, METI, NEDO
Aichi Pref.

Collaboration
U. Tokyo, NIMS
Kyoto U., Hokkaido U.
Uppsala U., Kalorinska I.
TORAY, Panasonic,
Toshiba, Tokai Rubber,
Takasago Elec., Cluster

Aichi Pref. Funding Program for Priority Res. Area

Plasma Nano Res. Center

Preventive Med. Eng. Center

Highly-Sensitive Electrochemical Imaging for Biosensing

T. Matsue
Advanced Institute of Materials Research (WPI-AIMR)
Graduate School of Environmental Studies
Tohoku University, Sendai 980-8579, Japan

Scanning Electrochemical Microscopy (SECM)
- Priciple & Imaging
- NanoSECM Systems
- Gene Expression at Single Cell Level

Addressable Microelectrode/Microwell
- Principle
- Bioimaging: Enzymes, Recombinant Cells
- Microring-ring, Interdigitated Array (IDA)

Ultrasensitive BioLSI

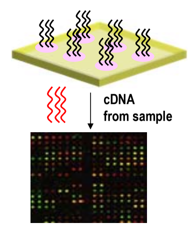
US-JAPAN WORKSHOP, Nov 12-13
Berkeley, CA, USA

Integrated Biochip

Array-type Biochip

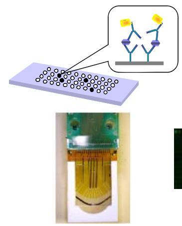
1st Genaration DNA Microarray → 2nd Genaration Protein Microarray, Lectin Microarray → 3rd Genaration Cellular Microarray

DNA microarray



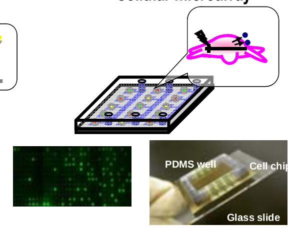
Scan fluorescence signals

Protein microarray



Enzyme, Antibody etc

Cellular microarray



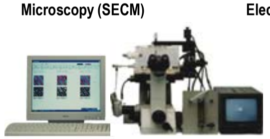
Microorganisms, Animal Cells
Plant Cells, Micro Tissues, Artificial Cells

Conventional Detection: Fluorescent

Is Electrochemical Imaging Possible?

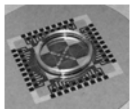
Bioelectrochemical Imaging

Scanning Electrochemical Microscopy (SECM)



Enzymes, Membranes,
DNAs, Cells, Gene Expression

Individually Addressable Electrode Array

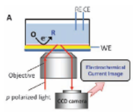


Hayashi et al., 2000
Kasai et al., 2005

CMOS-Based Electrode Array

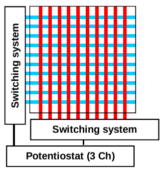
Ghindilis et al., 2007
http://www.combimatrix.com/index.htm

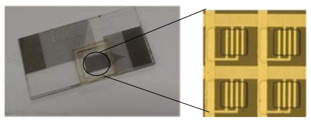
SRP-Based Electrochem. Imaging



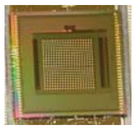
Shan et. al., 2010

3D-Microelelctrode-based Devices for Bioimaging



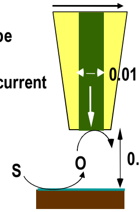


Addressable Microelectrode/Microwell Array



BioLSI

Scanning Electrochemical Microscope (SECM)
走査型電気化学顕微鏡



Signal: Redox current

Information: Chemical reaction or chemical species

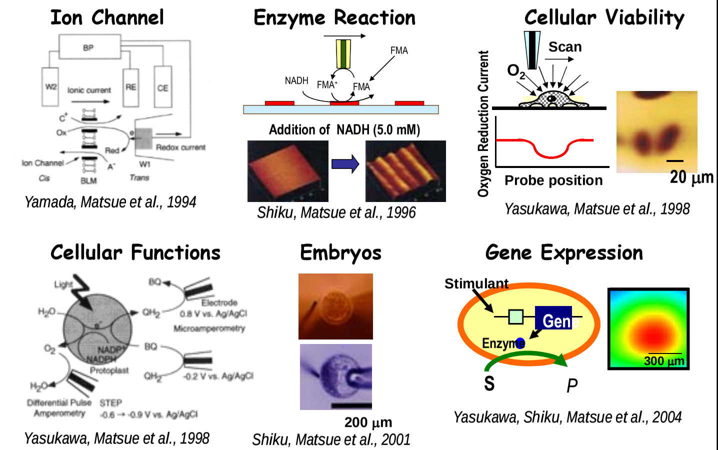
Resolution: 0.1 μm -

Enzymes, Membranes,
DNAs, Cells, Gene Expression

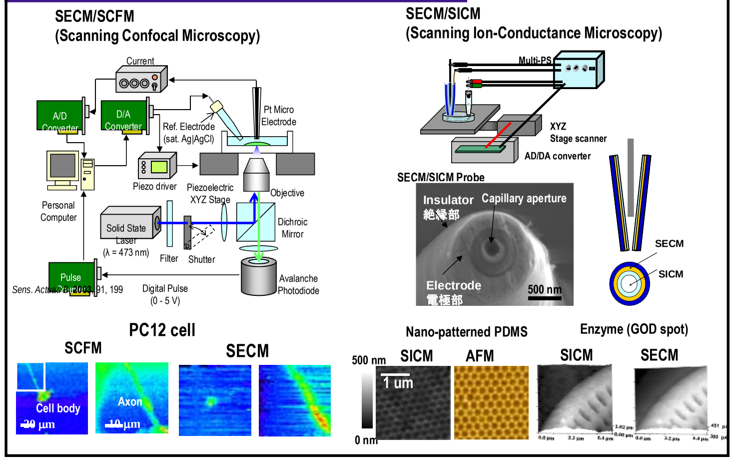
SECM can
detect localized chemical reaction
induce localized chemical reaction

SECM 局所化学反応の探索
局所領域に化学反応を誘起

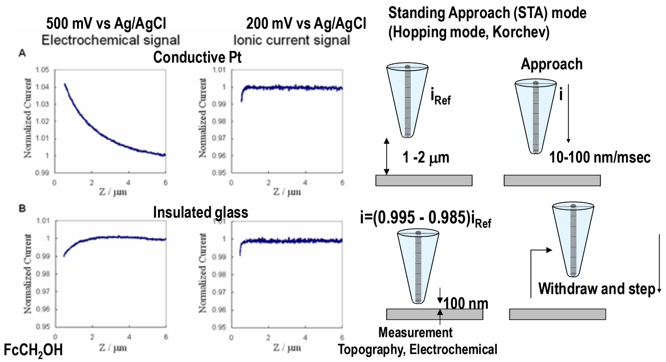
Application of SECM
Early Works



SECM Hybrid System



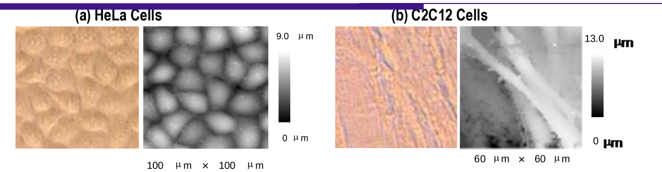
SECM/SICM System
Approach Curves



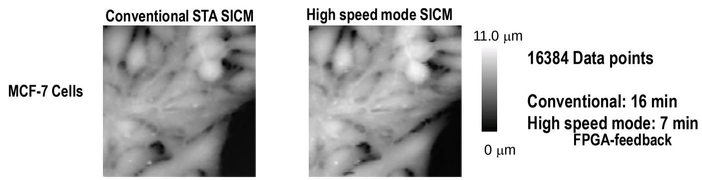
Approach curves of a SECM/SICM electrode to a (A) conductive Pt and (B) insulated glass surface in a 0.50 mM $FcCH_2OH$ + 0.1 M KCl solution for simultaneous electrochemical (left) and ion current (right) measurements. The SECM nanoring and SICM nanopipette electrodes were held at 500 and 200 mV vs. Ag/AgCl, respectively.

Angew. Chem. Int. Ed., 2011, 50, 9638; *JACS*, 2010, 132, 10118.

SECM/SICM System
Topography Imaging of Live Cells



Photograph (left) and SICM topographic images (right) of (a) HeLa and (b) C2C12 cells. Pipette aperture =100 nm. Applied voltage = -200 mV vs. Ag/AgCl. Step size = 1 μm. Scan range areas were 100x100 μm and 60x 60 μm, respectively. Cells were plated on Petri dishes and imaged in growth medium.

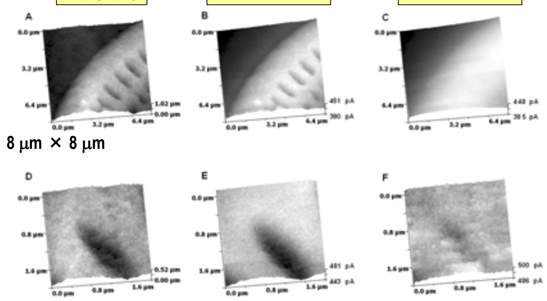


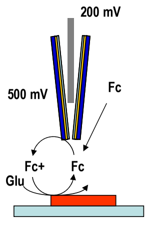
Photograph (a) and SICM topography of conventional STA mode (b) and high speed mode (c) topography images of MCF-7 cells. The pipette aperture was 100 nm. Applied voltage is -300 mV. The scan range was 100 μm x 100 mm, and the step size was 0.78 μm.

PCCP, 2010, 12, 10012

SECM/SICM Imaging
Glucose Oxidase (GOD): High Resolution Imaging

SICM Topography | SECM Distance=100 nm | SECM Distance=600 nm



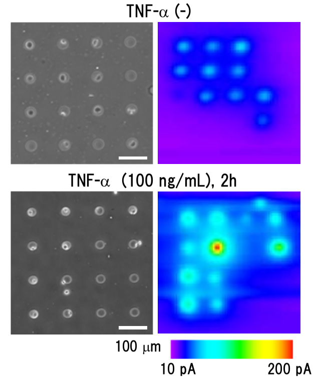


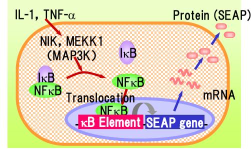
JACS, 2010, 132, 10118

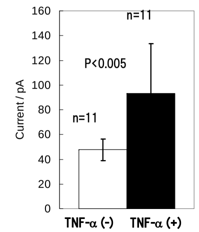
(A and D) Topographic and (B, C, E and F) electrochemical images of a GOD immobilized substrate adding 20 mM glucose in 0.50 mM $FcCH_2OH$ + 0.1 M KCl. The SECM nanoring and SICM nanopipette electrodes were held at 500 and 200 mV vs. Ag/AgCl, respectively. Upper and lower images were captured with 8 μm × 8 μm and 2 μm × 2 μm, respectively. The probe-sample distances were held at 100 nm (B and E) and 600 nm (C and F), respectively.

Imaging Cellular Array with SECM
Expression of HeLa-SEAP

Imaging of Electrochemical Signals



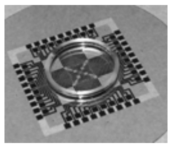




Biosensors & Bioelectronics, 2009, 25, 913

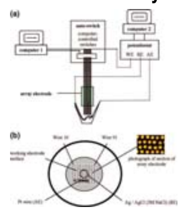
How to Realize Addressable Measurements?

Individually Addressable Electrode Array



Hayashi et al., Biosens.Bioelectron. 2000, 15, 523–529

Kasai et al., Sens Actuat., 2005, 108, 746-750



Lee et al., Anal Chem., 2008, 80, 3873-3881

1:1 mode for performing the electrochemical measurements.

Easy to fabricate
Individually addressable point is limited

CMOS-Based Electrode Array

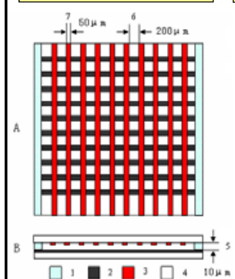
Ghindilis et al., Biosens. Bioelectron., 2007, 22, 1853–1860
http://www.combimatrix.com/index.htm

Addressable using CMOS switches

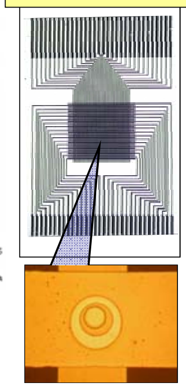
Large number of measurement points
Difficult to fabricate
Difficult to attain high sensitivity

Addressable 3D Electrochemical Array Devices for Electrochemical Imaging

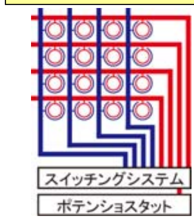
Cross-point Array 10x10



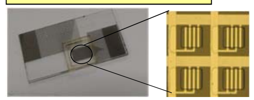
Microwell Array 32x32



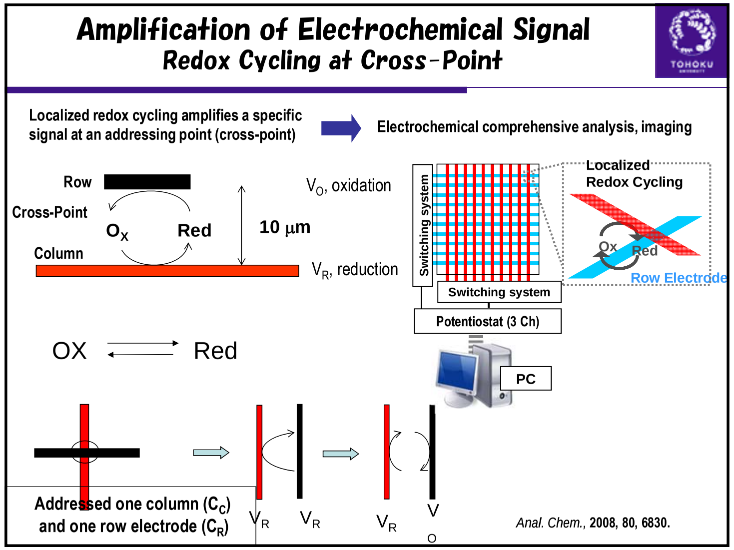
Microring-ring Array 4x4



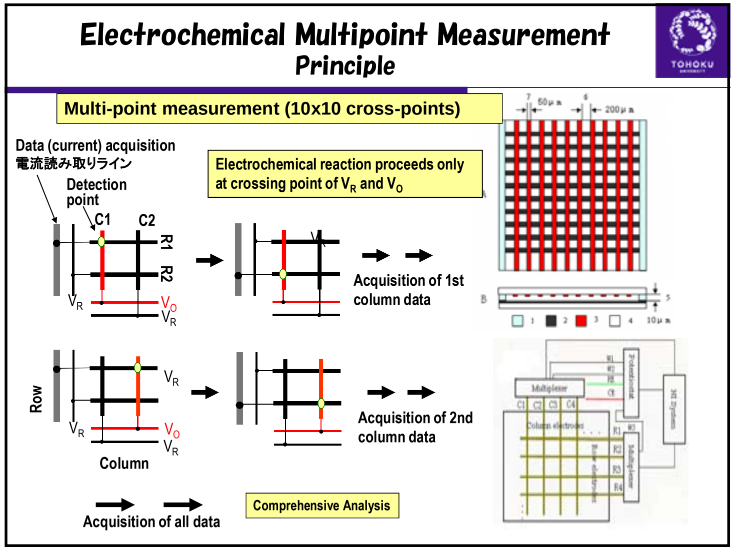
MicroIDE Array 32x32



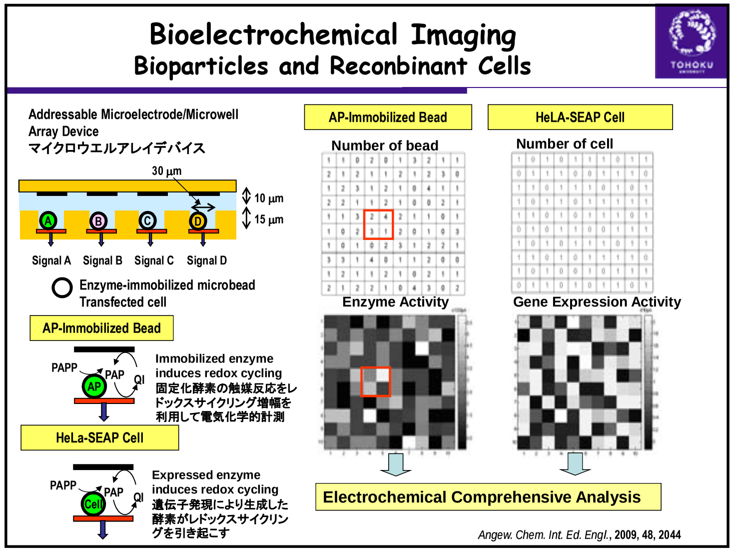
Anal. Chem., 2008, 80, 6830
Angew. Chem. Int. Ed. Engl., 2009, 48, 2044
Chem. Commun., 2010, 46, 559



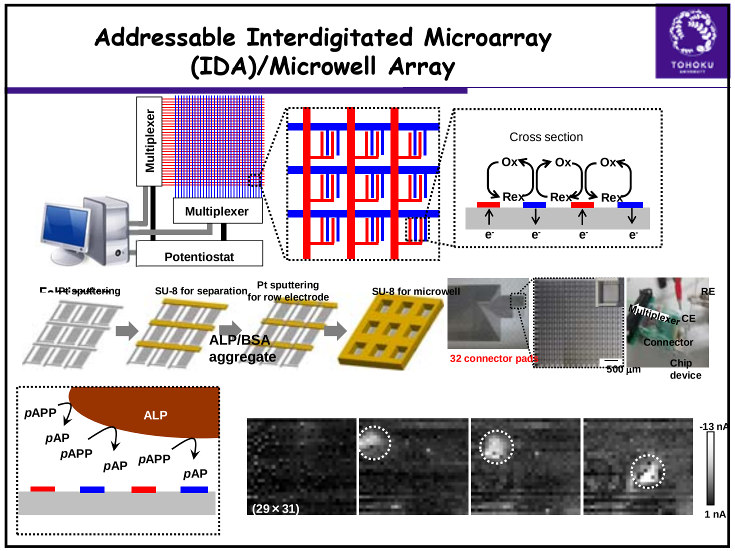
Amplification of Electrochemical Signal
Redox Cycling at Cross-Point
Localized redox cycling amplifies a specific signal at an addressing point (cross-point)
Electrochemical comprehensive analysis, imaging
Row
Cross-Point
Column
O_X
Red
10 µm
V_O, oxidation
V_R, reduction
Switching system
Switching system
Potentiostat (3 Ch)
PC
Localized Redox Cycling
Ox
Red
Row Electrode
OX
Red
Addressed one column (C_C) and one row electrode (C_R)
V_R
V_R
V_R
V_O
Anal. Chem., 2008, 80, 6830.



Electrochemical Multipoint Measurement
Principle
Multi-point measurement (10x10 cross-points)
Data (current) acquisition
電流読み取りライン
Detection point
C1
C2
R1
R2
Electrochemical reaction proceeds only at crossing point of V_R and V_O
Acquisition of 1st column data
Acquisition of 2nd column data
Row
Column
Acquisition of all data
Comprehensive Analysis

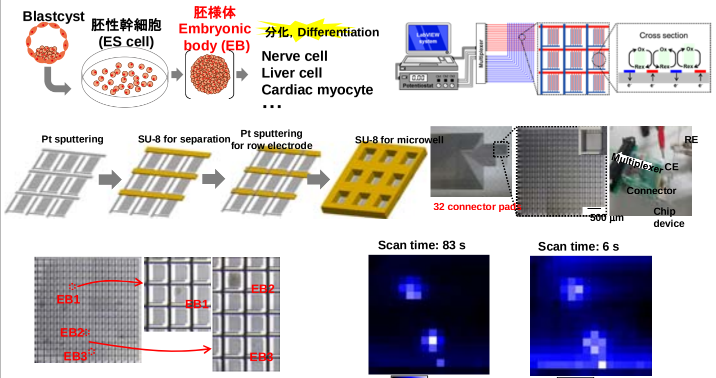


Bioelectrochemical Imaging
Bioparticles and Reconbinant Cells
Addressable Microelectrode/Microwell Array Device
マイクロウエルアレイデバイス
30 µm
10 µm
15 µm
Signal A
Signal B
Signal C
Signal D
Enzyme-immobilized microbead
Transfected cell
AP-Immobilized Bead
PAPP
PAP
QI
AP
Immobilized enzyme induces redox cycling
固定化酵素の触媒反応をレドックスサイクリング増幅を利用して電気化学的計測
HeLa-SEAP Cell
Cell
Expressed enzyme induces redox cycling
遺伝子発現により生成した酵素がレドックスサイクリングを引き起こす
AP-Immobilized Bead
HeLa-SEAP Cell
Number of bead
Number of cell
Enzyme Activity
Gene Expression Activity
Electrochemical Comprehensive Analysis
Angew. Chem. Int. Ed. Engl., 2009, 48, 2044



Addressable Interdigitated Microarray
(IDA)/Microwell Array
Multiplexer
Multiplexer
Potentiostat
Cross section
Ox
Rex
e-
SU-8 for separation
Pt sputtering for row electrode
SU-8 for microwell
ALP/BSA aggregate
32 connector pads
500 µm
Multiplexer
CE
RE
Connector
Chip device
ALP
pAPP
pAP
(29×31)
-13 nA
1 nA

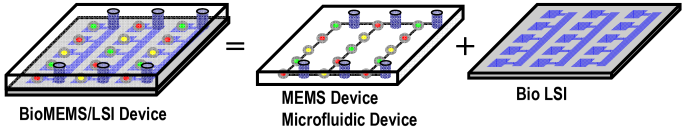
Imaging Embryonic Body:
Application to Tissue Engineering

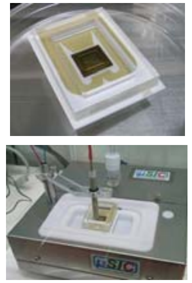


EBs were fabricated by using the hanging drop method (100 cells/20 ml). The EBs were cultured in differentiation medium for 10 or 11 days.

The image indicates the position of EB on the device
→ALP activity of EB was detected successfully.

Integrated Biodevice: BioLSI
集積型バイオデバイス：バイオLSI





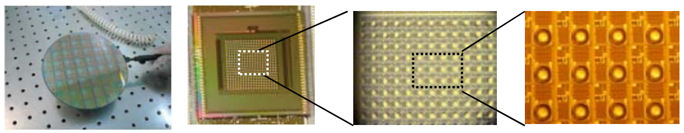
Rapid and addressable multi-point electrochemical measurements

Electrochemical Bioimaging & Comprehensive Analysis

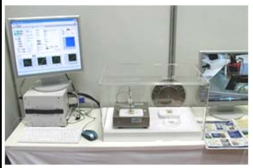
DNA array, Protein Array, Cellular Array
Drug Screening, Animal Test Alternative
Diagnosis, Environmental monitoring, Bioassay etc

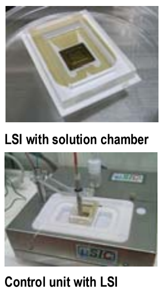
BioLSI developed in "Integrated Microsystem Project" supported by JST

Ultrasensitive BioLSI
Redox Current Measurements



BioLSI / Si Wafer





Fundamental Sciences
Medical
Artificial Biosystems
Environmental
Safety, Security

BioLSI Specification

20 x 20 Microelectrode array (400 electrodes)

Electrode: Disk-type Radius: 5 µm - 20 µm

Electrode Distance (center-center): 250 µm

Detectable current: 1 pA～100 nA

Temporal resolution: 100 msec/400 points～ (100 µsec/point)

超高感度 BioLSI：計測
Ultrasensitive BioLSI: Measurements

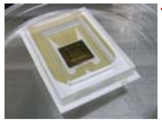
基礎科学：生物機能の探求
医療　　：診断，医薬品開発
人工バイオシステム（鼻，舌，組織，神経系　etc.）
その他　：環境計測，食品検査など
Fundamental Sciences, Medical
DNA array, Protein Array, Cellular Array
Drug Screening, Animal Test Alternative
Artificial Biosystems, Diagnosis, Environmental monitoring, Bioassay etc

BioLSIの利用
Application of BioLSI

超高感度 電流計測型 バイオLSI

Protein
Lipid
Lectin
DNA, RNA
Microorganisms
Cells
Micro Tissues
Artificial Cells
Artificial Tissues

Device
チップ化
デバイス化



Fundamental Science
基礎科学
→ **Explore Biological Functions**
生物機能の解明

Genetic Engineering
遺伝子工学
→ **Useful Cells**
Useful Genes
Useful Proteins
有用細胞
有用遺伝子
有用タンパク質

Drug Discovery
医薬品開発
→ **Drug Screening**
Animal Test Alternative
医薬品スクリーニング
動物実験の代替

Safety, Security
安全・安心
→ **Bioassay System**
バイオアッセイシステム
危険物質の検出
化学・バイオテロ対策

Medical
医療
→ **Cell & Tissue Diagnosis**
細胞診断：病気の診断、治療
微小組織診断：移植医療への適用

Bioassay using Organisms

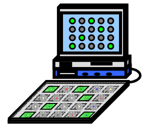
Huge number of chemicals: more than 30 million

WET (Whole Effluent Toxicity) Test→EPA (US Environmental Protection Agency)

Whole Effluent Toxicity (WET) refers to the aggregate toxic effect to aquatic organisms from all pollutants contained in a facility's wastewater (effluent).

・Bioassay using aquatic organisms
Daphnia magna (water-flea), Minnow (Zebra fish)
Typical bioassay Using Daphnia (ミジンコを用いた試験法)
Acute Toxicity Test (急性遊泳阻害試験): 48 hours
Reproduction Test (繁殖阻害試験): 21 days

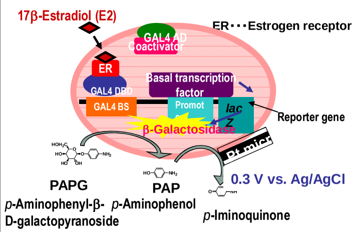
オオミジンコ



Is Rapid, Efficient, Accurate System Possible?

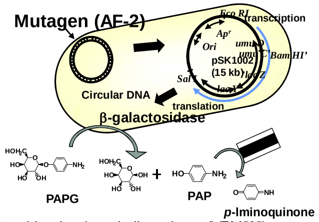
Bioassay Devices Using Recombinant cells
Detection of Hazardous Species

環境汚染物質の検出
Detection of Endocrine Disrupting Chemicals



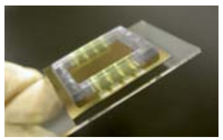
Recombinant *S. cerevisiae*
（組み換え酵母）

発がん物質の検出
Detection of Carcinogens



S. typhimurium (genetically engineered) (TA1535)
（組み換えサルモネラ菌）

AF-2: 2-(2-furyl)-3-(5-nitro-2-furyl)acryl amide



Bioassay Devices

Bioelectrochemical Imaging with Micro/Nanoelectrode Systems

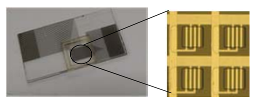
Is Electrochemical Imaging Possible?

High resolution bioimaging with NanoSECM
Enzymes, Recombinant Cells

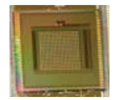
Bioimaging with Addressable Microelectrode/Microwell Array
3D-Microelectrode Array
Microring-ring, Interdigitated Array

Bioimaging with Ultrasensitive BioLSI

Nano SECM



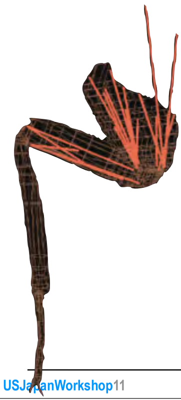
Addressable Microelectrode/Microwell Array

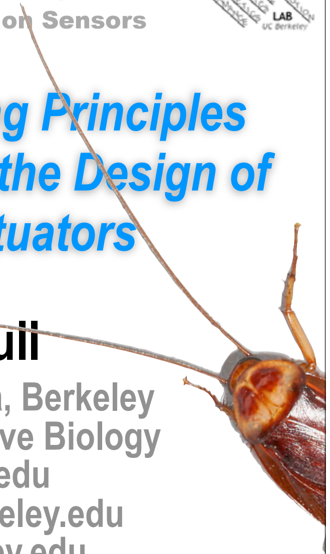


BioLSI

U.S.-Japan Workshop on Bio-inspired Engineering of Next-Generation Sensors and Actuators

Cautions on Extracting Principles from Nature to Inspire the Design of Sensors and Actuators





Professor
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Kim, Spenko, Trujillo, Heyneman, Mattoli, Cutkosky; Lanzetta and Cutkosky. Stanford University

Blind Biomimicry

Natural Selection is not Engineering

CAUTION

Evolution "just good enough"

Evolution is NOT Engineering

- Engineers often have final goals, whereas biological evolution does not.

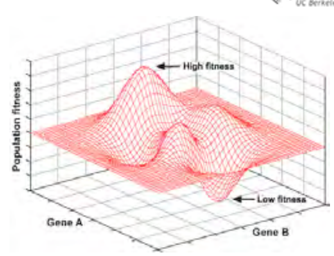
Jacob (1977)

- Organisms must do a multitude of tasks, whereas in engineering executing far fewer tasks will do.
- Trade-offs are the rule, severe constraints are pervasive and global optimality rare in biological systems.
- Biological evolution works more as a tinkerer than an engineer.
- Tinkerers never really know what they will produce and use everything at their disposal to make something workable.

Challenges of Biomimetic Approach

Extraordinary Opportunity for Design Ideas

Organisms are Not Optimally Designed



Evolution Often Fails to Keep Pace with the Rate of Environmental Change

Today's Adaptation is Tomorrow's Constraint

Specialization is Often an Evolutionary Dead End

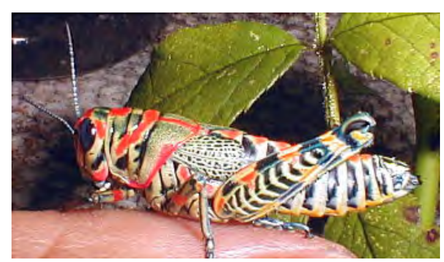
Behavior Changes Quickly Without a Change in Structure

All Traits are Not Equally Heritable
Trapped in Local Minima
Genetic Drift Counters Evolution

Reasons for Non-Optimal Bio-Designs

Natural Technologies

Must Grow



Neurons to Nowhere

**Adults lost ability to fly.
Flight muscles absent.
Neurons remain!**

Developmental Constraint

Organisms Must Grow

Imagine Requiring Engineers to Build an Auto that is 1cm , then 1m, then Full Size

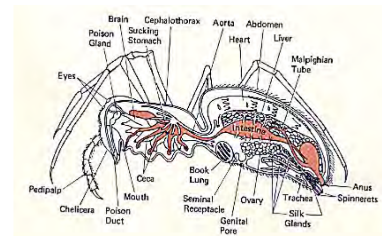
Final Design is Compromised

Developmental Constraint

Natural Technologies

Must be multi-functional

Jump, Run, Climb Using Hydraulic System to Extend Legs. No Extensor Muscles.



Hydraulic System is also Circulatory System Used for O_2, fuel and hormone delivery.

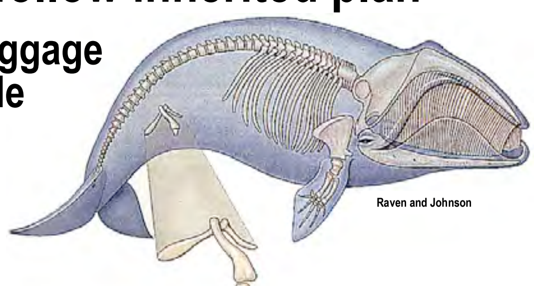
Functional Constraint

Natural Technologies

Must follow inherited plan

Evolutionary Baggage
Legacy Code

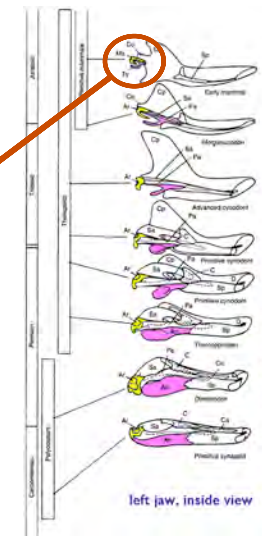
Pelvic bones in a whale



Evolutionary Constraint

Reworked Sensor

Inner Ear Evolved from Jaw Bones



Reasons for Non-Optimal Bio-Designs

Natural Technologies

Adaptive Solution for Another Problem Can Even Work in Direct Opposition to Natural Selection

Attracting a mate

Birds of paradise have highly elongated and elaborate feathers that reduce flight performance.

Sexual Selection

Biomimetic Approach Challenging Unlimited Opportunity for Innovation

Nature's technology represents the *only* known alternative to our own.

Looking at nature's designs liberates us from the constraints of our own habits, history, and outlook.

After Vogel

Biological Inspiration

Use Principles and Analogies from Biology when Advantageous. Integrate with Best Human Engineering to Design Something Better than Nature.

Learning from Nature

As human technologies take on more of the characteristics of nature, nature becomes a more useful teacher.

——— Vogel, 1998

Past Differences in Technologies

	Natural	Human
Size	Small	Large
Surfaces	Usually curved	Usually flat
Right angles	Rare	Widespread
Corners	Gentle	Abrupt
Solid materials	Pliant & tough	Stiff & brittle
Metallic materials	Absent	Ubiquitous
Composites	Common	Uncommon
Machinery	Reciprocating	Rotating
Sensors & actuators	Many	Few
Engines	Contracting	Expanding, rotating

Vogel, 1998

Design Lessons from Nature

1. Actuators are Multifunctional Materials
   - Managing the Flow of Energy
2. Sensors are Embedded in Structures
   - Interaction Provides Information and Control
3. Sensors and Actuators are Integrated Systems
   - Multi-modal Sensing with Tuned Actuation

Design Lessons from Nature

1. Actuators are Multifunctional Materials
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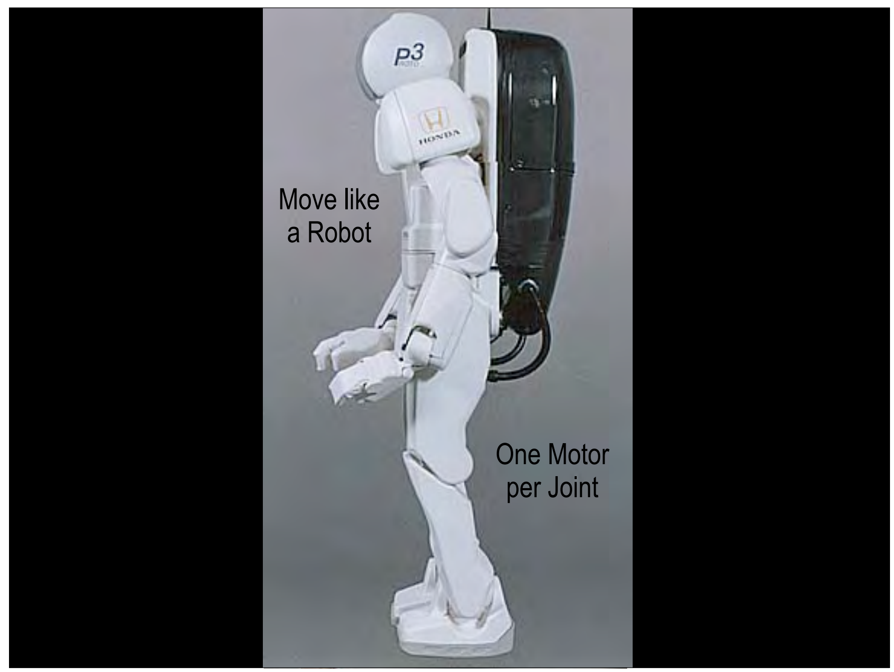
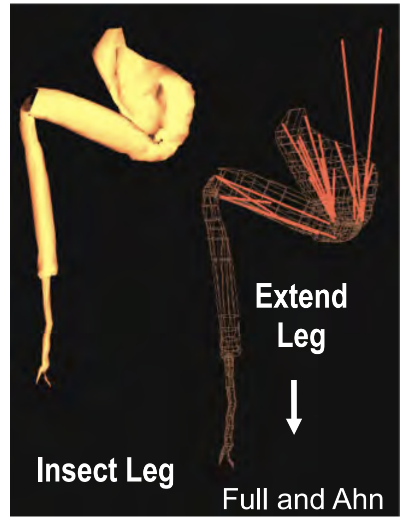


Discover - See How They Run

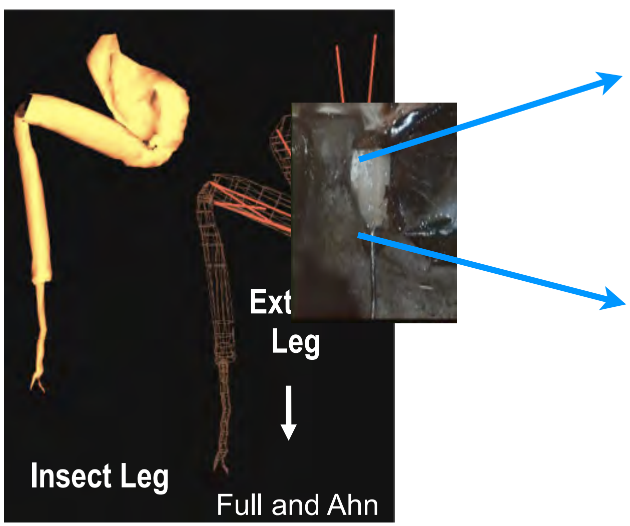
Programmable Material



Insect Muscle Simple to Study because one “wire” to each major muscle.

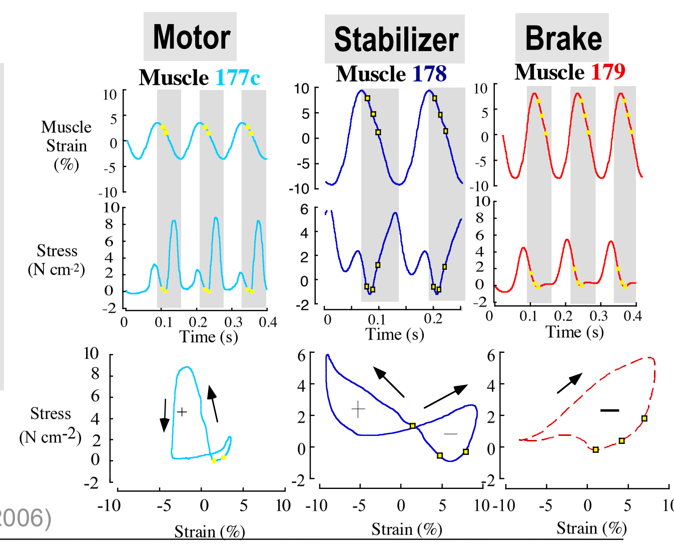
Muscles are not simply motors.

Programmable Material



Integrated Differential Function

Similar signal input. Different dynamic response output.

