1st Asilomar Bioelectronics Symposium

September 4th-8th, 2016

Asilomar Conference Grounds
Pacific Grove, CA, USA

SYMPOSIUM ORGANIZERS

Marco Rolandi, UC Santa Cruz, USA
Aleksandr Noy, LLNL & UC Merced, USA
David Cahen, Weizmann Inst., Israel

All meals are at CROCKER Dining Hall
All lectures and Poster sessions are in NAUTILUS room
All meals, including lunch on Thursday Sept 8th are included in the conference fee

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MEETING PROGRAM

Sunday, September 4th	
16:00	Registration and Check In
18:00	Dinner
Keynote Session chair: **Alex Noy**, Lawrence Livermore Nat. Lab & UC Merced	
19:00	**Charles Lieber**, Harvard U. Nano-Bioelectronics: From Biological Sensor Chips to Cyborg Tissues and Seamless Brain-Electronics Implants
20:00	Welcome Reception

Monday, September 5th	
Charge Transport in Proteins and Bacteria chair: **David Lederman,** UC Merced	
08:30	**Chris Nijhuis,** Nat'l. U. Singapore Biomolecular Spintronics Based on Ferritin
09:10	**David Waldeck,** U. Pittsburgh Charge Transport and Molecular Conductance of Nucleic Acids and Proteins on Electrodes
09:50	**Pau Gorostiza,** ICREA and IBEC Nanoscale Conductance Imaging of Electronic Materials and Redox Proteins in Aqueous Solution
10:30	Coffee Break
Charge Transport in Proteins and Bacteria (cont'd.) chair: **Martin Hohmann-Marriott,** Norwegian U. Sci. Technol.	
11:00	**Paul Meredith,** U. Queensland Hybrid Conductors for Bioelectronic Transducers
11:40	**Mohamed El Naggar,** U. Southern California Microbial Redox Networks: Biophysical and Structural Insights Into Extracellular Electron Transport at Biotic-Abiotic Interface
12:20	Lunch and Free Time (Box Lunch if Desired)
18:00	Dinner

Nanofabricated Bioelectronics chair: **Eric D. Glowacki,** JKU, Linz	
19:00	**Nick Melosh,** Stanford U. Heterogeneous Integration of Massively Parallel Electrode Arrays with CMOS Chips
19:40	**Alexander Sher,** UC Santa Cruz The Retina: What Can Go Wrong and How Can We Make It Better?
20:20	**Bianxiao Cui,** Stanford U. Nanoelectrodes for Intracellular Electrophysiology Recording
21:00	Poster Session

Tuesday, September 6th	
Organic Bioelectronics chair: **Cunlan Guo,** Weizmann Inst.	
08:30	**Daniel Simon,** Linköping U. Electronic Plants
09:10	**Fabio Biscarini,** U. Modena Electrolyte-Gated Organic Field Effect Transistors: Fundamentals and Applications to Biosensing
09:40	**George Malliaras,** E. de Mines-St Etienne Interfacing with the Brain Using Organic Electronics
10:30	Coffee Break
Printed Bioelectronics chair: **Jonathan Rivnay,** Xerox PARC	
11 00	**Michael McAlpine,** U. Minnesota 3D Printing Functional Materials and Devices
11:40	**Ana Claudia Arias,** UC Berkeley Design and Fabrication of Flexible Hybrid Bioelectronics
12:20	Lunch and Free Time (Box Lunch if Desired)
18:00	Dinner

Electroceuticals, Optogenetics, and Charge Transport chair: **Zahra Hemmatian,** UC Santa Cruz.	
19:00	**Valentin Pavlov,** Feinstein Inst. Med. Research Bioelectronics for Treating inflammation
19:40	**Xue Han,** Boston U. Neural Network Principles of Brain Disorders
20:20	**Caroline Ajo-Franklin,** Lawrence Berkeley Nat. Lab Making and Understanding Electronically-Controlled Organisms
21:00	Poster Session

Wednesday, September 7th	
Bio-inspired Bioelectronics chair: **Ramya Tunuguntla,** Lawrence Livermore Nat. Lab	
09:00	**Alon Gorodetsky,** UC Irvine Reflectin as a Material for Bioelectronic Devices
09:40	**Serdar Sariciftci,** Johannes Kepler U From Organic to Bioorganic Electronic Devices
10:20	Coffee Break
Bio-inspired Bioelectronics (cont'd.) chair: **Mostafa Baghbanzadeh,** Harvard U.	
10:50	**Chris Bettinger,** Carnegie Mellon U. Bioinspired Materials and Fabrication for Ultracompliant Neural Interfaces
12:10	Free Time (Box Lunch if Desired)
18:00	Dinner
19:00	**Selected Poster Talks** chairs: **Alex Noy,** Lawrence Livermore Nat. Lab & UC Merced **Marco Rolandi,** UC Santa Cruz
21:00	Farewell Reception

Thursday, September 8th	
08:00	Breakfast

PRESENTATION ABSTRACTS

Sunday, September 4th

Keynote Speaker

Nano-Bioelectronics: From Biological Sensor Chips to Cyborg Tissues and Seamless Brain-Electronics Implants

Charles M. Lieber
Department of Chemistry and Chemical Biology,
Harvard University

Nanoscale materials enable unique opportunities at the interface between the physical and life sciences, for example, by integrating nanoelectronic devices with cells and/or tissue to make possible communication at the length scales relevant to biological function. In this presentation, I will present an overview of bioelectronics, including general questions, primary research results, and future opportunities. First, general questions and issues for developing electronic devices for biological sensors through implants will be introduced. Second, transistor-based nanoelectronic chip-based platforms will be introduced and selected studies detection of biological analytes as well as neuron and cardiac cell action potentials will be briefly reviewed. Third, the design and implementation of new nanoelectronic probes capable of intracellular recording and stimulation at scales heretofore not possible with existing techniques will be discussed, including applications in neuroscience and the prospects of biologically-targeting of nanoscale devices. Fourth, a new concept will be introduced for seamless three-dimensional integration of addressable networks of multi-functional devices in engineered tissue, and exemplified with studies of cyborg cardiac tissue. Last, an 'out-of-the-box' approach for seamlessly merging nanoelectronic arrays with brain using syringe-injectable polymer-like mesh electronics will be discussed, including quantitative studies demonstrating unprecedented absence of tissue immune response and stable recording at the single neuron/neural circuit level for more than a year. Finally, the prospects for broad-ranging applications in the life sciences as the distinction between electronic and living systems is blurred in the future will be discussed, as well as future challenges.

Biomolecular Spintronics Based on Ferritin

Christian A. Nijhuis

Department of Chemistry, National University of Singapore.

The efficiency of electron transport (ET) over long distances in biological systems can be remarkably high and underlies many processes including enzymatic catalysis or photosynthesis. Unraveling the underlying mechanisms governing ET across such systems could lead to interesting technological applications in, for instance, the design of biomolecule-based sensors or single molecule devices. So far, long range ET via tunneling over a distance up to about 3.5 nm has been observed in a few systems based on azurin, cytochrome C or bacteriorhodopsine.[1,2] Here we show long range ET via tunneling across junctions based on ferritin (a cage-like protein that stores iron) over a distance of 12 nm (evidenced by temperature dependent measurements).[3] In addition, we show that these ferritin based junctions are efficient spin valves with a giant magnetoresistance of 15% at room temperature. In these junctions, monolayers of ferritin are formed on ultra-flat template stripped Ni surfaces which are contacted with EGaIn top-electrodes. The EGaIn top electrodes form non-invasive electrical contacts to these monolayers and make it possible to fabricate large numbers of junctions in high yields.[4,5] The monolayers of ferritin were characterized by XPS, AFM, and XMCD, from which we concluded that the Ni electrodes contained only small quantities of oxides and the packing density of was high. The XMCD data combined with the transport data made it possible to determine the mechanism of charge transport across the junctions.