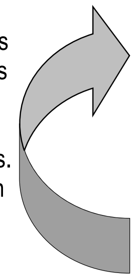


Ahn and Full (2006)

Multi-functional Material

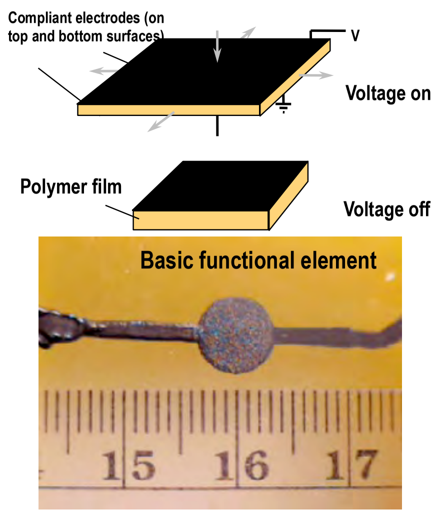
Mutualistic Interactions

Bio-inspired Artificial Muscles



Artificial Muscle

Soft ElectroActive Polymers (EAP)

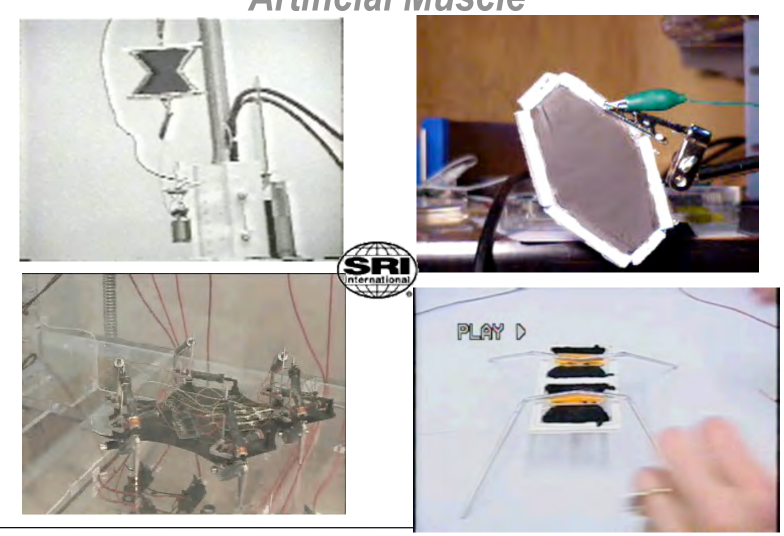


Well-known effect
Capability continues to develop

SRI International
R. Pelrine
R. Kornbluh

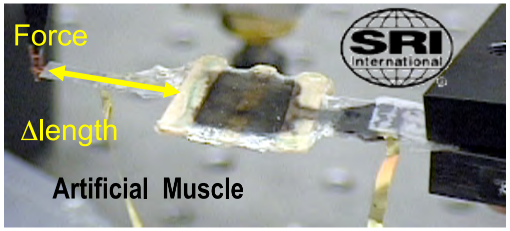
Electroactive Polymers

Artificial Muscle

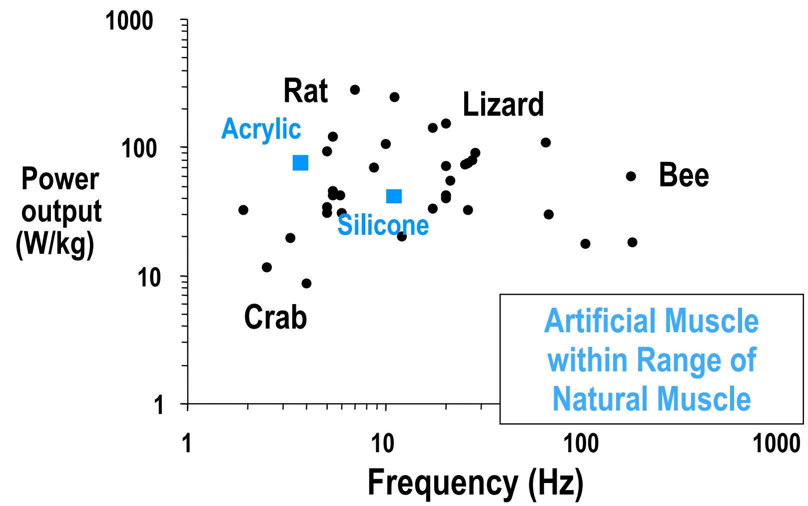


Real vs Artificial Muscles

Compare Power Output Directly to a Diversity of Species



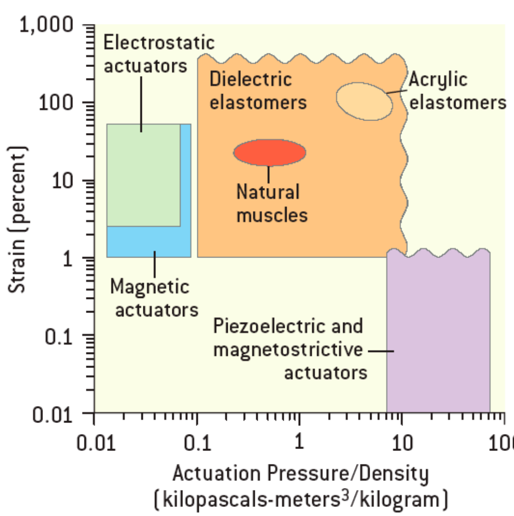
Power Output Comparison



Kornbluh, Full, Meijer, Pelrine, and Shastri (2002)

Real vs Artificial Muscles

Dielectric elastomers bound the range of natural muscle



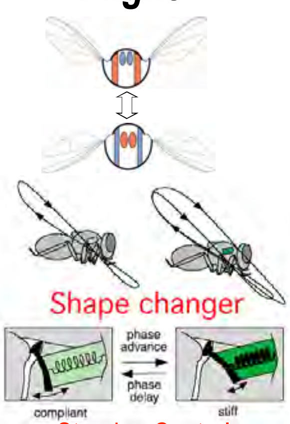
Electroactive Polymers

Altendorfer, Moore, Komsuoglu, Buehler, Brown, McMordie, Saranli, Full, Koditschek. 2000

Boston Dynamics Inc.
Commercial RHex

Common Actuator Theme

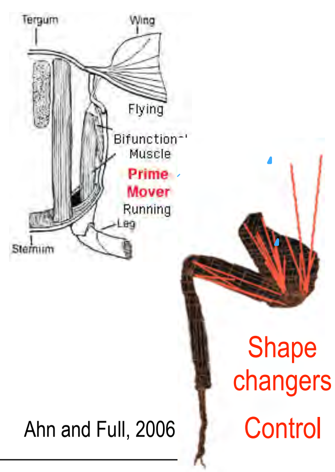
Flight



Steering Control
Tu and Dickinson, 1996

Large Prime Mover Muscles in Concert with Small Control Muscles

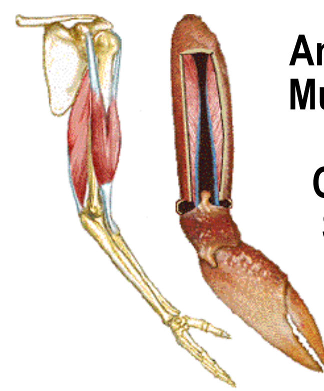
Ambulation



Ahn and Full, 2006

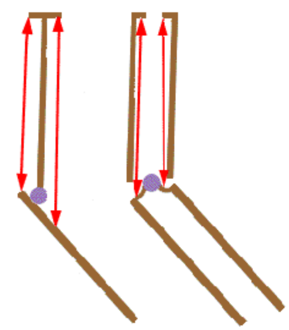
Skeletal Diversity

Endo-skeleton **Exo-skeleton**



Antagonistic Muscle Pairs Allow Control of Stiffness

Endoskeleton Bones on the inside **Exoskeleton Shell on the outside**

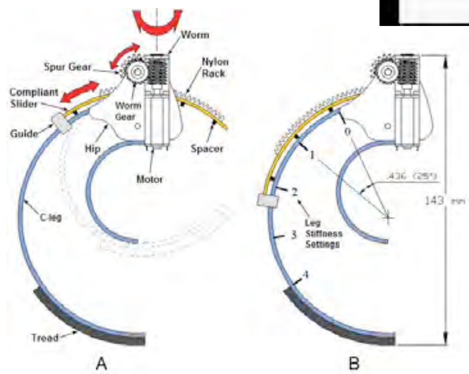


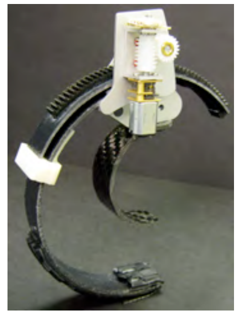
Variable Stiffness Device

Vary Morphology

Composite Tunable Leg Design

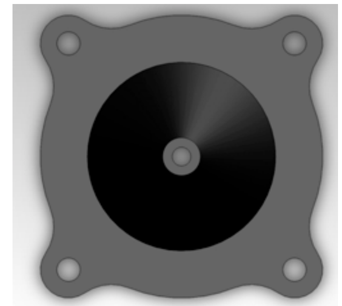
Galloway
Koditschek

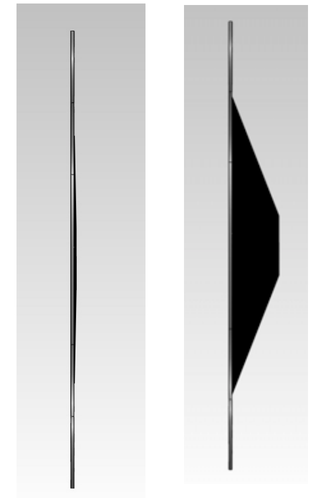




Variable Stiffness Device

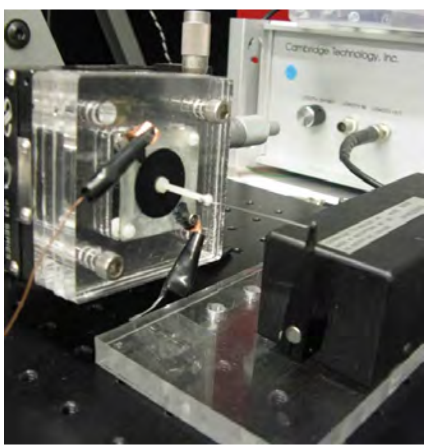
Annular
Dielectric Electroactive Polymer
(EAP) Actuators
Diaphragm geometry

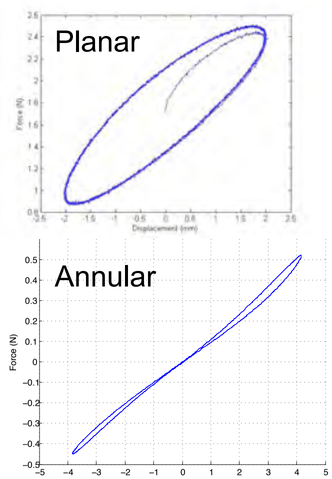




Dastoor & Cutkosky, ICRA 2012

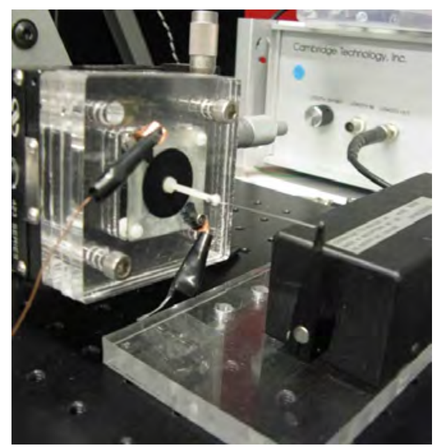
Variable Stiffness Device



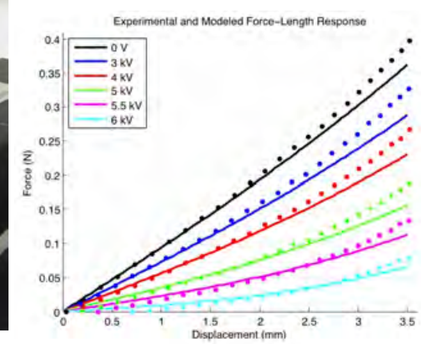


Dastoor & Cutkosky, ICRA 2012

Variable Stiffness Device



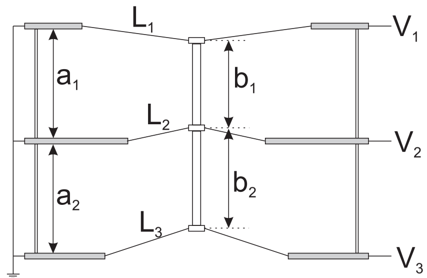
600-1000%
Change in Stiffness



Dastoor & Cutkosky, ICRA 2012

Multi-Unit Stacking

Custom Variable Stiffness Profiles

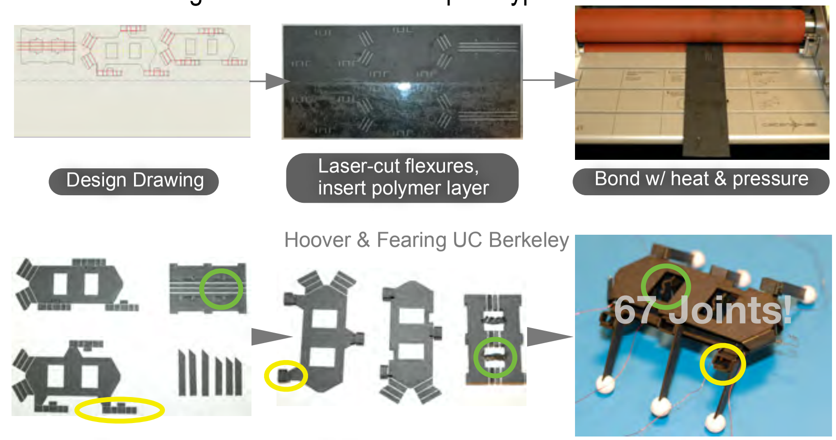


Dastoor & Cutkosky, ICRA 2012

Smart Composite Microstructures - SCM

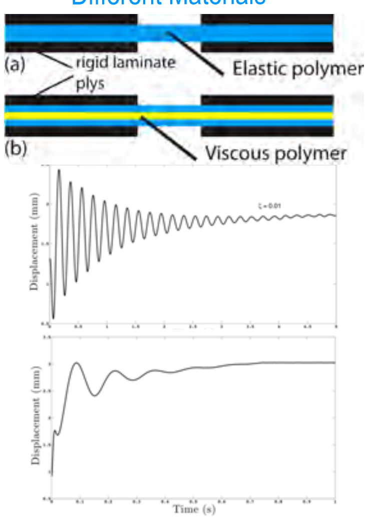
Rapid prototyping for fast iterative design

From design to functional scaled prototype in less than 1 hour!

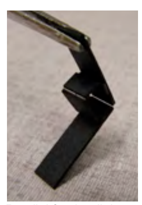


Test Hypotheses of Leg Design

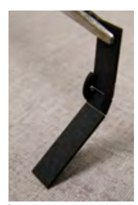
Different Materials



Different Geometries - produce legs that act as springs with different (linear and nonlinear) load/ displacement curves.



Parallel fourbar linkage



Simple rotational hinge

Sarrus linkage

Compliant hinge + polymer leaf spring

Palm-sized Hexapedal Running Robot

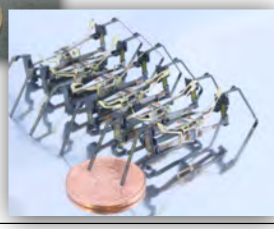
RoACH (Robotic, Autonomous, Crawling Hexapod)
- Fabricated from folded, compliant mechanisms
- Uses single drive motor
- Compliant legs (simple flexural knee joint) enable dynamic, Spring-mass gait
- Fabrication time < 3 hours
- Capable of 2-3 body lengths/sec
- Weight: 17g, Unoptimized power density: ~20 W/Kg

Hoover & Fearing ICRA (2008) UC Berkeley

Bio-inspired Legged Microbots

Fully assembled six legged skeleton with **50+ joints**

RoACH - 2.4 gram



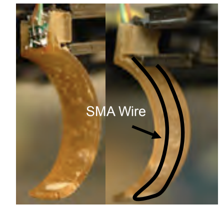
Wood
Harvard University
Fearing
UC Berkeley

Artificial Muscles for Control

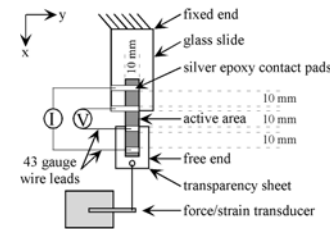
Simple robot legs can be tuned by artificial muscles that dynamically change leg shape and stiffness.

Artificial muscles can enhance stability, increase energy storage and return, and allow control for maneuvers such as steering.

When leg DOFs are increased for climbing, artificial muscles must play a role in perturbation rejection.



C-Leg with Shape memory alloy wires



DEAs with PDMS/EG Electrodes

Fearing UC Berkeley

Multifunctional Units

Artificial Muscles as Appendages

Robo-Snake?

Bipedal Octopus Disguised as a Rolling Coconut

Huffard C. L., F. Boneka, and R. J. Full (2005) Science. 307:1927.

Bipedal Octopus Disguised as Floating Algae

Huffard C. L., F. Boneka, and R. J. Full (2005) Science. 307:1927.

Beginnings of Soft Robotics

Huffard C. L., F. Boneka, and R. J. Full (2005) Science. 307:1927.

Sequences from *Incredible Suckers*, Oxford Scientific Films, Thirteen, WNET, and the BBC

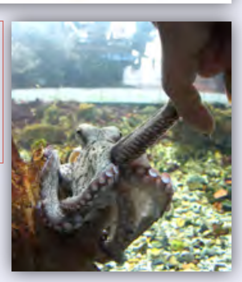
OCTOPUS IP (2009-2013)

Novel Design Principles and Technologies for a New Generation of High Dexterity Soft-bodied Robots Inspired by the Morphology and Behaviour of the Octopus

www.octopus-project.eu

Cecilia Laschi (Coordinator)
Barbara Mazzolai
Matteo Cianchetti
Laura Margheri

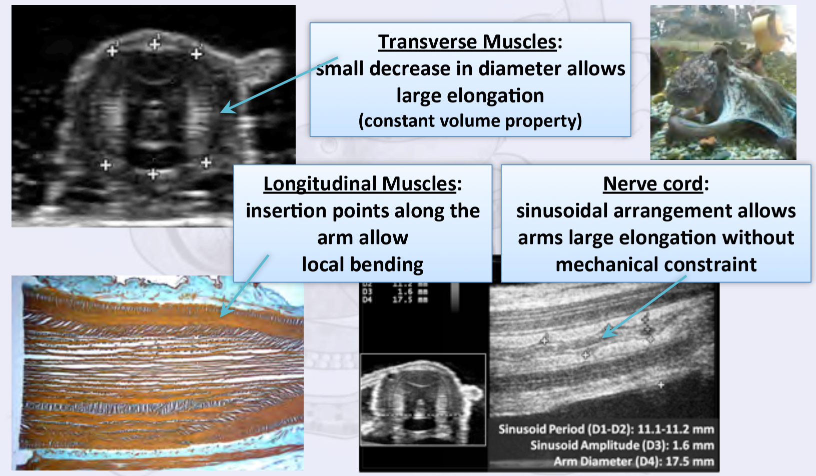
The OCTOPUS Integrated Project has the objective of designing and developing an 8-arm robot inspired to the muscular structure, neurophysiology and motor capabilities of the octopus (*Octopus vulgaris*).



Scuola Superiore Sant'Anna
University of Zurich
האוניברסיטה העברית בירושלים The Hebrew University of Jerusalem
iit Italian Institute of Technology
University of Reading
מכון ויצמן למדע Weizmann Institute of Science
FORTH

European Commission in the ICT-FET OCTOPUS Integrating Project, contract #231608

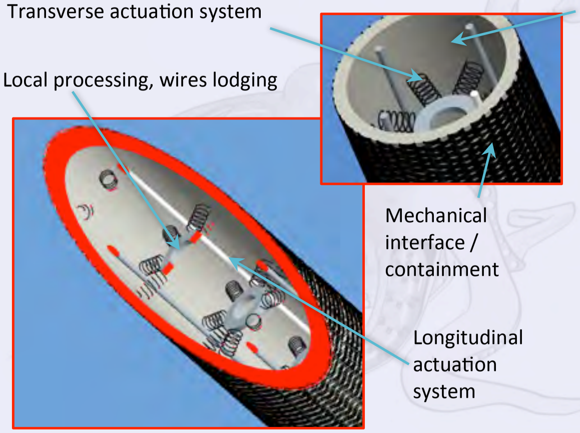
Robotic Design Concepts from Octopus Anatomy



L. Margheri, B. Mazzolai, G. Ponte, G.Fiorito, P.Dario, C. Laschi, "Methods and tools for the anatomical study and experimental in vivo measurement of the *Octopus vulgaris* arm for biomimetic design", IEEE RAS / EMBS - BioRob 2010

Design of the Artificial Muscular Hydrostat

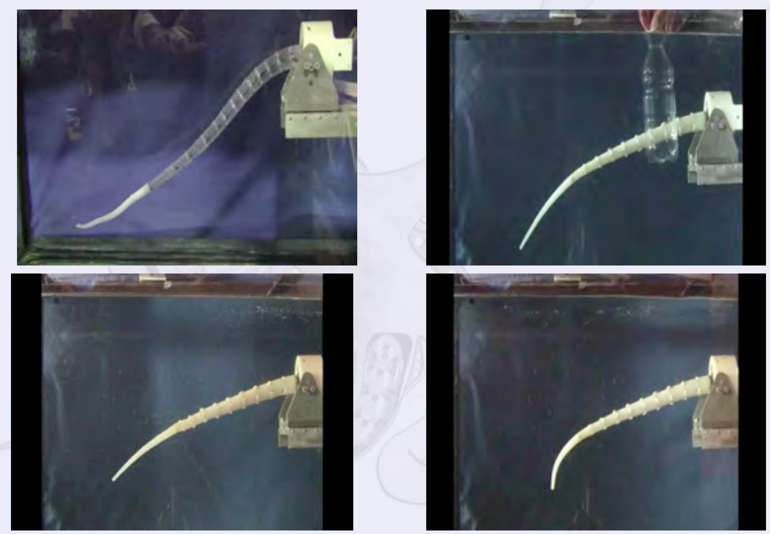
Arm description



Artificial Muscular Hydrostat Unit

PATENT PENDING

Robotic octopus-like arm prototype

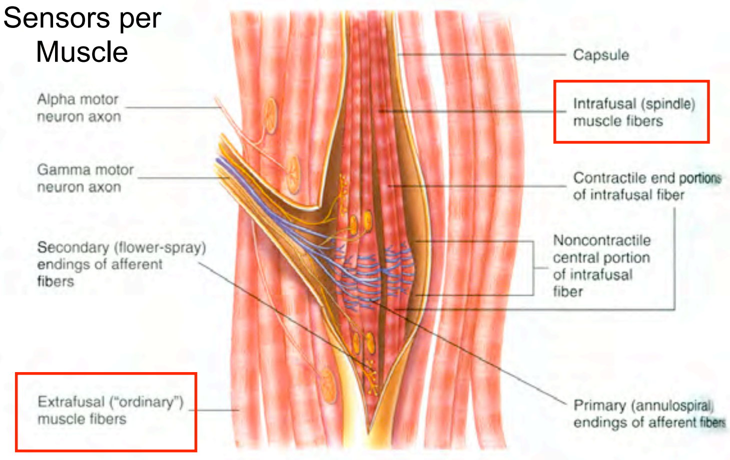


Design Lessons from Nature

1. Actuators are Multifunctional Materials
   - Managing the Flow of Energy
2. Sensors are Embedded in Structures
   - Interaction Provides Information and Control
3. Sensors and Actuators are Integrated Systems
   - Multi-modal Sensing with Tuned Actuation

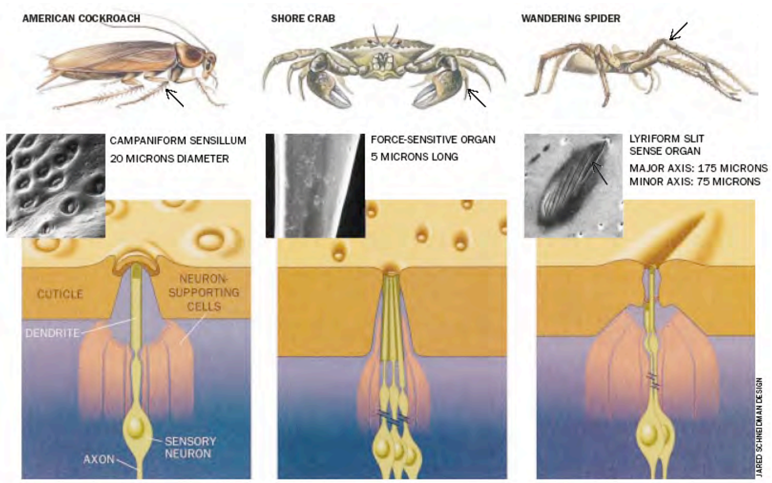
Sensors Integrated with Actuator

100's of Length Sensors per Muscle

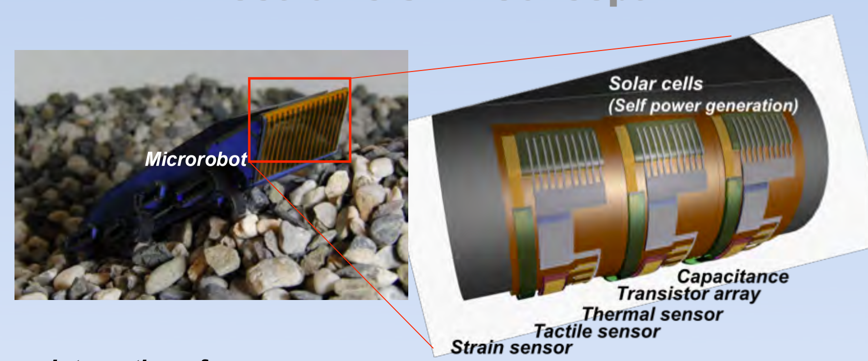


Exoskeletal Sensory Receptors

Force measurement by strain gauges in cuticle



Electronic Skin Concept



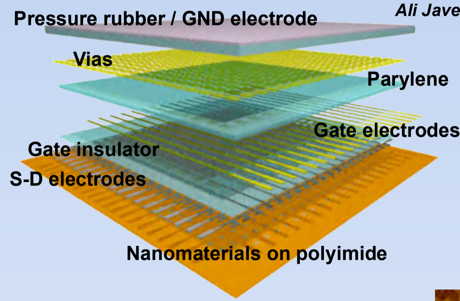
Integration of:
- *Circuits*
- *Tactile sensors*
- *Strain sensors*
- *Thermal sensors*
- *Chemical sensors*
- *Solar cell*

on microrobots and/or other objects to mimic biological skin

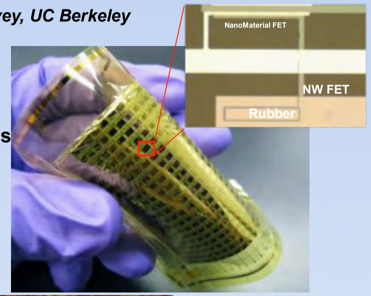
Ali Javey, UC Berkeley

T. Takahashi, et al *Nano Letters*, 2011, in press.
K. Takei, et al *Nature Materials*, 9, 821–826, 2010.

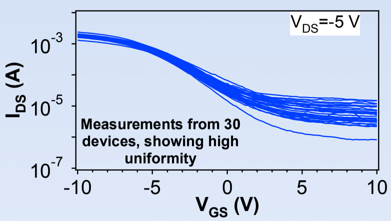
Macroscale flexible & stretchable skin electronics

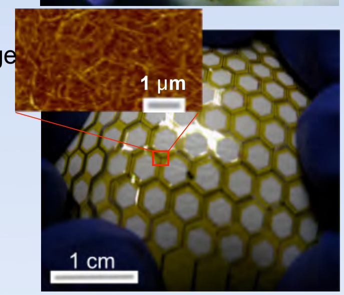


Ali Javey, UC Berkeley



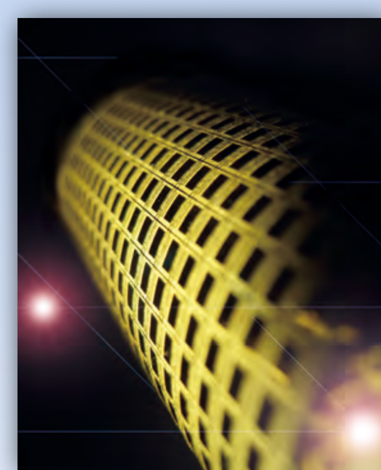
Transistor characteristics at low voltage





eSkin

Pressure-sensitive electronic material



First material from single crystalline semiconductors

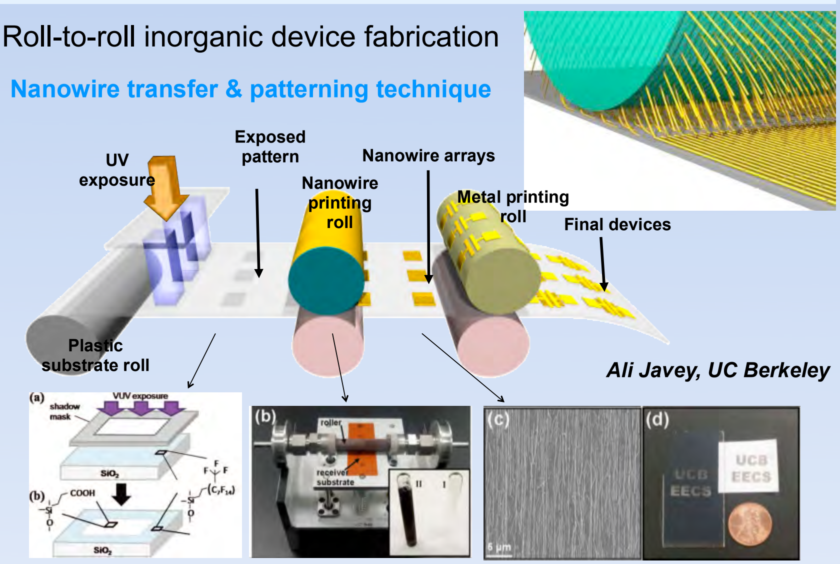
Nano-wires can sense the C

Ali Javey and Ron Fearing, UC Berkeley

Future Plan for Bendable Electronics

Roll-to-roll inorganic device fabrication

Nanowire transfer & patterning technique



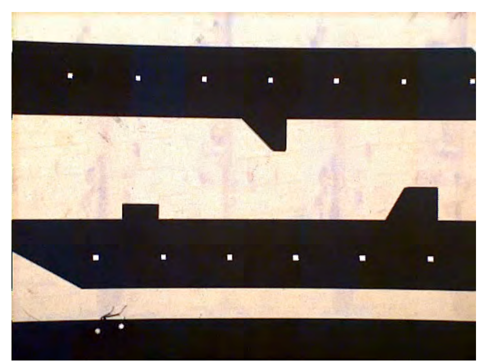
Ali Javey, UC Berkeley

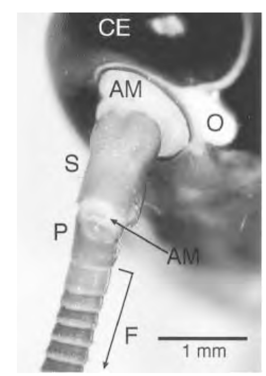
JACS, Vol.131, 2009 *APL, Vol. 91, 2007* *Adv. Mater. Vol.21, 2009*

Task Level Control

Insects Active in Low Light Levels

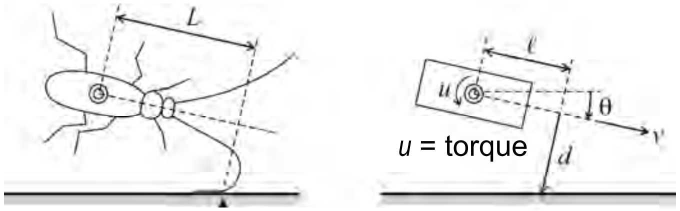
Rely on Non-visual Senses for Self-orientation and Navigation





Cowan, Lee and Full (2006)

Template Sensing Model



Simple Template Control Hypothesis

Proportional derivative (PD) feedback is required for stabilization

$$u = -K_P (d - d^*) - K_D \dot{d}$$

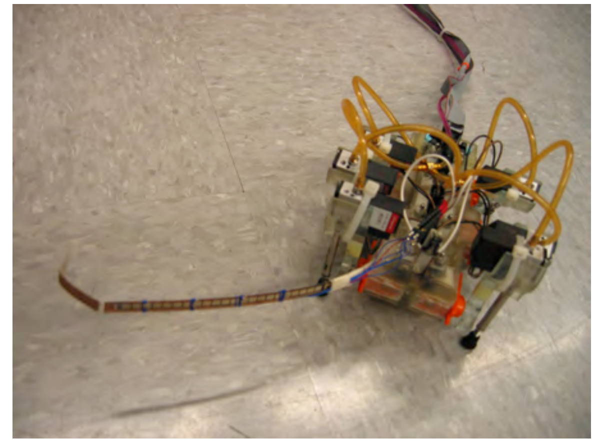
d^* - desired distance

Proportional   Derivative (Tactile Flow)   K - gain

Cowan, Lee and Full, (2006)

Bio-Inspired Antenna Design

Conductive Elastomer



Cowan, Full (UC Berkeley)
Cutkosky, Ma (Stanford)

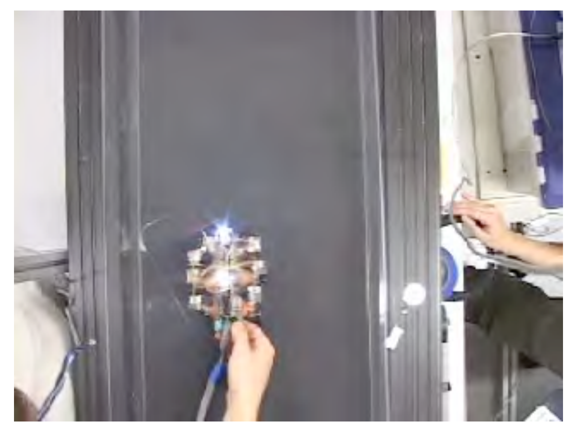
Bio-Inspired Antenna Design

Difficult to Control without velocity or phasic feedback

Cutkosky and Ma (Stanford)
Cowan (Berkeley/Johns Hopkins)

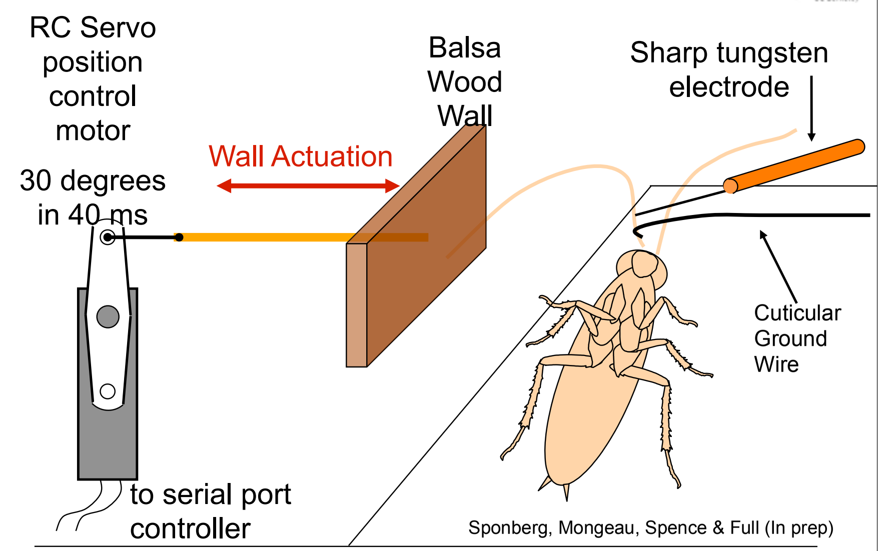
Bio-Inspired Antenna Design

Better Control with velocity or phasic feedback



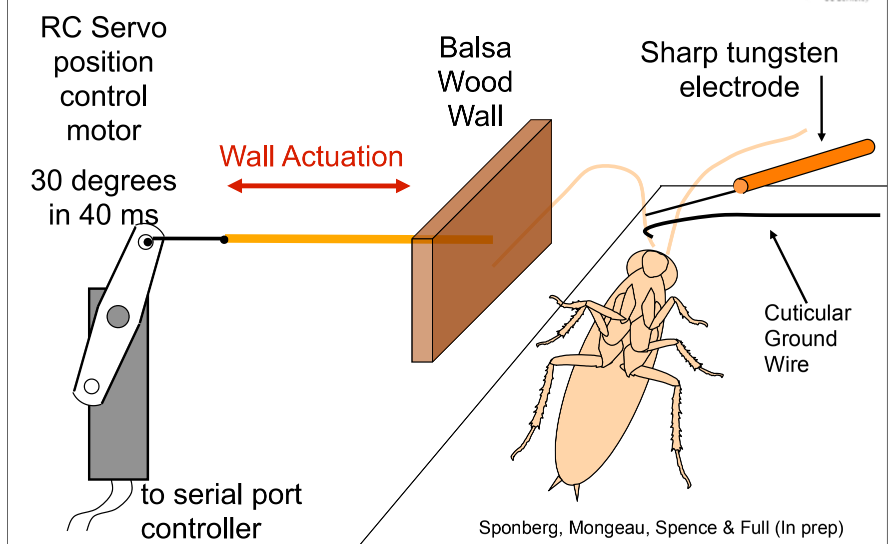
Cutkosky and Ma (Stanford)
Cowan (Berkeley/Johns Hopkins)

Virtual Turning - Test Derivative Control



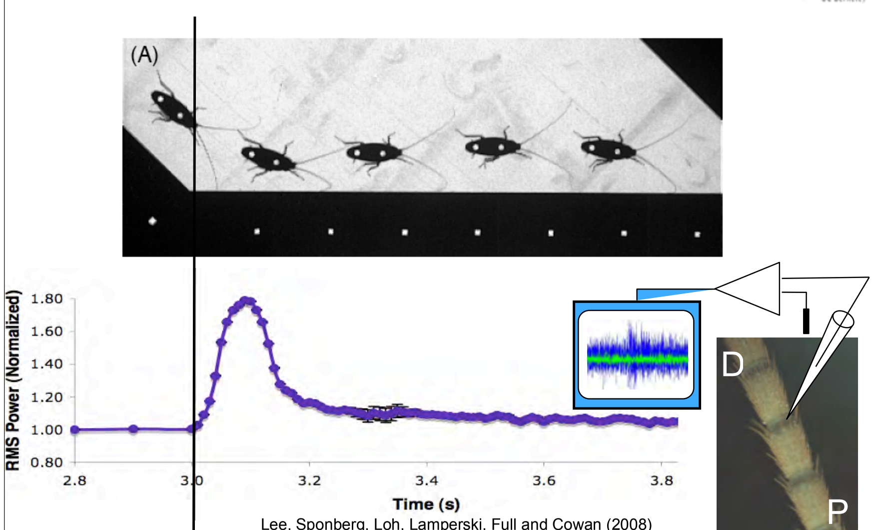
Sponberg, Mongeau, Spence & Full (In prep)

Virtual Turning - Test Derivative Control



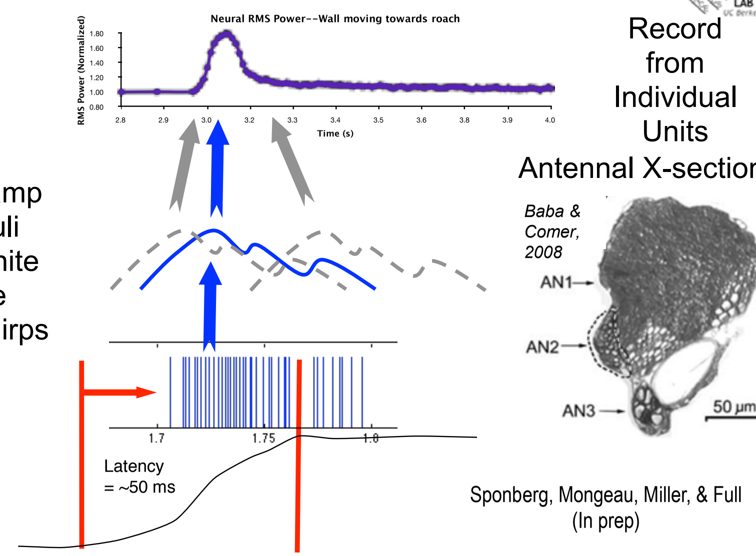
Sponberg, Mongeau, Spence & Full (In prep)

Support Phasic - Velocity Response



Lee, Sponberg, Loh, Lamperski, Full and Cowan (2008)

Velocity Dependence



1. Ramp Stimuli
2. White Noise
3. Chirps

Record from Individual Units

Antennal X-section

Sponberg, Mongeau, Miller, & Full (In prep)

Antenna Morphology

4 - 5 cm long

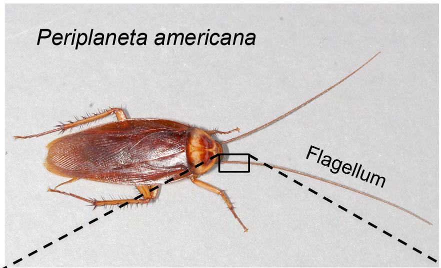
~150-170 segments

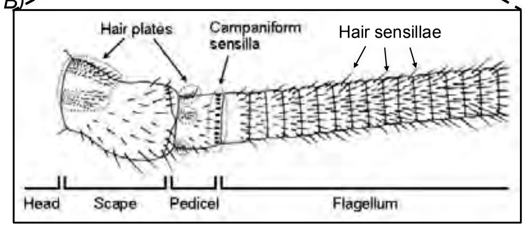
Flagellar Segment Mechanoreceptors

Hair sensillae (*S.Chaetica B*)
(~6,500 as peripheral rings)

Campaniform sensillae
(1 per flagellar segment)

Marginal sensillae
(in 3s on alternating segments)

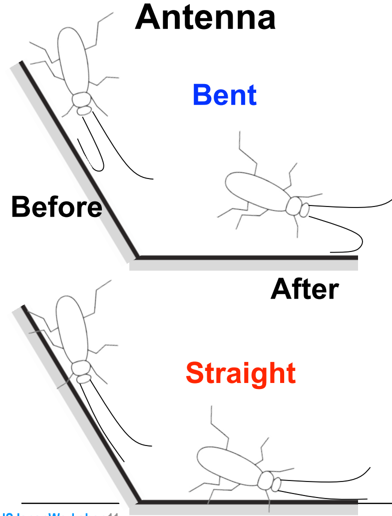


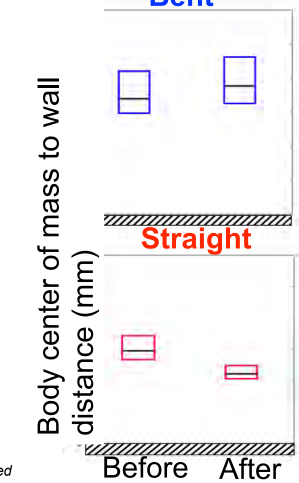


(Shafer, 1973; Toh, 1977; Camhi & Johnson, 1999; Okada, 2009)

Antenna Morphology

More Effective Control with Bent Antenna

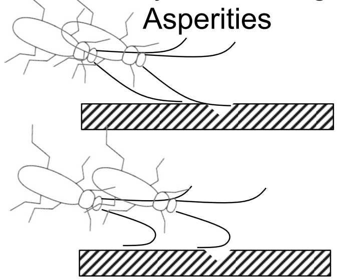




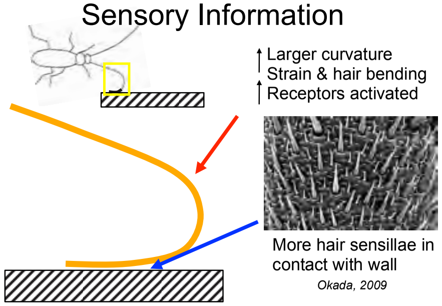
Lee et al. unpublished

Advantages of Bent Shape

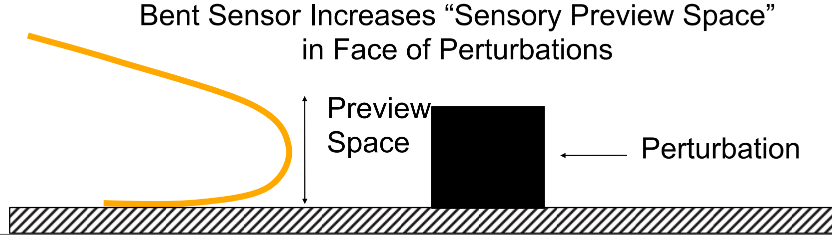
Bent Sensor Decrease Probability of Jamming into Asperities



Bent Shape Increases Sensory Information

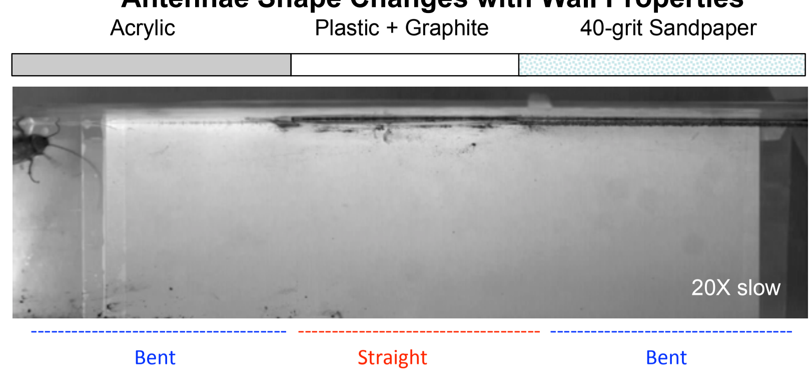


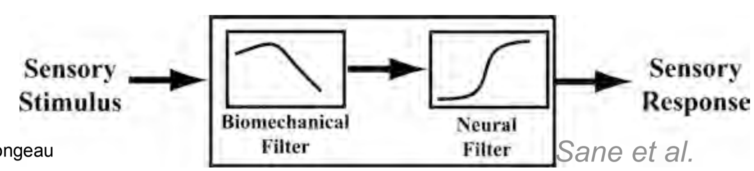
Bent Sensor Increases “Sensory Preview Space” in Face of Perturbations



Vary Wall Properties

Antennae Shape Changes with Wall Properties



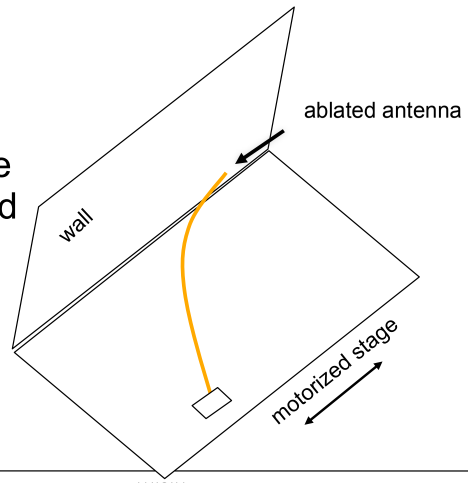


Mongeau

Sane et al.

Antennae Bend Passively

Procedure
Fix ablated antenna
Mount on a motorized stage
Drag along fixed wall

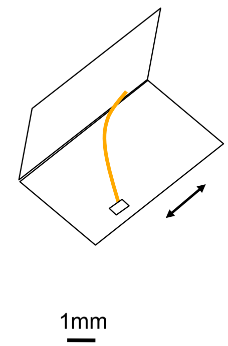


Mongeau

Antennae Bend Passively

Ablated antennae can bend passively.

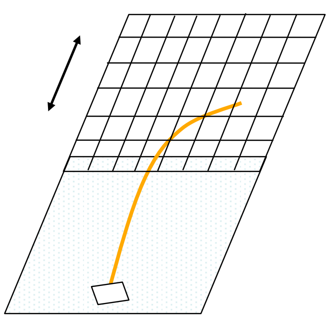
Performance comparable to natural running.



Mongeau

Evidence for Passive Mechanism

Freshly-ablated antennae passively displaced by moving surface with roughness.



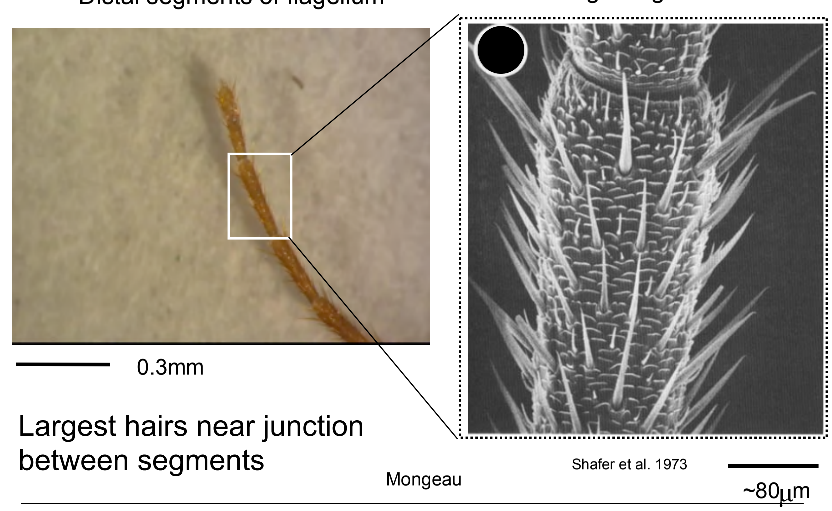
$1mm^2$ squares

Mongeau

Properties of Mechanosensory Hairs

Distal segments of flagellum

Single segment



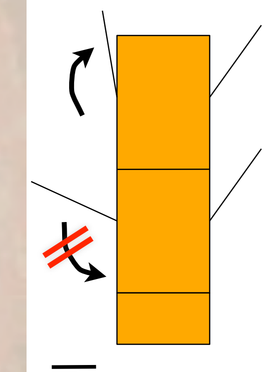
Largest hairs near junction between segments

Shafer et al. 1973

Mongeau

Hair Motion

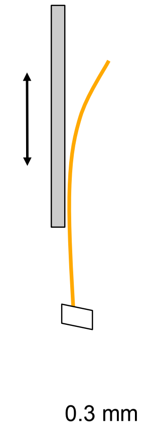
Hairs resist bending in one direction, but collapse toward flagellum in other.