References

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Charge Transport and Molecular Conductance of Nucleic Acids and Proteins on Electrodes

David H. Waldeck, Edward Beall, and Emil Wierzbinski
Chemistry Department, University of Pittsburgh

We present new results on charge transport in nucleic acids and on magnetic field effects on electron transfer with chiral molecules and proteins. Molecular conductances and electrochemical charge transfer are different manifestations of a molecule's ability to transmit electric charge. We report on recent experiments that compare the molecular conductance to the charge transfer rates. We present recent findings on the chiral induced spin-selectivity effect and its importance for understanding the fundamental nature of charge transfer with proteins.

Nanoscale Conductance Imaging of Electronic Materials and Redox Proteins in Aqueous Solution

Pau Gorostiza

ICREA and Institute for Bioengineering of Catalonia (IBEC)

Electron Transfer (ET) plays essential roles in crucial biological processes such as cell respiration and photosynthesis. It takes place between redox proteins and in protein complexes that display an outstanding efficiency and environmental adaptability. Although the fundamental aspects of ET processes are well understood, more experimental methods are needed to determine electronic pathways in these redox protein structures. Understanding how ET works is important not only for fundamental reasons, but also for the potential technological applications of these redox-active nanoscale systems.

Electrochemical Scanning Tunneling Microscopy (ECSTM) is an excellent tool to study electronic materials and redox molecules including proteins[1]. It offers atomic or single molecule resolution and allows working in aqueous solution, in nearly physiological conditions in the case of proteins, and under full electrochemical control. Beyond imaging, ECSTM allows performing current-potential and current-distance tunneling spectroscopy. We adapted the current-potential spectroscopy mode of ECSTM to include a sinusoidal potential modulation to the STM tip and current measurement by means of a lock-in amplifier, which renders a signal that is proportional to the differential conductance dI/dU of the studied surface [2]. With this setup we have recorded for the first time spatially resolved, differential conductance images under potentiostatic control (differential electrochemical conductance (DECC) imaging). We validated and optimized the technique using an iron electrode, whose reversible oxidation in borate buffer is well characterized [3].

We applied DECC imaging to gold Au <111> surfaces coated with P. Aeruginosa Azurin. This redox metalloprotein can be immobilized on single crystal Au <111> surfaces via a dithiol covalent bond, and constitutes a model system to study biological ET processes [4]. DECC imaging provides simultaneously the surface topography and local conductance with a resolution of a few nanometers, and reveals regions with different conductance within the protein. The characterization of conduction pathways in redox proteins at the nanoscale would enable important advances in biochemistry and would cause a high impact in the field of nanotechnology [5].

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Hybrid Conductors for Bioelectronic Transducers

Paul Meredith, Margarita Sheliakina, Shermiya Reinecker & Bernard Mostert

Centre for Organic Photonics & Electronics, School of Mathematics and Physics
University of Queensland

One of the critical tasks in realising a bioelectronic interface is the transduction of ion and electron signals at high fidelity, and with appropriate speed, bandwidth and signal-to-noise ratio [1]. This is a challenging task considering ions and electrons (or holes) have drastically different physics. For example, even the lightest ions (protons) have mobilities much smaller than electrons in the best semiconductors, effective masses are quite different, and at the most basic level, ions are 'classical' entities and electrons 'quantum mechanical'. These considerations dictate materials and device strategies for bioelectronic interfaces alongside practical aspects such as integration and biocompatibility [2]. In my talk I will describe some of these 'differences in physics' and exemplify how materials that can support both ion and electronic signals can be used in simple all-solid-state electrochemical transistors. I will focus on the melanin system which has been shown to be a predominantly proton conduction material [3], in a simple interface with a *p*-type conducting polymer. I will describe the basic physics of the conduction mechanism in melanin, and summarise new results as to how these properties can be perturbed by doping with transition metals. These models provide deep insight into how to design and realise optimise novel bioelectronic interfaces.

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Microbial Redox Networks: Biophysical and Structural Insights into Extracellular Electron Transport at Biotic-Abiotic Interfaces

Moh El-Naggar[1], Sahand Pirbadian[1], Poorna Subramanian[2], Hye Suk Byun[1], Yamini Jangir[1], Benjamin Gross[1], Shuai Xu[1], Aiichiro Nakano[1], Grant Jensen[2]

[1]University of Southern California
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Electron Transfer (ET) is the stuff of life. The stepwise movement of electrons within and between molecules dictates all biological energy conversion strategies, including respiration and photosynthesis. With such a universal role across all domains of life, the fundamentals of ET and its precise impact on bioenergetics have received considerable attention, and the broad mechanisms allowing ET over small length scales in biomolecules are now well appreciated. In what has become an established pattern, however, our planet's oldest and most versatile organisms are now challenging our current state of knowledge. With the discovery of bacterial nanowires and multicellular bacterial cables, the length scales of microbial ET observations have jumped by 7 orders of magnitude, from nanometers to centimeters, during the last decade alone!

This talk will take stock of where we are and where we are heading as we come to grips with the basic mechanisms and immense implications of microbial long-distance electron transport. We will focus on the biophysical and structural basis of long-distance, fast, extracellular electron transport by metal-reducing bacteria. These remarkable organisms have evolved direct charge transfer mechanisms to solid surfaces outside the cells, allowing them to use abundant minerals as electron acceptors for respiration, instead of oxygen or other soluble oxidants that would normally diffuse inside cells. From an environmental perspective, these microbes are major players in global elemental cycles. From a technological perspective, microbial extracellular electron transport is heavily pursued for interfacing redox reactions to electrodes in hybrid biotic-abiotic devices, including multiple renewable energy technologies.

But how can an organism transfer electrons to a surface many cell lengths away? What molecules mediate this transport? And, from a physics standpoint, what are the relevant length, time, and energy scales? We will describe new experimental and computational approaches that revealed how bacteria organize heme networks on outer cell membranes, and along the quasi-one-dimensional filaments known as bacterial nanowires, to facilitate long-range charge transport. Using correlated electron cryotomography and in vivo fluorescent microscopy, we are gaining new insight into the localization patterns of multiheme cytochromes along nanowires as well as the morphology and the formation mechanism of these

structures. In addition, we will examine the fundamental limits of extracellular electron transport, down to microbial energy acquisition by single cells. These findings are shedding light on one of the earliest forms of respiration on Earth while unraveling surprising biotic-abiotic interactions.

Heterogeneous Integration of Massively Parallel Electrode Arrays with CMOS Chips

Mina Hanna,[1] Matt Angle,[1] Victor Chang,[1] Jun Ding,[2] Andreas Schaefer,[3] **Nick Melosh**[1]

[1]Dept Materials Science and Engineering, Stanford University
[2]Dept of Neurosurgery, Stanford School of Medicine
[3]Crick Institute

Transitioning from small numbers of neural recording electrodes to the hundreds of thousands necessary to capture even a small fraction of a region's neural activity presents significant challenges to current brain interface approaches. Despite significant recent advances in planar cortical recording arrays, high channel count depth electrodes for stimulation or recording sub-surface regions in the brain are still lacking. Here we take a different approach to achieve high electrode counts, creating bundles of ten to one hundred thousand insulated microelectrodes, each of which can be a separate channel. Since the electrical properties and insertion of these types of microwires (~10-25 um diameter) are well known there is good confidence they can be inserted into the brain and record or stimulate neural activity.

One of the key questions for this approach is how to address such large numbers of electrodes; conventional soldering or flex connectors are inadequate at this scale. Instead, we are developing heterogeneous integration methods to merge non-planar electrode arrays onto CMOS microelectronic chips, such as those used for cameras or displays. These chips are already available with more than 1 million independent pixels, thus have room to spare to record or stimulate from 100k+ electrodes. The chip architectures have similar electronics and voltage/current ranges as neural interface systems, enabling use of even off-the-shelf chips. Here we present our efforts to build and test these massively parallel interface systems, including bundle preparation and connectivity yield with the CMOS pixels. We show that microelectrode bundles and nanowire arrays can be integrated onto CMOS platforms with reasonable connectivity yields, and each channel can produce physiologically relevant stimulation current or recording speed for highly dense electrical interfaces. These systems may provide a means to reach the electrode numbers and electronic readouts necessary for next-gen brain machine interfaces.

The Retina: What Can Go Wrong and How Can We Make It Better?

Alexander Sher

Santa Cruz Institute for Particle Physics

Mammalian retina is an amazing part of central nervous system that determines the visual perception of the outside world. Unfortunately, millions of people worldwide lose their sight due to a number of retinal neurodegenerative diseases. I will report on the investigation of the retinal ability to heal and to restore its function by making new synaptic connections. I will also discuss the sight restoration through photovoltaic stimulation of the retinal neurons.

Nanoelectrodes for Intracellular Electrophysiology Recording

Bianxiao Cui

Departments of Chemistry, Stanford University

The rapidly evolving field of nanotechnology creates new frontiers for biological sciences. Recently, we and other groups show that vertical nanopillars protruding from a flat surface support cell survival and can be used as subcellular sensors to probe biological processes in live cells. In particular, we focus on developing nanopillar as electric sensor, optical sensors and structural probes. As an electrode sensor, nanoelectrodes offer several advantages such as high sensitivity, subcellular spatial resolution, and precise control of the sensor geometry. We found that the 3D topology of nanopillars is crucial for its enhanced signal detection. The high membrane curvature induced by vertical nanopillars significantly affects the distribution of curvature-sensitive proteins and stimulates several cellular processes in live cells. Our studies show a strong interplay between biological cells and nano-sized sensors, which is an essential consideration for future development of interfacing devices.

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Electronic Plants

Daniel T. Simon

Laboratory of Organic Electronics, Dept. of Science and Technology, Linköping University

Organic bioelectronics has emerged in recent years as an optimal application of the combined electronic and "iontronic" capabilities of conjugated polymers and polyelectrolytes. The vast majority of the "bio" in bioelectronics has been centered on cell signaling applications, with a particular focus on neuromodulation for next-generation therapies. While our own group and many others have made great strides in this area, we have neglected to take a broader perspective on how organic electronics can impact our understanding and utilization of other parts of the biological world. In this talk, I will introduce our efforts to bring organic bioelectronic technology beyond the animal kingdom, and into plants. This effort includes not only the conversion of neurotransmitter delivery technology to plant hormone delivery components, but also an entirely new area of study: electronic plants. Liquid-phase processability is a well-known advantage of organic electronics over traditional electronic materials. This property is generally leveraged to facilitate thin-film fabrication, or to enable the use of printing techniques. We have instead used such conducting solutions to introduce self-organizing electronic functionality into living plants, using the plant's own vascular and gas-exchange systems as the template. We will present these results, focusing on conducting "xylem wires", organic digital logic circuits, and charge-storage capability, all inside of living roses. The talk will conclude with a look to the future, and how electronic plants can aid in a variety of agricultural and energy-harvesting applications.

Electrolyte-Gated Organic Field Effect Transistors: Fundamentals and Applications to Biosensing

Michele Di Lauro[1], Marcello Berto[1], Carlo Augusto Bortolotti[1], Marcello Pinti[1], Andrea Cossarizza[2], Michele Zoli[3], **Fabio Biscarini**[1]

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Organic field effect transistors (OFET) operated in aqueous environments are emerging as ultra-sensitive biosensors and transducers of electrical and electrochemical signals from a biological environment. Their applications range from detection of biomarkers in bodily fluids to implants for bidirectional communication with the central nervous system. They can be used in diagnostics, advanced treatments and theranostics. Several OFET layouts have been demonstrated to be effective in aqueous operations, which are distinguished either by their architecture or by the respective mechanism of doping by the ions in the electrolyte solution. In this work we discuss the chemical-physics of the electrolyte-gated OFET (EGOFET). We show how the substrate plays the role of a second bottom gate, whose potential is actually fixed by the pH/composition of the electrolyte and the gate voltage applied. The presence of the substrate can be exploited to modulate the capacitive coupling of the electrolyte solution with the semiconductor by almost one order of magnitude. We also show that this device, operated as a biosensor for a primary inflammatory citokine, i.e. TNF-alpha, responds super-exponentially in current vs analyte concentration in the sub-nM range, whereas responds linearly at concentrations greater than 1 nM. We unify the two regimes by introducing the density of states that is accessible upon the change of the electro-chemical potential of the organic semiconductor (pentacene) caused by the adsorption of TNF-alpha. We finally show that the response is modulated by the gate voltage applied, and the fit of the data allows us to extract the association binding constant of the antibody-antigen recognition, the molar free energy, and the electrostatic contribution to the free energy.

Acknowledgements: This work was funded by MIUR e Progetto Bilaterale Strategico Italia-Svezia "Poincarè.

Interfacing With the Brain Using Organic Electronics

George Malliaras

Ecole des Mines de St. Etienne

One of the most important scientific and technological frontiers of our time lies in the interface between electronics and the human brain. Interfacing the most advanced human engineering endeavor with nature's most refined creation promises to help elucidate aspects of the brain's working mechanism and deliver new tools for diagnosis and treatment of a host of pathologies including epilepsy and Parkinson's disease. Current solutions, however, are limited by the materials that are brought in contact with the tissue and transduce signals across the biotic/abiotic interface. The field of organic electronics has made available materials with a unique combination of attractive properties, including mechanical flexibility, mixed ionic/electronic conduction, enhanced biocompatibility, and capability for drug delivery. I will present examples of organic-based devices for recording and stimulation of brain activity, highlighting the connection between materials properties and device performance. I will show that organic electronic materials provide unparalleled opportunities to design devices that improve our understanding of brain physiology and pathology, and can be used to deliver new therapies.

3D Printing Functional Materials & Devices

Michael C. McAlpine

Department of Mechanical Engineering, University of Minnesota

The development of methods for interfacing high performance functional devices with biology could impact regenerative medicine, smart prosthetics, and human-machine interfaces. Indeed, the ability to three-dimensionally interweave biological and functional materials could enable the creation of devices possessing unique geometries, properties, and functionalities. Yet, most high quality functional materials are two dimensional, hard and brittle, and require high crystallization temperatures for maximal performance. These properties render the corresponding devices incompatible with biology, which is three-dimensional, soft, stretchable, and temperature sensitive. We overcome these dichotomies by: 1) using 3D printing and scanning for customized, interwoven, anatomically accurate device architectures; 2) employing nanotechnology as an enabling route for overcoming mechanical discrepancies while retaining high performance; and 3) 3D printing a range of soft and nanoscale materials to enable the integration of a diverse palette of high quality functional nanomaterials with biology. 3D printing is a multi-scale platform, allowing for the incorporation of functional nanoscale inks, the printing of microscale features, and ultimately the creation of macroscale devices. This three-dimensional blending of functional materials and 'living' platforms may enable next-generation 3D printed devices.

Design and Fabrication of Flexible Hybrid Bioelectronics

Yasser Khan and **Ana Claudia Arias**

Department of Electrical Engineering and Computer Sciences, University of California, Berkeley

Interfacing soft and hard electronics is a key challenge for flexible hybrid electronics. Bioelectronic interfaces require electrodes that are mechanically flexible and chemically inert as the conformal form factor allows pristine electrode contact to skin and tissue. The chemical properties and inertness prevents electrodes from reacting with biological fluids and living tissues. Typically a multi-substrate approach is employed, where soft and hard devices are fabricated or assembled on separate substrates, and bonded or interfaced using rigid connectors - this hinders the overall flexibility of the device, and is prone to interconnect issues. We have designed a system that uses a single substrate interfacing approach, where flexible sensors are directly printed on Kapton® polyimide substrates. Developing a process flow compatible with Flexible Printed Circuit Board assembly process, we demonstrated a wearable sensor patch composed of inkjet-printed gold electrocardiography (ECG) electrodes and a stencil-printed nickel oxide thermistor. The ECG electrodes provide 1mVp-p ECG signal at 4.7 cm electrode spacing and the thermistor is highly sensitive at normal body temperatures with α values of approximately 5.84 % K-1 and ß values of 4400 K.

Bioelectronics for Treating Inflammation

Valentin A. Pavlov

Center for Bioelectronic Medicine, The Feinstein Institute for Medical Research

Active ongoing research has identified several points of a reciprocal nervous system-immune system relationship. Vagus nerve-mediated and other neural circuits operating on reflex principles regulate multiple aspects of immunity and inflammation. Evaluating the anti-inflammatory efficacy of vagus nerve stimulation and advanced understanding of neural circuitry controlling inflammation has allowed implementation of conceptually novel platforms of disease treatment based on neuromodulation within the scope of Bioelectronic Medicine. The successful clinical exploration of vagus nerve stimulation in inflammatory bowel disease and rheumatoid arthritis is the beginning of the use of bioelectronic approaches targeting neuronal circuits to treat a broad spectrum of diseases.