Hairs are Sharp

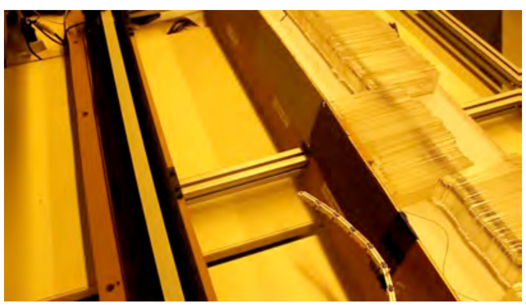
Mongeau

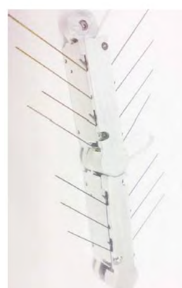
Hairs readily engage in soft surfaces with high friction and/or asperities



Bio-inspired Design

Novel antenna-inspired sensor with passive artificial spines being developed by the LIMBS Lab at Johns Hopkins Universitv

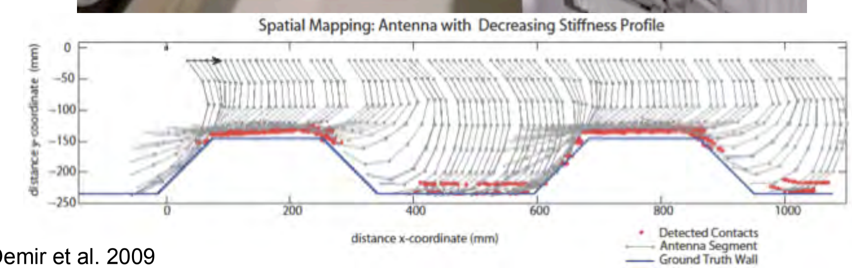




Artificial antenna as a physical model of cockroach antenna

Demir et al. 2009

Bio-inspired Design



Demir et al. 2009

Design Lessons from Nature

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2. Sensors are Embedded in Structures
   - Interaction Provides Information and Control
3. Sensors and Actuators are Integrated Systems
   - Multi-modal Sensing with Tuned Actuation

Gecko Feats

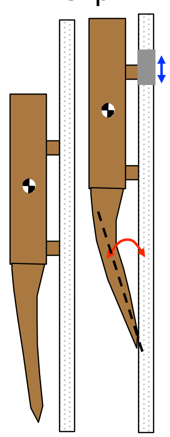
Rapid Climbing on Any Surface

Vertical Climb
1 m/sec
30 steps per second
Attaches in 8 msec
Detaches in 16 msec

Gecko

Discovery of New Tail Response

Triggered by Front Foot Slip



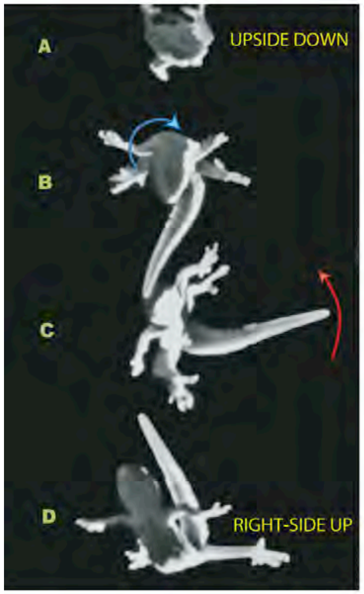
Slowed 10X

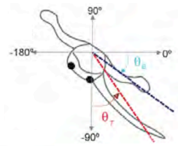
Jusufi, Goldman, Revzen & Full (2008) PNAS

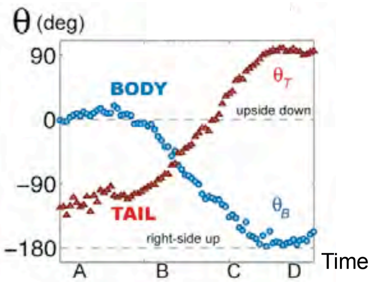
World's Fastest Air-righting Response

Jusufi, Goldman, Revzen & Full (2008) PNAS

Kinematics of Tail - induced Reorientation







Jusufi, Goldman, Revzen & Full (2008) PNAS

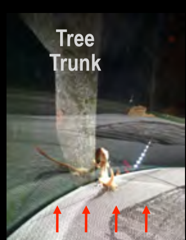
Air-righting Response with Tail in Robot

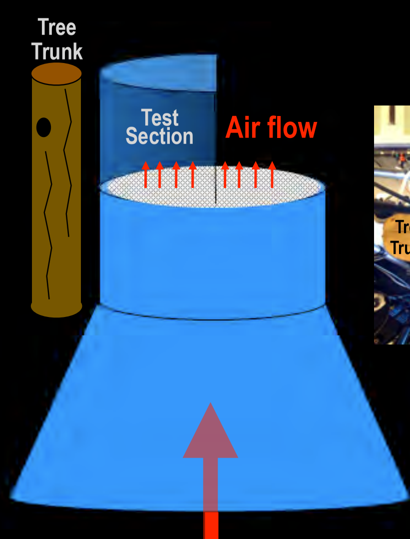
Active Tail

Slowed 10X

Vertical Wind Tunnel

Natural Landing Target





Top View Camera

Jusufi, Dudley and Full

Equilibrium Gliding

Jusufi, Goldman, Revzen & Full (2008) PNAS

Slowed 10X

Jusufi, Goldman, Revzen & Full (2008) PNAS

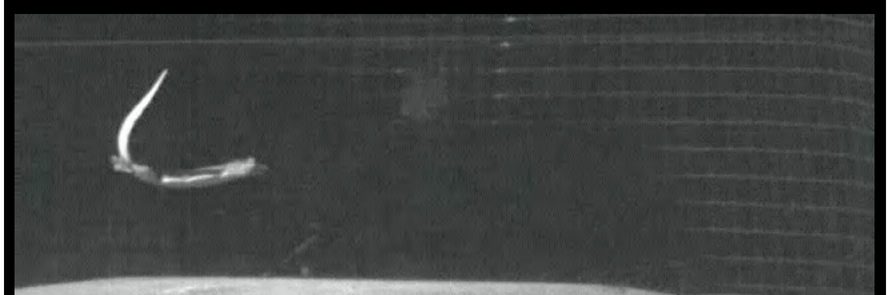
Libby Photo

Turning with Active Tail

Jusufi, Goldman, Revzen & Full (2008) PNAS

Slowed 25X

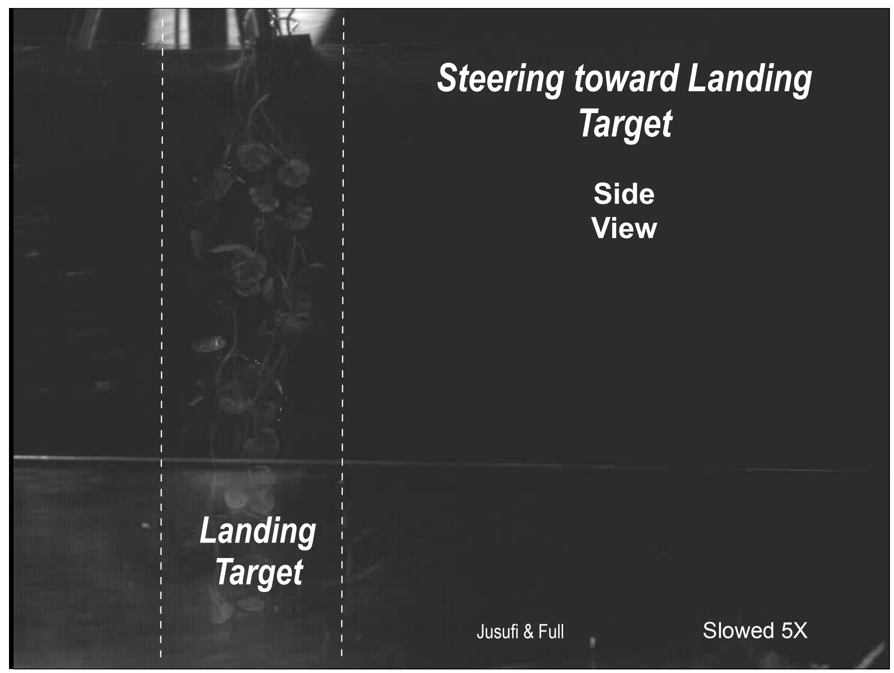
“Swimming” in Air with Active Tail

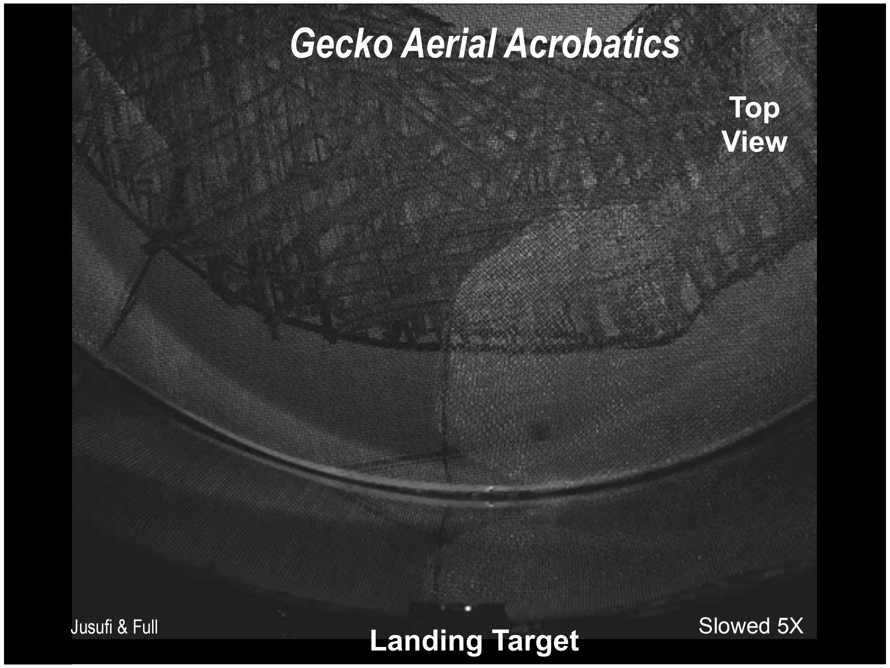


Watch Front Legs - Origin of Flight?

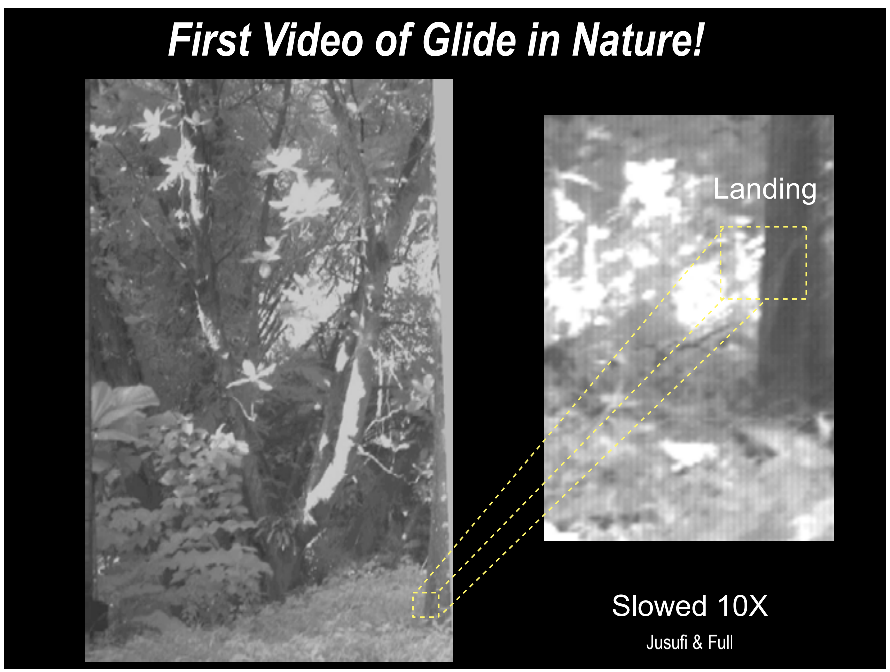
Jusufi, Goldman, Revzen & Full (2008) PNAS

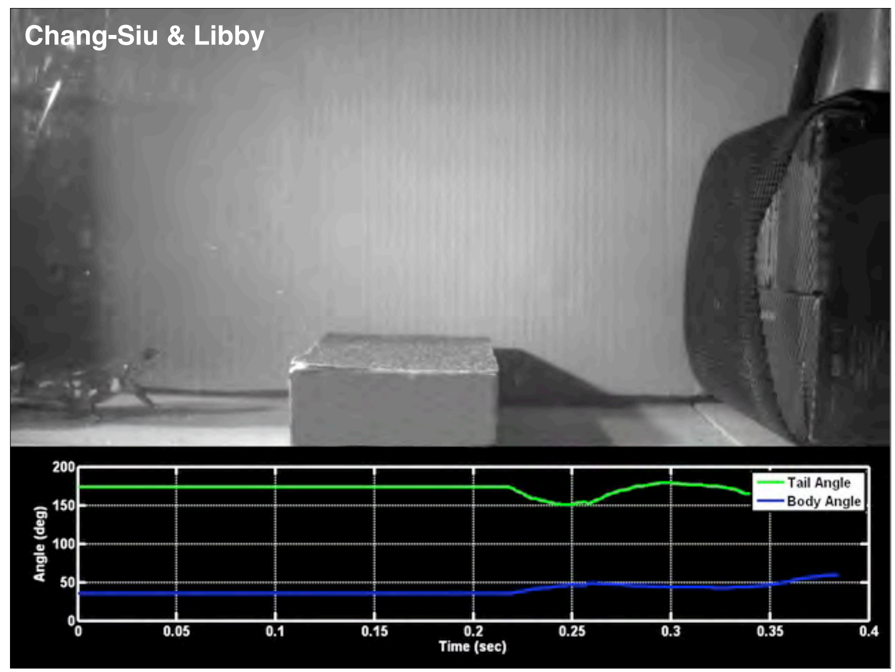
Slowed 10X

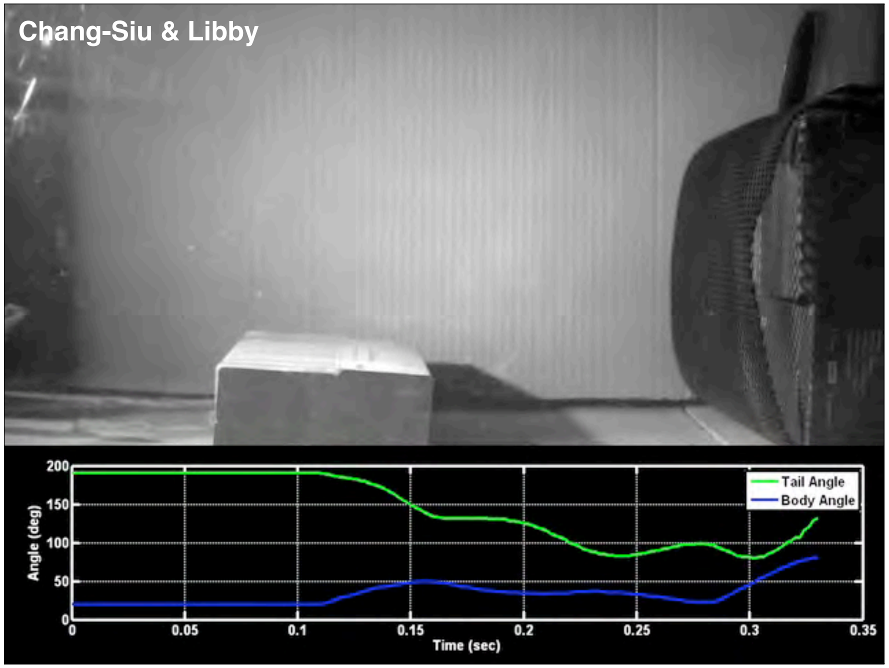



Gecko Aerial Acrobatics
Top View
Jusufi & Full
Landing Target
Slowed 5X

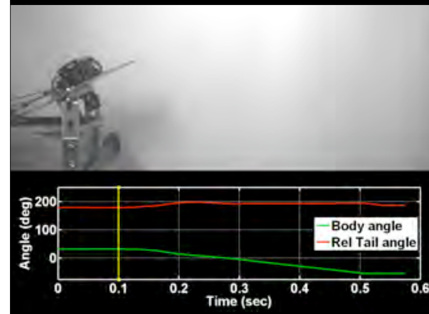

Do Geckos Glide in Nature?
Travel to Forests of Singapore & Southeast Asia
Jusufi & Full


First Video of Glide in Nature!
Landing
Slowed 10X
Jusufi & Full


Chang-Siu & Libby
Angle (deg)
Time (sec)
Tail Angle
Body Angle

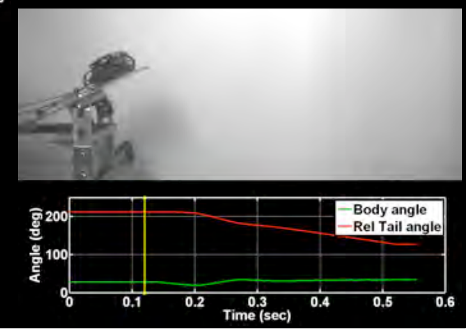


Body Attitude Control with Inertial Appendage



Tailbot

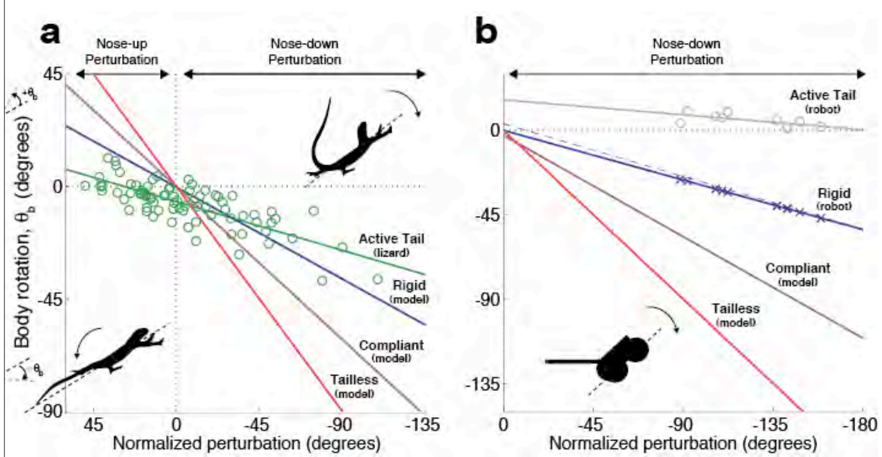
No Feedback Control



Feedback Control

Chang-Siu, Libby, Tomizuka and Full (Finalist Best Paper, IROS 2011)

Attitude Control

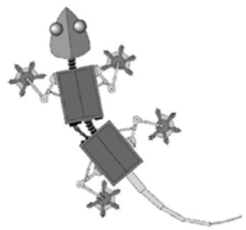


Thomas Libby, Talia Y. Moore, Evan Chang-Siu, Deborah Li, Daniel J. Cohen, Ardian Jusufi and Robert J. Full, ***Nature***, In Press

Grand Challenges

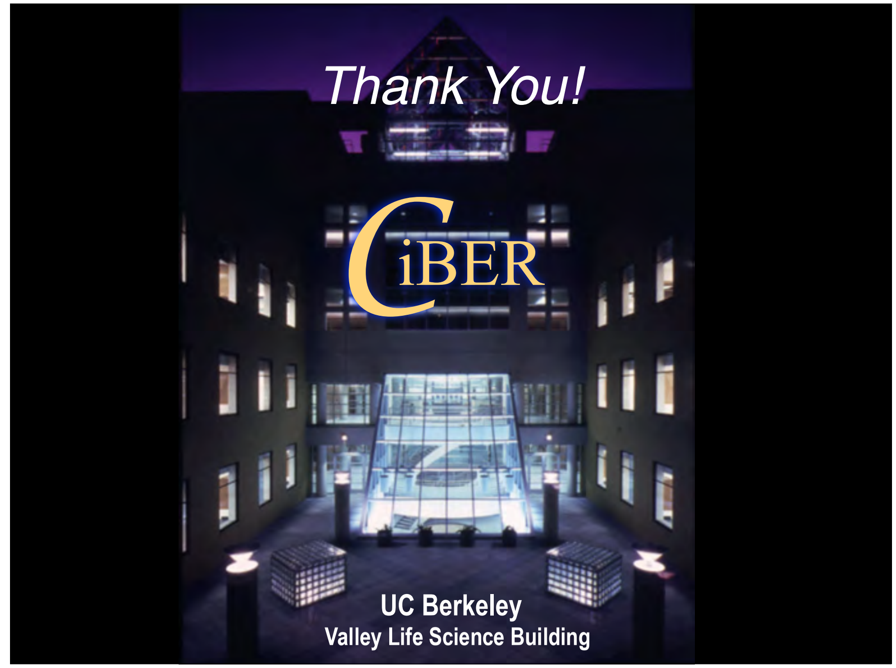
1. Integrate Multifunctional Materials
   - Small, Hybrid & Programmable
2. Work with Natural Dynamics of System
   - Managing the Flow of Energy
3. Effective Interaction with Environment
   - Organism and Environment are One
4. Build Robust and Sustainable Systems
   - Fault tolerant, Fail-safe, Self-repair, Adapt, Evolve

CENTER FOR INTERDISCIPLINARY BIOLOGICAL-INSPIRATION EDUCATION & RESEARCH



UC Berkeley
Director Robert Full

http://ciber.berkeley.edu

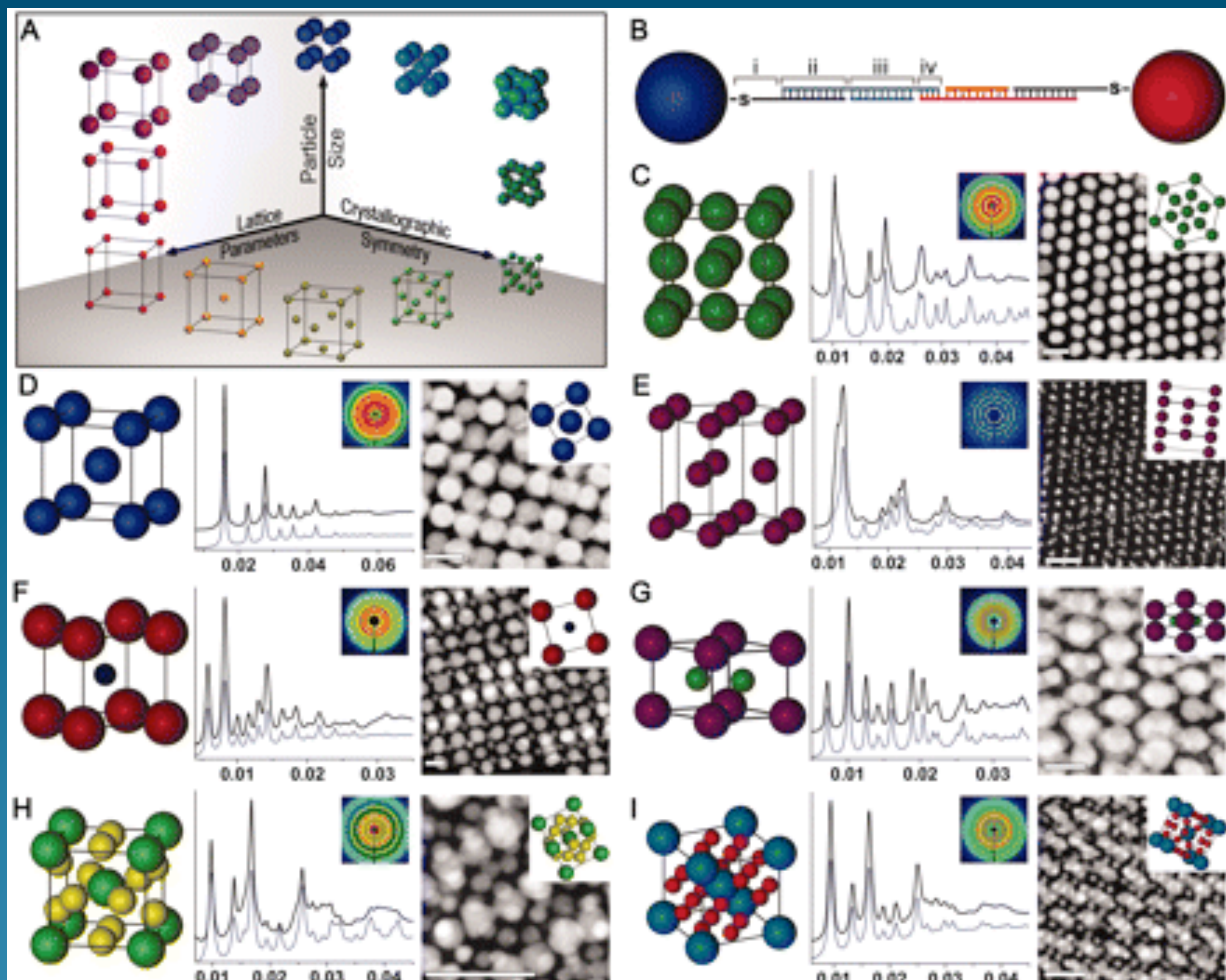


Biosensing based on Single Nanoparticles and Nanorods

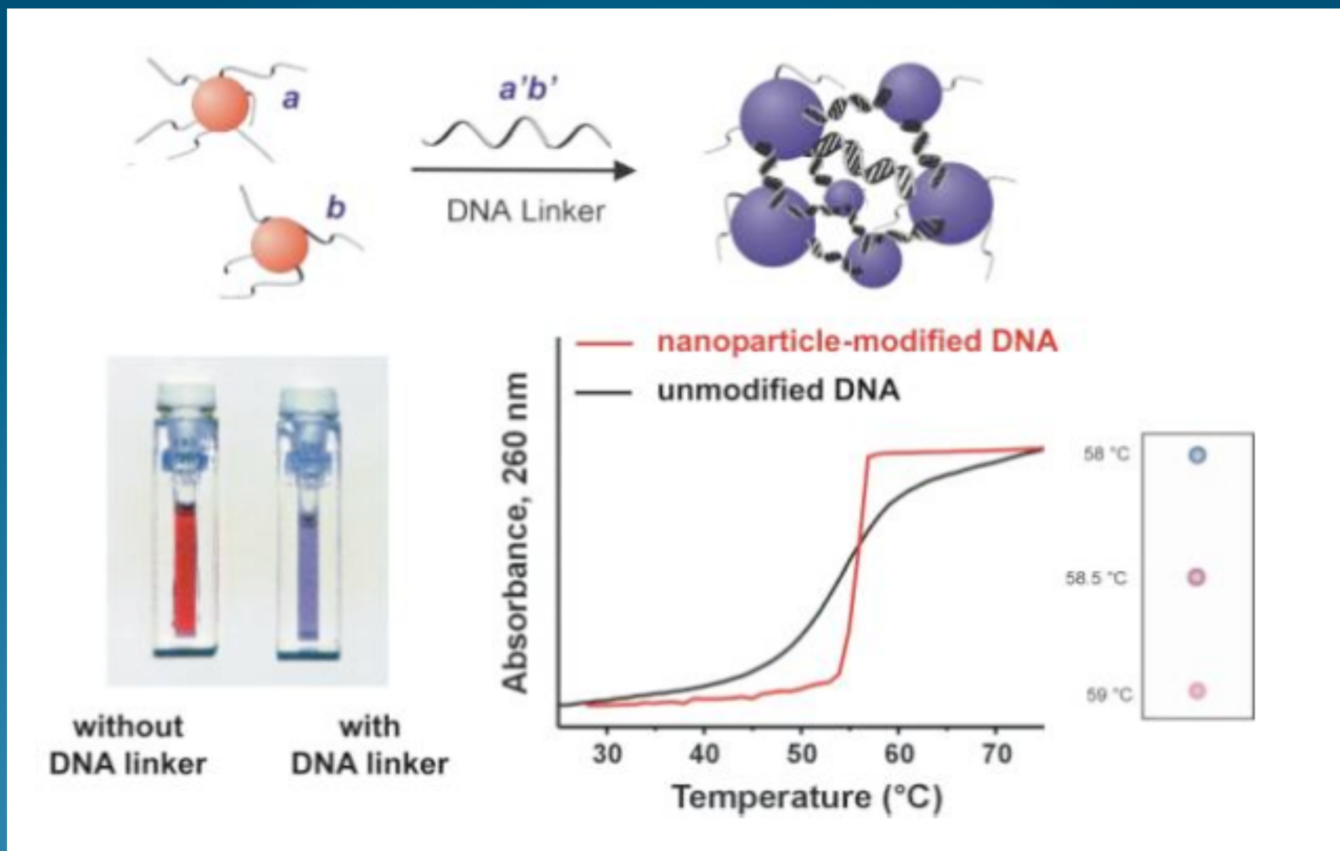
Edward S. Yeung, Ning Fang, Gufeng Wang, Lehui Xiao Lin Wei, YanXia Qiao, Yan He

Ames Laboratory DOE, Iowa State University
Biomedical Engineering Center, Hunan University

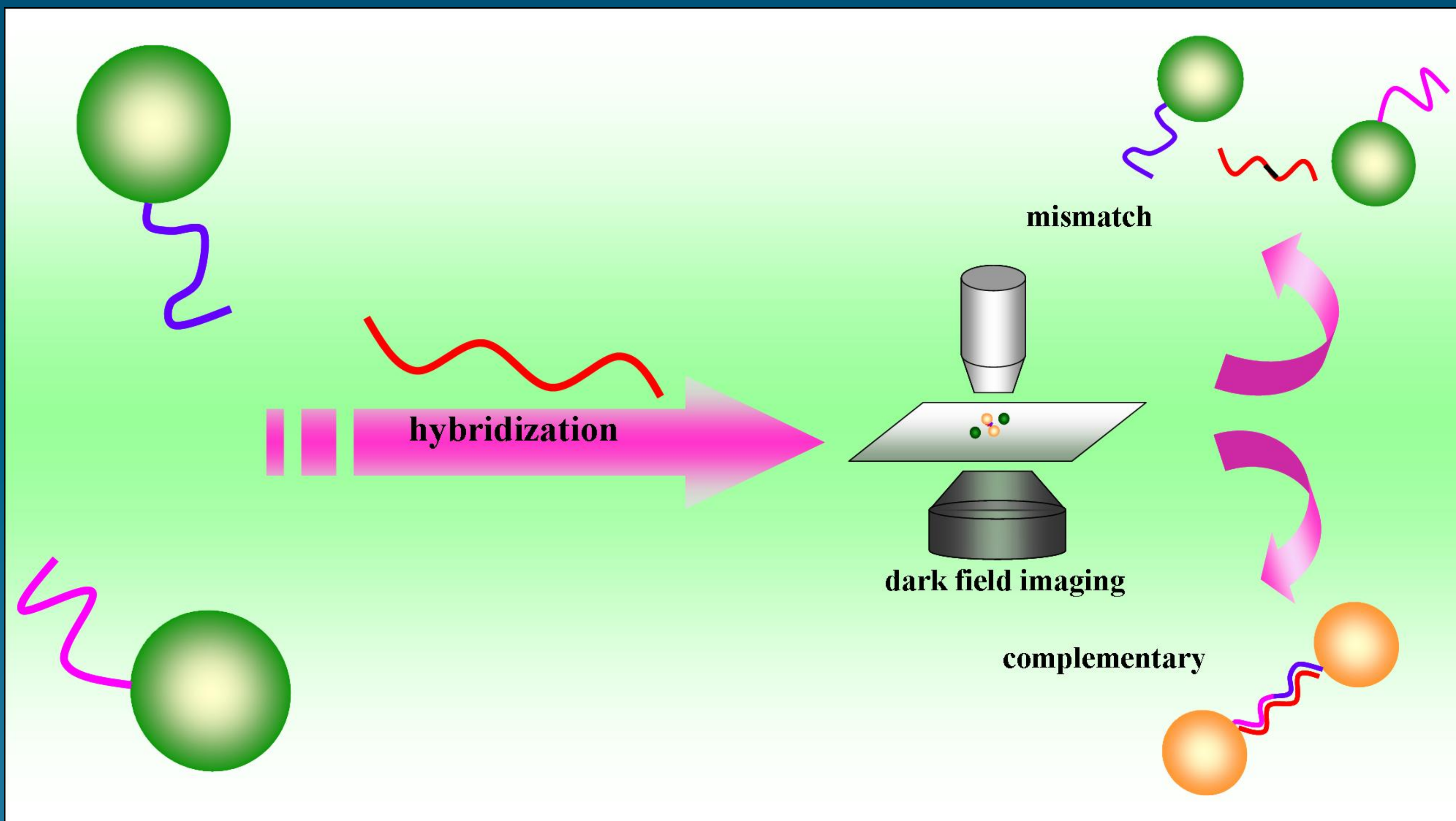
Controlled Assembly of Nanoparticles



Hybridization Assay based on Plasmonic Nanoparticles



Single Hybridization Event



Dark-Field – Light Scattering

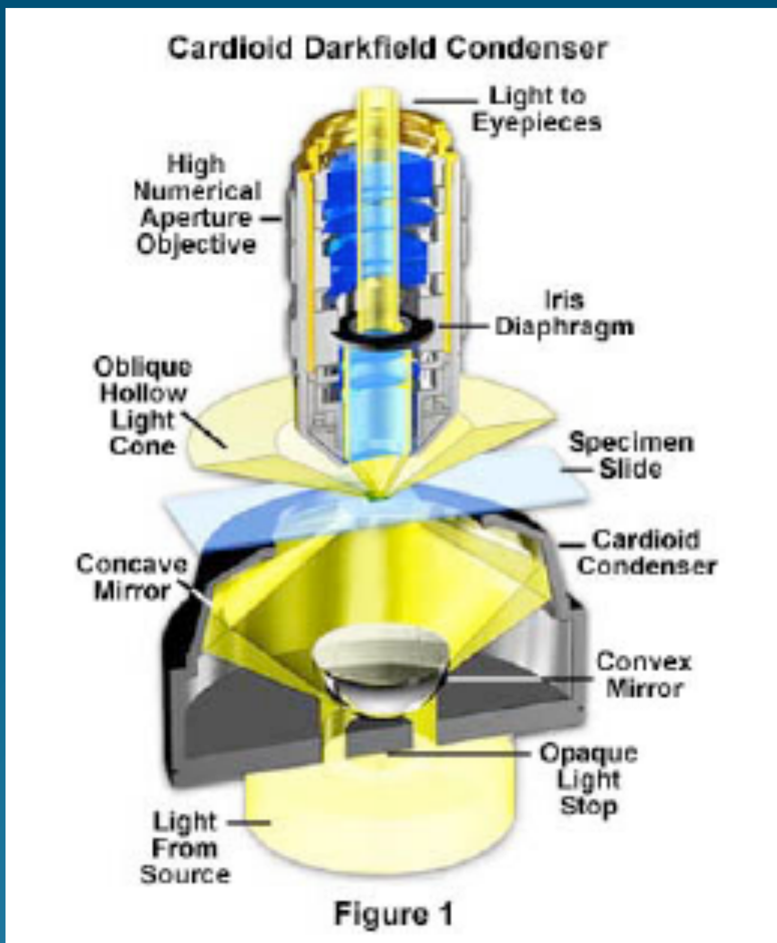


Figure 1

- Not fluorescence
- Not absorption
- Low background
- Conventional light source
- Plasmon resonance
- Polarization

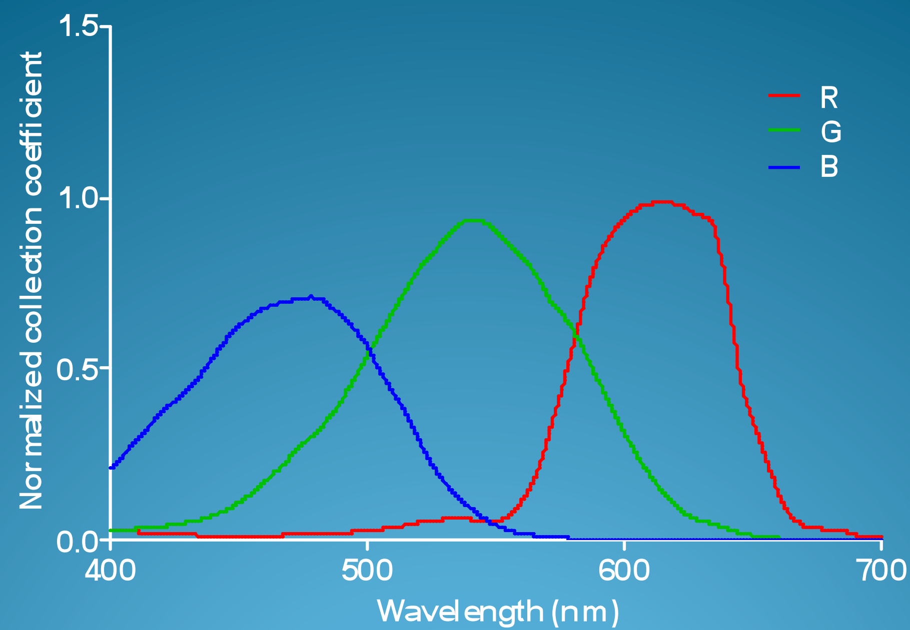
Red-shift on Dimerization

$$\frac{\Delta\lambda}{\lambda_o} \approx 0.18 \times \exp\left(-\frac{s/D}{0.23}\right)$$

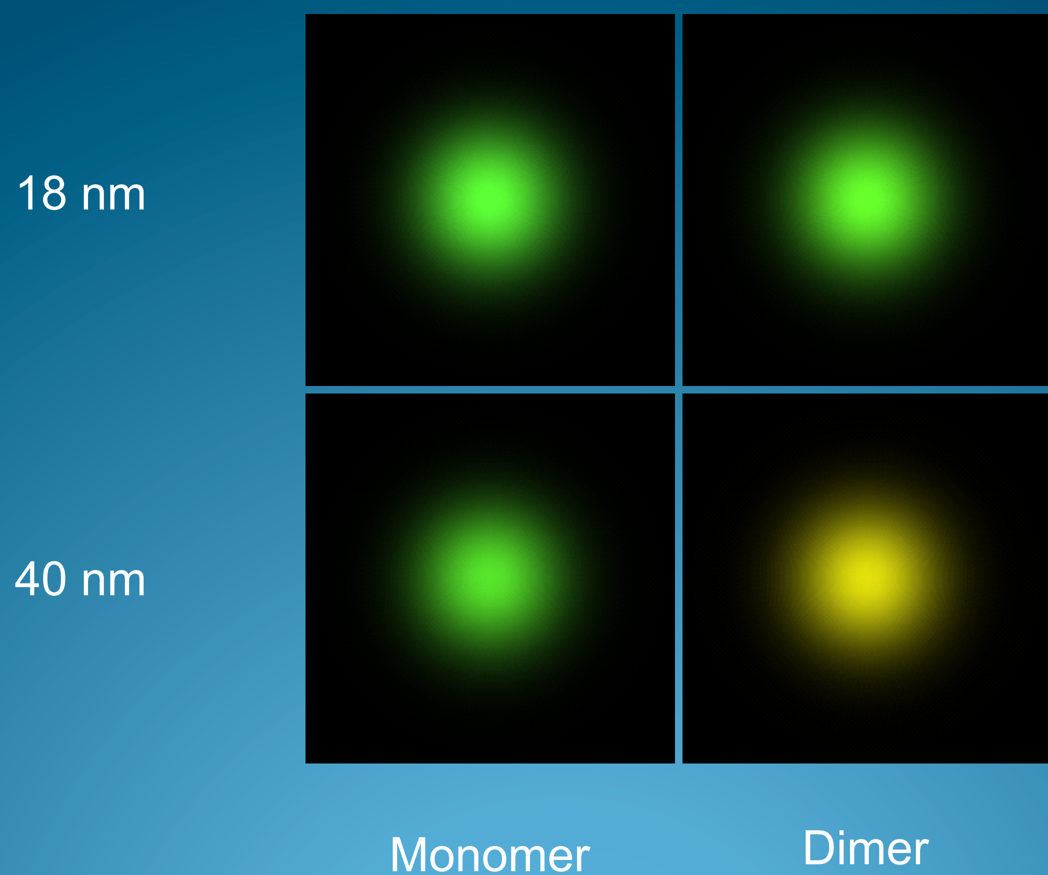
The eye vs. the spectrometer!