Neural Network Principles of Brain Disorders

Xue Han

Biomedical Engineering Department , Boston University

Neurological and psychiatric disorders affect about one billion people worldwide, and cost over $2.5 billion annually. My lab is interested in understanding the neural circuit mechanisms of brain disorders, with the ultimate goal of deriving network principles for designing next generation neuromodulation therapies. In this talk, I will describe our recent effort on understanding oscillation dynamics within the cortical-basal ganglion networks that are relevant for Parkinson's disease and deep brain stimulation therapy. In addition, I will highlight some of our recent technology development effort on improving the ability to interrogate neural networks. Specifically, I will describe a DNA nanoparticle based novel uncaging technique that allows rapid and light triggered delivery of arbitrary bioactive molecules, and a microRNA based gene targeting technique that mediates gene expression in defined neural cell subtypes using gene therapy viral vectors. Through integrating neurotechnology development effort with neural circuit analysis, we hope to identify features of network dynamics as potential biomarkers for neurological and psychiatric disorders.

Making and Understanding Electronically-Controlled Organisms

Caroline Ajo-Franklin

The Molecular Foundry, Lawrence Berkeley National Laboratory

Since both organisms and devices use electrons as information and energy carriers, interfacing living cells with electrodes offers the opportunity to control key biological processes electronically. In the first part of my talk, I will describe how we have transformed the industrial microbe Escherichia coli into an electroactive bacterium, whose behavior we can control and readout electronically. In the second part of my talk, I will discuss new structural understanding of how proteins can electronically interface microbes with materials. Together this work paves the way for rationally constructing electronically-controlled organisms.

Reflectin as a Material for Bioelectronic Devices

Alon Gorodetsky

Department of Chemical Engineering and Materials Science, University of California, Irvine

Cephalopods possess remarkable camouflage capabilities, which are enabled by their complex skin structure and highly advanced central nervous system. These animals' unique characteristics have therefore inspired the design of novel functional materials. Within this context, recent studies have investigated self-assembly, optical, and electrical properties of the cephalopod structural protein reflectin. We will discuss our work on reflectin-based bioelectronic devices that can directly communicate with single mammalian cells. Our findings may hold relevance for the design of both improved stem cell growth scaffolds and intrinsically biocompatible neural interfaces.

From Organic to Bioorganic Electronic Devices

Niyazi Serdar Sariciftci

Linz Institute for Organic Solar Cells (LIOS) at the Johannes Kepler University of Linz

Organic light emitting diodes (OLEDs), organic photovoltaic cells (OPVs) and organic field effect transistors (OFETs) are device elements for a future organic optoelectronics. Maturing from the academic research into the industrial development, such devices are entering the markets. Pure organic nanostructures and organic/inorganic hybrid nanostructures are comparatively studied for devices. This talk gives an overview of materials' aspect and devices with special emphasis on polymeric structures.

In order to account for a sustainable future, the application of biodegradable and biocompatible systems for organic optoelectronics are needed. The use of cheap electronic devices in a large scale will introduce a shift "from consumer electronics to consumable electronics". As such the contribution of electronic devices to urban waste is already increasing rapidly today. Therefore environmentally friendly materials are important to use. This is a next great challenge to material science in organic electronics. New developments of bio-inspired and/or bio-origin, bio-compatible materials are interesting. Such materials can also be used to interface the biological and biomedical research with the organic electronics field.

Bioinspired Materials and Fabrication for Ultracompliant Neural Interfaces

Wei-Chen Huang, Haosheng Wu, Hangjun Ding, Krzysztof Matjaszewski, **Christopher J. Bettinger**

Department of Biomedical Engineering, Carnegie Mellon University

Seamless integration of electronic devices with the human body could enable the next generation of medical implants that can monitor physiology, detect disease, and elucidate the complex function of the brain. Most excitable tissue in the nervous system, such as the brain or spinal cord, is mechanically compliant and modulates the flow of ions such a Na+ and K+. Conversely, most silicon-based computing devices and sensors are mechanically rigid and use electrons/holes as the primary information currency. Hence, there exist fundamental physical incompatibilities between the tissue that we want to interrogate and the implantable sensors that we use for this purpose. Incongruences in mechanical, chemical and physical properties can compromise the information density and integrity of the recording and reduce the overall performance of these implantable sensors. The next generation of brain-machine interfaces, implantable devices used to record neurological function in vivo, will benefit from novel materials that can better integrate electronically active materials with excitable tissue in the human body. Towards this end, two recent materials innovations are highlighted. First, the synthesis and characterization of intrinsically elastomeric conducting polymers will be described. Second, the design and fabrication of ultracompliant peripheral nerve interfaces will be presented. Taken together, these materials have the potential to improve the performance of implantable brain-machine interfaces.

POSTER ABSTRACTS

Poster-01

Organic Electronic Devices for the Controlled Transport of Signaling and Structural Compounds of Biological Systems

David J. Poxson[1], Hudson Pace[2], Roger Gabrielsson[1], Fredrik Höök[2], Daniel T. Simon[2], Magnus Berggren[2]

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Organic bioelectronics, in form of the organic electronic ion pump (OEIP), have been used to modulate cell and tissue function using flow-free delivery of small biological signaling compounds with high spatiotemporal resolution. To date, efforts have entirely focused on mammalian systems, particularly for neuroscience applications. Moreover, transport and delivery of compounds with OEIP devices has been achieved for small and non-aromatic substances only. Here we show the use of OEIP bioelectronic technologies that enables electronically controlled transport and delivery of large molecular structures based on cyclic alkaines or aromatic compounds. We fabricated OEIP devices based on a newly developed polyelectrolyte material system and demonstrated electrophoretic transport of a range of highly bio-relevant compounds. Our results provide a starting point for technologies enabling direct, rapid, and dynamic electronicically mediated, chemical interactions with living systems.

Poster-02

Ion-Selective Bio-interfaces for Organic Electrochemical Transistors

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Interfacing electronics with biology using organic electrochemical transistors (OECTs) has emerged as a new frontier in the field of bioelectronics to understand ionic and electronic transport in biological and/or biologically related media. Most OECTs use a conducting polymer film as a channel and are gated through an aqueous electrolyte, thereby offering intimate interfacing ability between electronic and biological materials. In addition to the strong correlation between ionic and electronic transport, the ability to transduce biological signals into electrical signals with high gain makes OECTs exceptional tools in the area of biosensor and bioelectronics. They have been widely used for many different purposes such as probing cell adhesion, measuring the integrity of barrier tissue, and sensing some biologically relevant ions, metabolites, hormones, and pathogens. [1] However, most of the sensing mechanisms in these devices lack selectivity. There is an obvious need to develop a selective detection and quantification approach for both fundamental and applied studies. Here, we report integration of ion-selective bio-interface that can be used to control and regulate selective ion-transport from sensing media to the transistor channel.

The present study aims to address the design and development of ion-selective bio-interface that is not only capable of direct sensing of biologically relevant ions, but also selectively sense enzymatically-generated ions in response to various levels of biological analytes. In addition to electroanalytical performance, we have also modelled our ion-selective bio-interface integrated OECT device to understand the effect of device parameters on performance characteristics such as barrier area, device area and particular resistance of the barrier layer of interest.

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Poster-03

How Does your E-Plant Garden Grow?

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The plant kingdom is vital for producing food, oxygen, materials, and aesthetics for the sustenance and comfort of all life on earth. Although great efforts have been made in plant genomics and biochemistry to conform plants to our needs, very few tools exist to monitor, control, and augment plant physiology. The Electronic Plant is the first attempt at integrating such functionalities inside roses using self-assembled PEDOT wires and electrochemical transistors inside the plant stem. These in-vivo devices could eventually create powerful tools for the agriculture industry. But in order to advance the field into relevant applications, future fabrication techniques must be able to construct devices at precise locations anywhere in the plant without disturbing its growth. In this work, we explore how we leverage natural plant functions and structures with modern nanotechnologies to create new fabrication methods for E-plants. Particularly, we use the powerful field of acoustofluidics to drive plant transpiration (the natural uptake of water) and construct simple devices in plant leaves. There is plenty of room to apply old techniques and devices in plant sciences that could help cultivate the future e-plant garden.

Poster-04

Soft Multi-Electrode Array (Soft-MEA)

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Contractile force and action potential are two important parameters in understanding cardio-physiology and cardiac disease. At single cell level, soft pillars (e.g. PDMS micropillars) are often used to infer the cardiac contractile force, while stiff electrodes (e.g. IrOx pillars) are used for action potential recording. Either spatial or temporary coupling between the beating force and action potential has to be sacrificed due to lacking of unified recording system. Herein, we present a bi-functional 8x8 electrode array for simultaneously recording action potential and contractile force. PEDOT:PSS/IL (poly(3,4-ethylenedioxythiophene) polystyrene sulfonate/Ionic liquid) was used to fabricate soft and bendable, while conductive micropillars (~1um in radius). The Soft-MEA provides a new platform for studying cardiac development and drug screening.

Poster-05

Electrically Controlled Neurotransmitter Release Within Tens of Milliseconds from Several Individually Controlled Sites

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The increased understanding of how perturbations to the nervous system are involved in a number of diseases makes implantable devices that can restore dysfunctional neural communication a promising therapeutic technology. The nervous system is extremely complex, however, and consists of billions of nerve cells where each cell can have several communication points, synapses, with other cells where messages are passed on within a few milliseconds. To replace dysfunctional neural communication and missing chemical synapses, an implantable device should thus be able to release chemicals to multiple micrometer-sized locations on demand within milliseconds.

We have developed chemical delivery circuits with several individually controlled delivery sites from which charged chemical compounds, such as neurotransmitters, can be released within tens of milliseconds after an electrical signal is applied. The delivery circuits are manufactured using standard microfabrication techniques and consist of patterned layers of polymers on glass substrates. Transport of the charged compounds is based on electrophoresis and the fact that a polyelectrolyte with a high concentration of either negative or positive charges can be used to selectively drive a cationic or an anionic current, respectively, through the polyelectrolyte. To individually control the release from several points, while using a single source reservoir for the delivered compound, we have placed an electronically and ionically conducting polymer control electrode at each delivery site. These control electrodes temporarily store the charged compounds and control the electrical potential gradient to the delivery site, and therefore the migration and release. The control electrodes also form the p- part of an ion bipolar membrane diode, which makes it possible to reduce diffusive leakage by reverse biasing the diode when delivery is not wanted. Controlling the potential of each control electrode controls the electric field across the outlet, i.e. the migration of charged compounds. Furthermore, the potential at the control electrode also transiently redox-switches the polymer, altering its charge state, so that the charged compounds are electrostatically repelled and delivered in short pulses. We found that we could release the neurotransmitter acetylcholine within about 50 ms and we verified that we could independently deliver ions from an array of six delivery points.

By delivering millisecond short pulses of neurotransmitters to micrometer sized locations we believe that our device may be useful for interactions with the nervous system, both in vitro as a tool for increased understanding of nerve cell communication, and in the future as a therapy in that it may replace damaged neurons.

Poster-06

Managing Brain Cancers with Electrical Fields

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Existing therapies for cancer treatment, namely, surgical resection, chemotherapy, and radiotherapy, cannot be used in many brain malignancies. This is particularly true in tumors that develop in inoperable brain regions, or for pediatric brain tumors wherein therapeutic intervention would be devastating to a child's neural development. To address the lack of available therapies, we examine the use of low power electric fields to consolidate and redirect tumor invasion, manipulate cancer cell fate, and alter the behavior of tumor-supporting cells.

Herein we report on an ensemble of in vitro experiments that screen various regimes of electrical stimulation and their effects on cancer cell invasion, proliferation, viability, and progression.

Poster-07

Organic Mixed Conductors for Bioelectronic Applications

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Direct measurement and stimulation of electrophysiological activity is a staple of neural and cardiac health monitoring, diagnosis and/or therapy. Such bi-directional interfacing can be enhanced by organic electronic materials that show mixed conduction properties (both electronic and ionic transport). Organic electrochemical transistors (OECTs) utilize such materials as the transistor channel, and have shown considerable promise as amplifying transducers due to their stability in aqueous conditions and high transconductance. These devices are fabricated in flexible, conformable form factors for in vivo recordings of epileptic activity, and for cutaneous EEG and ECG recordings in human subjects. The majority of high performance devices are based on conducting polymers such as poly(3,4-ethylenedioxythiophene):poly(styrenesulfonate), PEDOT:PSS. By investigating PEDOT-based materials and devices, we are able to establish a set of design rules for new formulations/materials. Introducing glycolated side chains to carefully selected semiconducting polymer backbones has enabled a new class high performance bioelectronic materials that feature high volumetric capacitance, transconductance >10mS (device dimensions ca. 10um), and steep subthreshold switching characteristics. A sub-set of these materials outperform PEDOT:PSS and shows significant promise for low power in vitro and in vivo biosensing applications.

Poster-08

Significance of the Double-Layer Capacitor Effect in Solution-Processable Polymeric Dielectrics and Exceptionally Stable Low-Voltage Organic Transistors

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High-performance FETs based on organic active materials are of particular interest due to their compatibility with low-cost, high-throughput processing and mechanical compliance with soft tissues. Due to the relatively low charge carrier mobilities of organic materials, often high operational voltages have to be applied and result in severe limitations. To overcome these issues high gate capacitance materials are needed. One appealing approach is the fabrication of ultra-thin dielectric layers, which, however, are technologically very challenging to make and suffer often from high leakage problems.
Here, we discovered that a polar fluorinated PVDF-HFP dielectric, despite of a low ion concentration, is able to induce an electric double-layer charging effect under an applied gate voltage. This polymer dielectric is solution-processable with a high static capacitance of about 0.3 µF/cm2 , even at a thickness of several micrometers. Furthermore it is highly compatible with solution processing of various organic semiconductors. Remarkably, the resulting devices showed both high current output and low bias stress in both ambient and aqueous conditions making it the ideal candidate for low-voltage and stable device operation.

Poster-09

Organic Field Effect Transistor-Based Biosensors

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Transistor-based biosensors offer a label-free, real-time, electronic detection for diagnostic applications. Organic field effect transistors (OFET) are especially attractive due to their molecular tunability, potential for low-cost fabrication, and mechanical compliance. However, many OFET sensors still suffer from bias stress and lack of aqueous stability. We have developed an OFET sensor platform with a polar fluorinated PVDF-HFP dielectric that enables for low-voltage driven sensor that is stable long-term with aqueous sensing. This sensor employs a functionalization scheme for modular receptor sites to enable a versatile sensing of a wide range of target analytes. Additionally, the sensor platform design is compatible with low-cost fabrication methods and production of a large array for multiplexed sensing, opening the door for a point-of-care diagnostic device.

Poster-10

3D Nanoelectrodes for Electrophysiology: How Size Affects Seal Resistance

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Three-dimensional (3D) nanoelectrodes fabricated on standard multielectrode array architecture have proven useful in monitoring intracellular electrophysiology of cardiomyocytes. The electrodes' mechanism of intracellular access involves a voltage pulse at the electrode which exceeds the dielectric breakdown of an engulfing cell's membrane, electroporating the cell and dramatically reducing the impedance to intracellular potential recording. The electroporation mechanism is non-invasive as the pores reseal. This gives rise to a method which is useful in its ability to multiplex, its technical ease of use, and non-invasiveness.
The driving phenomenon which yields this enhanced performance over planar electrodes is an enhancement of the seal resistance between the electrogenic center (the cell) and the recording center (the nanoelectrode). Cells in vitro engulf 3D electrodes such that the membrane-electrode distance is reduced compared to that of the membrane-planar electrode distance. This membrane-electrode distance is dependent upon the geometry of the electrode, but the electrical ramifications of this have not been characterized to date. Herein we explore this dependence by using electrochemical impedance spectroscopy in correlation with reduced-artifact FIB/SEM and electrophysiological measurement of chicken cardiomyocytes over an order of magnitude in 3D electrode diameter.