Color CCD Camera

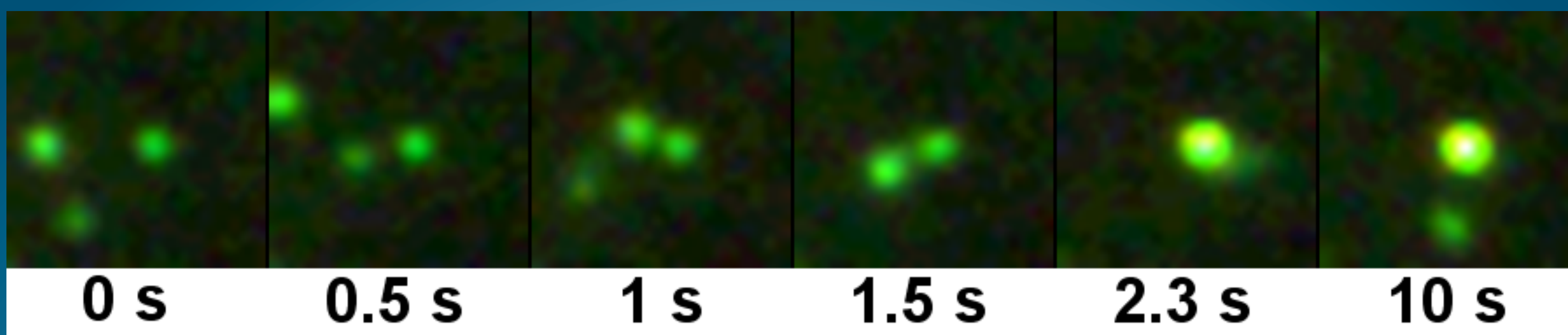
$$\int I(\lambda) \times x(\lambda) \times s(\lambda) d\lambda$$



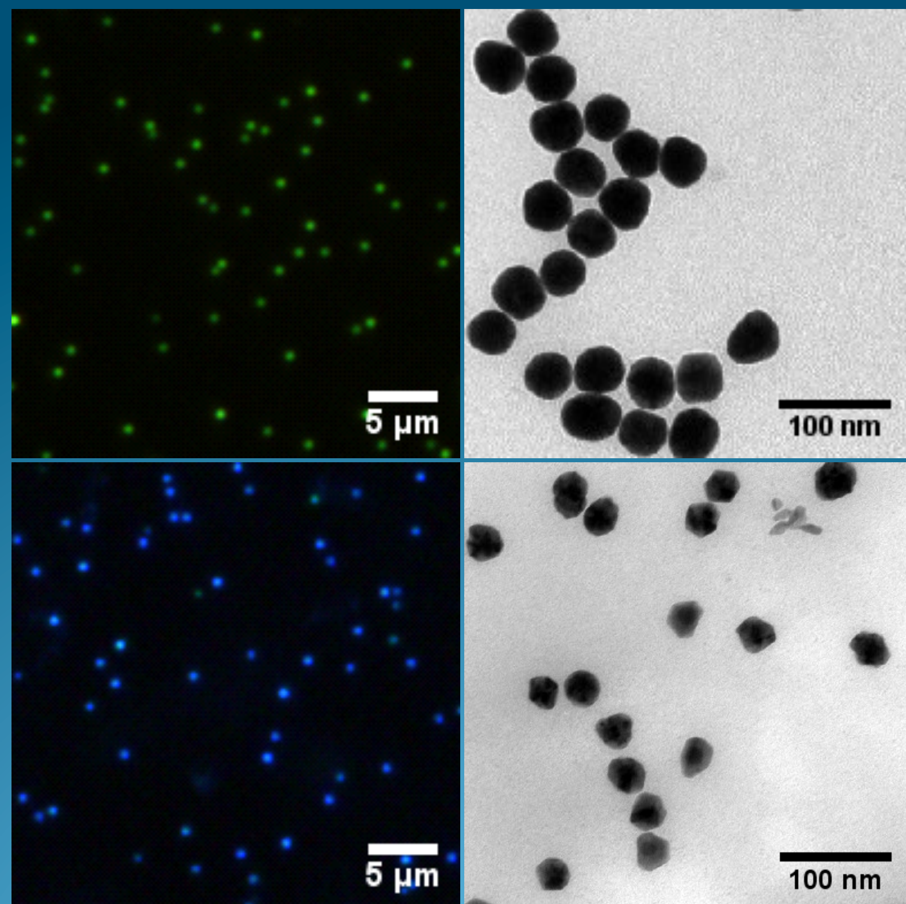
Optimal Dimerization



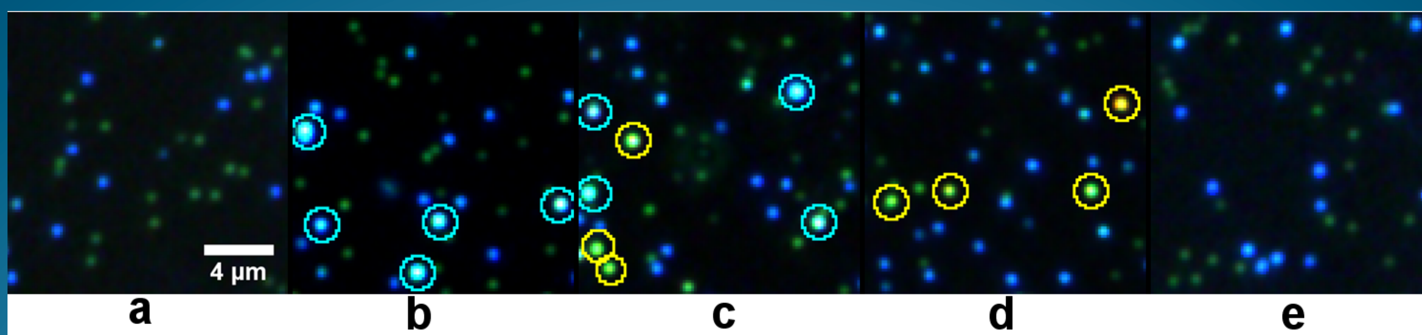
Hybridization in Real Time



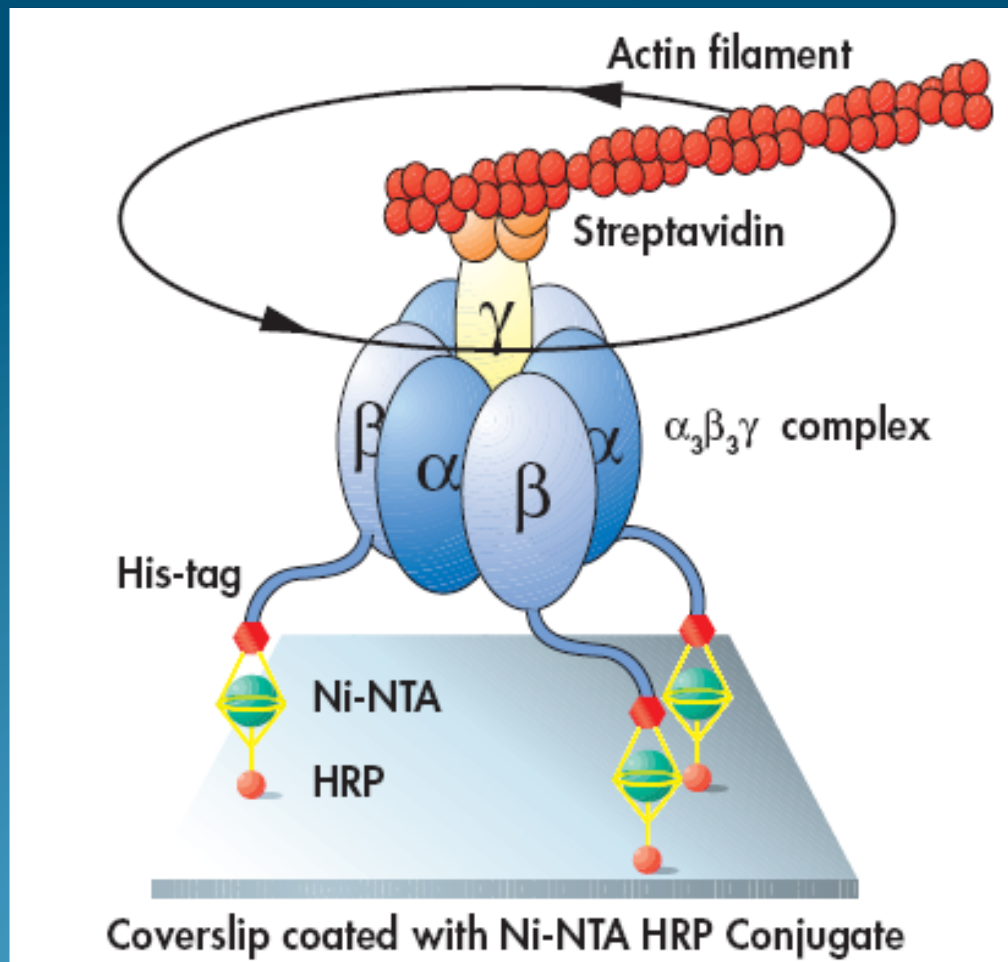
Au and Au/Ag Nanoparticles



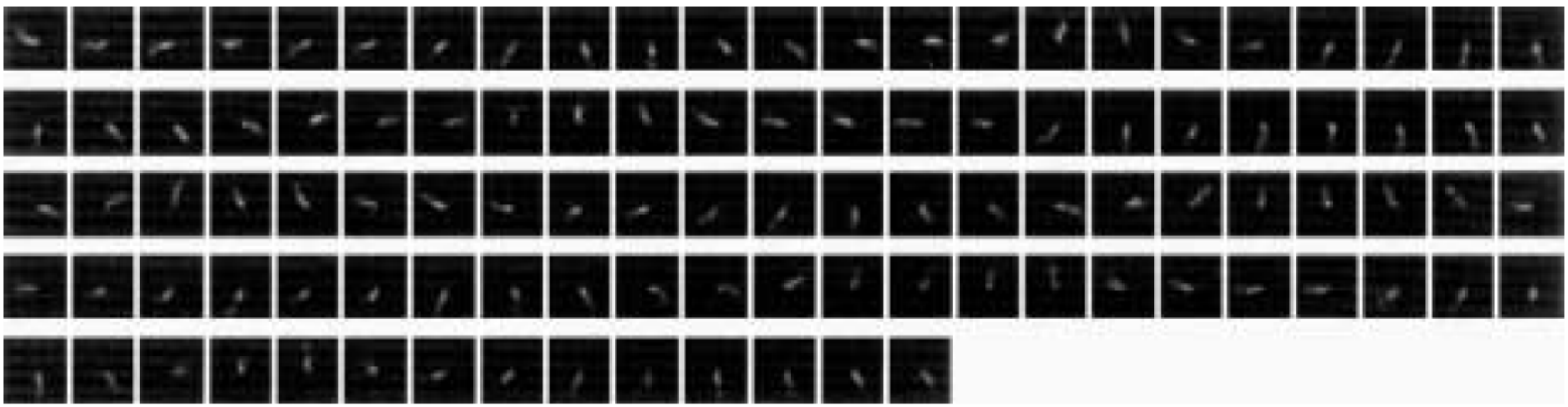
Multiplexed Detection



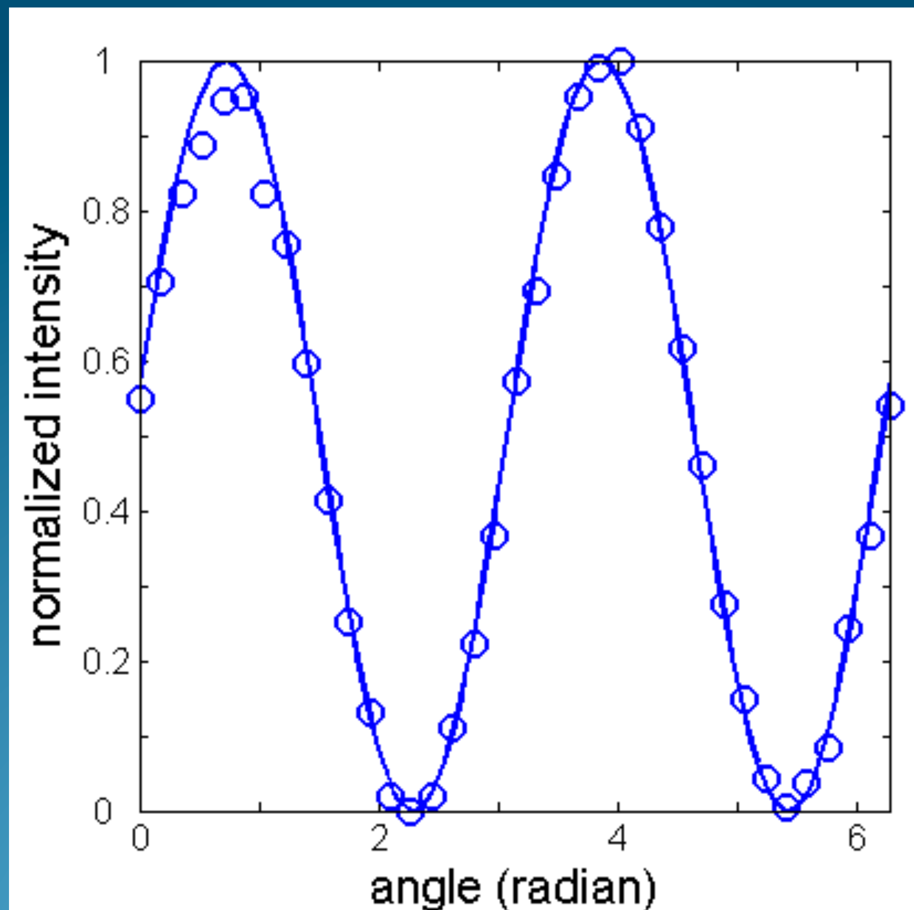
F1-ATPase Ion Pump



Video Record of 120° Steps



Polarization Modulation



3D Dark-field Scattering (Poynting Vector)

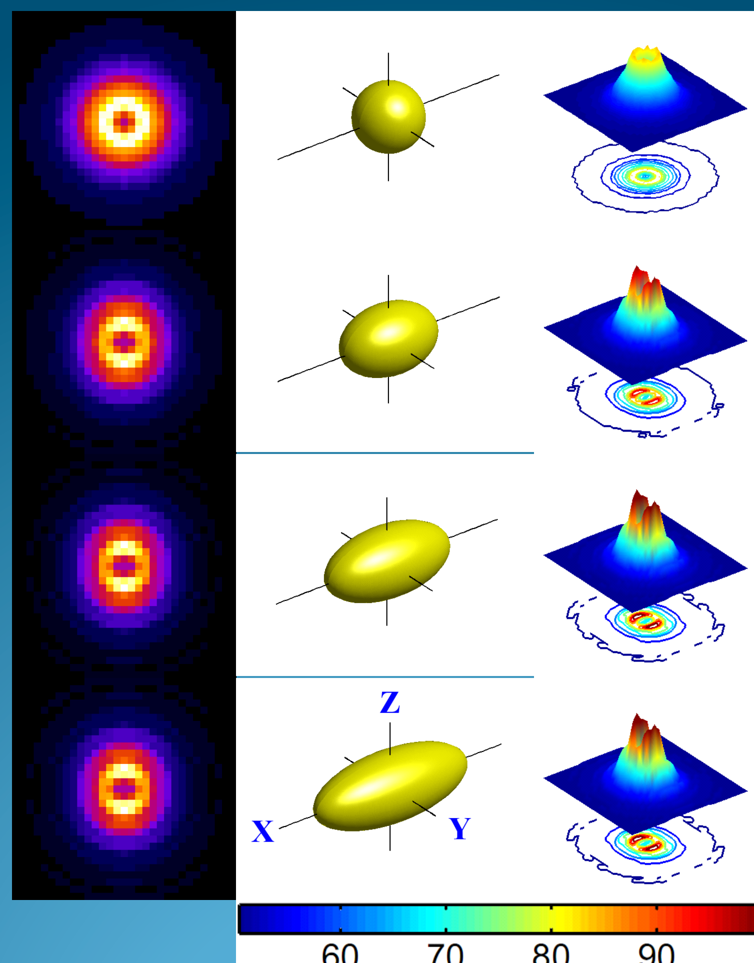
$$\langle S \rangle = \frac{1}{2}\hat{e}_z \operatorname{Re}\{E_{(scat)} \times H^*_{(scat)}\} = \frac{c\varepsilon_m^{1/2}}{8\pi}\hat{e}_z |E_{(scat)}|^2$$

$$\alpha_j = 4\pi xyz \frac{\varepsilon_r - \varepsilon_m}{3\varepsilon_m + 3L_j(\varepsilon_r - \varepsilon_m)}$$

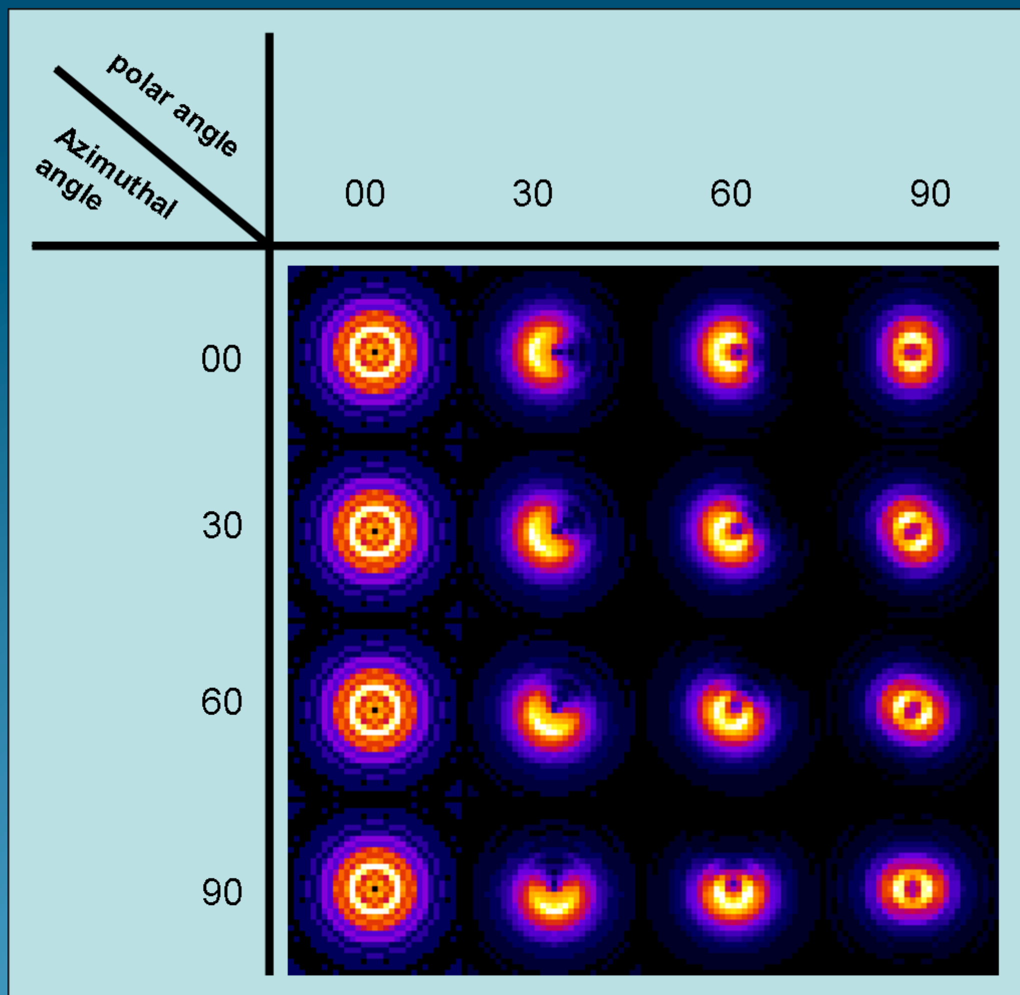
$$L_x = \frac{1-R^2}{R^2}\left(\frac{1}{2R}\ln\frac{1+R}{1-R} - 1\right)$$

$$R = \sqrt{1-\left(\frac{y}{x}\right)^2}$$

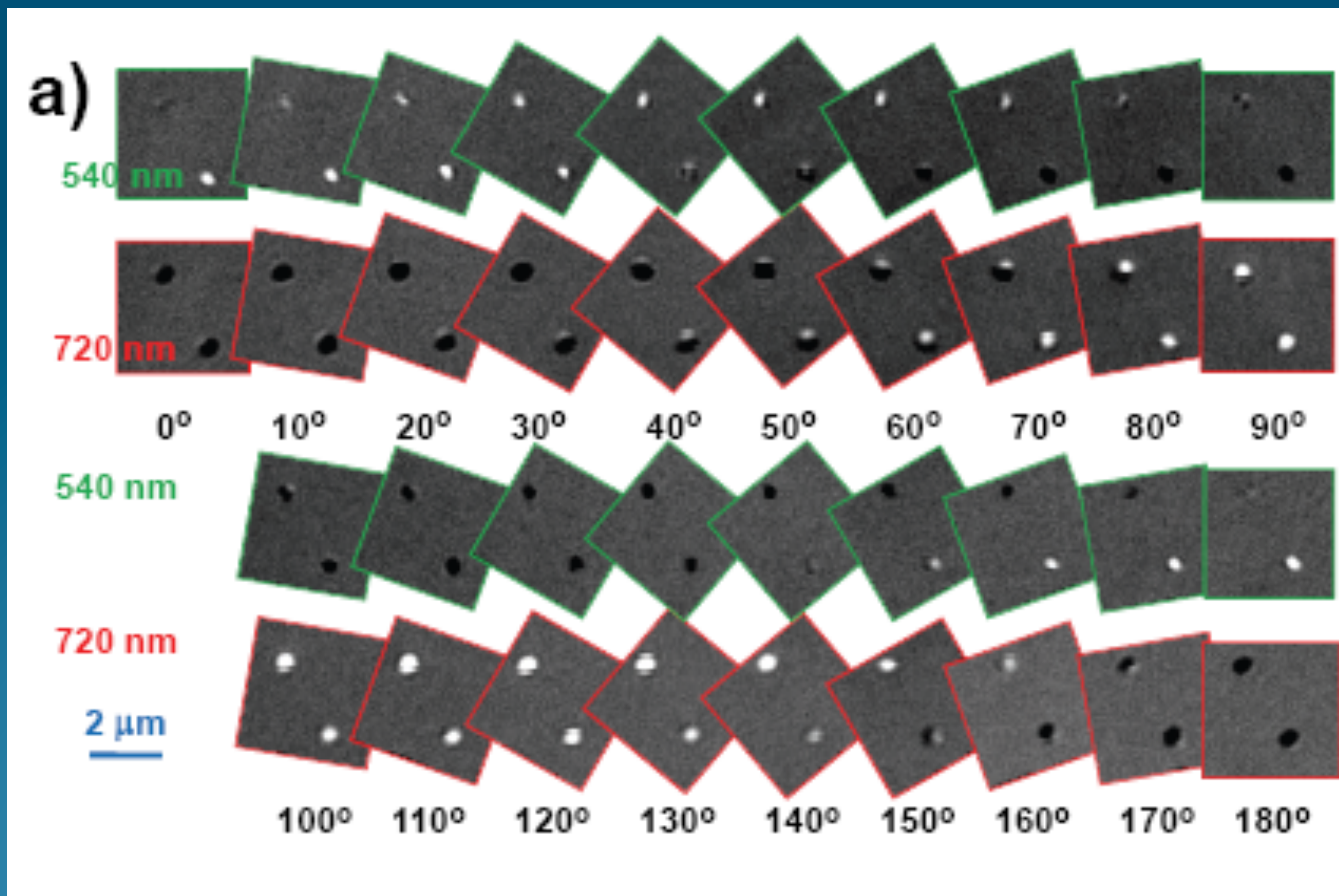
Asymmetric In-Plane Scattering



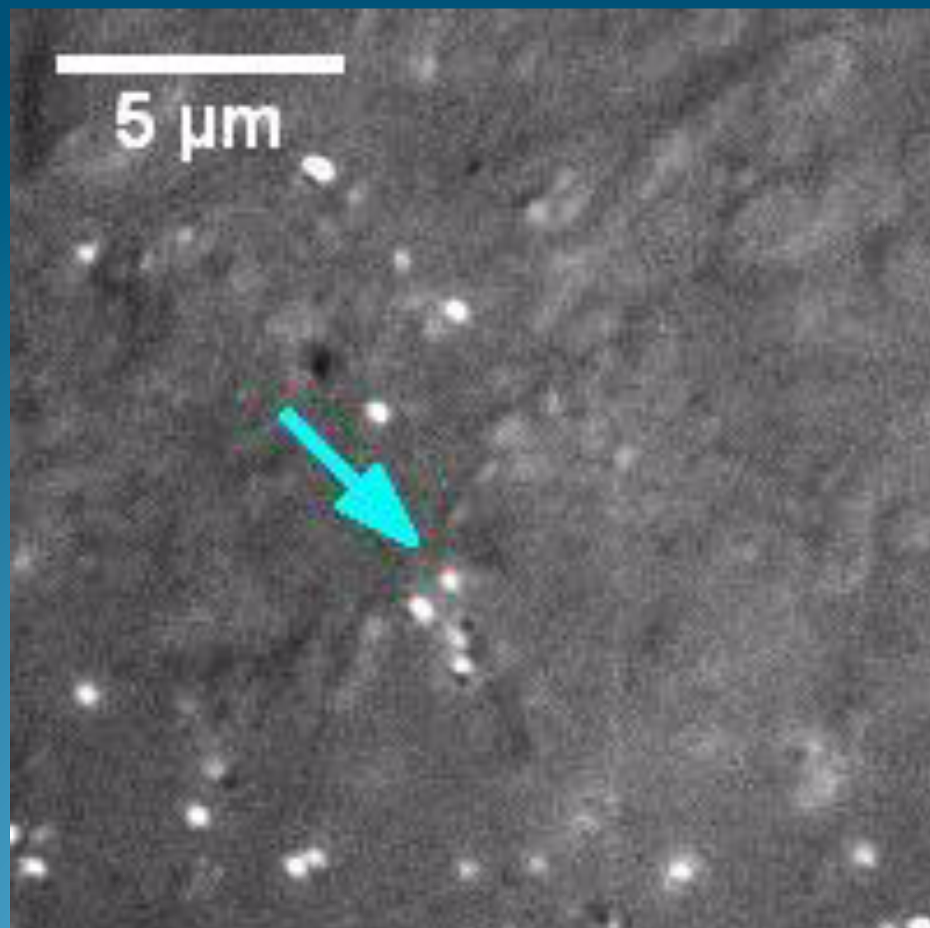
DF Patterns vs. 3D Orientation



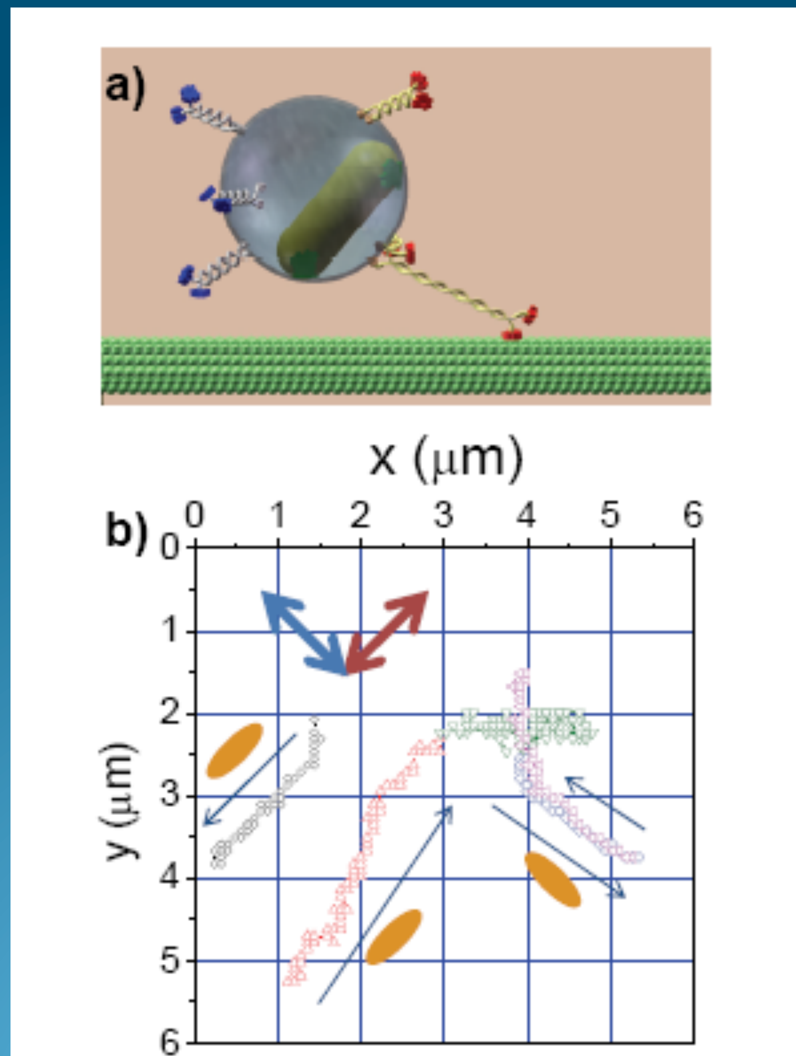
DIC Patterns vs. 3D Orientation



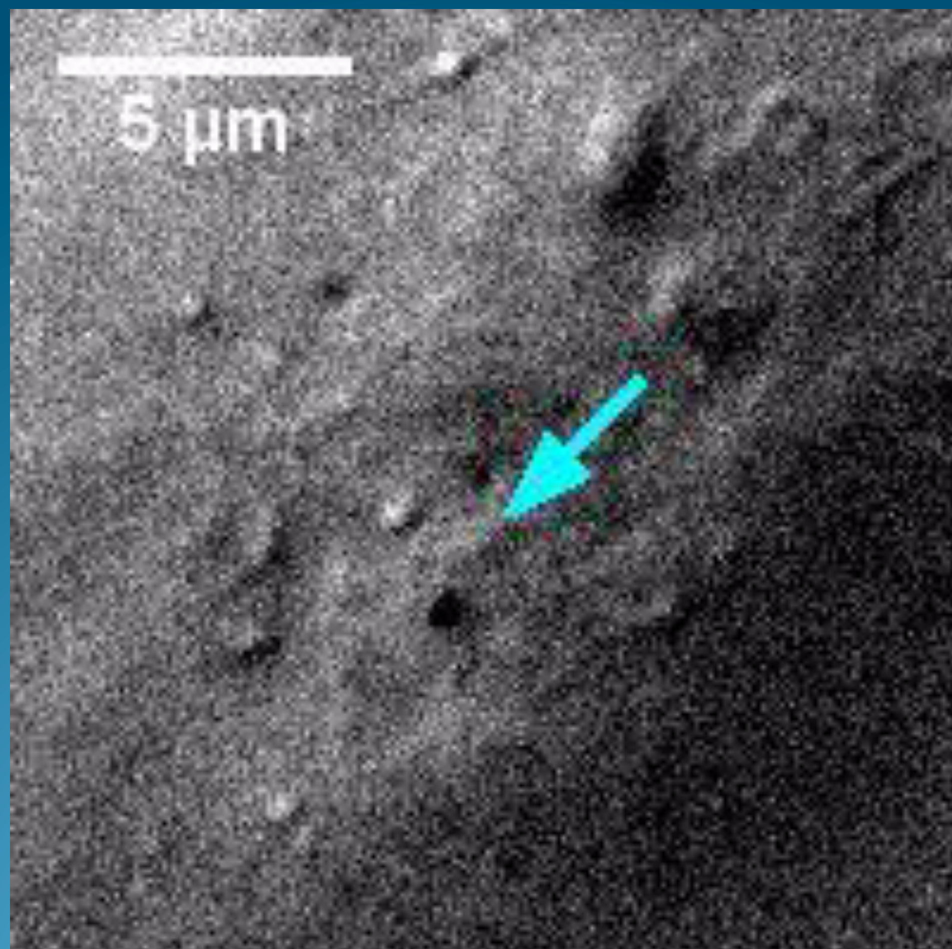
3D Orientation in Cellular Transport



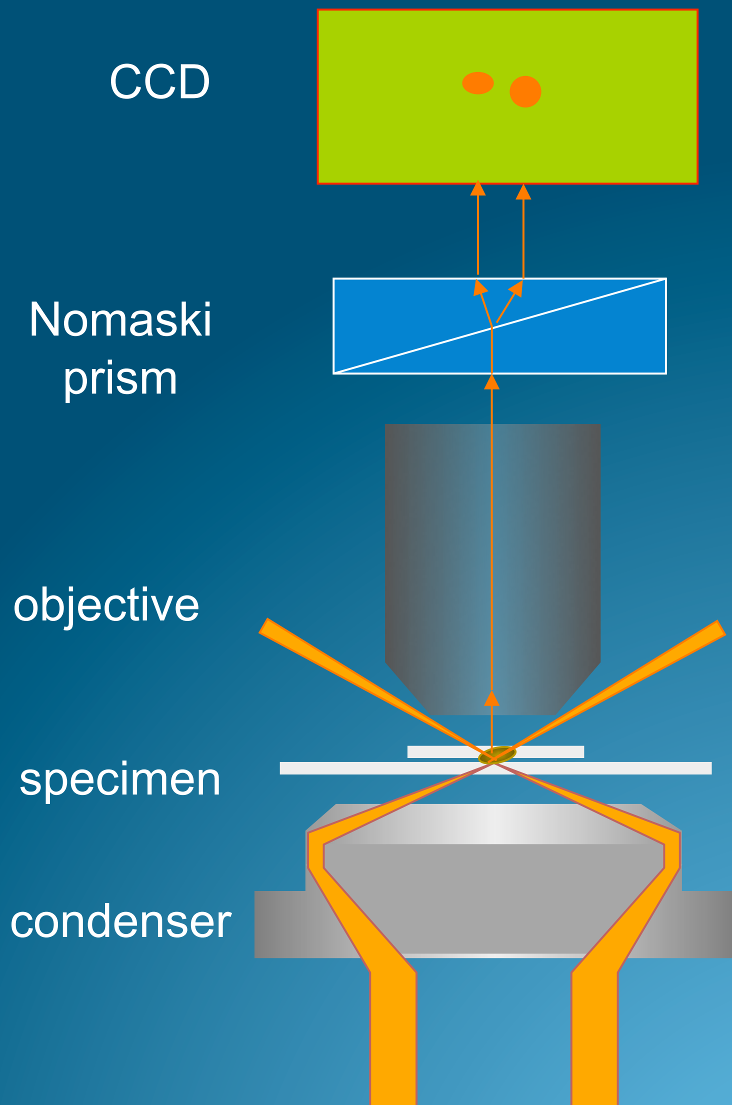
3D Orientation in Cellular Transport



3D Orientation in Cellular Transport

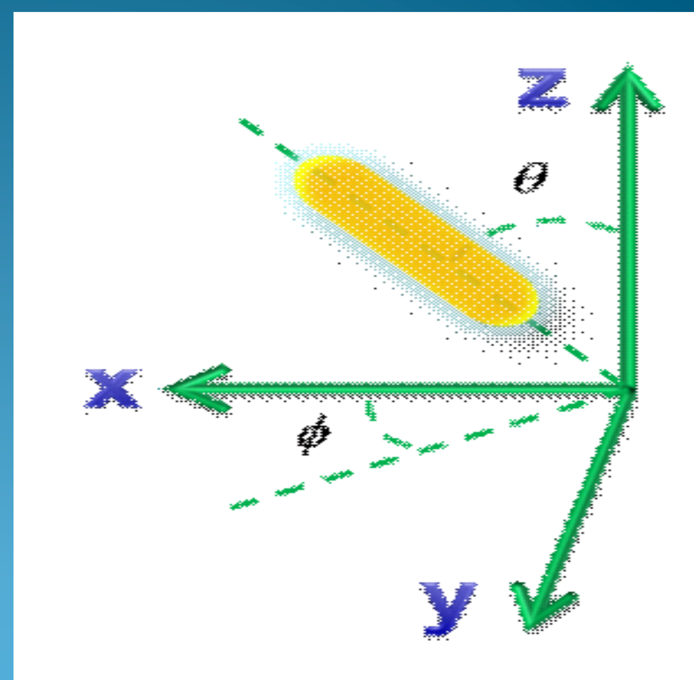


DF Polarization vs. Orientation

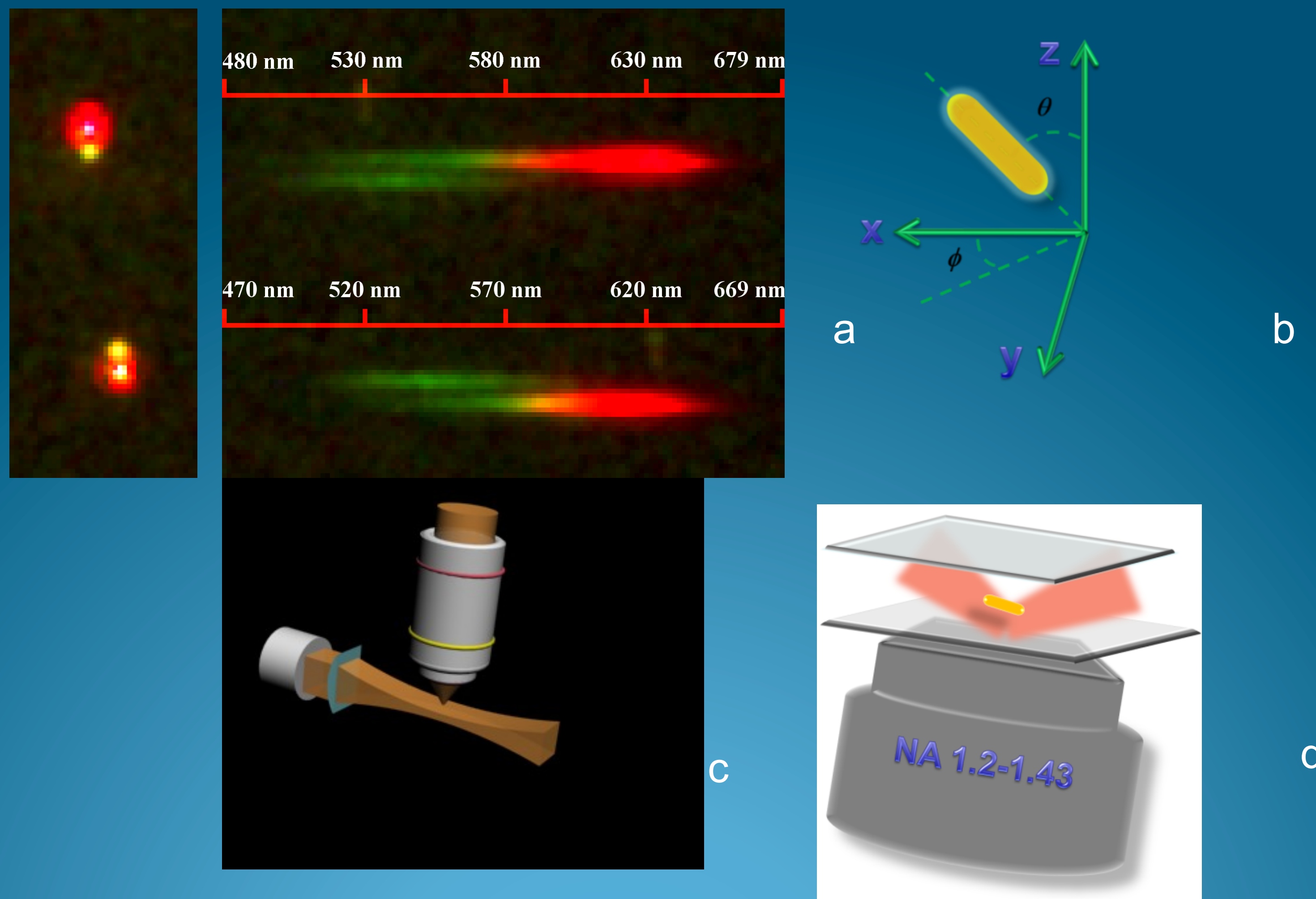


Emission polarization ratio

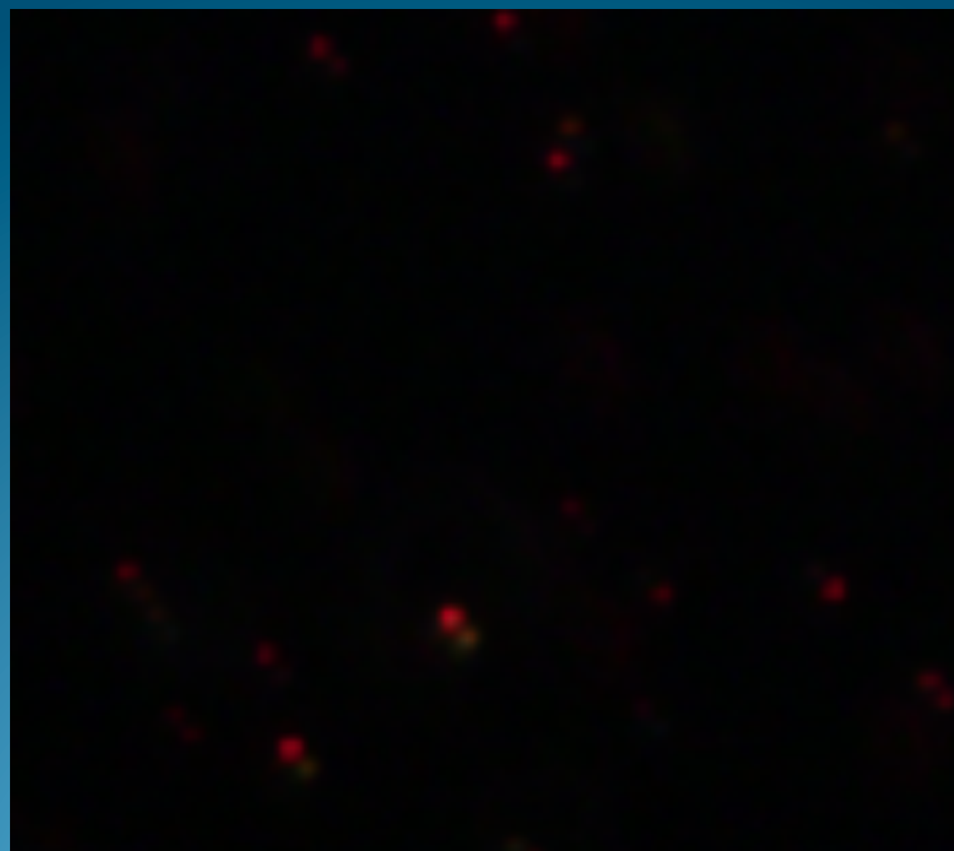
$$Q \equiv \frac{I_{ey}-I_{ex}}{I_{ey}+I_{ex}} = \frac{\sin^2\theta_e(\sin^2\phi_e-\cos^2\phi_e)}{\sin^2\theta_e(\sin^2\phi_e+\cos^2\phi_e)} = 1-2\cos^2\phi_e$$