Poster-11

Intrinsically Stretchable Bioelectronics

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Three-dimensional mapping of arrhythmogenic activity with high throughput and high spatial-temporal resolution at specific regions is critical for targeted therapies and patient specific diagnostic applications. No current technology can achieve high throughput, high resolution and anatomic precision with reproducible applicability in the clinical setting. Here, we introduce an intrinsically elastic electronic sheet containing hundreds of sensors that can map arrhythmogenic activity instantly on the beating heart during surgery with <100 μm spatial resolution and submillisecond temporal resolution. This elastic electronic sheet can be expanded up to 4 times of its original size to cover the whole epicardial or endocardial surfaces to provide a global activity mapping to roughly identify the arrhythmogenic region, and then relax to its original size to cover on the targeted region with high dense sensors array to further provide a high resolution mapping illustrating the origin of arrhythmogenic activity for therapies. Moreover, we employ intrinsically elastic materials to fabricate the sensor array so that the high dense sensors array can form an intimate mechanical coupling with cardiac tissue through the polymer-tissue interface and deform with the cardiomyocyte beating, while recording the signal at the same region through the elastic property of the materials. Together, this technology will allow for greater individualization of mapping, study and treatment of arrhythmias.

Poster-12

Physical Modelling of Bio Sensors Based on Organic Electrochemical Transistors

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Organic electronics, based on conductive polymers and organic small molecules has the continuous development since 1970s. Conducting polymers have been used in a wide range of electronic devices such as transducers and sensors for chemical detection of different types of analytes. One of the most promising categories of semiconductor-based sensors is organic electrochemical transistor (OECT). OECTs consist of three electrodes (source, drain and gate) and two active layers: electrolyte and conductive polymer. In conductive polymer layer the current modulation is generated by a dedoping effect produced by the positive ion penetration from electrolyte, followed by its recombination with negative conductive polymer ion. Since the amount of positive charge carriers in conductive polymer is decreased, current between source and drain electrodes also decreases. This kind of current variations is dependent on electrolyte concentration and gate voltage.
Despite the fact that OECT attracts a lot of attention in the last years, appropriate physical and chemical coupled model to describe precisely the interaction between ionic and electronic charge carriers haven't been yet developed. To understand the working mechanism of OECT device it is absolutely necessary to make modelling. 1,2
In each of the models should be considered the combination of three processes:
1) Movement of ions in electrolyte and polymer layers (electrochemical process)
2) Recombination of the electronic and ionic charge carriers in the polymer
3) Transport of the charge carriers (holes) inside polymer
The analytical model that was built by us shows a good fit to the experimentally obtained sigmoidal curves. From the model there could be extracted the set of very important parameters of the device, such as: minimum and maximum conductivity values and offset voltage. Knowing these parameters it is possible to calculate the current for any given set of gate and drain voltages.
The numerical model (2D finite elements approach) allows to understand an influence of different parameters on the charge carriers distribution and doping-dedoping proses in the polymer layer for the further optimization of the device. Simulation of electrolyte ion transport and dedoping process inside of the polymer performed with COMSOL Multyphysics software.
As a result, the combination of these two models would lead to the device optimization and building more efficient biosensor based on OECT.

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Poster-13

Visualization of the Nano-Bio Interface with 10 nm Resolution by FIB-SEM

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In recent years, 3D nano and micro-fabricated platforms have been used for multiple in vitro biomedical applications. In particular, nanostructured materials have gained large importance as a valid tool to manipulate cells and record electrical activity (i.e. action potentials) from electrogenic cells.1,2. Effectively, the geometry as well as the material nature of those 3D materials induce cells to have a specific response and often to re-adapt their shapes to the nanostructures3. This re-arrangement occurs at the cellular membrane as well as at the intracellular environment. In order to investigate these phenomena, a high resolution microscopical method is needed to visualize the actual proximity of the cell and the nanopillar at the cell-pillar interface.
Here, we developed an ultra-thin resin embedding method of cells with contrast-enhancing agents to improve the visualization of intracellular compartments as well as the cell membrane in SEM. Having an extremely thin resin layer on top of cells allows us to first visualize, with conventional SEM, entire cells spreading and growing on nanostructured materials (quartz nanopillars, PEDOT:PSS) while resolving very small intracellular and extracellular structures which can be damaged by standard SEM preparation techniques (i.e. critical point drying). This process is unlikely to be done with standard techniques such as TEM since the embedding resin is in the order of mm thick so that it is impossible to perform SEM imaging. In fact, our unique technique allows in situ SEM imaging of whole cells, followed by (spatially controlled) sequential transverse sectioning with FIB in order to visualize intracellular organelles in 3D in response to material. Besides individual sectioning with FIB, we were able to perform sequential cross sectioning to reconstruct a volume of interest including cells on nanostructures. Finally, we further enhance the cellular membrane at the interface with APEX2 for the first time in SEM, which allows proximity labelling of target protein on the membrane (CAAX).

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Poster-14

Bioprocessing Device Composed of Metalloprotein/Nucleic Acid/Nanoparticle Hybrid Material

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Nanoscale bioelecronic device based on hybrid biomaterial had emerged to generate new concept and technologies for the development of electronic devices (1). The biomaterial, especially metalloproteins, can be used as a functional unit in an electronic device. Major challenges in bioelectronic device include the miniaturization, and the demonstration of various functions implemented in biomaterial to overcome silicon-based electronic device technology. Metalloprotein-based conceptual biomemory device was developed which demonstrated memory characteristics including 'read', 'write' and 'erase' function (2). And multi-bit memory function and nanoscale memory function were constructed. Afterwards new hybrid material composed of metalloprotein/DNA/nanoparticle has been developed to construct bioprocessing device to achieve various functions (3). A metalloprotein that exhibits redox property was used as a biomemory signal source, and various nanoparticles with complementary DNA and metal ions were used as input signals to acquire processed output signals. Various functions including 'information reinforcement', 'information regulation' and 'information amplification' were accomplished in this device due to various input signals. Hybrid material including RNA/quantum dot were developed to construct nanoscale resistive biomemory (4). The electrochemical property in neural cell and synthesis property of nanoparticle in human cells have been investigated (5, 6). The proposed hybrid material-based bioprocessing device by the integration with neural cell should be a new type of platform for development of biomolecular-based biocomputing system.

Acknowledgements
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Poster-15

Protein-Based Bioelectronics

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Proteins that undergo redox reactions play a key role in the biological processes of organisms. Obtaining a fundamental understanding of how electrons are transported within the protein structure is not only important for biology, but may also help in the design of bioelectronic devices that directly couple to biological systems. Coupling to a biological system at the nanoscale to electronics would entail hybridization of the protein's electronic structure with that of the external electronic device, but very little is known about this biomolecule-solid state interface. In this talk, I will discuss recent efforts in my lab to understand this process better by fabricating and characterizing protein-based bioelectronic devices. Specifically, I will discuss single-electron transistors based on single myoglobin proteins and cytochrome P450 proteins localized on functionalized gold nanopillars. The importance of protein configuration in these experiments is important, and moreover, there seems to be a strong correlation between electron transport properties of the localized proteins and their biological viability.

Poster-16

Electronic Control of H^+ Current in a Bioprotonic Device with Gramicidin A and Alamethicin

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In biological systems, most of the communication between cells is mediated by membrane proteins and ion channels that passively allow or actively control the flow of ions and small molecules across the cell membrane. A bioelectronic device in which ion channels control ionic flow across a lipid bilayer with an applied voltage should therefore be ideal for interfacing with biological systems. Here, we demonstrate a biotic-abiotic bioprotonic device in which Pd contacts actively regulate proton (H+) flow across a supported lipid bilayer (SLB) incorporating the ion channel Gramicidin A (gA) and the voltage gated ion channel Alamethicin (ALM). This is the first time that H+ conducting channels have been integrated with Pd/PdHx H+-conducting contacts and that the H+ current flowing through these channels has been directly measured and controlled. This work opens the door to integrating more complex H+ channels such as bacteriorhodopsin at the Pd contact interface to produce responsive biotic-abiotic devices with increased functionality.

Poster-17

In Vivo Identification of Seizure Onset with Implantable OECT-Based Sensors

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In epilepsy, the reasons governing the evolution of a patient's brain state from healthy to pathological are unclear. However, seizures are fundamentally electrophysiological events and such events require brain-energy resources to begin and to be maintained. Therefore, it is our belief that the change in specific brain-energy substrates could be identified as an effective biomarker to identify seizure onset. The two primary energy-substrates in the brain, specifically glucose and lactate, are identified here as excellent candidates for biomarkers signaling seizure onset.

Transistors-based enzymatic sensor fabrication is combined here on our previously published flexible, non-invasive polymer probes, allowing high-resolution in vivo measurements. The conductive polymer utilized in this technology is PEDOT:PSS {poly(3,4-ethylenedioxythiophene) doped with poly(styrenesulfonate)} providing the basis for our organic electrochemical transistors (OECTs). The gates of these devices are then functionalized by a stable covalent enzyme immobilization process, creating enzymatic sensors for in vivo implant.

This design allows us to sense the biomarkers of interest, glucose and lactate, and at the same time exploit the amplification properties of the OECT, namely much larger currents and increased SNR in comparison to standard electrodes. We then correlate the consumption of glucose and the production of lactate during in vivo seizure onset.

Very clear changes in the slope of lactate increase can be seen preceding the onset of ictal (large seizure) events. This identified change occurring prior to the beginning of the pathological activity could potentially be used to for therapeutic local drug delivery to prevent epileptic seizure.

Additionally, in order to simultaneously monitor the levels of both glucose and lactate, cross-talk via H2O2 production between closely located sensors must be minimized. This has been done by the addition of a second enzyme layer using an 'enzyme stacking' process. In vivo use considerably profits from this addition as we additionally demonstrate that H2O2 changes firing patterns by disrupting ATP production in mitochondria.

Poster-18

Influence of Disorder on Organic Electrochemical Transistor Characteristics

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The mechanism for current modulation in organic electrochemical transistors (OECTs) endows OECTs with exceptionally high transconductance. Whereas charge modulation in field-effect transistors occurs only at the dielectric/semiconductor interface, in OECTs, dynamic electrochemical doping modulates the carrier concentration throughout the bulk of the semiconductor film. This bulk doping mechanism translates into gate-channel capacitances of hundreds of microfarads per square centimeter[1] and extrinsic transconductances exceeding 400 S/m.[2] Along with sub-1 V operation and the ability to operate in aqueous environments, the high transconductance in OECTs has made these transistors successful in applications ranging from biosensing[3] to digital logic[4] and neuromorphic circuits.[5] Although transconductance determines performance parameters in these applications, such as signal-to-noise ratio and voltage gain, its dependence on gate voltage and material properties is not yet understood. In particular, one ubiquitous property of OECTs is a non-monotonic dependence of transconductance on gate voltage. Here, we show that this dependence is due to the physics of charge transport in disordered semiconductors and the filling of a Gaussian-shaped density of states. We confirm that although gated contact resistance affects the performance of OECTs, it is not the primary cause responsible for the non-monotonic transconductance curve. Finally, we show that our model fits experimental data for both accumulation-mode and depletion-mode OECTs. Our model derives a central property of OECTs from fundamental semiconductor physics, and it provides guidelines for the development of new materials for optimizing transconductance in OECTs.

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Poster-19

A Bio-Protonic Platform Controls pH for Termination of Seizures in Neuronal Tissue

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Epilepsy is a chronic condition of the brain marked by reoccurring seizures. Seizures occur when neurons inside specific brain regions fire all together simultaneously. This increased excitability results in faulty signaling that manifests in uncontrollable motions. Targeted treatment to the closest proximity of the brain epileptic regions is a preferred over drug inhalation. This can be achieved by devices that can stimulate neurons, deliver drugs and locally control the pH. Acidosis is known to terminate epileptic seizures. Naturally, acidocis occurs as feedback mechanism by the increased production lactic acid during seizures or by increasing the levels of CO2 in the brain during breathing. However, breathing CO2 is not a practical way to treat epilepsy. Local pH changes can be achieved by bio-protonic devices. We present electrodes of palladium nanoparticles (protodes) able to change the pH in buffer conditions. Because of their high surface to volume ratio, palladium nanoparticles improve the proton injection resulting in modulation of pH in physiological media. As a proof of principle, we integrated brain slices with our platform and performed electrophysiological recordings under electroceutical pH modulation.

Poster-20

Large-Scale Silicon Probe Recordings Identify New Cell Types in the Mouse Superior Colliculus

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The mammalian superior colliculus (SC) is a midbrain structure that integrates vision with touch and hearing to initiate orienting movements of the eyes and head. As 70% of the mouse retinal ganglion cells project to the SC, it must be playing an important role in the visual information processing of mice, and therefore needs to be better understood.

We recorded, in awake, behaving mice, the visual response properties of a large population of neurons using 4-shank (200 μm pitch), 256-channel silicon probes in the mouse SC. This allows us to simultaneously record the electrical spiking activity from, on average, ~150 neurons in a single preparation. This provides the statistical power to classify the neurons into different cell types, to find rare cell types, and to determine their topological and functional organization.

Using this methodology, we have found cell types not previously reported in the mouse SC. For example, the 'suppressed-by-contrast' cells respond actively to visual stimuli with low contrast (e.g. a stationary gray screen), but respond weakly to stimuli of high contrast. This is unlike the vast majority of the visually-responsive SC neurons that respond very actively to visual stimuli with high contrast. These cells could be useful for the gain control of other cells.

Another cell type we have found in the mouse SC is the 'Y-like' cell. These cells have non-linear, frequency-doubled response to contrast reversing gratings with high spatial frequency. This cell type may be beneficial for the detection of moving objects that are finely textured.

Our experimental methods thus give important hints for understanding the functional and topological properties of the mouse SC as it responds to visual stimuli. In addition, our experimental method based on high channel count silicon probe recording provides the means to compare the SC functionality in wildtype versus genetically modified mice.

Poster-21

Eumelanin-Based Organic Electronics

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Eumelanins, the black insoluble pigments of human skin, eyes and substantia nigra (neuromelanin), stand today as a unique source of inspiration for the design and implementation of soft biocompatible multifunctional materials for bio-optoelectronic devices.1 Interest in eumelanins stems from bioavailability, biocompatibility and a peculiar set of physicochemical properties, i.e. broadband absorption in the UV-visible range, intrinsic free radical character, water-dependent hybrid ionic–electronic conductor behaviour, supporting optimistic feelings about a possible rise of eumelanin-mimics as innovative bio-inspired solutions for organic bioelectronics.2

However, a number of conceptual and technological gaps still hinder a rapid progress of melanin-based organic electronics and bioelectronics, including in particular the scarce solubility of the pigment in any solvent and the limited contribution of electronic conductivity under biasing.

Herein, we provide a concise overview of our recent advances in melanin-based technological applications. The attention will be focused mainly on: 1) the importance of the ammonia-induced solid state polymerization technique in the processing of eumelanin-based thin films, hybrids and 3D architectures; 2) the role of melanins in the field of organic electronics and bioelectronics; 3) the design and synthesis of melanin-inspired electroluminescent materials for opto-electronic applications.3

Basic structure-property function relationships, fundamental tailoring strategies and processing will be addressed to orient ongoing efforts toward efficient and competitive eumelanin-based technology.

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Poster-22

pH Sensing with Silicon Nanoribbon/Carbon Nanotube Porin Sensor

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Monitoring the acidity of cellular emnvironment in vivo is vital for cancer research since elevated glucose uptake and lactic acid release is the metabolic hallmark of cancer cells. Silicon nanowire field effect transistor (NW-FET) has been extensively studied as a pH sensing platform. However, the application of this sensor is limited by its anti-fouling stability and biocompatibility.

Recent studies have demonstrated that sub-1nm diameter carbon nanotube porins (CNTPs) embedded in lipid bilayers are efficient proton conductors. In this research, we focus on a bioelectronic approach towards designing pH-sensing devices. Specifically, we report an inorganic/organic hybrid device that integrates SiNW-FET and CNTPs and is capable of pH sensing in physiological conditions. We will also discuss potential applications for real-time monitoring of biological systems.