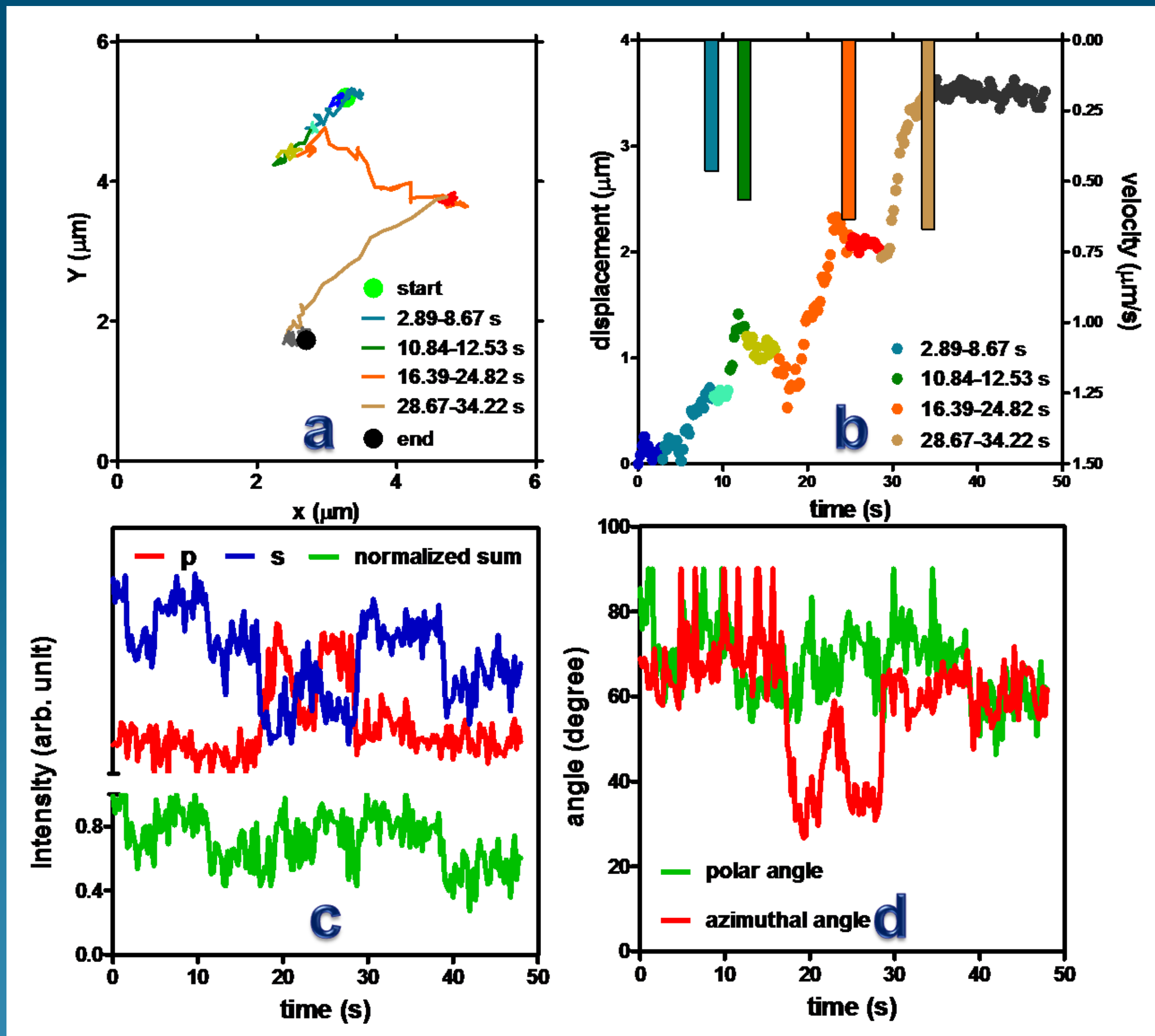
DF Polarization vs. Orientation



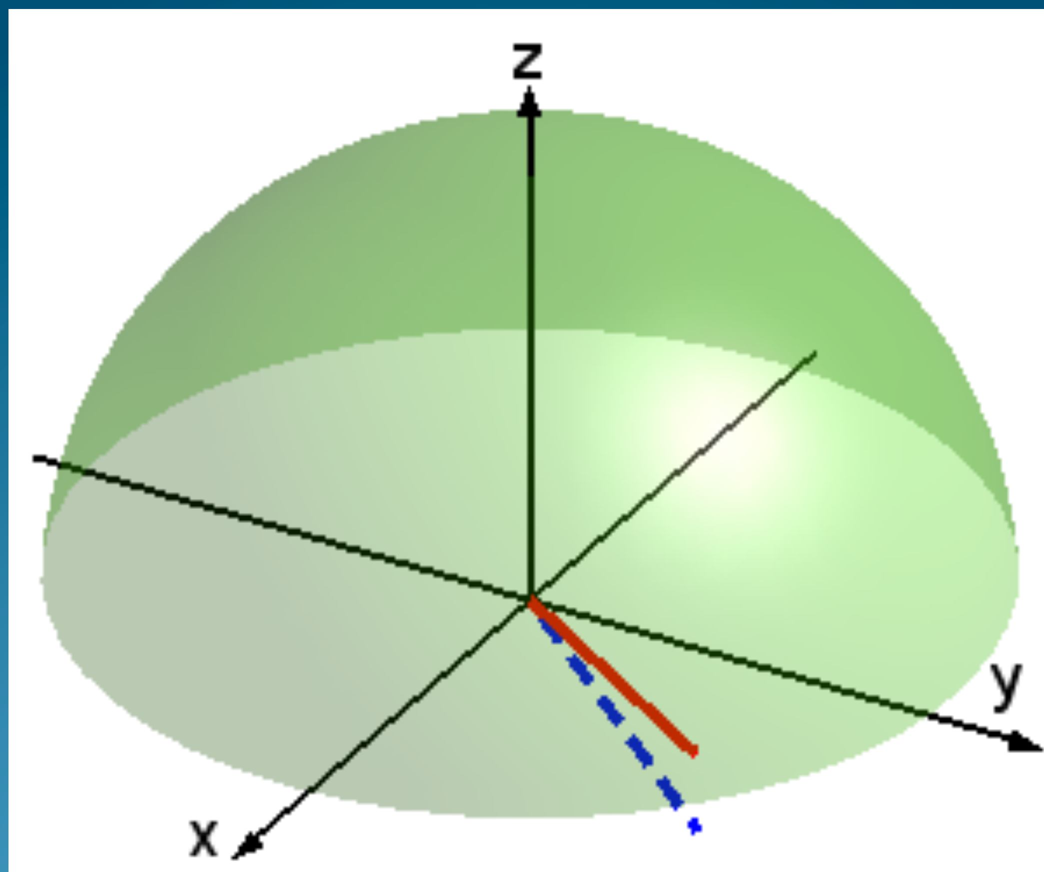
3D Orientation by Dark Field



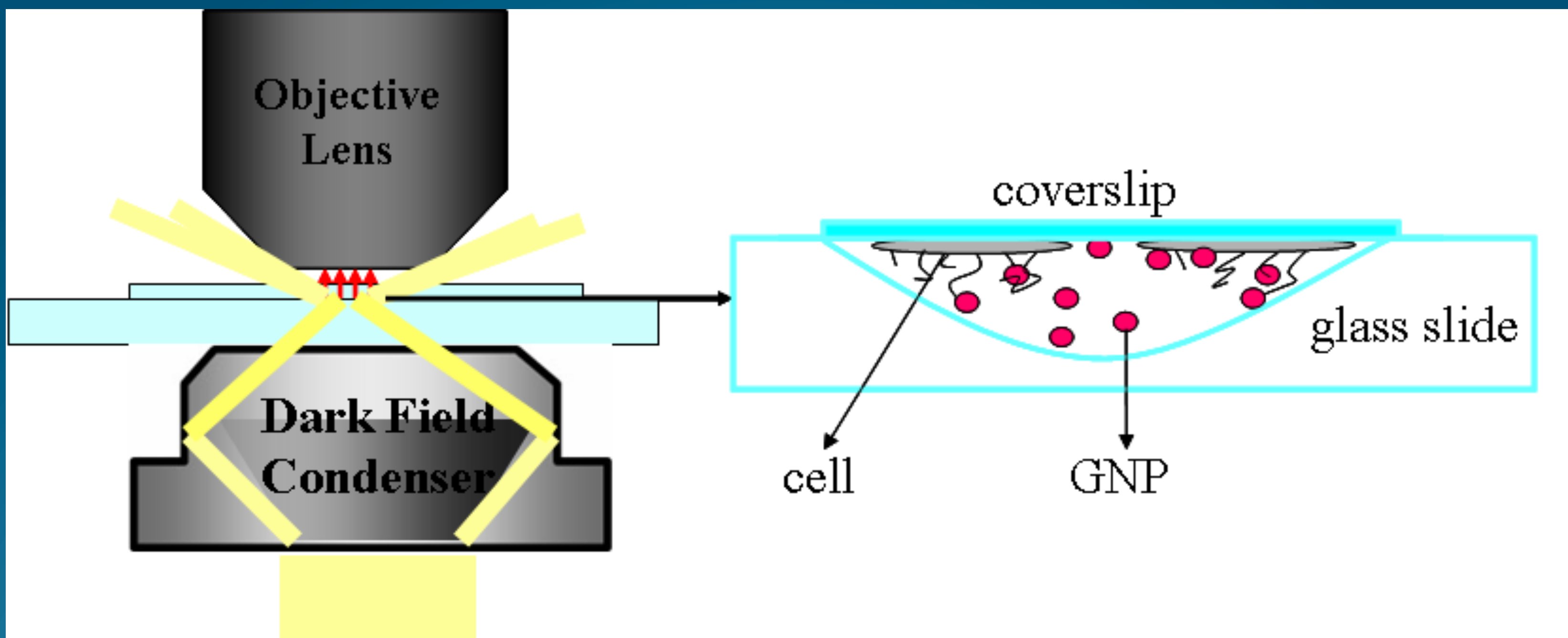
GNR Trajectory and Orientation



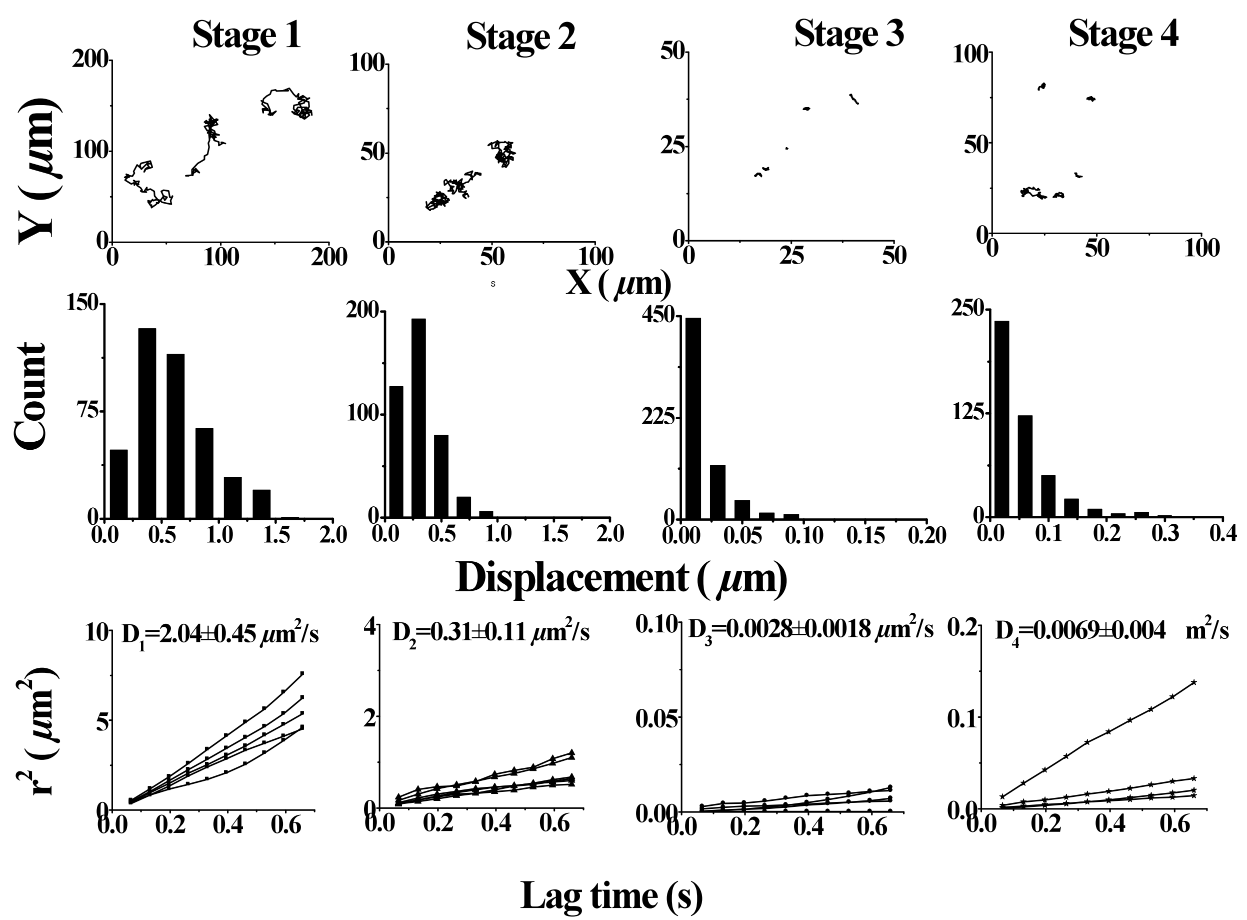
2-Color DF Microscopy: Orientation



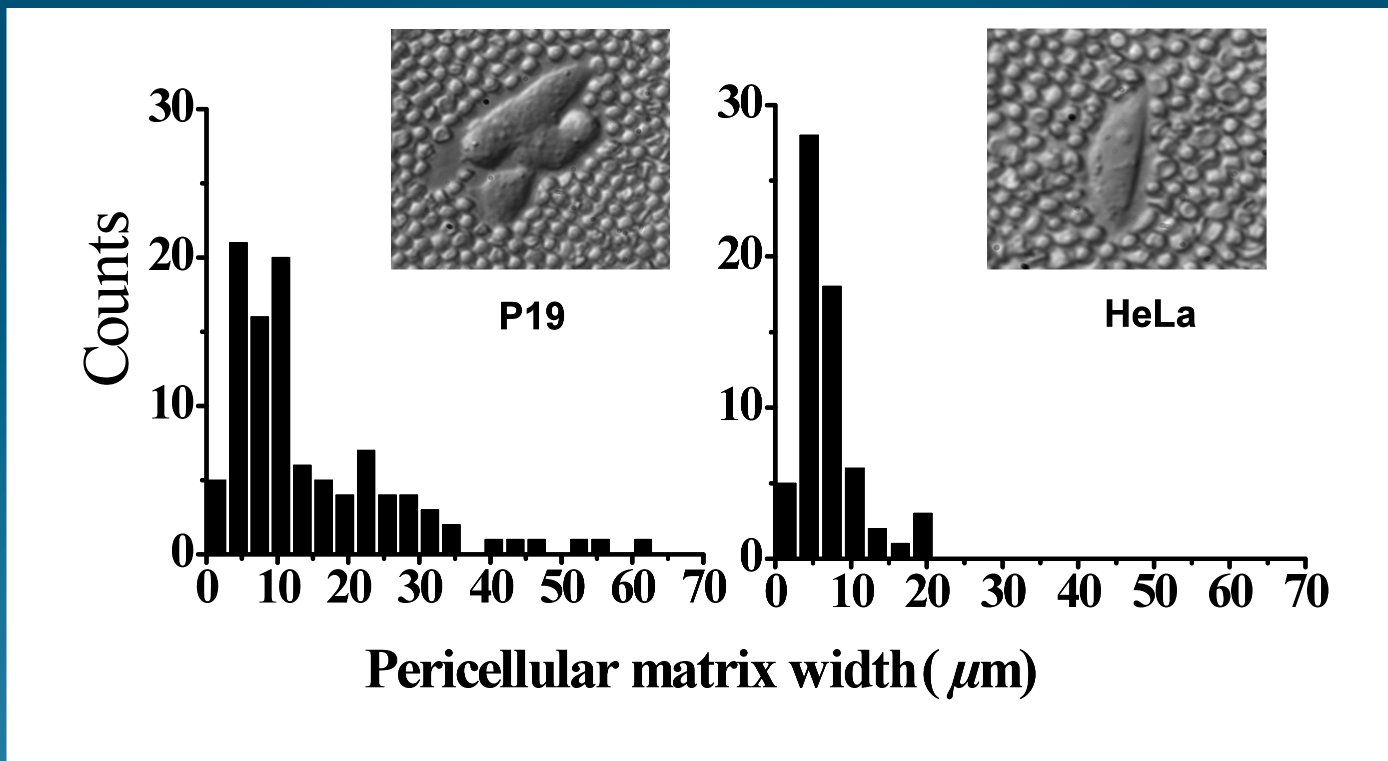
GNR Motion Near Cell Membrane

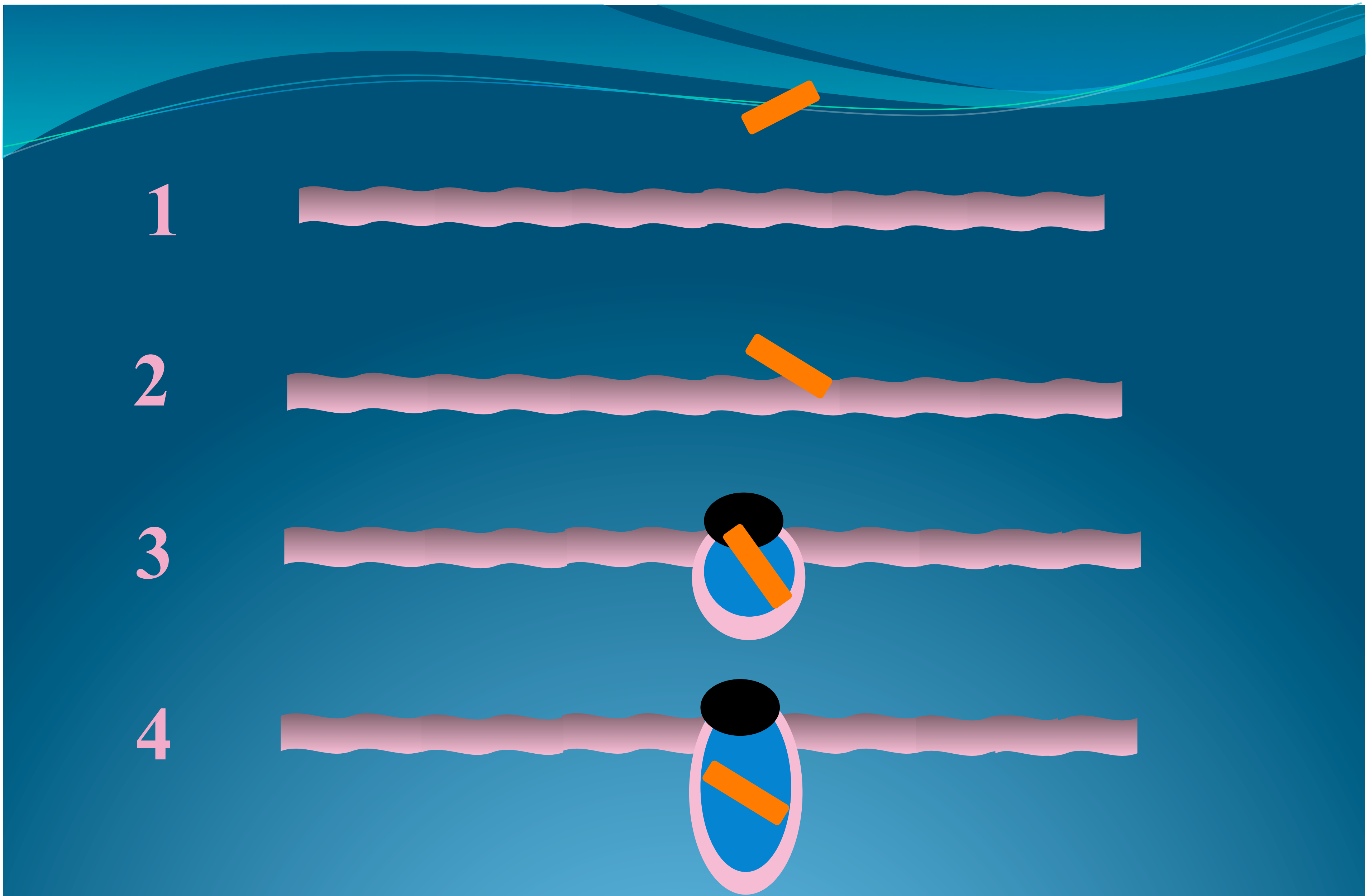


GNR Motion Near Cell Membrane



Extracellular Matrix





Biophysical Journal Volume 86 June 2004 4075–4093

Biographies and Statements

U.S. Delegates

Biography: Dr. Bharat Bhushan received an M.S. in mechanical engineering from the Massachusetts Institute of Technology in 1971, an M.S. in mechanics and a Ph.D. in mechanical engineering from the University of Colorado at Boulder in 1973 and 1976, respectively, an MBA from Rensselaer Polytechnic Institute at Troy, NY in 1980, Doctor Technicae from the University of Trondheim at Trondheim, Norway in 1990, a Doctor of Technical Sciences from the Warsaw University of Technology at Warsaw, Poland in 1996, and Doctor Honouris Causa from the National Academy of Sciences at Gomel, Belarus in 2000 and University of Kragujevac, Serbia in 2011. He is a registered professional engineer. He is presently an Ohio Eminent Scholar and The Howard D. Winbigler Professor in the College of Engineering, and the Director of the Nanoprobe Laboratory for Bio- & Nanotechnology and Biomimetics (NLB^2) at the Ohio State University, Columbus, Ohio. His research interests include fundamental studies with a focus on scanning probe techniques in the interdisciplinary areas of bio/nanotribology, bio/nanomechanics and bio/nanomaterials characterization, and applications to bio/nanotechnology and biomimetics. He is an internationally recognized expert of bio/nanotribology and bio/nanomechanics using scanning probe microscopy, and is one of the most prolific authors. He is considered by some a pioneer of the tribology and mechanics of magnetic storage devices. He has authored 7 scientific books, more than 90 handbook chapters, more than 700 scientific papers (h-index – 52+; ISI Highly Cited in Materials Science, since 2007), and more than 60 technical reports, edited more than 50 books, and holds 17 U.S. and foreign patents. He is co-editor of Springer NanoScience and Technology Series and co-editor of Microsystem Technologies. He has given more than 400 invited presentations on six continents and more than 160 keynote/plenary addresses at major international conferences.

Dr. Bhushan is an accomplished organizer. He organized the first symposium on Tribology and Mechanics of Magnetic Storage Systems in 1984 and the first international symposium on Advances in Information Storage Systems in 1990, both of which are now held annually. He is the founder of an ASME Information Storage and Processing Systems Division founded in 1993 and served as the founding chair during 1993-1998. His biography has been listed in over two dozen Who's Who books including Who's Who in the World and has received more than two dozen awards for his contributions to science and technology from professional societies, industry, and U.S. government agencies. He is also the recipient of various international fellowships including the Alexander von Humboldt Research Prize for Senior Scientists, Max Planck Foundation Research Award for Outstanding Foreign Scientists, and the Fulbright Senior Scholar Award. He is a foreign member of the International Academy of Engineering (Russia), Byelorussian Academy of Engineering and Technology and the Academy of Triboengineering of Ukraine, an honorary member of the Society of Tribologists of Belarus, a fellow of ASME, IEEE, STLE, and the New York Academy of Sciences, and a member of ASEE, Sigma Xi and Tau Beta Pi.

Dr. Bhushan has previously worked for the R & D Division of Mechanical Technology Inc., Latham, NY; the Technology Services Division of SKF Industries Inc., King of Prussia, PA; the General Products Division Laboratory of IBM Corporation, Tucson, AZ; and the Almaden Research Center of IBM Corporation, San Jose, CA. He has held visiting professor appointments at University of California at Berkeley, University of Cambridge, UK, Technical University Vienna, Austria, University of Paris, Orsay, ETH Zurich and EPFL Lausanne.

Grand Challenge: Design and modeling of nanostructured smart adhesion surfaces

Bharat Bhushan
Nanoprobe Laboratory for Bio- & Nanotechnology and Biomimetics, The Ohio State University, Columbus, OH 43210 USA

The mechanics of fibrillar adhesive surfaces of biological systems such as a lotus and a gecko is widely studied due to its unique surface properties. The Lotus leaf is a model for superhydrophobic surfaces due to its extreme water-repellent properties as well as self cleaning properties and low adhesion[1-4]. Geckos are well known for their exceptional ability to climb any wall and ceiling using their micro/nano fibrillar hierarchical structure with about a billion fibres on their feet[1,2,3,5]. The unique adhesion mechanism of geckos is based on so called division of contacts. Cumulative van der Waals attraction results in strong adhesion. In addition to strong adhesion, they have the ability to adapt to variety of surfaces, and exhibit wear resistance and self-cleaning. They can also detach via peeling action to provide reversible adhesion. A structured surface may exhibit low adhesion or high adhesion dependent upon fibrillar density and presents the possibility of realizing environmentally-friendly surface structures with tunable adhesion[6].

In one of our research thrust, an unconventional patterning technique is used to fabricate smart adhesion surfaces; single- and double-layer hierarchical synthetic adhesive structure surfaces with various fibrillar density and diameter that would allow the observation of either the lotus or gecko adhesion effects. The effect of the fibrillar array geometry on the adhesion mechanism is being studied to develop a model for surface roughness-dependent smart adhesion. Recent theoretical models of adhesion on fibrillar structures do not adequately address certain factors. For instance, in macroscale adhesion, there is a need to separately quantify shear and normal (peeling) adhesive modes. To model the normal adhesion, a glass ball attached to the AFM tip was used to obtain the adhesive forces via force-distance curves. In addition, models for fibrillar structures need to take into account the effect of humidity on the adhesion. The adhesive forces were obtained under various humidity conditions, and the adhesion mechanism of the smart adhesion surfaces was modeled taking into consideration the fibrillar geometry and humidity contributions to adhesion.

The challenge remains to develop methods to fabricate three-level hierarchical nanostructures using variety of materials for various applications.

[1]Nosonovsky, M. and Bhushan, B., *Multiscale Dissipative Mechanisms and Hierarchical Surfaces: Friction, Superhydrophobicity, and Biomimetics,* Springer-Verlag, Heidelberg, Germany, 2008.
[2]Bhushan, B., "Biomimetics: Lessons from Nature - An Overview," (invited), *Philos. Trans. R. Soc. A* 367, 1445-1486 (2009).
[3]Bhushan, B. (ed.), *Springer Handbook of Nanotechnology,* 3rd ed., Springer, Heidelberg, Germany, 2010.
[4]Bhushan, B. and Jung, Y. C., "Natural and Biomimetic Artificial Surfaces for Superhydrophobicity, Self-Cleaning, Low Adhesion, and Drag Reduction," *Prog. Mater. Sci*. **56**, 1-108 (2011).
[5]Bhushan, B., "Adhesion of Multi-level Hierarchical Attachment Systems in Gecko Feet," *J. Adh. Sci. Technol.***21**, 1213-1258 (2007).
[6]Nosonovsky, M. and Bhushan, B., "Green Tribology: Principles, Research Area, and Challenges," (invited), *Philos. Trans. R. Soc. A* **368**, 4677-4694 (2010).

Biography: Dr. Shantanu Chakrabartty received his B.Tech degree from Indian Institute of Technology, Delhi in 1996, M.S and Ph.D in Electrical Engineering from Johns Hopkins University, Baltimore, MD in 2002 and 2005 respectively. He is currently an associate professor in the department of electrical and computer engineering at Michigan State University. From 1996-1999 he was with Qualcomm Incorporated, San Diego and during 2002 he was a visiting researcher at The University of Tokyo. Dr. Chakrabartty's work covers different aspects of analog computing, in particular non-volatile circuits, and his current research interests include energy harvesting sensors and neuromorphic and hybrid circuits and systems. Dr. Chakrabartty was a Catalyst foundation fellow from 1999-2004 and is a recipient of National Science Foundation's CAREER award and Michigan State University's Teacher-Scholar Award. Dr. Chakrabartty is a senior member of the IEEE and is currently serving as the associate editor for IEEE Transactions of Biomedical Circuits and Systems, associate editor for the Advances in Artificial Neural Systems journal and a review editor for Frontiers of Neuromorphic Engineering journal.

Grand Challenge: Sensing-to-learn and Learning-to-sense – Exploiting biological symbiosis of sensing, computing, memory and adaptation for designing the next-generation of smart sensors.

Shantanu Chakrabartty
Associate Professor
Department of Electrical and Computer Engineering
Michigan State University, East Lansing, MI, USA

For ages biology has served as an inspiration to scientists and engineers but only in the last decade advancements in micro and nano fabrication technology has reached the point where ``truly" biomorphic sensors and systems can be designed that match the ``raw" sensing and computational capabilities observed biology. For instance, more than 100 silicon transistors can be packed inside a mammalian cell which is 10μm in diameter. It is now possible to fabricate piezoelectric nano-fibers whose dimensions are comparable and smaller than a cricket's or a spider's mechanoreceptors. The raw computational power of today's processor is comparable to that of the human brain. In spite of these remarkable technological advances, the performance achieved by specialized biological sensing systems makes even the most advanced man-made systems of today look crude and primitive. Therefore, current sensing technology has reached the cross-roads where biological scale devices can be fabricated, but the sensing and operational capabilities are still orders of magnitude inferior to those observed in biology. To understand how biological systems can achieve such a performance it is important to acknowledge that these systems have evolved in evolutionary environment, where energy resources were scarce and threat of predators were omnipresent. These constraints have led to remarkable designs of nature that seek to operate at fundamental limits of energy dissipation and performance. For example, the filiform hairs in crickets operate at fundamental limits of noise, the power dissipation of a mammalian cell is less than pico-watt, and the texture of shark's skin is optimized to reduce bacterial adhesion and growth. To achieve such performance, it is important to understand, what new principles can be learned from biology and then how it can be implemented, mimicked or morphed using man-made technologies.

The first grand challenge that needs to be addressed will be to achieve biological level of integration between sensing, memory, computation, actuation and communication functions. The auditory sensing epitomize this level of integration combining microfluidics, biomechanics, piezoelectrics, microelectronics and energy scavenging into a package, the size of pea. This might require advancements in multi-functional smart materials that can self-organize to perform specialized sensing tasks. Another grand challenge that needs to be addressed is to achieve the ubiquitous nature of any biological sensing system that is its inherent ability to adapt and learn not only at a cognitive level but at the level of the sensor. Learning will involve adaptation and altering the parameters or topology of the sensor over slow time-scales so that it can efficiently sense the signals of interest without dissipating too much energy and without requiring the use of precision computing or sensing devices. In this regard, most of the sensory processing in biology is inherently ``analog" and efficiency arises out of exploitation of computing and sensing primitives inherent in the device physics, like biochemical diffusion or feedback regulation. Also, unlike man-made sensors which consider device and sensor noise as nuisances, biology has evolved to use non-linear sensing techniques to exploit noise to its advantage and operate at or below fundamental limits. Thus, the concept of ``sensing-to-learn" and ``learning-to-sense" represents the need for a symbiotic understanding between biology and technology for designing the next-generation of biomorphic sensors.

Biography: Evan Chang-Siu is a PhD candidate at the University of California Berkeley. He also holds both a masters and bachelors degree in Mechanical Engineering at the University of California Berkeley. His current research interests are in the bio-inspired design of terrestrial robotics. More specifically, he is focused on uncovering and understanding the dynamic principles and behaviors involved in the multifunctional tail of a lizard and incorporating these novel behaviors into the next generation of search and rescue robots in order to improve their response times in hazardous, time-critical situations, and complex environments. Evan Chang-Siu is working closely with Professor Tomizuka and Professor Robert Full in an effort to bridge the gap between engineering and biology. He is currently a CiBER-IGERT NSF trainee, which is focused on bio-inspired motion systems in complex environments.

Grand Challenge: Improving Terrestrial Locomotion through Bio-inspired Tail Actuator

Evan H. Chang-Siu
PhD Candidate
Department of Mechanical Engineering
University of California Berkeley, Berkeley, CA, USA

One of the major difficulties that terrestrial robots face is in *quickly* overcoming complex terrain and completing transitions between different height and shape substrates. These difficulties can either completely inhibit the desired path or severely slow down the progress of a terrestrial robot. When quickly overcoming complex terrain, the obstacles can cause intermittent perturbations, which produce undesired aerial phases. When attempting to quickly transition, the ability to achieve a desired final orientation and compensate for initial perturbations is not always easy.

Treaded robots have been well developed to slowly overcome complex terrain. The new frontier for speeding up this task is through legged robots. However, at high speed, they can still be perturbed from their desired body orientation. Robot designs for climbing walls have also been accomplished, but quickly transitioning to a wall is still troublesome. The main limitation in all these types of robots is their sole dependence on affecting body posture only through robot-ground interaction. When the ground conditions are unknown, unpredictable results can occur.

Biology contains key inspiration that can be useful for this purpose; active tails, which can provide a more predictable control method. By the law of conservation of angular momentum, appendages have been used for their dynamic inertial properties to stabilize and control orientation in many biological systems; human gymnasts, skaters, skiers, falling cats, and even gliding lizards. Lizards have been discovered to use their largest inertial appendage, the tail, to stabilize their body pitch angle when faced with varying perturbations and for targeting.

We hypothesize that by adding an actuated and dynamic multi-functional tail-like limb to terrestrial mobile robots, they too can achieve improved stability when faced with perturbations or improved maneuverability when attempting to redirect their body posture. In this way, robot designers can improve upon limbs that were solely purposed for other tasks such as substrate contact.

The design challenge in this field will be in optimally selecting the best inertial, mass, and length parameters as well as developing the low level and high level control that will be involved in the myriad of tasks that the future of terrestrial robotics will face.

Biography: Daniel Ebert is a Ph.D. candidate in Mechanical Engineering at The Ohio State University. He received a B.S. in Mechanical Engineering from Ohio State in 2008. While in graduate school, he has interned at Hong Kong Polytechnic University (in 2008) and the Air Force Research Laboratory's Directed Energy Directorate (in 2010). He is currently working with Professor Bharat Bhushan in the fabrication of durable bio-inspired surfaces with extreme or unique wettability properties, such as the so-called "Lotus Effect."

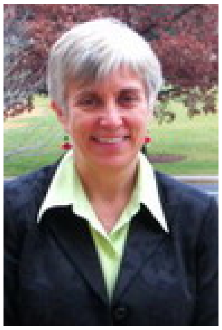
Grand Challenge: Fabrication of Durable Bio-inspired Surfaces with Special Wettability Properties

Daniel Ebert
Ph.D. Candidate
Department of Mechanical and Aerospace Engineering
The Ohio State University, Columbus, OH, USA

Surface wettability is of crucial importance as nanotechnology begins to permeate virtually all areas of modern life. Wetting of surfaces has been studied as far back as the 19^{th} century, but only since the inventions of the atomic force microscope (AFM) and scanning electron microscope (SEM) in the 1980s has the study of the nanoscale mechanisms responsible for extreme wetting behaviors been possible. For example, it was discovered that a dual-scale roughness of micro- and nanosized bumps gives the Lotus leaf its remarkable water repellency. Nanotechnology now allows us to imitate these natural phenomena to create surfaces with extreme wetting properties that are of growing engineering interest.

At small length scales, the domination of surface forces dictates careful study and optimization of surface properties. The affinity for water to spread on or repel from a surface becomes a central design parameter in many applications, such as in microchannels in MEMS devices, where fluid drag tends to be very high. As research in biosensors, lab-on-chip technology, and other microdevices progresses, manipulation of small droplets and intelligent control of fluid flow will be paramount.

The red rose petal (superhydrophobic with high droplet adhesion), the rice leaf (directional wettability), and the aforementioned Lotus leaf (superhydrophobic with self-cleaning effect) are just a few examples of natural surfaces that have generated significant interest. However, research in creating bio-inspired surfaces to take advantage of these properties is still in its early stages. In addition, many of the surfaces created thus far are not mechanically robust, which is generally necessary for real-world applications. The fabrication and characterization of durable bio-inspired surfaces with special wettability is therefore an important challenge for engineers and scientists as nanotechnology progresses.



Biography: Prof. Alison Flatau is a Professor of Aerospace Engineering and Director of the Aerospace Engineering Undergraduate Program at the University of Maryland. She holds a B.S.E. in Chemical Engineering from the University of Connecticut and M.S. and Ph.D. in Mechanical Engineering from the University of Utah. She joined Department of Aerospace Engineering at the University of Maryland in 2002 after serving as Program Director for the Dynamic Systems Modeling, Sensing and Control Program at the National Science Foundation from 1998-2002. Prior to that, she was on the Aerospace Engineering and Engineering Mechanics faculty at Iowa State University (1990-1998). Her experience also includes four years at the National Small Wind Systems Test Center in Golden, CO where she was a Senior Research Engineer in the Test Program. Her research interests are in dynamics of smart structures, with emphasis on actuator and sensor technologies and their application in noise, vibration and position control applied to rotorcraft and other aerospace systems. One of her key research areas is the development and application of magnetostrictive material actuators and sensors. A second research area is on the application of smart transduction materials in micro-systems, including synthetic jet design and bio-inspired micro- and nano-sensors. As the author of over 30 archival journal and book chapter contributions, Dr. Flatau currently serves as an Assistant Editor for the *Journal of Smart Structures and Materials* and she is the PI on a large team Multidisciplinary University Research Initiative (MURI) program on Structural Magnetostrictive Alloys.

Grand Challenge Research on BioSensors – Avoiding Information Overload

Alison Flatau
Professor
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There are countless aspects of biological systems that intrigue and inspire engineers and scientists. As an Aerospace Engineer, historical connections to bioactuation form the foundation of our field. Mimicry of the heavier-than-air, flight capabilities of biological systems date to ancient Greek myths and tales of Icarus and to Leonardo DaVinci's famous 15th century sketches of ornithopters. The Wright brothers and many of their peers literally credit years of studying avian models (bird-watching) for providing key insights and the essential understanding of flight control systems inherent in the designs that lead to their first successful manned flights. Within the past century, both evolutionary and revolutionary technology advances have enabled flight capabilities seen in jumbo jets, the space shuttle and hypersonic X-planes, systems that perform missions far removed from those of their predecessors. Yet, biological models continue to inspire creative new directions for aeronautical research, as demonstrated by major NASA and DARPA investments in morphing vehicle technologies and in (low Reynolds number) micro-air vehicles. We have over a century of experience in drawing inspiration from the macroscale behaviors of biological systems. With good reason, though, we remain in awe of the integrated sensing, decision-making, control and actuation capabilities of biological models.

Advanced MEMs and NEMs sensor systems offer means for increasing sensor density, and the quantity and quality of sensed information. However as implemented, they often provide only incremental performance gains associated with miniaturization of sensors and over-sampling of information needed only intermittently, and introduce the associated challenges of acquiring, digitizing, assimilating and storing many more channels of sensed information than previously possible. Somewhere short of creating a brain, and/or embedding artificial intelligence or cognition in inanimate objects, lie enormous opportunities for: *1) developing and validating models of the biological and biochemical processes with which biological systems efficiently manage large quantities of time-varying and spatially-distributed sensory information and 2) transitioning these processes to engineered (man-made) systems***.**

Over the past decade, the proliferation of here-to-fore unavailable instruments for studying biological, bioelectrical and biochemical processes in-vitro, in-vivo, and at the nanoscale offer unique capabilities needed for moving beyond miniaturization of macroscale sensor and actuator concepts. This will lead to revolutionary insights for implementing integrated nanotechnology-based components made possible through comprehension of biosensor and bioactuator processes. Returning to avian models, birds are continually processing information about their flight environment and coordinating their wing, body, tail feathers, feet and head positions to achieve immediate flight performance objectives in response to gusts and/or moving targets. The primary gust detection mechanism in birds is associated with the ability to sense wind direction as gusts ruffling the feathers stimulate distributed sensory receptors located in the skin around the base of their feathers. At a macroscopic scale, this might reduce to a feed-forward control loop process in which vision is the input sensor guiding and updating the brain/controller commands to wing muscles as needed to achieve maneuvering objectives. Yet little is understood of the biochemical and bioelectrical responses to sensing the distributed gust responses or visual cues of moving prey and subsequent processing of the significant quantities of time and spatially varying data that would at other times be irrelevant to the flight objective and ignored. Fascinating opportunities exist for drawing upon new insights into biosensors for changing how we design sensor arrays, choose the information to collect and prioritize processing of sensed information.

Biography: Robert J. Full, Chancellor's and Goldman Professor of Integrative Biology. Professor Full completed his undergraduate studies at SUNY Buffalo in 1979. He also did his graduate work at SUNY Buffalo, receiving a master's degree in 1982 and a doctoral degree in 1984. He held a research and teaching postdoctoral position at The University of Chicago from 1984 to 1986. In 1986 he joined the faculty of the University of California at Berkeley as an Assistant Professor of Zoology. He was promoted to Associate Professor of Integrative Biology in 1991, and to Full Professor of Integrative Biology in 1995, a position he holds today. Professor Full received a Presidential Young Investigator Award, has presented his research at the National Academy of Sciences and is a National Academy of Sciences Mentor in the Life Sciences.

In his 25 years at Berkeley, he has led a focused international effort to demonstrate the value of integrative biology and biological inspiration by the formation of interdisciplinary collaborations of biologists, engineers, mathematicians and computer scientists from academia and industry. Professor Full serves on the advisory boards of Harvard's Bio-inspired Design Wyss Institute, Research Corporation for Science Advancement, Science Education for New Civic Engagements and Responsibilities and the editorial board of the journal *Bioinspiration and Biomimetics*.

Professor Full is founder and director of CiBER, the Center for interdisciplinary Bio-inspiration in Education and Research focused on discovering fundamental principles of biology that inspire novel engineering and where engineers provide biologists with new hypotheses, approaches and techniques. The center has 32 faculty from 7 departments. Professor is the Principal Investigator on an NSF Integrative Graduate Education and Research Traineeship on Bio- and Bio-inspired Motion Systems Operating in Complex Environments that is training the next generation of biologists and engineers to collaborate in mutually beneficial relationships. Professor Full directs the Poly-PEDAL Laboratory, which studies the Performance, Energetics and Dynamics of Animal Locomotion (PEDAL) in many-footed creatures (Poly). His research program in comparative physiology and biomechanics has shown how examining a diversity of animals can lead to the discovery of general principles. His fundamental discoveries in animal locomotion have inspired the design of novel neural control circuits, artificial muscles, sensors, autonomous legged robots such as RHex, Sprawl, RiSE and Stickybot and the first, synthetic self-cleaning dry adhesive named one of top ten nanotechnology patents. Professor Full has authored over two hundred contributions and has delivered over three hundred national and international presentations.

Grand Challenge: Cautions on Extracting Principles from Nature to Inspire the Design of Sensors and Actuators

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Biological Inspiration is the use of principles and analogies from biology when advantageous to generate novel designs through integration with the best human engineering. Now more than ever before, nature can instruct us on how to best use new materials and manufacturing processes discovered by engineers, because these human technologies have more of the characteristics of life. Nowhere is this more evident than with respect to sensors and actuators. Natural technologies use an enormous number of small, robust sensors and actuators, whereas until now natural technologies have used few.

Yet, translating Nature's design ideas to devices remains challenging. Engineers seeking to benefit from this frontier should question whether the inspiration from biologists is a mere metaphor or a fundamental principle. Nature provides useful hints of what is possible and design ideas that may have escaped our consideration. Given the unique process of biological evolution and its associated constraints, identifying, quantifying and communicating these design ideas is demanding. Biologists offering advice need not only understand principles of structure and function, but use their knowledge of phylogenetic analysis, behavior and ecology to extract potentially valuable design ideas. Engineers should not blindly copy designs. We must remember that biological evolution works on the "just good enough" principle. Organisms are not optimally designed and natural selection is not engineering. Engineers often have final goals, whereas biological evolution does not. Organisms must do a multitude of tasks, whereas in engineering executing far fewer tasks will do. As a result, "trade-offs" are the rule, severe constraints are pervasive and global optimality rare in biological systems. Biological evolution has brought us amazingly functional and adaptive designs. However, biological evolution works more as a tinkerer than an engineer. The tinkerer never really knows what they will produce and uses everything at their disposal to make something workable. Organisms carry with them the baggage of their history. Therefore, they must co-opt the parts they have for new functions. Organisms are not an optimal product of engineering, but "a patchwork of odd sets pieced together when and where opportunities arose". Natural selection is constrained to work with the pre-existing materials inherited from an ancestor. Engineers can start from scratch and select the optimal raw materials and tools for the task desired, natural selection cannot. Organisms are not optimally adapted for the environment in which they reside. Biological evolution can't keep pace with the changing environments because not all phenotypic variation is heritable and if selection were too strong it could easily produce extinction. Natural selection can't anticipate major changes in environments. Behavior can evolve more quickly than morphology and physiology leading to mismatches. Engineers can optimize for one or a few environments and choose to add appropriate safety factors as dictated by previous experience.

Given these cautions and opportunities, principles can be extracted that can give actuators multi-functionality, greater force, faster velocities, more power over a great range of lengths and sensors small size, light-weight, increased sensitivity, function over a broad range and greater robustness.

Biography: Dr. Mory Gharib is Vice Provost for Research and the Hans W. Liepmann Professor of Aeronautics and Professor of Bio-Inspired Engineering at the California Institute of Technology. He received his B.S. degree in Mechanical Engineering from Tehran University (1975) and then pursued his graduate studies at Syracuse University (M.S., 1978, Aerospace and Mechanical Engineering) and Caltech (Ph.D., 1983, Aeronautics). After two years as a senior scientist at the Jet Propulsion Laboratory (NASA/CIT), he joined the faculty of the Applied Mechanics and Engineering Sciences Department at UCSD in 1985. He became a full professor of fluid mechanics in 1992 and, in January 1993, he joined Caltech as a professor of aeronautics. Dr. Gharib's current research interests include bio-inspired engineering for the development of medical devices, wind energy harvesting and propulsion systems. His other active projects include the development of advanced 3-D imaging systems, and nano and micro-fluidics. His biomechanics work includes studies of the human cardiovascular system and physiological machines. Dr. Gharib's honors and affiliations include: Fellow, American association for the advancement of science (AAAS), Fellow, American Physical Society (APS), Fellow, American Society of Mechanical Engineering (ASME), He has received 5 new technology recognition awards from NASA in the fields of advanced laser imaging and nanotechnology. For his 3-D imaging camera system, he has received R&D Magazine's "R&D 100 innovation award" for one of the best invention of the year 2008. Dr. Gharib holds 180 publications in refereed journal and 45 U.S. Patents.

Grand Challenge

Morteza Gharib
Professor
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Biological systems have learned through over three billion years of evolution to achieve local and global solutions to a variety of challenges. On the one hand, we can learn from these systems. On the other hand, evolution has occurred in the context of constraints that are different that those placed on engineered systems, and we can hope to improve on some of the evolved systems. Knowledge of diverse epigenetic factors is beginning to indicate the amazing flexibility of these systems' design that allows them to adapt to environmental conditions (evolvability). An example to mention is the case of embryonic heart valve growth where the onset of growth depends on the dynamics of blood flow as a shear inducing factor. Understanding the principles that allow flexibility based on sensing and feedback in response to epigenetic factors will provide unique and previously untapped sources of information from biology to guide engineering and will subsequently allow us to engineer robust components based on controllable epigenetic factors (at the level of molecules, gene networks, and organelles) to be used in clinical and industrial applications.

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Biography: Yingzi Lin is an Associate Professor with the Department of Mechanical and Industrial Engineering, Northeastern University, Boston, where she directs the Intelligent Human-Machine Systems Laboratory and co-directs the Virtual Environments Laboratory. In the prior year she was an Assistant Professor in the Concordia Institute for Information Systems Engineering at Concordia University, Montreal, Canada. She received a Ph.D. in mechanical engineering from the University of Saskatchewan (Saskatoon, Canada), and another Ph.D. in vehicle engineering from China Agricultural University (Beijing, China). Her research has been funded by the National Science Foundation (NSF), Natural Sciences and Engineering Research Council of Canada (NSERC), and major industries. She is a recipient of a few prestigious research awards, including a NSF CAREER award and a NSERC UFA (University Faculty Award). She has published over 100 technical papers in referred journals and conference proceedings. Her area of expertise includes: intelligent human-machine systems, smart structures and systems, sensors and sensing systems, multimodality information fusion, human machine interface design, and human friendly mechatronics.

Dr. Lin was the Chair of the Virtual Environments Technical Group of the Human Factors and Ergonomics Society (HFES) from 11/2007 to 11/2010. She is on committees of the Transportation Research Board (TRB) of the National Academy of Sciences: Committee on Simulation and Measurement of Vehicle and Operator Performance (AND30); Committee on Vehicle User Characteristics (AND10). She is also on the program committee of the SPIE Smart Structure/NDE Conference, Conference on Sensors and Smart Structures Technologies for Civil, Mechanical, and Aerospace Systems since Mar. 2010. She serves as an Associate Editor of the *IEEE Trans. on Systems, Man and Cybernetics - Part A: Systems and Humans*, and *Structural Health Monitoring: An International Journal*. In addition, Professor Lin has been a reviewer for many professional journals and conferences. She has also been on the organizing committee of a number of professional meetings in the areas of Advanced Sensors, Mechatronic Systems, Dynamic Systems and Control, and Advanced Smart Materials and Smart Structures. She served as the Workshop Chair of the 2011 American Control Conference (ACC); Chair for Local Arrangement of the 2010 IFAC Symposium on Mechatronic Systems, held jointly with 2010 ASME Dynamic Systems and Control; Chair for Invited Sessions of the 2009 ASME Dynamic Systems and Control Conference (DSCC); Conference Secretariat of the 2009 The Fifth International Workshop on Advanced Smart Materials and Smart Structures Technology (ANCRiSST). She was the host of the 2008 New England Chapter of the Human Factors and Ergonomics Society Student Conference.

Grand Challenge: Biosensing in Human-Machine Interactions

Yingzi Lin
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Northeastern University, Boston, USA

Human-Machine Systems are pervasive in our society. In particular, operator-machine interaction systems are one of the most sophisticated human-machine systems and also a safety critical system that has a great impact on human lives, public safety and society. Broadly speaking, any machine system should be viewed as a human-machine system, as they are always operated or used by a human. However, the current machine systems have not fully addressed human aspects, such as human cognitive and/or emotional states. Machines often come equipped with sensors and gauges so the human operator is aware of what state the machine is running in. There are currently very few machines equipped with sensors to give the machine awareness of the user's state. Development of such sensors will move human machine "operation" closer to human machine "collaboration." Specifically, the following fundamental research problems need to be investigated in great depth:

(1) how to measure human cues naturally and non-intrusively? An awareness or annoyance from cue measurement can alter the state of mind of the operator, producing "false cues." With that in mind, the most accurate method of measurement is the least intrusive method.

(2) how to infer human's state from the cues? Psychophysiological studies have proven a link between human state and the activity of the Autonomic Nervous System (ANS). Using these fundamentals, human state can be inferred though measurement of physiological states such as heart and respiration rate.

(3) how to assist the human based on the information obtained from the above? Enabling machine awareness of human cognitive state will allow the machine to adjust settings to better suit the user to increase efficiency or prevent harm, or to provide useful feedback/suggestions for the user.

Following the momentum generated by the NSF initiative on biosensing and bioactuation, Dr. Lin targets her research program on non-intrusive biosensor technology and cognitive inference algorithms, which include the systematic study and development of biosensors and of test beds. This program will lay a foundation for a new discipline – Bridging cognitive science and sensor technology. Dr. Lin has been trained and worked on this interdisciplinary field in the past years and published over a hundred articles, which provide evidence of both the usefulness and feasibility of this new area. Her research has consistently moved forward in the general areas of human-machine interface design sensor development, information fusion, and cognitive states inference. With her preliminary work covering the general areas and with her diverse knowledge related to the field, she is very confident with her unique position.

Drawing upon bio-inspired cognitive concepts, Dr. Lin's long term goal is to establish this interdisciplinary field of human-machine systems, with a major focus on bio-sensing systems, which are applied to human systems. Research of micro- and nanofabrication technologies in Dr. Lin's lab has proven the feasibility of biosensor design that can naturally and non-intrusively detect human cues. During operation, the human user almost always has to come into contact with the machine at specific points. The development of thin, flexible sensors that can cover these specific points will enable measurement through natural contact, which is almost completely non-intrusive. One of such sensors that take advantage of micro-fabrication processes has been developed for proof of concept. Dr. Lin's research group will continue to examine the above research problems and use the research results to further solidify her current efforts and lead to groundbreaking results in the human-machine systems.

Biography: Dr. Yang Liu is a research fellow in the Department of Civil and Environmental Engineering at the University of Michigan. Dr. Liu completed his graduate studies at Michigan State University where he received his Ph.D. in Electrical Engineering in 2010. Prior to attending Michigan State University, Dr. Liu received his M.S. degree in electrical engineering from Institute of Intelligent Machines, Chinese Academy of Sciences, Hefei, in 2004 and he received his B.S. degree in Electrical Engineering from Hefei University of Technology, Hefei, China, in 2001. His current research interests include carbon nanotube based thin film sensor design, bioelectronics and biosensors, hybrid biological/solid-state devices, and mixed-signal very-large scale integrated design for biomedical and life science applications. Dr. Liu also actively pursues entrepreneurship and he was a recipient of "The Entrepreneurial Faculty for the 21st Century University" fellowship, 2008–2009, awarded by Michigan State University. Dr. Liu is a member of Sigma Xi. He is a member of US-China Association of High-level Professionals.

Grand Challenge: The Next Generation of Hybrid Biological/Solid-State Sensing Devices

Yang Liu
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In many areas of science and technology, biological systems represent ideal prototypes whose performance is still unmatched by human-engineered systems. For example, one of the remarkable biophysical phenomena observed in nature is the ability of migratory birds and certain species of fishes to be able to accurately navigate using earth's magnetic field which is as low as 50 micro Tesla. Several recent anatomical studies have discovered cryptochrome mediated photochemical reactions in bird's eye which produce spin-correlated radical pairs acting as the primary sensor in a magnetic field-dependent signaling cascade. The question is can we build a human-engineered systems, which exploit the nanoscale, ultra-sensitive magnetoreceptive phenomenon observed in biology to design next generation biosensing devices that demonstrate detection sensitivity superior than the existing state-of-the-art? To solve this problem, we need to bring together researchers from the field of biochemistry, biosystems engineering, information theory, and integrated circuits and we need to train a new breed of researcher capable of crossing the bio/nano/info boundaries and for developing next generation bio-inspired sensors and systems.

However, with advances in nanotechnology and micro-fabrication technology, it is now possible not only to monitor the biological processes at macro, micro and nano-scales but also to seamlessly integrate synthetic nano-microsystems with biological units. I believe that creating a symbiotic relationship between the world of biology and human-engineered systems is the key towards achieving “biological level” performance while ensuring “synthetic level” reliability. It is at this interface I believe will play a key role in addressing some of the important technological challenges in the next decades.

One example of hybrid biological/solid state sensing devices is to conjugate biological entities with solid-state circuits. Inherent electrical properties of biological entities (e.g DNA carries intrinsic negative charges) make their interface with solid-state circuits feasible and promising. For instance the biological entity could be used for improving the detection of desired targets (antigens and proteins) whereas the solid-state circuit can process the signal acquired from the interface to improve/enhance the detection reliability. Possible future research in this area will focus on the role of CMOS in sensing and actuation in direct contact with a biological recognition layer, which will lead to the design of hybrid biological/solid-state devices. For example, interfacing magnetotactic bacteria (MTB) with silicon could integrate memory and actuation with applications in life-sciences and sensor design. In future research, DNA and Aptamers electronics can appear because of their high specificity and affinity, which can improve the performance of bioelectronics. The beauty of DNA electronics lies in the fact that it uses the techniques of genetic engineering which nature has perfected under harsh conditions over billions of years. This new research area is highly interdisciplinary, merging physics, biology, engineering and so on, to use individual DNA molecules for producing a new range of electronic devices that are much smaller, faster and more energy-efficient than the present semiconductor-based electronic devices.

Biography: Dr. Kenneth Loh is an Assistant Professor of Civil and Environmental Engineering at the University of California, Davis; he is also a member of the Department of Mechanical and Aerospace Engineering graduate group. Dr. Loh is also the director of his research laboratory, the Nano-Engineering and Smart Structures Technologies (NESST) Laboratory. Dr. Loh completed his graduate studies at the University of Michigan, Ann Arbor where he received his Ph.D. in Civil Engineering in 2008, M.S. in Civil Engineering in 2005, and a second M.S. in Materials Science and Engineering in 2008. Prior to attending the University of Michigan, Dr. Loh received his B.S. in Civil Engineering from Johns Hopkins University in Baltimore, MD. The overarching goal of Dr. Loh's research is to enhance structural performance, integrity, and serviceability using new materials and multifunctional systems. Specifically, his current research interests are in the areas of multifunctional and bio-inspired materials, nanocomposite sensors and actuators, wireless sensors and sensor networks, and alternative energy systems. Some of Dr. Loh's more current research has been focused on developing bio-inspired photocurrent-based thin film sensors, carbon nanotube sensing skins for spatial structural sensing, and piezoelectric zinc oxide-based sensors/actuators.

Grand Challenges

Kenneth J. Loh
Department of Civil & Environmental Engineering
University of California, Davis

Recent advancements in the nanotechnology domain have brought forth a plethora of novel nanomaterials (*e.g.*, nanotubes, nanowires, nanoparticles, quantum dots, among others) and materials' fabrication methodologies. When combined with state-of-the-art nano- and micro-imaging and analyses techniques (*e.g.*, scanning tunneling microscopy (STM), tunneling electron microscopy (TEM), Raman spectroscopy, among others), a new generation of hybrid materials and high-performance multifunctional systems have emerged. For instance, by intentionally manipulating molecular structures and orientations, a variety of sensing and actuation transduction mechanisms can be encoded within multi-component nanocomposite architectures to create high-performance piezoresistive, piezoelectric, thermoelectric, or self-healing systems.

In addition to creating higher performance multifunctional systems, the versatility of nano- and micro-fabrication have permitted the design and fabrication of bio-inspired and biomimetic structures that far exceed the performance of current-generation devices. Nature has successfully demonstrated that its creations balance between various unique materials, assemblies, and architectures to achieve optimal performance and functionality. For example, human skins are inherently multifunctional (*i.e.*, capable of multi-modal sensing, actuation, healing, among others), birds can fly and change its wing structure under different conditions, and amphibians possess unique respiratory structures that allow them to adapt to both aquatic and land environments. As a result, advanced material systems such as the morphing wing for improving aerodynamic performance, artificial hair cells for monitoring fluid flow, and self-healing cementitious composites are some of the attempts that have been proposed to imitate the various functions observed in nature's creations. Despite the recent progress in developing bio-inspired material systems, the performance of these artificial structures cannot match their biological counterparts. Particularly, the current generation of bio-inspired structures only seeks to mimic biological function through the use of materials and technologies that are drastically different than those offered by nature.

Thus, so as to match and even exceed the performance of biological structures, further developments in the bio-nanotechnology field of study is direly needed. Not only should bio-inspiration be drawn to mimic the final performance of the material, but also, the design, fabrication, and assembly of next generation sensors and actuators should also follow biological and cellular assembly of nanostructures and functional molecules. By unlocking the mysteries of how nature assembles its complex and unique structures (*e.g.*, filiform hairs, muscles, wings, among others) beginning at cellular length scales, one can mimic bio-manufacturing and further enhance or tailor its performance for the desired application. Understanding the interactions between all components of complex biological structures can also enhance the feasibility to imitate and create novel and sophisticated bio-sensors/actuators. It is expected that future self-assembly fabrication techniques will be autonomously driven by DNA-like coded instruction sets already built into the molecular structure of materials and the fabrication environment.

Biography: Dr. Jerome Lynch is an Associate Professor of Civil and Environmental Engineering at the University of Michigan; he is also holds a courtesy faculty appointment with the Department of Electrical Engineering and Computer Science. Dr. Lynch completed his graduate studies at Stanford University where he received his PhD in Civil and Environmental Engineering in 2002, MS in Civil and Environmental Engineering in 1998, and MS in Electrical Engineering in 2003. Prior to attending Stanford, Dr. Lynch received his BE in Civil and Environmental Engineering from the Cooper Union in New York City. His current research interests are in the areas of wireless structural monitoring, feedback control systems, and sustainable built environments. Specifically, Dr. Lynch's work aims towards addressing challenging problems associated with the health of aging infrastructure systems and the performance of infrastructure during and after natural hazard events. Some of Dr. Lynch's more current research has been focused on the design of building automation systems based on wireless decentralized control architectures. Dr. Lynch was recently awarded the 2005 Office of Naval Research Young Investigator Award, 2007 University of Michigan Henry Russel Award, 2008 College of Engineering (University of Michigan) 1938E Award, 2009 NSF CAREER Award and the 2010 Rackham Distinguished Faculty Award. He was also featured by Popular Science magazine in their 2009 "Brilliant 10" annual issue.

Grand Challenge: Learning and Mimicking Biological Systems for Next-Generation Sensors and Actuators for Health Monitoring of Civil Infrastructure Systems

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Department of Electrical Engineering and Computer Science
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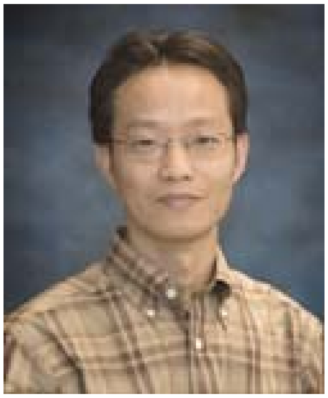
By definition, engineering is the profession engaged in "*the application of science for directly useful purposes, as construction, propulsion, communication or manufacture*"(Oxford 2002). The engineering fields have for the past three centuries adopted scientific understanding and discovery from many of the natural sciences including physics and chemistry. Consider the case of sensors; some of our oldest sensor concepts are derived from the laws and concepts of physics. For example, force-balanced accelerometers use inertial masses coupled with electrical feedback circuits to measure acceleration. In the late 1970's, a complete paradigm shift emerged within the engineering field due to the emergence of miniaturization technologies based on integrated circuit technology; technologies including microelectromechanical system (MEMS) were strongly influenced by the field of chemistry. For example, MEMS accelerometers made from thin film poly-silicon allow the sensor to be small and low-cost, yet accurate and reliable. The one field of science that remains to be explored is biology. Bio-inspired sensing and bio-inspired actuation (BSBA) represent an exciting and unexplored opportunity as we look to design and manufacture a new generation of sensors and actuators for the protection of civil infrastructure systems.

Nature has evolved to offer a rich set of sensing and actuation capabilities that can be found at all length-scales in life. Borrowing concepts from or mimicking nature can lead to exciting new sensor and actuation technologies applicable to the field of structural health monitoring. What has renewed recent interest in biomimicry has been the availability of technological tools that allow scientists to explore matter and life at atomistic length-scales. Nanotechnology allows for bioelectrical and biochemical processes to be observed at the cellular-level; such insight promises to yield advances in the design of future engineered systems. Recent discoveries made at the nano-scale are leading to a more comprehensive understanding of how nature yields living organisms with impressive sensing and actuation mechanisms at the macro-scale. Insight to how nature elevates functionality up length scales is also inspiring researchers to adopt "bottom-up" assembly techniques to new materials.

There is a pressing need for new paradigms that advance the current state-of-art in the smart structure field. While great advances have been made on many technological fronts, there still remain few implementations of SHM systems in operational civil and mechanical engineering structures. One factor for this may be the limitations inherent to current sensor technologies. For example, sensors in common use do not detect damage directly; rather, sensors make measurement of structural responses with physics based models necessary to correlate measurements to damage states. Given the many complexities inherent to this inverse problem, robust algorithms that are generically applicable have yet to be devised. Another shortcoming in sensors is that they are point based devices. To accurately identify damage which can be spatially distributed, a dense network of point based sensors coupled with analytical models are necessary to extrapolate point measurements to the entirety of the instrumented component. Through the mimicking of biological systems, it is highly likely the engineering profession will be able to offer sensors that can detect damage directly, can provide a spatial context to their measurements and still below cost and easy to fabricate. Opportunities also exist to mimic the social interaction of animals to rapidly advance the algorithmic tools necessary to make decisions based on the sensor data generated.



Biography: Dr. David Ma is an Associate Professor of Civil and Environmental Engineering at the University of Hawaii at Manoa. Dr. Ma completed his graduate studies at University of California, Santa Barbara, where he received his PhD in Mechanical Engineering and MS in Electrical and Computer Engineering both in 2003. Prior to attending University of California, Dr. Ma received his MS in Design Theory from University of Science and Technology, Beijing, and his BE in Naval Architecture and Ocean Engineering from Shanghai Jiao Tong University, China. His current research interests are in the areas of structural control and monitoring, system identification, and smart sensor technology. Some of Dr. Ma's more current research has been focused on harvesting energy from ambient structural vibrations.

Grand Challenge: Adaptive Energy Harvesting:
A Grand Challenge in Bio-Inspired, Self-sustained Sensing/Actuation Systems

David T. Ma, Associate Professor
Department of Civil & Environmental Engineering
University of Hawaii at Manoa

While continuously advancing technology keeps bringing engineering systems to higher levels, biological systems, which seem to be stationary in a macroscopic sense, are still far more complex and superior in many aspects. A "simple" biological system contains numerous fundamental units with various functions (e.g. cells), and yet, these units work seamlessly and efficiently to provide desired functionality of the system. Learning from biological systems is beneficial to the development of future engineering systems.

One of the features of biological systems that has been longed for in engineering systems is self-sustainability. A living biological system has the capability of obtaining energy from the environment to power its functionality. Furthermore, it often can adjust its energy collection and consumption in an efficient way depending on the environment and need. For an engineering system, be it sensing or actuation, self-sustainability is key for it to become truly autonomous, long lasting and maintenance free.

While there have been significant advances in the area of harvesting energy from the environment, the efficiency and effectiveness of current energy harvesting technology are still limited. Especially for applications in uncertain environments, adaptivity, although crucial to energy harvesting performance, has not yet received much attention. Thus, there is an imperative need to invest in the area of adaptive energy harvesting technology. Successful research in this area has the potential of breaking the bottleneck of current energy harvesting technology; it will provide a solid foundation for the development of next-generation smart sensing and actuation systems.

Biography: Dr. Gerard Marriott received his PhD from the University of Illinois in 1987 under Gregorio Weber, a pioneer in fluorescence spectroscopy. He was awarded postdoctoral fellowships from the Alexander von Humboldt Stiftung and the Japan Society for the Promotion of Science to study with Profs. Thomas Jovin (Max Planck Institute, MPI) and Kazuhiko Kinosita (Keio University), respectively. Marriott was appointed C3-professor at the MPI for Biochemistry in Martinsried in 1992. He was recruited to the University of Wisconsin-Madison in 1999 to lead a Biophotonics initiative and remained there as a full professor of Physiology until 2009. Marriott joined the Department of Bioengineering at UC-Berkeley in 2009 as a full professor, and as staff scientist in the physical biosciences division at the Lawrence Berkeley National Laboratory. He is a guest professor at both Tsinghua University Graduate School and South East University, China. His research interests centre on understanding the molecular basis of protein function during cell motility and muscle contraction. A parallel program is focused on developing tools that will allow for controlled assembly of proteins and hybrid materials in vivo and in artificial cells. These studies are being advanced through the development of new imaging techniques and optical probes. His research program is currently supported by grants from the NIH and the NCI.

Grand Challenge: Developing new molecular tools, tool-kits and design principles for the generation and regulation of biomimetic systems

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The performance of proteins, biomaterials, and multi-component entities including cells, tissues and organisms serve as a source of inspiration and benchmarks for biomimetic products and biomaterials. Energy, health and nanomedicine and biomaterials are key target areas for bio-inspired engineering. One of the grand challenges in this emerging area of bioengineering requires developing modular molecular tools that collectively endow the product with specific properties from a broad palette of synthetic molecules, genes, proteins and hybrid nanomaterials. A related challenge is to develop molecular tool-kits that allow engineers to automate the selection and integration of these modular tools into natural and hybrid materials. The availability of these tools and tool-kits will greatly accelerate the discovery, optimization and production of bio-inspired drugs and materials. Some advantages of bio-inspired engineering and associated challenges are highlighted as below.

Bioenergy and high-worth organic products: Even the lowly bacterium holds secrets for engineers embarking on the design, construction and performance of nanoscale machines, bioreactors and hybrid materials that convert light or biomass into biofuels and natural polymers. Biofuels and polymers production could be generated cheaply and locally, reducing impacts on the environment and climate.

Drugs and Nanomedicine: Natural products already provide inspiration and guidance for the development of drugs to treat diseases in humans, animals and plants. These drugs are usually produced with low efficiency using organic chemistry. Advances in synthetic biology however, allow for high-yield production of drugs such as *artemesin* in E. coli from component genes and abundant precursors.

Biomaterials: The application of stem cells to treat human disease and related health conditions requires a complete understanding of the factors that lead to the differentiation and organization of the stem cell into the desired cell or tissue type. The environment in which these cells grow is critical for robust differentiation and bio-inspired materials are being developed to mimic these complex environments. These materials must also consider both the chemical composition and diffusive characteristics of the polymer surrounding the stem cell and the role that molecular force in the matrix plays in determining cell fate. This is a complex problem since forces are both exerted on the matrix by the cell for example during contraction while the matrix exerts force on the cell that changes during its remodeling by the cell.

Self-organizing systems and regulation: A key feature of biological systems is their ability to sense and adapt to changes in their environment. Regulation is facilitated by the biological structures themselves, which are self-organizing and undergo quasi-continuous cycles of assembly and disassembly. It is hard to imagine how a macro-scale machine such as a lathe periodically and automatically breaking down to its component nuts and bolts and then spontaneously reassemble in order to ensure optimal performance. Building this property into a bio-inspired structure requires continuous probing of the system with key signal levels initiating the disassembly and reconstruction without human intervention. Another grand challenge one can identify in our quest to exploit bio-inspired engineering will be to design and integrate optical-based multiscale sensing, regulation and self-organizing and repair functions into the system.

Biography: Matt McHenry is interested in the sensory biology and biomechanics of aquatic animals. He is an Assistant Professor of Ecology and Evolutionary Biology at the University of California, Irvine. His graduate study on the scaling of swimming hydrodynamics was conducted under the guidance of M.A.R. Koehl at the U.C. Berkeley. After receiving his Ph.D. in Integrative Biology, Matt began study on the biomechanics of flow sensing by the lateral line system of fish when he was supported by a Bioinformatics Postdoctoral Fellowship from the National Science Foundation. This research was conducted in collaboration with George Lauder at Harvard University and Seitse van Netten at the University of Groningen in the Netherlands. Matt established his laboratory 2005 and has since continued his investigations on flow sensing and the biomechanics of locomotion. His research is currently supported by a CAREER grant from the National Science Foundation.

Grand Challenge: Biological research for biologically-inspired engineering

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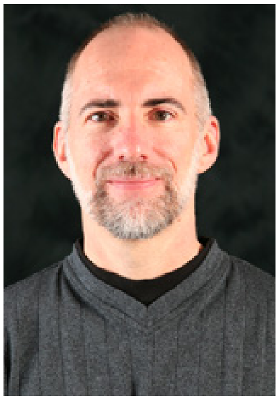
The sensory and motor performance of animals may be the envy of engineers, but nature's design secrets may be hard to discern from the biological literature. The complexity of biological systems certainly challenges biological investigators. However, I would argue that we biologists generally do not organize our investigations or communicate our findings in a manner that is conducive to the development of improved sensor or actuator design. This could mean that biologists are missing a receptive audience for their work and that engineers may not be aware of many of nature's solutions that are commonly understood by biologists. Some measures offer the potential to aid in bridging biological research on muscles and sensory systems to bio-inspired engineering. Journals and conferences on bio-inspiration offer a common forum for communication. Cross-disciplinary funding opportunities provide incentive for common-cause research. Biologists may be able to offer the engineering community more if they were made more aware of the grand challenges in bio-inspired engineering.



Biography: Dr. Mark Nelson is a Professor of Molecular & Integrative Physiology at the University of Illinois, Urbana-Champaign (UIUC). He is also a member of the UIUC Neuroscience program, the Biophysics & Computational Biology program and the Bioengineering program. Dr. Nelson is a full-time faculty member in the Beckman Institute, where he heads the Electrosensory Signal Processing Laboratory, serves as group leader for the Beckman NeuroTech group, and co-chairs the Biological Intelligence research theme. Professor Nelson received his Ph.D. in Physics from the University of California, Berkeley in 1983, completed postdoctoral training in Physics and Computational Neurobiology at Caltech in 1990, and has been a faculty member at UIUC since 1991. His areas of professional interest are computational neuroscience, neural coding, and biological signal processing. His research focuses on the electrosensory system of weakly electric fish as a model system for understanding the neural mechanisms and computational principles that animals use to actively acquire sensory information in complex, dynamic environments. Dr. Nelson is a Fellow of the American Association for the Advancement of Science.

Grand Challenge: Harnessing the Capabilities of Smart Mobile Devices to Create a Bio-inspired Infrastructure for Adaptive Emergency Response

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In nature, animals are constantly confronted with time-critical decisions that impact their chances of survival. Similarly, time-critical decisions must be made in human society in the aftermath of major disasters, such as earthquakes, typhoons, wildfires, and terrorist attacks. A grand challenge for bio-inspired engineering is to leverage insights from biological communications and information processing networks to enable rapid, efficient, and adaptive acquisition and communication of mission-critical information in the first few hours after a major disaster. Success in this domain would contribute directly to saving lives and reducing injury to both disaster victims and first responders.

A bio-inspired approach to the problem would draw on systems-level information processing principles from neurobiology as well as distributed task management in social insect societies to create adaptive, self-organizing communications networks for optimally sensing, encoding, communicating and responding to complex, dynamic emergency situations. These bio-inspired engineering principles could be applied to a broad range of problems in which sensing and communications networks are needed to rapidly inform, assess and coordinate large groups of individuals (campus emergency response scenarios, mass transit disruptions, widespread power outages, breakdown of communications infrastructure, emergency evacuations at airports, stadiums, high-rise buildings, etc.). The development of such an engineering framework would require cross-disciplinary teams of researchers with expertise in neurobiology, animal behavior, civil engineering, computer science, and emergency response management.

Such a framework could be implemented in part by harnessing the computing and communications capabilities of smart mobile devices. Cell phones represent a ubiquitous, but under-utilized resource for adaptive emergency response. Indeed, the number of mobile phone subscriptions worldwide is approximately 5 billion, which is approximately 70 percent the world's population. In major metropolitan areas, disaster victims are almost always in close proximity to one or more cellular phones. However, the existing emergency communications infrastructure does not make good use of the inherent sensing and networking capabilities of these mobile devices. The current solution for obtaining information from disaster victims is the universal emergency phone system (US 911, Japan 119), which works well for isolated, small-scale emergency events, but can easily become overloaded in major disasters.

In a bio-inspired framework, the inherent communication and computation capabilities of individual cell phone nodes could be utilized in analogy to the individual neurons in the brain. Like neurons, cell phones are capable of establishing local connections with their neighbors (through ad-hoc networking) as well as longer-distance connections with distant targets (via internet and cell tower infrastructure). Cell phones also have a variety of sensor input capabilities (e.g. sound, video, location, motion sensing) that have analogies with the sensory capabilities of biological systems. These analogies can provide useful guidance in translating information processing principles from biological systems to engineering solutions for efficient acquisition, filtering and transmission of task-relevant information in emergency response scenarios.

Biography: Dr. Manuel L. B. Palacio is a senior research scientist at the Nanoprobe Laboratory for Bio- & Nanotechnology and Biomimetics (NLBB) at the Department of Mechanical and Aerospace Engineering of the Ohio State University. He received his Ph.D. in Materials Science and Engineering from the University of Minnesota in 2004. Prior to this, he obtained his B.S. in Chemistry from the University of the Philippines. Dr. Palacio's research interests include the mechanical properties of materials, nanotribological properties of surfaces, and the applicability of polymers as biomaterials. To date, he has published over thirty articles in these research areas. One of his publications has been recognized as among the most cited articles in Elsevier's *Journal of Colloid and Interface Science* from 2008-2009.

Grand Challenge: Block Copolymers as Platforms for Bioinspired Biosensing Systems

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Porous materials are of interest as biomolecular encapsulants in biosensors due to their large surface area. Moreover, they have the ability to confine biomolecules such as proteins, enzymes and antibodies, which is thought to simulate the crowded environment of living cells. There are numerous experimental studies that have demonstrated that this confinement can maintain the native state of biomolecules, which is a necessary condition for the proper operation of biosensor devices. However, there are also studies that indicate how certain confining materials can denature biomolecular structures.

Block copolymers composed of known biocompatible blocks are attractive as materials for biosensors due to their ability to form nanostructures, which can be tuned by modulating the block composition and arrangement. These materials have been demonstrated to facilitate the native conformation of proteins. Porosity can be introduced on block copolymers with the appropriate synthesis and processing conditions. Therefore, block copolymers are attractive as a class of materials for immobilizing biomolecules in a biologically inspired biosensing platform. Therefore, one of the grand challenges in the development of bioinspired biosensing systems is to establish the viability of block copolymers as materials that can provide the appropriate morphology and enable the immobilization of biomolecules in their native conformation. More fundamental research will be needed to establish empirical guidelines on controlling block copolymer surface morphology. Addressing this challenge would also entail the development of experimental approaches for the immobilization of biomolecules, with the goal of obtaining an improved understanding of the factors that influence their conformational variation when confined in a biomaterial.

Biography: Courtney A. Peckens is a doctoral student in Civil and Environmental Engineering at the University of Michigan. Courtney obtained a M.S. degree from the University of Michigan in Civil and Environmental Engineering in 2008 and is also currently working toward completion of a M.S. degree in Electrical Engineering. Prior to attending the University of Michigan, Courtney received her B.S. degree in Mechanical Engineering from Hope College in Holland, Michigan. Courtney's primary research interests include wireless sensing networks for structural health monitoring applications and specifically, distributed computing architectures in wireless sensing units.

Grand Challenge: Drawing Inspiration from Biological Systems for Next-generation Sensors in Civil Infrastructure

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Humans have always looked to nature when attempting to solve engineering problems. One of the earliest examples of bio-inspired engineering was Leonardo da Vinci's attempt to create a "flying machine" by drawing inspiration from the anatomy and flight techniques of birds. The later successful Wright Brothers also studied various birds in flight while perfecting their airplane design. Nature is a natural source of inspiration because biological systems have been functioning efficiently and robustly for centuries. In addition, over the past several decades the field of biology has made great advances in their understanding of the natural world, making it a prime time for engineers to draw inspiration from biological concepts in their own systems. One area of engineering that will benefit from bio-inspired systems is the field of structural health monitoring (SHM). While SHM has made many advances over the last several years, there are still few implementations of SHM systems in civil engineering applications. Although there are many factors for this, one limitation of SHM systems may be in the data collection and processing techniques used by the sensors.

Biological systems are extremely efficient and robust for sensing and processing data. In particular, the biological nervous system represents a highly efficient method of sensing and transmitting information from the external world through a condensed format. Additionally, the system is capable of aggregating information from various sources and actuating based on the perceived external stimulus. The system is able to accomplish this entire process in a relatively small amount of time. If sensors used in SHM utilized the same mechanisms that are used in biological sensors the overall system would be more efficient and have the capability of operating without any processing latencies. Additionally, biological systems often collect and process data from a dense array of sensors and use algorithmic mechanisms to process and actuate on the provided information. SHM sensors are often point based which limits the depth of information that can be collected about the system. Engineers should draw inspiration from these biological data processing capabilities to create dense arrays of SHM sensors that are also capable of easily processing vast amount of information. Thus biological systems present a natural source of inspiration for engineering sensors and if properly mimicked many engineering deficiencies can be overcome.

Biography: Dr. Philen is currently an Assistant Professor in the Department of Aerospace and Ocean Engineering at Virginia Polytechnic Institute and State University. His research interests focus on biomimetic systems, adaptive structures, and smart materials. He has published over thirty papers in the areas of structural health monitoring, biologically inspired systems, structural vibration control, adaptive optics, and active control of variable stiffness structures. He is a member of AIAA, ASME, and ASEE. He established the Aerospace Structures and Materials Laboratory, which is a state-of-the-art facility used for both education and research. He recently received a $1.95 million NSF Emerging Frontiers in Research and Innovation (NSF 08-599) grant under the subtopic BioSensing & BioActuation: Interface of Living and Engineered Systems (BSBA). This project is a collaborative research effort in the design and development of advanced material systems having distributed sensing, actuation, and intelligent control inspired by fish. He received the 2009 ASME Adaptive Structures and Material Systems Best Paper Award in Structural Dynamics and Control (coauthor). He also received the *2011 Dean's Award for Excellence in Teaching*, *2010 Dean's Award for Outstanding Assistant Professor,* and the *2009 Certificate of Teaching Excellence*.

Grand Challenge: Bio-Inspired Sensors: Making sensors smaller

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In recent years, researchers have been looking towards nanotechnology for creating new and societally important bio-inspired sensors. The advancements made in nanotechnology and our greater understanding of biology has provided new opportunities for developing advanced sensors. Developing a sensor with the robustness, efficiency, and sensitivity found in biology will have a profound effect on our society and will lead to new advancements in medical, industrial, and military technologies. For example, bio-inspired nanosensors could provide for real-time diagnostics of patients, early detection and treatment of currently incurable diseases, airborne chemical or other toxin detection, artificial hairs for sensing in advanced prosthetics, and new robotic devices to perform minimally invasive and micro surgeries. These nanosensors can lead to a new class of autonomous vehicles such as micro-aerial and underwater vehicles that can sense surrounding changes in the fluid for object tracking and performance optimization.

As inspired by the olfactory systems of mammals and insects, Andrei Kolmakov, an assistant professor at Southern Illinois University at Carbondale, and his group are developing 'e-noses' that utilize electron transport through nanowires for creating electronic devices that can discriminate between various gases (Sysoev, 2006). Similarly, Dr. Lehui Lu, a professor at the Changchun Institute of Applied Chemistry, and his team are developing simple, environmentally friendly, and highly sensitive sensors for detecting cyanide in water using gold nanoclusters (Liu, 2010). Recently, an interdisplinary team consisting of researchers from Virginia Tech, Harvard University, and Drexel University are developing state-of-the-art sensors inspired by the mechanosensory lateral line system that allows fish to locate, track, form hydrodynamic images of the environment, and perform complex schooling maneuvers.

Achieving a paradigm shift in the development of bioinspired sensors within the next 10 to 20 years requires that multidisciplinary teams consisting of biologists, scientists, and engineers work together to transform the concepts and operating principles found in nature into technologies and engineered systems. More fundamental research and integrative thinking among biologists, scientists, and engineers along with advancements made in nanotechnology with provide the foundation for developing the next generation of sensors which will be smaller, exhibit increased sensitivity and robustness, and consume less power. By making sensors smaller and better, there will be new and exciting opportunities for revolutionizing the quality of life.

Biography: Donghyeon Ryu is a PhD Candidate of Civil and Environmental Engineering at the University of California, Davis. Prior to attending UC Davis, he received his MS in Civil and Environmental Engineering in 2008 at Yonsei University in Seoul, South Korea. He also obtained his BS in Civil and Environmental Engineering from Yonsei University. His current research interests reside in the areas of bio-inspired multifunctional material systems, optoelectronic nanocomposite characterization and optimization, and nanomaterials synthesis and optimization. Especially, Mr. Ryu is focusing on developing a photosynthesis-inspired multifunctional monitoring system using optoelectronic nanocomposites. In addition, he is conducting research on metal nanoparticles-based optical sensing thin film. Mr. Ryu was currently awarded the 2010 NSF Micro and Nano Scale Phenomena in Tribology Fellowship.

Grand Challenge: Application of Bio-Inspired Sensors and Actuators for Large-Scale Civil Infrastructures

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Civil engineers have been contributed to the quality of life by building large-scale civil infrastructures (*e.g.*, bridges, tunnels, and dams). However, the infrastructures are aged and damaged by diverse types of external stimuli (*e.g.*, earthquake, impact, fatigue, and corrosion). If the structures are not timely inspected and maintained, there should be catastrophic disasters imposing huge cost on public society. For preventing the disaster, the civil infrastructures are visually inspected based on the regular schedule. Although the visual inspection is widely employed in the civil infrastructures inspection, it is limited due to subjective evaluation, unreachable location, and high labor cost. Therefore, many interdisciplinary research groups have vigorously proposed diverse types of novel sensors (*e.g.*, wireless, ultrasound-based, piezoresistive nanocomposite-based sensor). Nevertheless, the novel type sensors are still disadvantageous due to high energy demand and large form factor. Consequently, there is a pressing need to find a new paradigm in order to overcome the aforementioned bottlenecks. In contrast, nature has been evolved its creatures into the most efficient sensing body. Therefore, the biological principles have been arising as the most promising candidate for solving the encountered limitations.

Likewise the bio-inspired sensors in the other fields, the bio-inspired sensors in civil engineering are advanced by employing the biological sensing concepts. For example, the high energy demand can be solved by using photonic energy from abundant sun light by mimicking plant photosynthetic reaction. Also, human skin is inspiring researchers to advance the current point-based sensors to the two dimensional spatial sensors. Furthermore, the multifunctional sensing capacity of human skin inspires civil engineers to develop the multifunctional sensors for monitoring civil infrastructures. The state-of-the-art bio-inspired sensors use "bottom-up" methodology for engineering the novel bio-inspired sensors by mimicking biological membranes. In consequence, nano-scale materials are used for assembling the higher-scale structures for embedding the sensing capacities inspired from biological systems. Also, micro- or nano-scale fabrication techniques are employed during the sensor fabrication procedure. However, contrary to the sensors for mechanical and biological structures, the sensors for civil structures are required to be instrumented on the mega structures. However, the current state "bottom-up" assembly methodology is still limited for deploying the sensors to the large-scale civil structures due to high fabrication cost for nanomaterials and complicated fabrication process. Due to the limitations, the bio-inspired sensors are not widely used in civil infrastructures. *Therefore, the grand challenge encountered while developing bio-inspired sensors can be defined as the high cost and complicated fabrication procedure.*

Also, a lot of novel bio-inspired actuators have been proposed by several researchers. Among them, vibration controlling system with a shape memory alloy is inspired by carnivorous plant reaction on the external stimuli. In practice, the shape memory alloy-based actuators have been developed for controlling civil infrastructures exposed to seismic forces. However, the bio-inspired actuator applications for civil structures are limited likewise the bio-inspired sensors. *The scarce application can be attributed to mainly two reasons: 1) heavy weight and 2) brittle structural members. Accordingly, the grand challenge for the bio-inspired actuator can be two intrinsic properties of civil infrastructures.*

Biography: Spencer, Jr. received his Ph.D. in theoretical and applied mechanics from the University of Illinois at Urbana-Champaign in 1985. He worked on the faculty at the University of Notre Dame for 17 years before returning to the University of Illinois at Urbana-Champaign, where he currently holds the Nathan M. and Anne M. Newmark Endowed Chair in Civil Engineering and is the Director of the Newmark Structural Engineering Laboratory. His research has been primarily in the areas of smart structures, fatigue reliability, stochastic computational mechanics, and natural hazard mitigation. He is a Fellow of ASCE, an elected Foreign Member of the Polish Academy of Sciences, the North American Editor in Chief of Smart Structures and Systems, and the president of the Asia-Pacific Network of Centers for Research in Smart Structures Technology.

Grand Challenge: Smart Sensing Technology: A New Paradigm for Structural Health Monitoring

Dr. B.F. Spencer, Jr.

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The ability to continuously monitor the integrity of civil infrastructure in real-time offers the opportunity to reduce maintenance and inspection costs, while providing for increased safety to the public. Furthermore, after natural disasters, it is imperative that emergency facilities and evacuation routes, including bridges and highways, be assessed for safety. Addressing all of these issues is the objective of structural health monitoring (SHM).

Smart sensors densely distributed over structures can provide rich information for structural health monitoring using their sensing, computational, and wireless communication capabilities. Though smart sensor technology has seen substantial advances during recent years, implementation of smart sensors on full-scale structures has been limited; interdisciplinary efforts to address issues in sensors, networks, and application specific algorithms have only now begun to germinate. Following an overview of these issues, a new paradigm for structural health monitoring employing a network of smart sensors will be presented. Because of its ability to meet the demands of data intensive applications such as SHM, Intel's Imote2 is adopted for this research. The performance of the proposed SHM system is first evaluated through experimental studies employing a three-dimensional truss structure. Subsequently, full-scale implementation on a historic bridge in Mahomet, Illinois is conducted. The system is investigated from the sensing, network, and SHM algorithmic perspectives and shown to perform effectively.

Biography: William Stewart is a PhD graduate student in the department of Ecology and Evolutionary Biology at the University of California, Irvine. William received a BS and MS in Biology from Old Dominion University in Norfolk, VA. His research has focused on biomechanics in fluid environments, including the locomotion and sensory biology of aquatic animals. William is currently studying the sensory abilities of fishes during predator-prey interactions. Specifically, he is interested in the sensory signals that alert prey fish to approaching predators, and how predator detection facilitates evasion.

Grand Challenge: Matching the flow sensing abilities of fishes in bio-inspired applications

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Recent studies in sensory biology and biomechanics are revealing the extensive flow sensing abilities of fishes. Using a series of flow-sensitive receptors located along the body, collectively known as the lateral line system, fishes can detect and respond to nearby water motions. Fishes employ this flow sensing ability during a diverse suite of behaviors, such as predator detection, prey localization, rheotaxis (body orientation to water currents), and navigation. While the lateral line system has been acknowledged for some time, recent studies are revealing an incredible sensitivity of the system when detecting flow stimuli. For example, blind cave fish lack vision and use the lateral line to successfully navigate through complex environments while avoiding obstacles. Other studies have shown that fishes can detect the location and behavior of complex flow stimuli, such as vortices, as they interact with the body.

The high sensitivity of the lateral line system is especially evident during predator-prey interactions. While many have assumed that prey fish most often detect predators visually, my colleagues and I, in a present study, are finding that larval fish primarily use the lateral line to detect predators, even in light conditions. Furthermore, prey fish often respond to an approaching predator quite early, before the predator has come into close proximity or even opened the mouth during a strike. In spite of this, prey fish rarely respond to unimportant water motions in the background. These findings attest to the lateral line's ability to detect subtle stimuli generated by a relatively distant predator, and a fish's ability to distinguish important flow stimuli generated by predators from other flows in the environment.

In light of these findings, we face a grand engineering challenge to mimic the sensitivity and precision of the fish lateral line in bio-inspired sensors. While flow sensors resembling the receptors of the fish lateral line have been developed to monitor the direction and velocity of water motions along surfaces, we must develop more sophisticated sensor systems with increased sensitivity and an improved ability to recognize and distinguish different, complex water motions. Such systems would facilitate in the navigation of underwater vehicles, or the detection of moving underwater objects in dark conditions. With the fish lateral line as inspiration, we can implement this "sixth sense" in engineering applications that is employed so well in fishes.

Biography: Masayoshi Tomizuka was born in Tokyo, Japan in 1946. He received his B.S. and M.S. degrees in Mechanical Engineering from Keio University, Tokyo, Japan and his Ph. D. degree in Mechanical Engineering from the Massachusetts Institute of Technology in February 1974. In 1974, he joined the faculty of the Department of Mechanical Engineering at the University of California at Berkeley, where he currently holds the Cheryl and John Neerhout, Jr., Distinguished Professorship Chair and serves as Executive Associate Dean of Engineering. He teaches courses in dynamic systems and controls. His current research interests are optimal and adaptive control, digital control, signal processing, motion control, and control problems related to robotics and rehabilitation, vehicles and mechatronic systems. He served as Program Director of the Dynamic Systems and Control Program of the National Science Foundation (2002-2004). He has supervised more than 90 PhD students to completion. He has published over 550 articles in professional journals and conference proceedings.

He served as Technical Editor of the ASME Journal of Dynamic Systems, Measurement and Control, J-DSMC (1988-93), Editor-in-Chief of the IEEE/ASME Transactions on Mechatronics (1997-99), and Associate Editor of the Journal of the International Federation of Automatic Control (IFAC), Automatica. He served as President of the American Automatic Control Council (AACC) (1998-99), and he currently chairs the IFAC Technical Committee on Mechatronic Systems. He is a Fellow of the ASME, the Institute of Electric and Electronics Engineers (IEEE) and the Society of Manufacturing Engineers. He is the recipient of the J-DSMC Best Paper Award (1995, 2010), the DSCD Outstanding Investigator Award (1996), the Charles Russ Richards Memorial Award (ASME, 1997), the Rufus Oldenburger Medal (ASME, 2002) and the John R. Ragazzini Award (AACC, 2006).

Grand Challenge: Cross Disciplinary Collaboration toward Bio-inspired Engineering Systems for Betterment of Society and Human Life – Workshop Organizer's Point of View

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Sensing and actuation technologies play a key role in the design, construction and operation of modern engineering systems. Sensing technologies are generally defined to include sensing transducers, sensor networking architectures and signal processing techniques. Actuation technologies include actuation devices along with associated control and decision making methods that define a system's actuation objectives. The designers and operators of control systems must consider how sensing and actuation technologies interact with a physical system, as well as with each other, to ensure they are synergistically integrated. Synergy may be considered in terms of system complexity, performance, cost, physical dimension, time for development, ease of installation, among other factors. Sensors and actuators are ubiquitously integrated with many of the systems that make our society safer, secure and economically prosperous. For example, modern aircraft employ dense arrays of sensors and actuators that aid in flying the plane, ensure the safety of passengers and control the fuel efficiency of the plane. Also, sensors and actuators are key elements in the design of "green" systems that adapt to user preferences in comfort while minimizing energy consumption.

Researchers have recognized for many years that living systems have vastly superior sensors and actuators than the best engineered systems. Superiorities and characteristics of sensors and actuators that we may learn from bio-systems include: sensing and actuation principles; materials; efficiency of energy usage; physical dimensions and weights; sensitivity, noise filtering and dynamic range; processing and transmission of massive signals from distributed sensors and coordination of distributed actuators; built-in fault tolerant mechanism, and so on. Any item in this list provides us motivation for bio-inspiration. For some people, e.g. chemists and nano-scientists, bio-inspiration may imply analysis (understanding) and synthesis (engineering) of fundamental mechanism and chemistry of bio-sensors and bio-actuators. For others, e.g. roboticists, bio-inspiration means analysis and synthesis of functionality of bio-systems; such examples include walking robots, humanoid robots and swimming robots. While each of such bio-inspired research activities makes sense by its own right, research on bio-inspired systems will be elevated to higher levels when multiple of different types of bio-inspired research activities are integrated and pursued to achieve a common goal via truly cross disciplinary collaborations, generation and initiation of which is a grand challenge. Successful cross disciplinary collaborations will make unprecedented impacts on engineering and technologies that affect our daily life such as health care, rehabilitation and environmental among others.

Biography: Ming Wang is a Professor of Civil and Environmental Engineering at the Northeastern University. He was formerly a full professor in the Department of Civil and Materials Engineering at the University of Illinois at Chicago (UIC) and before that at the University of New Mexico (UNM). Before that, he taught as a visiting professor in the Departments of Civil Engineering at Princeton University and at Northwestern University. His research has had a large influence on the health monitoring of civil infrastructures and the development of new sensor technologies for civil infrastructure applications. In addition, his research is having a strong international influence on futuristic monitoring technologies for large structural systems. His improvements of the electro-magnetic (EM) sensor to directly measure the stresses of large steel cables for cable-stayed bridges have gained much attention. Practical applications have been done in the United States, China, Japan, Europe, and in Taiwan. He has published more than 200 papers in various journals, conference proceedings, chapters, and edited books. Dr. Wang was also awarded a United States patent (number 5,254,857) on the "Fast Scanning Electron Microscope" in 1993. He has also filed several disclosures and patents on EM sensor technologies currently under worldwide use.

Grand Challenges Bio-inspired Monitoring and Warning Systems for Earthquakes

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Earthquakes are extremely lethal in part because they cannot be predicted. Furthermore, early warning systems for earthquakes remain a difficult technology to implement in practical settings. To save human lives, new sensors for development of bio-inspired early detection system for warning of eminent earthquakes are a primary interest for future Taiwan-US collaborations.

The biological structures and mechanisms that contribute to the exceptional hearing and sensing abilities of animals such as frogs, fish, lizards and snakes, among others, will be explored to create novel sensors that can be used for early detection systems for earthquakes. For example, it is widely known that animals exhibit unusual activities proceeding major earthquakes. Ultimately, we hope that an understanding of animal detection and recognition mechanisms will eventually help in the development of bio-inspired sensors for earthquake monitoring and warning. We will emphasize mechanisms and modeling of biological detection of information that can be used in warning of eminent seismic events in lieu of (and as a complement to) research on prediction of seismic events. Several challenging topics include:

1) Studying and mimicking exceptional hearing mechanism of animals to provide insight into the design of a sensor to detect infrasound for frequency below 20 Hz. For example, elephants use infrasound waves for communication over extremely long distances (*e.g.*, over hundreds of kilometers). Frogs and fish are also endowed with impressive low frequency detection mechanisms.
2) Other animals such as lizards, snakes, and birds will likely provide clues for mimicking their abilities to sense and detect a major earthquake and to provide a few extra seconds (perhaps minutes) warning people to seek safety from the arriving earthquake.

Biography: Dr. Ian White is an Assistant Professor in the Fischell Department of Bioengineering at the University of Maryland. He received his Ph.D. in Electrical Engineering from Stanford University in 2002 and his B.S. in Electrical Engineering from the University of Missouri in 1997. After receiving his doctoral degree, Dr. White worked at the Sprint Advanced Technology Labs from 2002 until 2005. At that time, Dr. White accepted a post-doctoral fellowship at the University of Missouri in the Biological Engineering Department. In 2008, Dr. White became an Assistant Professor of Bioengineering at the University of Maryland. Currently, Dr. White's research group develops microsystems for biological and chemical analysis at the cellular and molecular level. Specific research tracks in Dr. White laboratory include: microsystems for novel studies of the cellular and molecular mechanisms of cancer metastasis, microsystems for the point-of-care diagnosis of infectious diseases, and chemical and biological sensors based on surface enhanced Raman spectroscopy.

Grand Challenge: Real-time diagnosis of infectious disease from blood samples using bio-inspired methods in microsystems.

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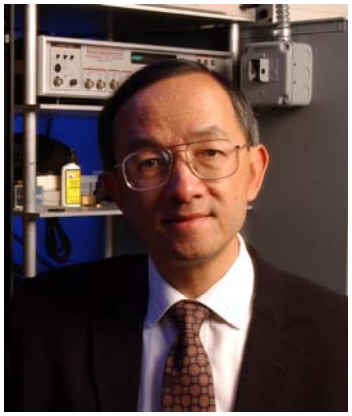
Today the standard technique for the diagnosis of blood-borne infectious disease is to perform blood cultures, which may take between two and seven days to produce a result. During this extended time, the pathogen can spread and the patient's condition can worsen; additionally, the patient may be treated with broad-spectrum antibiotics that are not appropriate for the infection, that can harm the patient, and that may lead to drug-resistant strains of pathogens. There is a widely recognized need to develop a diagnostic technique that can provide a real-time identification of the species and strain of the infectious agent. This would increase patient health, reduce the spread of pathogens, and cut dramatically the use of broad-spectrum antibiotics.

Polymerase chain reaction (PCR), a technique in which DNA is exponentially amplified, is currently being investigated as a rapid diagnostics technique for infectious disease. PCR represents one of the most successful adaptations of bio-inspired design in biotechnology. For infectious disease diagnosis, the assay attempts to amplify DNA sequence signatures specific to a pathogen species and/or strain to determine if it is present. Currently, PCR shows great promise for diagnosing nosocomial infections without the need for cultures. However, detecting pathogens in blood continues to present a tremendous problem because of the complexities of the sample. For example, bacterial infections may present with 10 colony forming units – or alternative approximately 10 copies of bacterial genome – per milliliter of whole blood. In addition, the same milliliter of whole blood contains billions red blood cells, millions white blood cells, platelets, proteins, etc. Today it is costly, complex, and time consuming to purify such a low number of bacteria from whole blood, which thus prohibits the use of PCR in diagnostic environments, such as an emergency room or clinic. Thus, until sophisticated and automated sample processing techniques are developed, there is still a tremendous need for a non-culture-based diagnostic technique for infectious disease from blood samples.

While it is difficult to perform PCR amplification of pathogen DNA from samples of whole blood, mammalian evolution has proceeded to enable components of the blood to sense pathogens; likewise, microorganisms have developed methods to recognize and attach to tissues while circulating in whole blood. These facts seem to present clues to bioinspired techniques to develop microsystems for the speciesspecific and possibly even strain specific identification of pathogens in blood. For example, an infected patient with a responsive immune system has circulating cells that have been engineered to identify the surface of pathogens. Therefore, engineering a microsystem decorated with a large surface area decorated with pathogen like surfaces (specific to species or strain) could be recognized by activated immune cells drawn from the patient's blood. Conversely, a microsystem could be engineered by presenting a large surface area that mimics the cell membrane components that enable viral capsids to bind and inject DNA or RNA across the synthetic surface; the recovered nucleic acids could subsequently be used to identify the source of the infection. These are only a few of the many examples in which microsystems could be engineered with synthetic biological components to enable the real time diagnosis of infectious disease from complex samples, including blood.



Biography: Dr. Edward Yeung received his A.B. from Cornell University and his Ph.D. from the University of California at Berkeley. Since then, he has been on the chemistry faculty at Iowa State University, where he is Robert Allen Wright Professor and Distinguished Professor in Liberal Arts and Sciences. His research focuses on measurement systems for biological and material sciences. His expertise includes optical and mass spectroscopies, single cell and single molecule monitoring, and physical phenomena at restricted domains. He was an Associate Editor of *Analytical Chemistry* and is currently a co-editor of *Annual Review of Analytical Chemistry*. He has received an Alfred P. Sloan Fellowship, the ACS Division of Analytical Chemistry Award in Chemical Instrumentation, 4 separate R&D 100 Awards, the Lester W. Strock Award, the Pittsburgh Analytical Chemistry Award, the L. S. Palmer Award, the ACS Fisher Award in Analytical Chemistry, the Frederick Conference on Capillary Electrophoresis Award, the Eastern Analytical Symposium Award in Analytical Chemistry, the ACS Award in Chromatography, the International Prize of the Belgian Society of Pharmaceutical Sciences, the Eastern Analytical Symposium Award in Separation Science, the Ralph N. Adams Award in Bioanalytical Chemistry, the Golay Award, the Chicago Chromatography Discussion Group Merit Award and the ACS Division of Analytical Chemistry Award for Distinguished Service.

Grand Challenge: Small, Simple and Sensitive Measurement Systems

Edward S. Yeung
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While chemical measurements within biological systems have been around for centuries, we are constantly faced with new situations that require different concepts, instrumentation, or information content. The grand challenges are to make the measurement system as small as possible, as simple as possible, and as sensitive as possible. Not all of these goals are necessary or can be achieved simultaneously, so one needs to specify what the results are used for. We marvel at nature's ability to detect single photons (human eye), sense single molecules (insect pheromones), or distinguish identical twins. Future designs of measurement systems could benefit from these tried-and-true examples.

Size – Miniaturization refers to the entire measurement process. Often not discussed are the bulky lasers, pumps, sample dispensers, CCD cameras, etc., that feed microfluidic devices. So, even though the chemical reactions are performed in admirably small volumes, the portability of the complete system remains open for new ideas. Efforts in integrating the components in the measurement system during manufacturing are already paying off. The ultimate goal is to reduce the size of optical components further, to the micron regime if not to the diffraction limit. For example, light emitting diodes can certainly be made to 1 micron square. The reduced light intensity is not an issue because the irradiated area is also small. As for the detector, current CCD pixels are only a few microns across. The electron-multiplier version can approach single photon performance. Best of all, they already have built-in spectral analysis through the RGB filters. Micron-scale optics can be derived from light guides and/or gradient index lenses. All these can be integrated during manufacturing. The challenge then shifts from making the sensors to adapting them to serve particular needs in chemical measurements.

Simplicity – It is not always true that the more functions the better the instrument. Inherent to having multiple capabilities is decreased ruggedness, increased size and mutual interference. Indeed, often instruments provide too much information that may cloud the interpretation in practical applications. The challenge therefore is to design highly specific measurement schemes, one for each piece of relevant information. For example, although academically "home test strips" may not be glamorous, they constitute an important screening step that can reduce critical response time. The elimination of fancy computation and data manipulation further make the results more rugged and the conclusions more intuitive. Simplicity also enables operation by untrained personnel and lowers the cost of manufacturing.

Sensitivity – Everyone seems to be constantly chasing the next detection limit. We have already achieved single-molecule detectability. However, the best detection limit may not be always relevant. More important are issues of specificity, interference and dynamic range. Single molecule fluorescence contains little information so one challenge is to incorporate the appropriate labeling scheme to take advantage of the signal. Sensitivity also relates to temporal response, since one can almost always increase the sensitivity by accumulating more data. For applications to biodynamics or microscale mechanics, the additional challenge is to move from the second scale to the millisecond scale for measurement time, if not lower. Moreover, measurements need to be repeatable at a similar time scale to follow entire events. Kilohertz CCD cameras are already available, but the signal-to-noise ratios still leave much to be desired.

Biography: Dr. Xiong (Bill) Yu is an assistant professor at Department of Civil Engineering, Case Western Reserve University. He also holds courtesy appointments in the Department of Electrical Engineering and Computer Science, Department of Mechanical and Aerospace Engineering. He also involves in the research activities of the Applied Platform Technology center. Dr. Yu received his B.S. and M.S. degree from Tsinghua University, China, his M.S and Ph.D. degree from Purdue University in 2003. His current research focuses on sensor technology and multifunctional infrastructure materials. In the area of sensor technology, he has developed an active research program is the health monitoring of civil infrastructure. He specialize the development of innovative sensors based on guided electromagnetic wave principles. His research also incorporates smart materials and bio-inspired sensing and signal processing principles for various applications, i.e., non-invasive sensors for human health and bio-inspired technology for detection of critical hazardous events. In conjunction with sensor development research, his research also aims to understand the multi-scale and multi-physical processes in materials. His previous research has produced two U.S. patents, one pending U.S. patent application and a few invention disclosures. He received a NSF CAREER award in 2009 and ASNT fellowship in 2010.

Grand Challenge: System and Interdisciplinary Vision for Bio-Inspired Sensor Technologies

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Department of Electrical Engineering and Computer Science (courtesy)
Department of Mechanical and Aerospace Engineering (courtesy)
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I have been frequently fascinated by the remarkable skills developed in the biological systems. The Nature produces biological system with unmatchable sensitivity and amazing speed in processing the huge amount of data. In my opinion, we need to overthrow the barrier between engineering and science to catalyze a breakthrough in this area. The mission of science is to understand the basic principles and enhance the existing knowledge. The mission of engineering is to serve the welfare of the human being through advancing in technological fields. A strong connection between engineering and science will provide a channel to timely place the advancement in science into the hands of engineers. Huge amount of study on the sound sensing mechanism in aquatics (i.e. fish) are available in the fields of biology and zoology. These studies uncovered various transduction mechanisms in biological organs. Most these study, however, have not gone beyond to address how to reproduce such transduction mechanism? Aware of the limitations of man-made sensors, more and more engineers resort to learning from the sensing mechanism in biological systems. The wealth of scientific knowledge provide a resource reservoir for such exploration, although the exact nature of knowledge that engineers sought might or might not be in place. Therefore, I believe the advancement in bio-inspired technologies will greatly benefit from close dialogues between scientist (biologist, neurologist, etc) and engineers. This will set the foundation to explore the unprecedented opportunities by bio-inspired design. The success in engineering applications will prompt interest in fundamental science.

Another important task is to prompt interdisciplinary education in engineering arena. Development of bio-inspired technologies involves multiple disciplines such as material science and engineering, chemical engineering, electrical engineering, etc. Civil engineering and other disciplinary provide testbed and opportunities to implement such advancement. The long term success in the area of bio-inspired design requires promoting interdisciplinary education and rewarding interdisciplinary research. A paradigm change in the current promotion criteria for faculty as well as the core curricular for engineering students will be necessary.

From the technical side, I think we need to catalyze advancement in technology and materials to achieve the sensitivity, miniaturization, energy supply, and signal processing requirements that is similar or superior to biological system. The community is making progresses yet significant investment and joint efforts are still required.

Biography: Dr. Susan Zhou becomes Assistant Professor of Chemical Engineering at Worcester Polytechnic Institute (WPI) in 2005 after holding postdoctoral and teaching positions at the University of California, Irvine. She directs the Microfluidics and Bionanotechnology Laboratory in WPI's Life Sciences and Bio-engineering Center at Gateway Park. Her active areas of research currently include micro- and nano-bioelectronics, BioMEMs (microelectromechanical systems), microfluidics, biosensors, and bio-nanomaterials. She holds a Ph.D degree in Materials Science from University of California, Irvine. She received her MS in Chemical Engineering from Clarkson University in 1999.

Grand Challenge: Implantable responsive drug delivery system

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Successful drug delivery requires not only right choice of drug, but also proper delivery to the site of action. Drug delivery has been studied quite extensively recently and is an extremely broad area of research. Each drug molecule, small molecule or large biomolecule, has its own individually unique profile of absorption, distribution, metabolism, excretion, and toxicology. Moreover, timing of the drug release may affect the pharmacological efficacy. Therefore, how the drugs can be actuated and controlled is of significant importance. It will be no surprising that microelectromechanical system (MEMS) may lead to substantial advances over conventional drug delivery system due to its ability to generate two dimensional or three dimensional device structures accurately and reproducibly.

External drug delivery systems include microneedles and other micromachined systems for enhancing transdermal, ocular, or buccal delivery. Another category, internally implanted devices, includes microreservoir systems, non-Fickian release depots, and immunoisolation capsules for therapeutic cells. Ultimately, MEMS-based drug delivery may rely on implantable microfluidic networks that carefully meter out an entire drug regime under the guidance of integrated circuits with built-in sensors and telemetry.

One challenge for drug delivery is rupture, with potential drug dumping. In some cases, e.g., insulin, a dump could be fatal. Another challenge for implantable drug delivery system is immunoisolation. Even if a drug delivery device successfully averts encapsulation by fibrous tissue, it still runs the risk of fouling, where antibodies or other proteins migrate through exit orifices and inhibit the metering mechanism of the device. With the ultimate goal of developing intelligent drug delivery devices that can sense when and how much the dose is needed and then automatically release it from reservoirs, other challenges include restriction of undesired uptake by nontargeted organs; and improvement of stimuli-triggered or programmable drug release systems.

Japan Delegates

Biography: Dr. Yoshinobu Baba is a Professor of Department of Applied Chemistry, Graduate School of Engineering, Nagoya University. He is also a Presidential Advisor of Nagoya University, Director of FIRST Research Center for Innovative Nanobiodevice, Nagoya University, Professor of Department of Advanced Medical Science, Graduate School of Medicine, Nagoya University, and Research Advisor, Health Research Institute, National Institute of Advanced Industrial Science and Technology (AIST). He is an Associate Editor of *Anal. Chem.* and serving to over 20 scientific journals, including *Nanoscale* and *Biomicrofluidics*, as an editorial/advisory board member. He is a co-initiator for the world largest Nanotech/Nanobio International Meeting and Exhibition in Japan and Internaitonal Academy of Nanomedicine. He is a general chair of numerous international meetings (microTAS, MSB, NanoBioEXPO, ISMM). He has been admitted as a Fellow of the Royal Society of Chemistry and received numerous awards for his contributions in nanobiotechnology: MERCK Award in 2004, award from the Applied Physics Society of Japan in 2006, and The CSJ (Chemical Society of Japan) award for creative work in 2008. His major area of interest is nanobiosicence and nanobiotechnology for omics, systems biology, medical diagnosis, tissue engineering, and molecular imaging. He is the author or co-author of 702 publications, including research papers, proceedings, reviews, and books and is also an inventor of over 70 patents. He has delivered more than 641 plenary and invited lectures at conferences. His work has been cited on 265 occasions by newspapers and televisions.

Grand Challenge: Nanobiodevice for Future Personalized Medicine and Evidence Based Healthcare

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FIRST Research Center for Innovative Nanobiodevice, Nagoya University, Nagoya, Japan

Nanobiodevice is a piece of contrivance, equipment, machine, or component, which is created by the overlapping multidisciplinary activities associated with nanotechnology and biotechnology, intended for biological, medical, and clinical purposes. During the past decade, nanobiodevice has progressively begun to focus on the establishment of main four fields of biomedical applications of nanotechnology, including 1) diagnostic devices, 2) molecular imaging, 3) regenerative medicine, and 4) drug delivery systems. The research efforts in my laboratory have been focused on the development of novel nanodevices, nanomatrials, and nanotechnologies intended for biomedical applications, including genome and proteome analysis, biosensor for blood biomarker, actuation of single biomolecule, analysis of biomolecules and cells, diagnosis of diseases, *in vivo* imaging, stem cell therapy, tissue engineering, and gene delivery system.

Since nanobiodevice has tremendous advantages, it is applicable to fast analysis of biomolecules developed by appropriate small space, which has short distance to diffuse biomolecules, which have extremely small diffusion constants. Highly sensitive detection and single molecular analysis will be possible by use of nanobiodevice, because of the large surface to volume ratio and the use of extremely small volume, such as fL (10^{-15} L) and aL (10^{-18} L). Nanobiodevice is also suitable for single molecular and single cellular manipulation, since the laminar flow, which is characteristic in the low Reynolds number (Re) of micro- and nano-fluidics, is valuable for separation and manipulation of single biomolecules and single cells, and it is possible to fabricate the nanostructure and nanomaterials, of which the size is comparable to the size of biomolecule and cell. Nanomaterials, such as quantum dots, are essential to develop highly bright and long life fluorescence materials even in the near infra-red region, which will be indispensable for molecular sensing and *in vivo* imaging.

For future personalized medicine and evidence based healthcare, we need to develop novel nanobiodevices, including 1) multifunctional nanobiodevices for single-platform bioimaging and targeting therapy (theranostic nanodevices); 2) ultra-high sensitive, highly specific, low invasive and reliable (robust) multiplexed detection technologies, which will enable diagnosis through the ability to detect disease processes at their inception, e.g., a single diseased cell or pathophysiology at molecular level, for early cancer detection; 3) remote disease monitoring through the ability of nanotechnology to provide on-line sensing and information relay; 4) construction of tissue-growth facilitating structured cell sheets for organ repair and replacement; 5) application of biological nanostructures (i.e., nucleic acids, proteins) in bioelectronics and environment-friendly nanofabrication processes; 6) single cell interventions and diagnostics, including stem cell growth and differentiation and cellular level genomics and proteomics; 7) stem cell differentiation and site-specific delivery by devices that allow protective delivery and can serve as growth and templates that include nano-architecture surfaces.

Biography: Toshio Fukuda received the B.A. degree from Waseda University, Tokyo, Japan, in 1971, and the M.S and Dr. Eng. from the University of Tokyo, Tokyo, Japan, in 1973 and 1977, respectively.

In 1977, he joined the National Mechanical Engineering Laboratory. In 1982, he joined the Science University of Tokyo, Japan, and then joined Nagoya University, Nagoya, Japan, in 1989. Currently, he is Director of Center for Micro-Nano Mechatronics and Professor of Department of Micro-Nano Systems Engineering at Nagoya University, where he is mainly involved in the research fields of intelligent robotic and mechatronic system, cellular robotic system, and micro- and nano-robotic system. He is Distinguished Professor, Seoul National University since 2009. Dr. Fukuda is IEEE Region 10 Director-Elect (2011-2012) and served President of IEEE Robotics and Automation Society (1998-1999), Director of the IEEE Division X, Systems and Control (2001-2002), and Editor-in-Chief of IEEE / ASME Transactions on Mechatronics (2000-2002). He was President of IEEE Nanotechnology Council (2002-2003, 2005) and President of SOFT (Japan Society for Fuzzy Theory and Intelligent Informatics) (2003-2005). He was elected as a member of Science Council of Japan (2008-). He received the IEEE Eugene Mittelmann Award (1997), IEEE Millennium Medal (2000), IEEE Robotics and Automation Pioneer Award (2004), IEEE Robotics and Automation Society Distinguished Service Award (2005), Award from Ministry of Education and Science in Japan (2005). IEEE Nanotechnology Council Distinguished service award (2007). Best Googol Application paper awards from IEEE Trans. Automation Science and Engineering (2007). Best papers awards from RSJ (2004) and SICE (2007), Special Funai Award from JSME (2008), 2009 George Saridis Leadership Award in Robotics and Automation (2009), IEEE Robotics and Automation Technical Field Award (2010), ROBOMECH Award 2010 (2010), The Society of Instrument and Control Engineers Technical Field Award (2010), Distinguished Service Award, The Robotics Society of Japan (2010), World Automation Congress 2010 (WAC 2010) dedicated to Prof. Toshio Fukuda, Best Paper Award in 2010 International Symposium on Micro-Nano Mechatronics and Human Science (MHS2010), IEEE Fellow (1995), SICE Fellow (1995), JSME Fellow (2001), RSJ Fellow (2004), Honorary Doctor of Aalto University School of Science and Technology (2010).

Grand Challenge: Micro and Nano Robotics Manipulation toward Nano-surgery System for Single Cell

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Micro-nano robotic technologies, micro-nano manipulation technique, have been widely developed and applied for various academic and industrial applications. We have been proposed “Nano Laboratory” consisted of the capabilities of nanofabrication, nanoinstrumentation and nanoassembly based on nanorobotic manipulation system [1]. Recently, we constructed the bio-nanomanipulation system using single cell analysis technique to control, measure, and manipulate of biological cells using various micro-nano tools [2]. Based on the system, the single cell nanosurgery system was proposed to realize the single cell diagnosis, extraction, cutting, injection and embedded the micro-nano devices (Fig. 1).

For example, we proposed the single cell adhesion force measurement using a nanofork. The nanofork was used to pick-up a single cell on a line-patterned substrate through nanomanipulation system inside environmental-scanning electron microscope (E-SEM) [3-5]. The line-patterned substrate was used to provide small gaps between the single cells and the substrate. Therefore, the nanofork could be inserted through these gaps in order to successfully pick-up a single cell. Adhesion force was measured during the cell pick-up process from the deflection of the cantilever beam. The nanofork was fabricated using focused ion beam (FIB) etching process while the line-patterned substrate was fabricated using nanoimprinting technology. The line-patterned substrate is fabricated by Nano-imprinting technique. Typical E-SEM images during the cell release experiment are shown in Fig. 2. This method can be implemented in various applications such as in a bio-medical research.

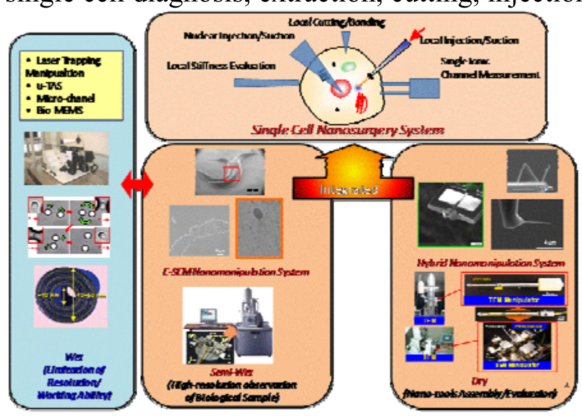

Fig. 1. Single cell nanosurgery system based on micro/nanomanipulators under various microscopes (wet/semi-wet/dry conditions).

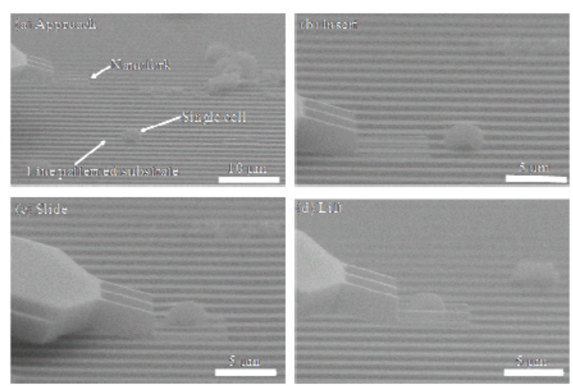

Fig. 2. Typical sequences during the cell release experiment by Nanofork on a line-patterned substrate.

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Biography: Mr. Xiaofang Gao is currently a Ph. D student in Kitamori Lab at the University of Tokyo. He received his bachelor and master degree in Tianjin University from the major of electrochemistry and chemical engineering in 2003 and 2007, respectively. His current research is focused on the construction of cell-based microdevices for micro continuous chemical engineering. He also has a broad interest on the development of bio-related applications in the field of microfluidics and nanofluidics. He recently published his own work in the journal of *Analytical Sciences*. He aimed his research at the combination of cell functions with microfluidics for the future application in medical care portable devices and novel concept of cell-based micro chemical engineering.

Grand Challenge: Combining biosensors with micro- and nanotechnology for a novel methodology applied in the future medical care

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From the last century when Clark and Lyon first gave the tentative idea of biosensor, there has already been over 40 years for the development of biosensor. As an interdisciplinary subject between biotechnology and information technology, biosensor has been applied in many areas such as environment monitoring, food chemistry, clinical medicine and military engineering. From the viewpoint of analytical chemistry, one of the improvements is the reduction of detection limit. Therefore, more sensitive sensor with an extreme low limit of reaction is one of the future developments for the scientific research and industry.

Accompanied by the adventure and rapid progress of micro- and nanotechnology, it brought a big opportunity for the future biosensor and actuator. Micro- and nanotechnology allow us to observe and manipulate working units such as cells and biomolecules in their similar living circumstances in vitro. So it is possible to mimic a real space for sensing matters to give feedback from the outside circumstance at single cell and single molecule level. It can supply and magnify very weak signals from a certain biochemical reaction but maybe extremely important for some pathological changes. For example, scientists made a change to the concentration of some transcription factors by the cell programming technology so as to transform stem cells to some certain cells. Novel biosensors by micro- and nanotech and detect the activities of transcription factors to insure the stem cell to be right programmed. It can at the same time confirm which factor has been activated in the patient's cancer cell and which has been inhibited so as to use the corresponding medicine to cure the patient.

By using more and more micro- and nanodevices into the area of bioinspired sensors and actuators, such progresses of biochemical activities *in vivo* became possible to be manipulated and applied. By the construction of micro- and nanodevices with cell functions, both detection and various chemical engineering operations can be replicated at organ level. Conclusively, it is of great opportunity and challenge to face the biomimicking in micro- and nanoscale that maybe bring a huge changing for our life.

Biography: Dr. Itaru Hamachi, Department of Synthetic Chemistry & Biological Chemistry, Kyoto University; Itaru Hamachi received his B. S. in 1983 from Kyoto University, M. S. in 1985 from Kyoto University, and Ph. D. in 1988 from Kyoto University (advisor: Iwao Tabushi & Teruo Matsuura). Then he joined the faculty of Kyushu University as an assistant Professor (Prof. Toyoki Kunitake's group) in 1988, and was promoted to be an associate Professor of Kyushu University (Prof. Seiji Shinkai's group) in 1992. In 2001, he became a full Professor of Kyushu University in 2001 and moved to Kyoto University in 2005. He was a PRESTO investigator supported by JST for 7 years and now a CREST team leader supported by JST (since 2009-2014). Award: Chemical Society of Japan Award for creative work (in 2006). His research interest covers Bioorganic Chemistry, Chemical Biology, In cell/in vivo Organic Chemistry, Molecular Recognition, Supramolecular Biomaterials Tel: +81-75-383-2754, Fax: +81-75-383-2759, E-mail: ihamachi@sbchem.kyoto-u.ac.jp

Grand Challenge Statement in Bioinspired Engineering of Next Generation of Biosensors and Actuators

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As a grand challenge in the field of next generation of biosensors and actuators, I would like to propose development of sophisticated molecules and materials where biosensing and the responsive work (functions) are efficiently coupled n order to not only detecting biological events, but also treat them actively. For constantly curing human diseases, such intelligent materials are desired that are ideally expected to work within human bodies with artificial intelligence. In order to facilitate development of these materials, various directions of researches should greatly progress, such as highly selective and sensitive biosensors, biocompatible materials, intelligent materials, highly ordered soft-materials, and so on.

Biography: Dr. Noritada Kaji is a designated associate professor of the Graduate School of Scienceand a group leader of Engineering Technology Group of ERATO Higashiyama Live-Holonics Project at Nagoya University. He obtained a Bachelor degree in Pharmaceutical Sciences in 2000 and PhD degree in 2004 from the University of Tokushima, Japan. In his PhD study, he worked on NanopillarChips which are state-of-the-art TAS combining nano-fabricated structures for DNA analysis. After his postdoctoral research, he started working as an assistant professor of the department of Applied Chemistry at Nagoya University from February 2005. His research interests are mainly divided into three parts; Nano-biodevices for biomolecule analysis, Single molecule biophysics, and Biological process on TAS for plant science.

Mimicking Intracellular Environment by Micro- and Nanotechnologies towards a Better Understanding of Biochemical Reactions *in vivo* as a System

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Most biochemical experiments such as biochemical assay and biophysical kinetic measurements are done with so-called "diluted" solution ranged from few μg to mg/ml. However cytoplasm includes high concentration of polymers such as DNA, RNA, protein, and polysaccharide, from 200 to 400 mg/ml concentration range. These molecular crowding conditions might strongly affect biochemical reaction kinetics as well as dynamics. One of the major approaches to defeat the problem is adding molecular crowding reagents like PEG (polyethylene glycol) and Ficoll into the reaction solutions and mimicking cytoplasm environment. This biochemical approach is powerful to understand biochemical reactions in cell more quantitatively. But some concerns are still remained; reactivity of molecular crowding reagents and target polymers, influences on the higher-order structures of the target polymers and so on. Therefore one of challenges to understand biochemical reaction *in vivo* using test tubes is to find a suitable molecular crowding reagent depending on the intended reactions.

To compensate the above drawbacks of the molecular crowding reagent system, we are trying to apply cell-sized reaction chambers as a confinement space for biochemical reactions. In particular, micro- and nanochambers ranged from 0.5 to 5 cubic μm were fabricated by "top-down" approach using electron beam and photolithography, dry etching, and PDMS (Polydimethylsiloxane) cast. The fabricated micro- and nanochamber device was a powerful tool to provide confinement space for biochemical reactions and enable single enzyme assay. We applied various sizes of micro- and nanochambers for kinetic measurements of enzyme reaction and revealed that the reaction space affects the kinetics of enzyme and the confinement decelerates the reaction speed. The result indicates the reaction space become smaller and smaller, unexpected influence was observed in this experimental system. So our grand challenge is to understand the observed phenomena by comparing the molecular crowding system, and develop precisely reproduced intracellular environment by micro- and nanofabrication techniques. We believe that these approaches are essential to provide precise information of biochemical reactions in live cells and understand a cell as a system network of biochemicals, systems biology.

Biography: Dr. Yutaka Kazoe is an Assistant Professor of Department of Applied Chemistry at the University of Tokyo. He received BE, ME and PhD degrees from Keio University in 2004, 2006 and 2008, respectively. He has been a research fellow of JSPS in Keio University from 2008, and a postdoctoral fellow in Georgia Institute of Technology from 2009. From 2010 to 2011, He has been a research scientist of the University of Tokyo. His research mainly focuses on micro- and nanofluidics. He has developed optical flow measurement techniques by fluorescence imaging. Quantitative imaging of surface electrostatic potential (zeta potential) and near-wall velocity measurement were achieved by developing optical system, image processing and fluidic control system. Electrokinetics with surface chemistry and momentum transport of fluid, which are fundamental for miniaturized flow systems such as μTAS and Lab-on-a-chip, have been revealed through the developed techniques. Now he is investigating dynamics of nanochannel flows.

Grand Challenge: Experimental Investigation of Small Scale Fluid Dynamics for Further Development of Micro- and Nano Chemical Systems

Yutaka Kazoe
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Fluid dynamics has been a basic science of engineering fields such as nuclear engineering, aerospace engineering, biological engineering, chemical plant engineering, e.g. From 1990s, microscale fluid dynamics has been investigated with rapid development of micro chemical systems for analysis and synthesis, which integrate chemical processes (mixing, separation, reaction, detection) on a microchip. As well as numerical studies, experimental approaches by measurements played important roles for the development. Measurement schemes were developed based upon optical methods using flow tracers such as molecules and particles. They revealed that the flow is simply laminar but strongly affected by surface chemical properties such as wettability, chemical affinity and electric charge.

Recently, miniaturized flow systems are downscaling to 10^{1}□10^{3} nm for development of novel chemical analysis and synthesis. The regime of this scale is between single molecule and continuous phase, and specific properties such as high proton mobility, high viscosity and low permittivity has been revealed (Hibara *et al.*, *Anal. Chem.*, 2002; Tsukahara *et al.*, *Angew. Chem. Int.*, 2007). However, the fluid behavior and mass transport in this scale are not well explored owing to the lack of measurement methods. Simply applying the schemes of microscale flow measurements is difficult because the spatial resolution is restricted to the optical diffraction limit. In addition, flow tracers of nanometer-size are subject to the significant diffusion. Therefore, novel measurement technique is strongly required to understand the nanosale fluid dynamics.

My grand challenge is to develop a measurement technique and reveal the nanoscale fluid behavior and mass transport. The near-field optics, nanosensor technology based on particle synthesis, and data processing are being combined in order to achieve nanometer-order spatial resolution. Constructing basic science of nanoscale fluid dynamics related to nano-physical chemistry will contribute to create new fluid engineering field for single cell and single molecule analysis, specific chemical synthesis, and fluidic based electronic devices.

Biography：Dr. Takehiko Kitamori is a full professor at the Department of Applied Chemistry, School of Engineering, The University of Tokyo, and Dean of the faculty of Engineering, and Councilor of The University of Tokyo. He moved from Hitachi Ltd. as an Assistant Professor in 1989 and arrived at a full Professor in 1998. He was a project leader of Microchemical group of Kanagawa Academy of Science and Technology (KAST) for 1998-2009 and performed quite an achievement. His research activity covers analytical chemistry, applied laser spectroscopy, and micro and extended nano chemistry. He especially focuses on the miniaturization of the chemical, medical and bio equipments on microchips as novel device technologies. They are based on chemistry, physics, spectroscopy, and instrumentation. He organizes a number of domestic and international symposiums. Prof.Kitamori is now serving as Vice-President of the largest international academic society of this field, Chemical and Biological Microsystem Society(CBMS), and also I have been appointed as Fellow Member of The Royal Society of Chemistry (UK). In the domestic academic societies in Japan, he was President of the Society for Chemistry and Micro and Nano System, and was Senior Vice-President of Japan Society of Analytical Chemistry.
Because of his achievements, he has received several prestigious awards like (selected):
1991 Ichimura Award of Science
2006 The Chemical Society of Japan Award for Creative Work
2008 IBM Faculty Award
2009 The Japan Society for Analytical Chemistry Award2009
2009~ Adjunct Research Professor to the Ian Wark Research Institute, University of South Australia

Grand Challenge: Creation of fluid engineering in extended-nano space and development of novel devices using its unique properties

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【Purpose and Background of the Research】

Nanotechnology exploiting quantum effects and near-field light and so on has developed science and engineering in electronics and photonics fields. By contrast, our group has studied on micro chemical systems integrating various chemical operations such as reaction and extraction in microchips with microchannels in μm order by using micro-fabrication technology (Fig.1). So far, rapid, efficient micro chip technology has been developed exploiting space characteristics that surface properties affect on fluid behavior due to size effects and applied it to rapid diagnosis systems and so on. Such technologies are summarized in Fig. 1 focusing on size order. The extended nano scale, 10^1–10^3 nm scale is larger than macromolecular and smaller than micro fabrication field. Also, extended nano scale is larger than single molecule and smaller than size where liquids keep their original properties. Therefore, extended nano space is scientifically interesting, but there has been no experimental tools.

Therefore, in this study, (A) the basic technologies are established including fabrication, fluidic control methods, single molecule detection methods, (B) the physics and chemistry in extended-nano space are clarified, and finally (C) novel devices using unique properties of extended-nano spaces are developed.

Therefore, in this study, (A) the basic technologies are established including fabrication, fluidic control methods, single molecule detection methods, (B) the physics and chemistry in extended-nano space are clarified, and finally (C) novel devices using unique properties of extended-nano spaces are developed.

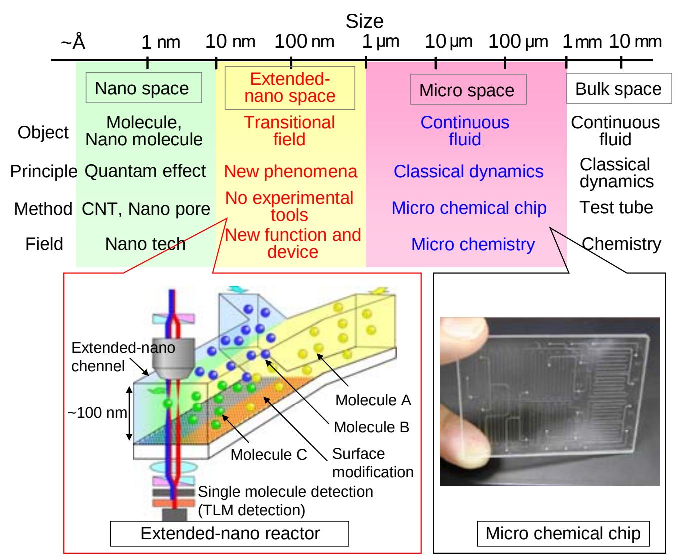

Fig. 1. Research Concept

【Research Methods】

Plan A: Establishment of technology

A-1) Fabrication and modification

In addition to top-down fabrication, partial chemical surface modification method in extended-nano channels is developed.

A-2) Fluid control

Surface wettability are controlled to control fluid in extended-nano space where mechanical fluidic devices are difficult to be incorporated.

A-3) Detection

Single molecule detection is realized applying our original sensitive non-fluorescent molecule detector, thermal lens microscope (TLM).

Plan B: Physical/chemical property solution

B-1) Liquid properties and structures

Liquid Properties (density, specific heat and refractive index) and structures are measured by spectroscopic analytical method.

B-2) Chemical reactions

Chemical reactions in extended-nano space are realized and investigated.

B-3) Properties in bio-extended-nano space

Bio-extended-nano space imitating space between cells is realized and investigated.

Plan C: Novel device development

C-1) Single cell analysis device: Single cell, single molecule analysis devices are created using extremely small volume of extended-nano spaces (fL ~ aL).

C-2) Super chromatography: Efficient chromatography is realized using surface dominant property of extended-nano spaces.

C-3) Heat pipe without electricity: A heat pipe is developed using capillary condensation effect in extended-nano space.

C-4) Light fuel cell: A fuel cell working with light is created using near-field light and proton transfer increasing effects in extended-nano spaces.

【Expected Research Achievements and Scientific Significance】 This study not only opens new disciplines, but also gives new engineering methods. This study can give molecular sketch to electric double layer, and can be applied to various novel devices such as ultra effective analysis devices and new principle energy devices.

Biography: Dr. Masahiro Kurata is an Assistant Professor of the Division of Earthquake Hazards, the Disaster Prevention Research Institute at Kyoto University. Dr. Kurata completed his graduate studies at the Georgia Institute of Technology where he received his Ph.D. in Civil and Environmental Engineering in 2009 and M.Eng. in Civil and Environmental Engineering in 2007. Prior to attending the Georgia Institute of Technology, he received his B.S. degree in Architecture and M.S. degree in Architectural Engineering from Kyoto University. He also completed post-graduate training and research in Earthquake Engineering and Engineering Seismology at the ROSE School, University of Pavia, Italy. His current research interests are in the area of smart building system, post-disaster structural damage screening, wireless monitoring system, and sustainable structural rehabilitation.

Grand Challenge: Enhancement of Post-Hazard Actions using Bio-Inspired Smart Buildings and Regional Damage Estimation System

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The reaction of biological systems against environmental or physical stimuli depends on the intensity of stimuli as well as the experience of the biological systems to similar phenomenon. Combined with intuition or reasoning acquired from the past, information obtained thorough biological sensing system severs as a clue for biological systems to select appropriate reactions. The quantitative measure of the intensity of various events (*e.g.*, pressure, heat and acid), whether or not it causes (has caused) critical damage in the parts of biological systems, is reasoned by comparing the stimuli received from a current event with memorized perceptions.

In the field of earthquake engineering, the damage intensity of a seismic event stands on an empirical correlation between the damage of buildings and the magnitude of strong ground motions observed in past events. The benefit of such intensity measure is timeliness where an automated system computes and announces the intensity of seismic damage to the public; such system is named Earthquake Early Warning (EEW) system. However, this measure does not provide information on the state of individual buildings (*i.e.*, operationability of damaged buildings). Consequently, one may wait for weeks or months, especially for a large seismic event in a heavily populated area, until damage estimates based on visual inspections by certified structural engineers become available.

The estimates on regional building damage in a seismically affected region can be significantly improved by the inclusion of biological reasoning and learning processes that works on sensing and information technologies. In the system, spaciously-distributed smart buildings (*i.e.*, buildings interfaced with sensors) self-diagnosis their healthiness by referencing to a biological database inspired by a cognitive-type neural database model where sensor information and damage states of individual buildings in past events and numerical simulations are pre-memorized. Here, a small number of smart buildings are selected to represent various structural types (*e.g.*, steel, concrete, or timber structure; old or new construction) in a region whose estimates are invoked to the rest of non-smart buildings (without sensors) in the region. A cyberenvironment specifically designed for combining multiple layers of information and experience (*e.g.*, actual damage estimates, past and numerically simulated damage, regional database for structures, and strong ground motion records) supports a biological reasoning process in the proposed regional building damage estimating system. The proposed system helps inspectors for prioritizing the list of buildings to be inspected. Such estimates released in a rapid manner can serve as the first basis for planning post-earthquake restorations by local communities.

Biography: Dr. Tomokazu Matsue is currently a professor of Advanced Institute of Materials Research (WPI-AIMR) at Tohoku University, Japan. He is also an adjunct professor of the Graduate School of Environmental Studies and faculty of engineering at the same university. Dr. Matsue received BS degree from Tohoku University in 1976 and Ph. D from the same university in 1981. His research interests are in biosensing and bioelectronic devices/systems, characterization and application of cellular functions, micromanipulation and micropatterning for biomaterials, intelligent biosystems with micro/nano technology, and electrochemical instrumentations. Dr. Matsue has been active in academic societies. He worked for Japan Society for the Promotion of Science (JSPS) as a program officer in 2006-2008. Currently, he is a Japan Representative of International Society of Electrochemistry (ISE), an editor of Electrochimica Acta (a society journal of ISE), technological advisor of Japan Science and Technology Agency (JST), technological advisor of New Energy and Industrial Technology Development Organization (NEDO), and an advisor of several research organizations in Japan. Dr. Matsue received several awards including Award for Young Electrochemist from the Electrochemical Society of Japan (1986), Award for Creative Work from the Electrochemical Society of Japan (2002), and Award for Technical Achievements from the Electrochemical Society of Japan (2006). He published 250 original papers, 62 review papers and 33 books.

Grand Challenge: Highly-Sensitive Electrochemical Imaging for Biosensing

Tomokazu Matsue
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Bioimaging has been a key technology to support rapid developments of fundamental and applied biosciences. The methods developed so far are usually based on fluorescence detection since fluorescence measurement usually has a high sensitivity and a variety of tools for performing the measurements are commercially available. However, fluorescence detection has some drawbacks such as undesired fluctuations due to quenching or emission from other materials, shielding by a turbid solution or vessels, and need for labeling non-fluorescent species, which may cause toxic side effects in the analytes. Bioimaging based on electrochemical measurements has also been attempted. The electrochemical method has been considered to have some advantages, including high compatibility with micro- and nanomachining technologies, system simplicity, small size, reliability, ease of use, and high sensitivity, but so far it only showed limited successes. I will show recent status and perspective of bioelectrochemical imaging with integrated microelectrode arrays and scanning electrochemical microscopy (SECM).

SECM has been widely applied for imaging of electrochemical reactions proceeding at various surfaces, including enzyme reactions, cellular functions, and membrane-related processes. Owing to recent efforts for incorporation of sophisticated nano-positioning control and multi-functionality to SECM systems, modern systems afford high-resolution imaging of non-contact topography and electrochemical signals of biomaterials. However, SECM imaging is not a high-throughput method; acquisition of full images usually requires more than 10 min.

Bioimaging with an individually addressable microelectrode array has also investigated. The conventional way to individually address each electrode of an array is to connect the electrode line to a corresponding bond pad. The electrochemical measurements are then carried out on each electrode sequentially. This method is easy to implement from a technological point of view; however, the number of individually addressable electrodes is limited since sufficient space for bond pads is not available on the chip border. Another way to realize the individual addressability with array electrodes is to use an integrated circuit (IC). However, it is difficult to detect very low currents (pA to nA) with an IC-based array.

Recently, new types of highly-sensitive bioelectrochemical imaging methods using 3D micro/nanoelectrode arrays and bio-LSI have been proposed. I will report the applicability of these devices to high-throughput bioimaging for Grand Challenge.

Biography: Dr. Kazuma Mawatari is an Associate Professor of Department of Applied Chemistry at The University of Tokyo. Dr. Mawatari completed his master course studies at Department of Applied Chemistry of The University of Tokyo in 1998. Then, he attended Asahikasei Corporation where he worked on development of point-of-care medical systems utilizing microfluidic chips. In 2003, he moved to The University of Tokyo and worked as a researcher in Kitamori Lab. From 2004-2009, he worked at Kanagawa Academy of Science and Technology and developed fundamental technologies for microsystem . In 2006, he received his PhD in Department of Applied Chemistry at The University of Tokyo. In 2009, he moved to The University of Tokyo as a lecturer, and he became an Associate Professor in 2011. His current researches are integration of chemical processes in micro/nano space, application of microfluidic system for analysis and diagnosis, and basic research on fluidics and chemistry in extended nanospace (10-1000nm). He is also developing analytical and energy devices utilizing the unique characteristics of extended nanospace such as single cell analytical device, chromatography device, heat pipe device, and fuel cell device.

Grand Challenge: extended nanospace for mimicking intracellular space and application to sensing technology

Kazuma Mawatari
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Department of Applied Chemistry
School of Engineering
The University of Tokyo, Tokyo, Japan

Spaces of 10-100 nm between cell membranes like synaptic gaps are believed to play very important roles in cell functions such as tissue formation and signaling process. In this space, some specific solution properties (viscosity increase and enhancement of proton transfer rate) are suggested near cell membranes (*Chem. Rev.* 2006). So, it is necessary to make a tool for investigating solution properties between them. By investigating the relationship between the liquid properties confined in 10-100 nm and the cell functions, next generation biomimetic devices can be expected. These devices will contribute to artificial tissue formation device or sensing device using the cell function.

However, it is quite difficult to directly measure the liquid properties *in vivo*. In addition, there was no experimental tool *in vitro* due to the very small space. Therefore, a big issue is to develop an engineering tool to investigate the liquid properties and to realize an artificial device utilizing the cell functions. In our laboratory, we made the 10-1000 nm extended nanospace channel in glass substrates and found many specific water properties, such as higher viscosity and faster proton transfer rate etc. It is revealed that there are similarity of solution properties between the extended-nano space and intercellular spaces. Therefore, we believe the biomimetic extended-nano space can be developed by modifying the wall of the channel by cell membranes, which leads to artificial biomimetic devices in future. At present, we could modify the channel with lipid bilayers and obtained preliminary results on direct evidence of enhancement of proton transfer rate below 1000 nm. However, many properties (viscosity, liquid structure, etc.) should be clarified. Technologies should be also developed to embed functional molecules on the lipid and to detect the very small amount of molecules inside the extended nanospace.

Biography: Dr. Akira Mita is a Professor of Department of System Design Engineering at Keio University. He received his PhD in Applied Mechanics and Engineering Sciences from the University of California at San Diego in 1986, MS in Architectural Engineering in 1981 from Kyoto University. Dr. Mita completed his undergraduate study at Tohoku University and received BS in Architectural Engineering in 1979. From 1981 through 2000, Dr. Mita served as a research engineer and a chief research engineer at Shimizu Corporation, one of the largest construction companies. His current research interests include sensors, system identification, structural health monitoring and biofied building. Especially, the last research topic, biofied building, is to develop a building embedding four adaption mechanisms, namely, sensory adaption, adaption by learning, physiological adaption and evolutionary adaption. In this research, sensor agent robots play an important role as moving sensors. Dr. Mita was awarded Encouragement Prize of Architectural Institute of Japan in 1991 and the Prize of Architectural Institute of Japan in 2009. He served the chair for the first Asia-Pacific Workshop on Structural Health Monitoring in 2006.

Grand Challenge: Biofied Building Embedding Adaption Mechanisms of Biological Systems for Safe, Energy-Efficient and Comfortable Living Space

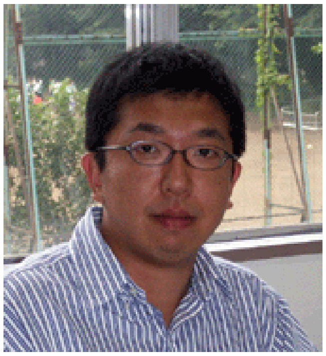
Akira Mita
Professor
Department of System Design Engineering
Keio University, Yokohama, Japan

Living things have been surviving thanks to adaptive mechanisms as categorized into four, sensory adaption, adaption by learning, physiological adaption, and evolutionary adaption. The latter two adaption mechanisms give the living things an ability of conquering harsh events such as unseen virus infection and drastic change of living environment. We do not have such capabilities in our engineering systems. To embed the adaption mechanism, we are particularly interested in using robots as moving sensor agents, that we call sensor agent robots. They gather information of buildings and residents, and more importantly interface buildings and residents. The information includes emotion and unconscious feeling of humans. Introduction of the robots will open a new era for buildings that talk to residents explicitly as well as implicitly. We call this concept "biofied building" or "biofication of living spaces" and are working to integrate the concept.

The smart house was proposed to make a house to be safer, more comfortable, energy-efficient, more durable, responsive to individual needs, and safer for aging and handicapped people. However, the smart house relies on scenario-based control systems so that the smart house does not have capability to deal with unexpected events. In addition, many sensors and actuators should be embedded in the house. Thus, the system is not flexible to adapt to a new generation of technologies. Once it is completed, it will immediately start becoming obsolete.

We propose the use of sensor agent robots to minimize the number of sensors embedded in building spaces. The sensor agent robots will be pets for residents. As the robots are self-contained systems, they are portable to be used at any building spaces. When the robots become degraded, they will be replaced by new robots while the data taken by the old robots will be inherited to the new robots. Thus the whole system can be always up-to-date by keeping the robots to be new. One of the most promising control methods for the robots to control the environments, homeostasis control mechanism has been studied at our laboratory. The homeostasis control mechanism is not based on scenarios so that it will be useful even for unexpected events such as failure of devices. However, the system requires that the feeling and emotion of the residents be obtained by the sensor agent robots.

One of the most important research topics in biofied building is to develop sensors to be implemented into the sensor agent robots to acquire information on inherent feeling, health conditions, emotions and activities of the residents in the building spaces. By detecting all important information on residents by bio-integrated sensors, buildings will evolve to biofied buildings.



Biography: Dr. Keisuke Morishima is a Professor, Department of Mechanical Engineering, Osaka University, JAPAN; he graduated from Nagoya University where he received his PhD in Engineering from Nagoya University, in 1998. In 1997, he was JSPS Postdoctoral Research Fellow. From 1998 to 2001, he was a Postdoctoral Research Associate in Prof. Richard N. Zare Lab at Department of Chemistry, Stanford University, USA. He joined Kanagawa Academy of Science and Technology as a Research Scientist in 2001. Meanwhile, he was a Research Fellow at the Research Association of Micro Chemical Process Technology and a Visiting Research Fellow. In 2004, he was a Visiting Research Fellow at Lund Institute of Technology, Sweden. In 2005, he joined Tokyo University of Agriculture and Technology. At present, he is Associate Professor of Department of Bio-Mechanics and Intelligent Systems and Department of Mechanical Systems Engineering, Tokyo University of Agriculture and Technology, Japan. He is mainly engaging in the research fields of Micro-Nano Robotics and its application to the micro-nanomanipulation, bio automation, BioMEMS, MicroTAS, microactuators, medical applications, living machine, soft & wet nano robotics, regenerative medicine. In recent years, he received 2009 Best Paper Award, The Robotics Society of Japan, 2009 The Young Scientists' Prize, The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology, 2006 Young Scientist Award, Ando Foundation.

Grand Challenge: Learning from Nature, and Engineered Top down and Bottom up approach will lead us an innovative fundamental change of New Design and Emergent Functionality of Regenerative Bionic Systems Powered by Chemical Energy for Cellular Build Up Wet Machines

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There have been so far many studies on downsizing and integration of "man-made machines"; not only semiconductor devices but also mechanical systems and chemical systems, such as micro electro mechanical systems (MEMS) and micro total analytical systems (µTAS). Those systems and devices are driven by external energy power source. Most of their fabrication process is based on "top-down approach." However, this top-down approach generally need a large-scale external system and have many issues regarding energy conversion efficiency, energy supply system, and sensitivity. Here we propose an environmentally robust hybrid (biotic–abiotic) robotic system that uses living components, called "Cellular Build Up Wet Nano Robotics". Our group has already presented a bioactuator using rat heart muscle cells, but it is difficult to keep rat heart muscle cells contracting spontaneously without maintaining the culture conditions carefully. By contrast, insect cells are much robust over a range of culture conditions (temperature, osmotic pressure and pH) compared to mammalian cells. Therefore, insect cells are more practical use of a hybrid wet robotic system, and they can be driven without precise environmental control.

From this point of view, to utilize robust biological components as a functional systems and self assembly process and their emergent functionality, and to build up such a soft and wet machines will lead us an innovative fundamental change and produce a new principle and design to future man-made systems. We demonstrate the example of a micro bioactuator and mechanical systems driven by biochemical energy. This novel muscle-powered bioactuator successfully show autonomous beating at room temperature for a long time without maintenance. Experimental results suggest the possibility of constructing an environmentally robust hybrid wet robotic system with living components and open up a new science and technology, biorobotic approach, medical, environmental monitoring, agriculture and industrial application.

Future Perspective: Cellular Build Up Wet Nano Robotics

Key: Soft and Wet Science &Technology and Understanding of Control Architecture

Application:

- **Healthcare & Medicine**
  Novel Micromachine inside Human with Chemical Energy
  Bioautomation and Biofactory for producing Wet Machines, Wet Lego using Stem cells and iPS cells
- **Environment & Energy**
  High Energy Efficient Device, such as a Biofuel Cell
  Environmental Monitoring system using robust Insect Cells
  Less Polluted-Mass Production System for Bio-Hybrid devices
- **Safety & Security**
  Novel Biosensor for Environmental monitoring

Biography: Dr. Tomonori Nagayama obtained his B.S. (2000) and M.S. (2002) in civil engineering from the University of Tokyo and his Ph.D. (2007) in civil and environmental engineering from the University of Illinois at Urbana-Champaign. He is currently an assistant professor at the Department of Civil Engineering at the University of Tokyo. His research interests include smart wireless sensor technology, structural health monitoring, earthquake engineering, and structural dynamics. He is a recipient of the 2007 ASCE Raymond C. Reese Research Prize.

Grand Challenge: Multilevel Sensing Fusion and Evolutionary Algorithm Refinement Toward Infrastructure Monitoring

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As infrastructure ages, their efficient management is a common and important issue in many countries including Japan and the U.S. Objective condition assessment of infrastructure based on sensing technologies is considered to improve this management allowing extraction of bridges, pavements, and other infrastructure components needing maintenance. Also, condition assessment of newly built structures and those after maintenance work can be used to evaluate the quality of the design and work. Such feedback would help improve the quality of the current infrastructure and that in the future. However objective condition assessment based on sensing technology has not matured yet. Characteristics of infrastructure, such as the large size, designs different from each other, large numbers of components, continuous service operation, pose limitation on the application of currently available technologies.

One possible break-through approach is one analogous to biological systems. Biological systems consist of a large number of sensing components. Many kinds of sensors are used simultaneously and the outputs are combined to reach the final decision. Such information fusion is performed on multiple phases. Low level perception (e.g., combination of vision and hearing) and high level logical judgment (e.g. combination of current information and past experiences) are jointly utilized. Recent advance in smart sensing technologies possibly allows sensing of a variety of physical quantities, storing data efficiently, and analyzing them. However, simply combining sensing, storing, and analysis capabilities would not solve the problem. In biological systems, among many possible DNA combinations, only a few successful ones exist. Refinement of the combination depending on the environment and/or purpose is necessary. For infrastructure monitoring, combinations of several sensing capabilities are being studied. However, these efforts need to be tailored toward condition assessment purposes with more emphasis on application needs.

Biography: Dr Onoshima received his Ph.D. in Applied Chemistry from Nagoya University in 2008. He completed his degree in the laboratory of Prof. Yoshinobu Baba (an expert in nanobiotechnology) where he worked on the development of miniaturized analytical systems for molecular biology. During his initial postdoctoral works, he studied single-particle tracking techniques to visualize the motion of biomolecules at MEXT Innovative Research Center for Preventive Medical Engineering, Nagoya University. He is now a postdoctoral fellow at FIRST Research Center for Innovative Nanobiodevice in Nagoya University where he studies the interaction of biomolecules at a single molecule level. He uses several approaches in his study, including electrophoresis, microfluidics, fluorescent imaging and statistical data analysis. The latest advances of his study were selected as an excellent work for oral session in The 12th and 14th International Conference on Miniaturized Systems for Chemistry and Life Sciences (MicroTAS 2008 and 2010). He received CJS Presentation awards 2009 from The Chemical Society of Japan (CJS), and more recently received the support of a Grant-in-Aid for Young Scientist (Start-up) (FY2009) from Japan Society for the Promotion of Science.

Designing a Nano-Interface in a Microfluidic Chip to Probe Biological Processes and Living Cells: Challenges and Perspectives

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Micro- and nanoelectronics technology would enable fabrication of a biosensor array capable of rapid high content screening to identify and investigate pharmacological agents or toxins. For instance, dielectrophoresis in microfluidic chip has been proposed for positioning cells, proteins, or DNA on the substrate, and the control of viral protein or DNA positioning shows promise for guiding self-assembly of molecular electronics circuits in the push for smaller, faster, more energy-efficient device designs. These examples illustrate recent advances in the measurement and control of mechanical, biochemical, and electrical interactions at the interface between biomaterials and living cells. Thus, new tools are becoming available at a time when biologists are learning more about molecular mechanisms such as physiology and pathology. However, the elucidation of disease mechanisms and increased sensitivity to detect small amounts of biological agents requires improved robustness and spatial resolution for fabricating nanostructured surfaces within microfluidic chips. A major challenge for the next 5–10 years is the reproducible placement and seamless interfacing of functionalized nanoscale features and messaging systems within a chip-based device to measure and interpret complex biological processes in real time.

Existing technologies to manipulate a single intact cell or to measure biological processes within a microchip environment include chemical, optical, and electrokinetic, each of which take advantage of different physical forces at the micrometer length scale. Biochemical approaches have been traditionally used by biologists and biochemists to characterize cell populations, and more recently these methods have been adapted for use in microdevices. The most prominent example is the development of a chip-based DNA purification and PCR technique that rapidly synthesizes thousands of copies of a DNA fragment, thus amplifying the amount of DNA above the detection threshold. Biochemical tags or cues or inhibitors of cellular functions can be delivered to a single cell either in soluble form or immobilized on a solid surface. The introduction of soluble biochemical cues within microchip systems is limited by micromixing and by characteristically slow diffusion of reagents in small channels. However, the surface area of a microchannel wall is large compared with channel volume, which enables presentation of controlled concentrations or spatial gradients of chemical stimuli or sensors over a relatively large area with respect to the cell surface. The quantitative measurement of cell responses from such chemical cues remains a challenge. Fluorescence-based techniques show promise for single molecule detection in systems with ideal optical imaging conditions, but accurate quantification is difficult at such small length scales. In addition, advances in nanotopography fabrication on both horizontal and vertical surfaces in a microfluidic channel are required to accomplish chemical trapping of single biomolecules and cells at a given location. Finally, rapid throughput and analysis are required to determine whether results from only a few molecules used in the microdevice are indicative of a population behavior.

Biography: Mihoko Otake is a researcher, inventor and innovator based on the expertise in robotics. She holds BE (1998) and PhD (2003) in Mechano-Informatics from the University of Tokyo. She developed world first "Gel Robot" during her PhD studies, which has published as world first monograph “Electroactive Polymer Gel Robots - Modelling and Control of Artificial Muscles” (2009) from Springer-Verlag, and opened the novel interdisciplinary field. Gel Robot is a whole body deformable mechanism made of smart materials. She has been on faculty of the University of Tokyo since 2003. She is currently the Associate Professor with Research into Artifacts, Center for Engineering the University of Tokyo. She won the Doctoral Scholarship Award from the Japan Society for the Promotion of Science (2001), and the Young Investigator Award from the Robotics Society of Japan (2003) for the contribution to the development of Gel Robot. Then, she extended her skill of modelling, design and control from smart materials to smart machines, the human brain and mind. She won the PRESTO Fellowship Award from the Japan Science and Technology Agency for the development of human neural model (2004) and individually adapted cognitive activity support (2010) for both healthy and disabled people. She invented Coimagination Method (2006), the cognitive enhancement method supporting interactive recall and knowing via data-driven conversation. She founded Fonobono Research Institute (2007), and became a founding director in order to investigate the method as well as to innovate social environment towards heart warming (fonobono) humanitarian society through the permeation of the philosophy of Coimagination Method. She is developing technologies for modelling and identifying internal state of humans from multiple sensor data and monitoring human reactions.

Grand Challenge: Agent Model of Smart Materials for Bioloically Inspired Robots

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In this statement, I introduce design philosophy of gel robots, biologically inspired robots based on agent model of one of the smart materials, electroactive ionic polymer gels, from my monograph "Electroactive Polymer Gel Robots" pp.213, for presenting future direction.

In the field of artificial intelligence, agent is defined that anything that can be viewed as perceiving its environment through sensors and acting upon that environment through actuators. This definition also applies to smart materials. Among various types of agents, we can model smart materials as model-based reflex agents, which maintain some sort of internal state that depends on the percept history and thereby reflects at least some of the unobserved aspects of the current state. Internal state functions are determined based on the electrochemomechanical property of each material.

Knowing about the current state of the environment is not always enough to decide what to do, the agent needs some sort of goal information that describes situations that are desirable. The agent program can combine this with information about the results of possible actions in order to choose actions that achieve the goal. However, goals alone are not really enough to generate high-quality behavior in most environments. Goals just provide a crude binary distinction between desirable and undesirable states, whereas a more general performance measure should allow a comparison of different world state according to exactly how desirable they would make the agent if they could be achieved. If one world state is preferred to another, then it has higher utility for the agent. A utility function maps a state onto a real number, which describes the associated degree of desirability.

Control system for smart materials should contain modules which represent goal or utilities, since smart materials are modeled as simple reflex agents with internal state without goal or utility by its nature. Therefore, we modeled on of the typical electroactive polymers, and include the model into control systems. Then, the utility function was added in order to determine the appropriate action or electrical stimuli to the material from the control system. Simulation had been conducted in various situations so that condition action rules are determined. The controller with condition action rules was necessary for real-time operation.

Future direction includes modelling smart materials as agents for applying artificial intelligence theories to design biologically inspired smart sensors and actuators.

Biography: Dr. Kenji Sueyoshi is an Assistant Professor of Graduate School of Engineering at Kyoto University. Dr. Sueyoshi completed his graduate studies at Kyoto University where he received his PhD in Engineering in 2008, MS in Engineering in 2005. Dr. Sueyoshi received his BE in Chemical Engineering from Kyoto University in 2003. His current research interests are in the areas of separation science, especially, capillary and microchip electrophoresis (CE and MCE). Specifically, Dr. Sueyoshi's work aims to develop novel analytical methods based on CE and MCE with easy experimental procedure. Some of Dr. Sueyoshi's more current research has been focused on the improvement of both the separation efficiency and sensitivity of the bioanalytes such as peptide, protein, and DNA. Dr. Sueyoshi was recently awarded the 2009 CSJ Presentation Award.

Grand Challenge: Development of Biologically Functionalized Microfluidic Device for Rapid, High-sensitive and High-resolution Bioanalysis Based on Electrophoresis

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In studies on *Life Science*, one of the important fields is *Separation Science* because a numerous amounts of analytes take part in biosystems in human being. In addition, most of the biogenic compounds are positively or negatively charged, thus electrophoretic analyses play a significant role to clarify the relationships between the biosystems and health. Considering the electrophoretic separation, a molecular sieving effect of a slab gel has been utilized for the size separation of proteins and DNAs in the early stage of the study on Life Science. Especially, the developments of the blotting methods after the slab gel electrophoretic separation provide valuable information, e.g., presence/absence of the specific DNA related on genetic disorder, immunoaffinity analysis of specific proteins, and so on. However, the slab gel immuno-blotting has numerous drawbacks such as troublesome manual operations, requirement of long analysis time, and so forth, which disturb the study on Life Science.

Capillary electrophoreses (CE) is also used for the separation of bioanalytes due to some advantages e.g., high resolution, small consumption of reagents/samples, short analysis time, and many versatile separation modes. In CE, some biologically important parameters such as the isoelectric point, molecular size, specific interaction between bioanalytes and ligands can be rapidly estimated by capillary isoelectric focusing, capillary gel electrophoresis (CGE), and affinity capillary electrophoresis, respectively. Especially, it is well-known that a paradigm shift emerged within genomics by the development of a DNA sequencer based on the multi-array CGE. Furthermore, it is also reported that the direct sampling from the living body was employed by the capillary equipped with a microdialysis probe. In a microelectro-mechanical system (MEMS), microchip electrophoresis (MCE) was developed to realize further high throughput electrophoretic analysis. Additionally, MCE can be combined with some microfluidic devices as a separation and detection scheme of a micro total analysis system (μ-TAS). Resent investigations on μ-TAS also allow the immuno-blotting techniques in slab gel electrophoresis to be carried out in the microdevice, providing a rapid immunoassay with an easy experimental procedure. Hence, the progress of the microfabrication techniques makes CE/MCE versatile techniques for the separation of the numerous kinds of biogenic analytes.

As a next step, it will be important to emulate/mimick the biological systems and processes in CE/MCE for the investigation of the molecular recognition on the cell membrane, measurement of the activity of enzyme in the internal organs, highly sensitive and specific detection of targets by employing affinity sensor, and so on. However, the emulation of the biosystems is still difficult for the CE/MCE equipment due to some experimental reasons, e.g. the difficulty of the cultivation of the living cells in the capillary/microchannel, the joule heating due to a high ionic strength of the body, tissue and culture fluids, the durability of living cells under the applied electric field during the analysis, and so on. Through the application of biological systems to CE/MCE analyses, it will become possible to realize a rapid and sensitive biogenic and diagnostic analysis based on the biogenic interaction. There is a pressing need for new paradigms that advance a novel electrophoretic analysis which can be carried out with overcoming these difficulties.

Biography: Dr. Madoka Takai is a Professor of Department of Bioengineering at The University of Tokyo. Dr. Takai completed her graduate studies at Waseda University where she received her PhD in Engineering in 1998. She received her MS in Applied Chemistry of Engineering in 1995, and her BE in also Applied Chemistry of Engineering in 1990 at Waseda University. Her current research interests are in the areas of biosensing devices by novel biomaterials based on molecular design with strong inspiration from the phospholipid structure of cell membrane surface. The novel biomaterials can inhibit surface-induced clot formation effectively, even when they contact with blood in the absence of anticoagulant. Recently she found that activity conservation of biomolecules immobilized on the phospholipid polymer surface comparing with activity of a physically adsorbed biomolecuels. The phenomenon is also very important function to develop every bioconjugated devices such as biosensor. Now she starts analyzing the cause based on the interaction between biomolecules and materials focus on water structure surrounding of material surface. Dr. Takai was recently awarded the 2010 Incentive Award in Society of Chemical and Micro/Nano System, 2006 Technology Prize in The Surface Finishing Society of Japan, and 2003 Honda Memorial Young Researcher Award.

Grand Challenge: Bio-inspired Active Soft Materials for Biosensing System for Next Generation Medicine

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Nature provides a wide range of materials with different functions and which may serve as a source of bio-inspiration for the materials scientist. In contrast to artificial materials natural materials such as wood, bone and shells are composed of only limited number of basic components. They gain their diversity in mechanical properties by hierarchical structuring which allows them to fulfill a variety of functions e.g. self-healing, mechanical stability, high toughness. Thus, bio-inspired materials science – also referred to as biomimetic materials science– is a rapidly growing of increasing interest in many diverse fields, such as biosensing, bioactuating, biomedical engineering, and bionanotechnology inspired in part by the paper of Heuer et al. published by 1992[A. H. Heuer, et al., *Science* 1992, *255*, 1098]. The embryonic tendency is to focus on just a few hard biological materials, such as wood, bone and shells. There is however much more to be discovered but the access to the knowledge about relevant biological systems is difficult.

The challenging field of bio-inspired materials science focuses on developing a fundamental understanding of the synthesis, directed self-assembly and hierarchical organization of naturally occurring materials, and uses this understanding to engineer "new bio-inspired" artificial materials for diverse applications. The main thrust in the developing of "new bio-inspired" materials is the artificial multi-functional materials involving an active biological network system, instead of looking at the relationship between biological materials and functions only one point of view.

Cell membrane is a perfect example as biological materials control a biological sensing network system such as cell-cell communication, conjugation, recognition, and signaling. Sugar chain and membrane protein that are sensing unit implant in the phospholipid bilayer coordinates response of a cell to its external environment specifically. Materials exploration of a radically new approach for the design of "cell-inspired" is synthetic polymers with environmentally responsive mechanical- chemical- biological- properties. The external stimulus causes a reversible change of the specific unit in the polymers, and the change of the mechanical properties proceeds to next response in sequence. The specific signal can be distinguished under perfect materials platforms that have unresponsive, non-specific properties like phospholipid bilayer. Characteristic manner in the "cell-inspired" materials is soft polymers that can work dynamically active in nano/micro scale in a chain reaction. Among them a liquidity structure of cell membrane plays an important role in a signaling mechanism of biological system. That is a grate challenge to develop "new bio-inspired" soft- and active- materials having multi-functions for biosensing system for next generation medicine. To obtain further advancing functions for creating active sensing device system, the hybrid, composite materials with organic and inorganic substances appear promising. Fusion nanotechnology, which defies the boundaries of organic/inorganic materials, bottom-up technology based on self assembly/top-down technology is needed for creating bio-inspired materials.

Biography: Dr. Yasuteru Urano is current a professor of Graduate School of Medicine, The University of Tokyo. He received the Doctorate of Pharmaceutical Sciences (PhD) awarded from the University of Tokyo in 1995. He was a postdoc fellow in the University of Tokyo from 1995-1997.

Grand Challenge: Seeing the Unseen in vivo for Possible Revolution of Personal Medicine; Evidence-based Diagnosis and Therapy of Disease by Developing Rationally Designed Chemical Tools

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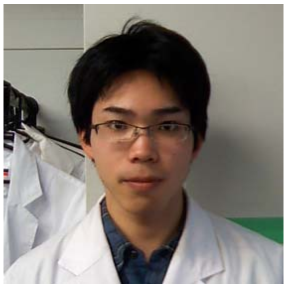
So many men, so many diseases. In these several years, much attention has been paid on the concept of personal medicine. Even if two men suffer from the same disease, different therapies should be applied based on personal characteristics like activities of metabolism. For acquiring personal characteristics, genetic features of patients' extracted genes have been extensively examined sofar, however, I think examining "living" features of patients' personal disease cells have much impact and efficiency for achieving real personal medicine.

Chemical tools have been extensively utilized in biological fields as critical methods for exploring the nature of life. Small molecule agonists and antagonists are good examples of great contribution of chemical tools to biological researches. Further, nowadays, chemical probes like fluorescent probes and photosensitizers are frequently used in biological researches which offer chances of critical observation and perturbation of responses in living cells and organs. In other words, these chemical tools afford precise examination of living features of cells and organs.

However, these tools have been rarely utilized for medical purposes, i.e., visualization and therapy of disease. In principle, in situ diagnosis of disease cells in living human should afford true personal evidence-based therapy, because doctors are able to understand the nature of disease site. Forachieving this goal, we must know exact and much characteristics of living normal and disease cells and organs in human body by using various chemical probes and metabolome approaches. Based on these "live" information of every normal and disease cell and organ, doctors can suggest one by one efficient strategy to cure diseases. These approaches would lead to possible revolutionof personal medicine. For achieving these unmet medical needs, probes and instruments for visualizing various targets such as disease marker proteins, protein-protein interactions, and epigenetics in vivo.



Biography: Mr. Tadahiro Yamashita is a Ph. D student of the University of Tokyo; he is also a research fellow of Japan Society for the Promotion of Science (JSPS) from 2010. Mr. Yamashita received BE in Applied Chemistry and ME in Bioengineering from the University of Tokyo. His research mainly focuses on microfluidics and biomaterial chemistry. Combining the knowledge, he has developed a separable microchip that enables cell culture in the microfluidic environments and noninvasive recovery of them from the device. Utilizing this new microchip, fundamental cell culture and recovery scheme of vascular cells were demonstrated. Applying this new device, his current work aims *in vitro* construction of a vascular tissue in m scale.

Grand Challenge: Bioinspired self maintenance system for long term and robust biosensors

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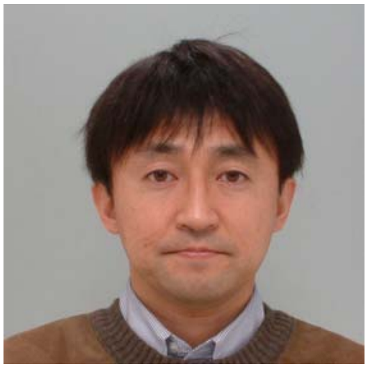
Sensing in this document indicates ‘detecting’ that means discovering or identifying the presence or existence of something. When we develop a sensor, which includes some necessary steps: (1) detecting something and generating a signal (2) transfer the signals to another part (3) interpreting the signal to get some information. In nature, many animals have many kinds of fully integrated sensing system such as five senses that includes all components noted above.

About a half century ago, bioinspired specific sensors called ‘Biosensor’ was conceived. In the sensor, biomolecules or organelle immobilized onto the electrodes to detect the chemicals, and signals from them are transduced to electric information through electrodes. As the science and technologies advance, this concept has been widely expanded involving other fields. For example, electrodes are integrated to electric circuits and microfluidic environments utilizing microelectro mecanichal systems (MEMS) techniques, and not only biomolecules but also living cells and cellular spheroids have been applied for sensing modules.

Practical application of biosensors has become wider. However, these devices have a limited useful life-span because the sensing part is not immortal. And this mortality has made it unable to long term (such as several month) monitoring by biosensors. To overcome the difficulty, I suggest a new function for biosensors (4) self maintenance and self renewal. For example, in the living body, almost living cells increase and dead cells are cleared off to maintain the living tissue. To mimic the life for the longevity of the biosensors, active maintenance system for in vitro cell culture should be developed. For example, integrating a miniaturized cell culture platform, biosensors and the controlling unit, the concentration of analytes and cellular conditions are monitored simultaneously. All information is fed back to the controlling system and it adjusts the environment to maintain the cellular condition. This integrated sensing system would enable the robust biosensors for long term monitoring. And that would also provide a new cell culture and analysis platform for medical use such as cellular engineering, tissue engineering, and drug screening.



Biography: Dr. Kenji Yasuda is an Professor of Institute of Biomaterials and Biosystems at Tokyo Medical and Dental University. He received his PhD degree in Physics from Waseda University, Japan in 1995. Then, he studied Biophysics as researcher in Advanced Research Laboratory, Hitachi Ltd. Japan until 1999. During this period, he studied energy exchange mechanism of single molecular motors, physical properties of nebulin and titin in skeletal muscle sarcomeres, and invented acoustic tweezers for non-contact handling of biomaterials within the microfluidic pathways with several fundamental Lab-on-Chip technologies. From 1999 to 2006, he was an associate professor (and professor in 2006) in University of Tokyo. During this period, he started a series of on-chip single cell-based researches and developed several single cell measurement technologies. He used microcultivation chambers and optical tweezers to compare the behavior of two isolated sister *E. coli* cells to understand the limit of genetic control for their behaviors. He also invented agarose photo-thermal etching technology for real-time microfabrication on chip even during cultivation, and developed a method for fully-direction control of neuritis like axons and dendrites for formation of real neuronal network on a chip exploiting this etching technology. He measured the importance of community effect of cardiomyocytes for the stable beating quantitatively, and he also observed that the synchronization of two cardiomyocytes having different beating intervals occurred by choosing the cell having more stable beating frequency rather than the faster one. In 2005, he was also a visiting professor in Genome Technology Center (Prof. R. Davis) at Stanford University for developing nano pipette-based post genome measurement technology together. From 2006 to date, he has been a professor in Institute of Biomaterials and Biosystems at Tokyo Medical and Dental University, and from 2008 to date, he also is a head of research team in Kanagawa Academy of Science and Technology to develop the several technologies for characterizing single cells within the network, such as 3-min ultra high speed single cell PCR analyzer, on-chip *in situ* genome/proteome measurement system and so on.

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Grand Challenge: On-chip Cellomics Technology for Re-Constructing quasi-*in vivo* Pre-Clinical Toxicity Measurement using hES/iPS Cells and Their Community Effects

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Prof. Yamanaka team have reported a new way to create pluripotent cells from human somatic cells in 2007. The advent of induced pluripotent stem (iPS) cell technology has a great impact on the patient-specific cell therapy and also might have a great promise as a research tool to improve predictive power of toxicology testing. One of the advantages of the iPS cell technology is that iPS cells can be prepared from healthy volunteers of different races, sexs and also from patients with various diseases, and they can differentiate into any types of human tissues (endodermal, mesodermal and ectodermal tissues) to provide an ideal testing platform, distinct from the traditional in vitro testing using immortalized cell lines and primary cultured cells. .

However, there are many hurdles to validate testing systems. For example, we have not yet known the detailed mechanisms for reprograming and how closely iPS cells resemble conventional ES cells, or how closely the provided human cells from iPS cells resemble human tissue cells. The efficiency of derivation of human somatic cells remains low. Supply of standard iPS cell-derived specific cell types, how to identify and open protocol are important to validate testing systems among participating companies and academics. Moreover, as we only can acquire human cells, not tissues nor organs, we need to develop and validate a new *in vitro* testing systems and protocols which can expand its ability to *in vivo* screening indexes, i.e. *quasi-in vivo assay*.

Consequently, as an initial step, our research team have focused on the risk assessment of QT prolongation using human iPS/ES cell-derived cardiomyocytes. QT prolongation is still a major safety concern for selecting and developing candidate compounds. The current integrated assay systems using hERG-transfected HEK-293/CHO-cells (hERG assay), isolated animal tissues (APD or MAP assay) and conscious and/or anesthetized whole animals (QT or Map assay) may identify QT prolongation, but cannot fully predict the potential lethal arrhythmias such as Torsades de Pointes (TdP) or ventricular fibrillation (VF) by drug candidates. There is, therefore, an urgent need for a surrogate marker that can distinguish the torsadogenic potential better than the QT interval duration. Added to the current testing systems, human iPS cell derived cardiomyocytes might provide further insight into the extrapolation of preclinical data to human clinical settings or could replace existing in vitro and in vivo models to the *quasi-in vivo* model.

Understanding the importance of spatial and temporal regulation of cellular orientation, community size and shape, variety and interactions are the keys to resolving mechanisms of epigenetic processes in highly complex heart system for expanding conventional *in vitro* cell assay to cell-network assay and *quasi-in vivo* assay. To investigate the meaning of the spatial distribution of cells, an on-chip cell network cultivation system has been developed, and extra-cellular signals (field potentials: FP) of human embryonic cardiomyocytes in geometrically patterning chambers have been recorded with an on-chip multi-electrode array (MEA) system.

In our research project, especially, we have focused on the strategy of an on-chip assay for providing further insight into the extrapolation of preclinical data to human clinical settings or for expanding or replacing existing in vitro and in vivo cardio- toxicity models as the special topics as follows:

1) TdP prediction by evaluation of temporal fluctuation of ion channels. Abnormal triggering (temporal dispersion) causing lethal arrhythmias have been estimated by analyzing the time course FP dispersion of single human cardiomyocyte cells using Poincaré plotting.
2) TdP prediction by evaluation of spatial fluctuation cell-to-cell propagation. Spatial dispersion of cells causing fluctuation of signal propagation and spiral re-entry have been measured by using a cell network loop which can choose different propagation pathways of human cardiomyocyte cells among neighboring circulations. Especially, addition of human fibroblasts into the cell network has a potential for representing the more close to real heart tissue propagation model.
3) Evaluation of the inhibition on the trafficking pathway of ion-channel proteins. Expanding the testing of the conventional direct inhibition to the ion channels, the inhibitory effects on the protein synthesis, protein maturation, and intra cellar vesicle transport in human heart cells have been measured.
4) Genetic/epigenetic variety of human heart cell sources provided from variety of human iPS cells. In the workshop, we hope to discuss the trends and potentials of single-cell-based re-constructive approach for creating *quasi-in vivo* assay in a chip.

Biography: Takao Yasui is a PhD student of Department of Applied Chemistry, Graduate School of Engineering in Prof. Yoshinobu Baba's laboratory at Nagoya University; he is also working with FIRST Research Center for Innovative Nanobiodevice at Nagoya University. He completed his MS in Department of Applied Chemistry, Graduate School of Engineering, and his BE in Department of Chemical and Biological Engineering, School of Engineering from Nagoya University in 2009 and 2007, respectively. His research interests focus on label-free DNA detection and DNA separation with micro/nanostructures.

Grand Challenge: Development of micro/nanostructures with bio- and medical sensing applications

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New nanomaterials and nanostructures using semiconductor, nanofabrication and chemical technologies have been developed. The grand challenge is to develop new structures with bio- and medical sensing applications via label-free biomolecule separation and detection at ultrahigh resolution with a wide range of molecular length. To achieve this challenge the appropriate micro/nanostructures for DNA, protein or cell analysis should be selected, resulting in the most appropriate personalized medicine.

For several years nanotechnology has been applying to disease diagnosis, especially the detection of biomarkers, SNP (single nucleotide polymorphism) analysis and DNA sequencing. Now, some medical groups work to develop very-early-stage cancer detection based on single cell or biomolecule analysis. System biologists also would like to analyze expression profiles of genes from human. For this aim, nanostructures for analyzing over 20000 genes in a single run and in parallel need to be developed, even though the scale of analysis of genetic materials is still small. The nanotechnology is a key technology for targeting the biological, medical, or system biological fields. Personalized medicine has a wide variety of goals. For example, the detection of SNPs to predict side reactions of drugs has been already used. But SNPs are only a small part of personalized medicine. The real personalized medicine will take more than 10 years to reach because there is no knowledge from system biology at present. An expression profile of all genes and all expressed proteins, all modifications of proteins and all other reactions in the cell should be categorized. To do that, a number of nanotechnological break through are desired. *In situ, in vivo* real time single molecule analysis is also an important goal. The very small number of expressed proteins can be a key issue for cancer and other diseases. To look at interactions between small numbers of molecules, very small volumes are necessary but conventional technologies use large volumes. Using large volumes it is easy to detect single molecules, for example single molecule DNA or single molecule proteins. But if interactions between proteins, proteins and DNA or molecules and cells would be detected, very small nanostructures which could deal with very small volumes would be required because biological reactions occur at micro- to nano-, even pico-molar concentrations. Chip-based technology means very small volumes can be available, making nanotechnology key for this kind of work.

Another challenge is making older people feel happier, because the aging population is increasing and 10 years from now 25% of the Japanese population will be over 65. Nanotechnology would be also used as a measure of happiness, stress levels and health. And also the stages of cancer or diabetes would be measurable, since genomic research would tell us which genes relate to which diseases. The next stage is that the analysis of proteomics and glycomics in more detail and measurement of the brain function to look at happiness and stress. The control of disease and measurements of health means happiness for some people. To develop that technology we could measure the happiness. The definition of happiness is different for each of us so a personalized happiness measurement based on nanotechnology is needed. That is an important target, too.

Biography: Dr. Takashi Yatsui is currently Associate Professor of School of Engineering at University of Tokyo. He received the B.E. degree from Keio University, Tokyo, Japan, in 1995, and M.E. and D.E. degrees from Tokyo Institute of Technology, Tokyo, Japan, in 1997 and 2000, respectively. From 1999 to 2000, he was a Research Fellow of the Japan Society for the Promotion of Science. Following his postdoctoral research at the Japan Science and Technology Agency, he joined the faculty at University of Tokyo. His current research interests include nanofabrication using optical near-field and its application to nanophotonics. Dr. Yatsui received 1st prize in Paper Contest from IEEE Student Branch at Tokyo Institute of Technology in 1998, and the excellent research presentation award form the Japan Society of Applied Physics in 2000, Tejima Doctoral Dissertation Award from Tejima Foundation in 2001, and German Innovation Award in 2011.

Grand Challenge: Learning and Mimicking Biological Systems for Next-Generation Sensors and Actuators for Health Monitoring of Civil Infrastructure Systems

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It is well known that the light-trapping system in photosynthetic bacteria was formed under the illumination of the sun light [1]. Mimicking such a biological system, we have developed photon-assisted fabrication process, and have shown that the device was formed as an optimum structure.

One example was the nano-scale waveguide that consisted of the metallic nanoparticles chain [2]. Instead of conventional top-down method such as electron-beam lithography, we deposited metallic nanoparticles chain using sputtering under the illumination with a photon energy that will be used as a nano-scale waveguide. We realized self-assembly of the uniform chain structure of the metallic nanoparticles, in which the separation was optimized for the application of nano-scale waveguide.

Another example was the solar cell [3]. To fabricate the electrode of the semiconductor solar cell, we also performed laser-assisted deposition. As a result, we succeeded in the increase in the photo-current conversion efficiency at a wavelength region that was used for the electrode deposition.

Based on our achievement, if the certain sensor or actuator which utilize light during operation is given, we believe their performance can be optimized when the device was fabricated under the illumination.

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Biography: Dr. Genki Yoshikawa is a MANA Independent Scientist at the WPI Center for Materials Nanoarchitectonics (MANA), National Institute for Materials Science (NIMS), Japan. Dr. Yoshikawa received his BS (1999), MS (2001), and Ph.D. (2004) degrees in Science from University of Tokyo, Japan. He was a COE Researcher at Department of Chemistry, University of Tokyo, Japan (2004-2005), Assistant Professor at Institute for Materials Research (IMR), Tohoku University, Japan (2005-2008), Visiting Scientist at Department of Physics, University of Basel, Switzerland (2007-2009), Research Associate (2008-2009), and ICYS-MANA Researcher (2009-2011) at MANA, NIMS, Japan. His current research topics include: Nanomechanical Sensors, Cantilever Sensors, Biosensors, Finite Element Analysis, Analytical Modeling, Surface Science, Physical Chemistry, Materials Engineering, and Cell Biology. Currently, Dr. Yoshikawa's research focuses on the comprehensive development of a really useful sensor system based on the Membrane-type Surface stress Sensor (MSS) which he invented and developed in collaboration with Dr. Heinrich Rohrer and the MEMS team in the Institute of Microengineering (IMT), Ecole Polytechnique Federale de Lausanne (EPFL), Switzerland.

Grand Challenge: Rapid Identification of Pathogenic Bacteria

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How many times have you ever dosed yourself with “antibiotics”? With or without our knowledge, each time we take antibiotics, we are taking the following serious risks:

a) Fostering antibiotic-resistant bacteria

b) Upsetting the natural balance of bacteria in our body

As we experienced in our history, such as the Spanish influenza which killed more than 20 million people all over the world (this is still one of the top records of the death toll among all kinds of causes, including World War II (~ a few tens of million in total)), antibiotic-resistant bacteria can cause a global crisis. The number of deaths is estimated up to millions or even billions once highly toxic and infectious bacteria which have resistance to any kinds of antibiotics emerge at somewhere in the world.

The risk b) has been gradually becoming clear recently. Although this issue has received far less attention, it can be equally serious. Antibiotics kill the bacteria we do want, as well as those we don’t. Recent studies indicate that, sometimes, our friendly flora never fully recover. These long-term changes to the beneficial bacteria within people’s bodies may even increase our susceptibility to infections and disease. Overuse of antibiotics could be fuelling the dramatic increase in conditions such as obesity, type 1 diabetes, inflammatory bowel disease, allergies and asthma, which have more than doubled in many populations.

The critical problem for the current situation is the absence of a good sensor which can rapidly identify pathogenic bacteria, while the conventional method takes at least a few days. Accordingly, medical doctors prescribe an antibiotic based on their experiences (empiric therapy) as the first choice. Since it is impossible to identify the exact bacterial species, they give a broad spectrum antibiotic which acts on a wide range of bacteria in most cases, thereby running the above risks a) and b) everyday all over the world.

The sensor must be small, low-cost, and easy to use anywhere in the world because evil bacteria can easily spread globally irrespective of its place of emergence. We are now trying to address this Grand Challenge by means of a recently developed sensor, namely a membrane-type surface stress sensor (MSS; Fig. 1) [1]. If we can solve this challenge, such a sensor system can be also utilized as a versatile tool for the daily health-care by placing it at bedside, in a toilet, etc, connected to a health-care cloud, in addition to saving the world and the future from the threats related with bacteria.

[1] G. Yoshikawa, T. Akiyama, S. Gautsch, P. Vettiger, H. Rohrer, Nano Letters 11, 1044-1048 (2011).

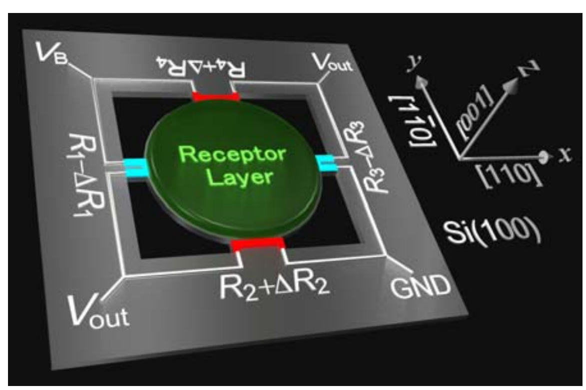

Fig. 1: Membrane-type Surface stress Sensor (MSS)

Biography: Dr. Hiroyuki Yoshikawa is an Assistant Professor of Department of Applied Physics at Osaka University. In 1999 he obtained his PhD in Applied Physics from Osaka University studying on picosecond near-field microspectroscopy of organic microcrystals. He has published many papers regarding photochemistry and photophysics of nanomaterials in small domains utilizing confocal and near-field microspectroscopies, optical trapping and control of molecular nano-assembly, surface enhanced nonlinear Raman scattering from optically-trapped silver nanoparticles. He has started researches regarding biosensors in collaboration with Prof. Tamiya from 2007. His current research interests are in the areas of nanophotonic biosensors with plasmonic metal nanostructures.

Grand Challenge: New design concepts for nanophotonic biosensors

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Advanced biosensing and bioanalysis researches are mainly focused on the high sensitivity and ultramicroanalysis, and nanotechnology is used to improve their performances. The problem is that advanced biosensing and analysis using precise and complicated micro- nanostructure and special expensive apparatuses are difficult to be widely used. A new concept is necessary to utilize advanced nanobiotechnologies for public health and safety.

Biosensor using interaction between photons (light) and nanostructures is both scientifically and technologically interesting and important. Not only high sensitivity and ultramicroanalysis, but also high throughput, low cost, and easy and safety operation are expected by the development of nanophotonic biosensor.

So far, in nanophotonic biosensors, light has been used as a signal probe. But light, especially a focused laser beam has potentials to induce photochemical reactions, temperature elevation, trapping of small objects, and so on. By using these effects induced by a focused laser beam, unique nanophotonic biosensors can be designed. For example, gold or silver ion reduction and their nanoparticle deposition by a focused laser beam is demonstrated by some researchers. Thus a focused laser beam has a potential to fabricate metal nanostructures, which are applicable to nanophotonic biosensors based on localized surface plasmon resonances (LSPR) and surface enhanced Raman scattering (SERS). If a focused laser beam can be used both as the energy source of metal nanostructure fabrication and a signal probe, time-consuming and expensive nanofabrication process can be skipped.

A focused laser beam is quite commonly used in daily work and life. A small optical device called “optical (laser) pickup” is used for reading and recording of an optical disc and equipped in CD and DVD recorders, game hardware, and personal computers. In optical pickup devices, a laser beam emitted from a laser diode is tightly focused by a lens on a surface of an optical disk. A reflected or backscattered light of the laser beam is corrected by the lens and introduced to a photodetector and converted into electric signal. The position of the beam is precisely controlled.

By using such widely used devices, I think sophisticated nanophotonic biosensing systems can be realized without both complicated nanofabrication processes and expensive apparatuses, and such biosensors can contribute to public health and safety.