Poster-23

Proton Conductance in Carbon Nanotube Porins in Lipid Membranes

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The maintenance and regulation of ion gradients, specifically the electrochemical proton gradient, ΔμH+, across biological membranes has been established as a necessary intermediate in biological energy transduction that is crucial for proper cellular function. In recent years, artificial membrane channels have attracted much attention due to the key role of proton channels in performing a number of specific functions in different cells. Carbon nanotube (CNT) structures are similar to biological channels (e.g. aquaporins) with their smooth, narrow (ca. 1.5 nm), hydrophobic inner pores. The hydrophobic walls of the CNT facilitates the formation of 1D hydrogen bonded water chains and results in weak interactions with water molecules that enable nearly frictionless water transport. CNTs can provide a functional mimic of biological channels, and to that end we have created shortened CNT-porins and investigated osmotically-driven transport of ions, uncharged species, and water through CNT porins and showed that these porins are capable of transporting ions, water, and small molecules and reject large nonpolar species. This presentation will discuss proton permeation through carbon nanotube porins that have dimensions comparable to biological proteins.

Poster-24

Biophysical Investigations of Electron Transport in Bacterial Nanowires of Shewanella oneidensis MR-1: New Insights from Simulations and Electron Cryo-Tomography

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Dissimilatory metal-reducing bacteria are able to extract free energy from their environment by coupling their respiration to the reduction of solid-phase electron acceptors. There are important implications of this extracellular electron transport (EET) in global elemental cycles and renewable energy technologies. Bacterial nanowires represent one of the pathways of EET in the metal-reducing bacterium Shewanella oneidensis MR-1. These biological filaments are able to transport respiratory electrons to electron acceptors microns away from the cell surface. Here we report our latest findings on the electron transport dynamics and the ultrastructure of bacterial nanowires. Using fluorescent and atomic force techniques, we recently found that the Shewanella nanowires are extensions of the outer membrane and periplasm that contain decaheme cytochromes MtrC and OmcA. The localization of these cytochromes along nanowires supports a multistep redox hopping mechanism, allowing long-range electron transport along a membrane network of heme cofactors that line the nanowires. Here, to investigate the electron transfer dynamics of Shewanella nanowires, we use a combination of atomistically informed kinetic Monte Carlo and coarse-grained molecular dynamics simulations. Our results show how electron flux along nanowires resulting from a multistep redox hopping mechanism strongly depends on the cytochrome density, topology, and orientation. In addition, we report our latest results from electron cryo-tomography (ECT) of Shewanella nanowires, demonstrating ultrastructural details of these filaments in a near-native state. The high resolution of ECT reveals particles along nanowires that are consistent in size with MtrC, thus paving the way for investigating the localization patterns of cytochromes on nanowires. Finally, we report how ECT is allowing us to gain new insight into the morphology and the formation mechanism of these structures. Together, these studies help shape a biophysical understanding of bacterial nanowires, these redox-functionalized membrane and vesicular extensions, as a microbial strategy for electron transport and energy distribution.

Poster-25

Back to Basics - Solutions for Next Generation Electronics and Bioelectronics from 19th Century Dye Chemistry

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Organic pigments have been ubiquitous throughout history and are widely produced today industrially as colorants in everyday products as various as cosmetics and printing inks. Largely regarded by chemists as "yesterday's research" there are many attractive properties of these materials that should be rediscovered in the context of modern technologies. I will cover what are some critical features of these materials and what they have to offer to semiconductor-based devices, especially in the context of applying semiconductors at the interface of biology. I will discuss methods to transform commercial pigments into nano and micro-structured semiconducting crystals, and will highlight two emerging applications: catalysis and cellular interfacing.

Poster-26

Cellular Photostimulation with Hydrogen-Bonded Organic Semiconductor Microcrystal Interfaces

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Successful bioelectronics should rely on an active material that is biocompatible and interfaces intimately with cells. We report on biocompatible hydrogen-bonded semiconductor nanostructured crystals for cellular photostimulation. The biomimetic hierarchical crystals show impressive affinity for cellular coupling and efficient stimulation. The close interface between the nanostructured crystals and cells was elucidated using electron microscopy. Light irradiation was found to elicit a reversible electrophysiological response, measured using patch-clamp technique, only in cells that grow in contact with the nanostructured crystals. The mechanism of action was studied by investigating the effects of photoexcitation on specific ion channels. In total, three different types of ion channels and two types of cells were studied. We discuss the interplay between capacitive, faradaic, and thermal effects on cellular electrophysiology. Over the presented materials would be a potent candidate for cellular photostimulation, which is highly relevant to the new generation of wireless retinal implants.

Poster-27

Protonic Conductivity of Glycosaminoglycans

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The ampullae of Lorenzini are electroreceptive organs found elasmobranchs that are capable of detecting small electric fields on the order of 5nV/cm. An individual ampulla consists of a pore at the skin-seawater interface and interior cavities lined with electrosensing cells, connecting these is a jelly-filled canal. A recent discovery of proton conductivity in the jelly may hint at a mechanism for electrosensory function. Proton conduction of the ampullae jelly has been proposed to be facilitated by acidic groups on keratan sulfate, a sulfated glycosaminoglycan. Here we demonstrate the proton conductivity of keratan sulfate and other glycosaminoglycans with devices utilizing palladium contacts capable of directly inducing and measuring a proton current. These measurements of conduction in glycosaminoglycans aid in the understanding how protons are conducted in biomaterials and the relevance to electrophysiology.

Poster-28

Highly Controlled Assembly of Nanoprobes in 3D for Cellular Electrical Interrogations

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For centuries efforts have been invested in the exploration of the intricate way cells communicate. Basic research at the tissue level of the heart and brain electrical activity, for example, has led to the development of tools to treat various ailments, such as pacemaker and deep brain stimulation electrodes for the treatment of cardiac arrhythmias and Parkinson's disease respectively. Currently, there is a critical need to develop new ways to explore how cells communicate at the cellular level with exquisite details.

Here we demonstrate a state-of-the-art nanoprobe arrays assembled in three-dimensions (3D) with subcellular spatial resolution and microsec temporal resolution to directly monitor the development of electrical activities of microscale tissues (microtissues, ca. 200-400um). Studying the mechanism of cell-cell communication and understanding the electrical signal propagation within a microtissue will greatly impact our basic understanding of signals transduction in complex cellular assemblies, and will create new avenues for bidirectional communication (sensing and stimulation) with electrically active tissues. The developed nanomaterials-based measurement platform will set the ground for further investigations of the relationship between electrical signals and reported diseases such as Alzheimer, Parkinson's disease and Arrhythmias.

Poster-29

Interface Investigation of Electrogenic Cells on 3D Laser-Patterned PEDOT Structures

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Interfacing OECT's with ionic barriers and biological systems holds considerable promise not only for building sensitive biosensors and diagnostic tools, but also for recording biological process in live cells and neurons. In fact, organic transistors or multi (organic) electrode arrays can record action potentials from electrogenic cells as well as send electrical stimuli to trigger certain electrical patterns within cells. Traditional devices are planar, and a cleft between cells and device typically forms, affecting the recorded signal quality. Recently, 3D modifications of the electrode surface have been successfully proposed for traditional metal electrodes. Here, we present a novel patterning method using a direct-write femtosecond laser process, to create well-defined micro patterns into PEDOT:PSS films. The direct-write technique is straightforward and does not involve complicated lithography or etching steps while the ultrafast nature of the process ensures a high resolution and low impact. Electrogenic cells can sense 3D cues inducing spatially guided outgrowth and stretching. Furthermore, we investigate the effective interface of electrogenic cells by using an innovative embedding procedure for scanning electron microscopy and focused ion beam sectioning and comparing that with the transconductance measured on functionalized organic electrochemical transistors. By doing so we can both effectively visualize the point contacts of the cell membrane on to the 3D PEDOT structures as well as provide an estimate of the resulting electrical contact resistance and capacitance of the cleft. These in vitro morphological studies represent the first step towards a 3D implantable organic electrodes.

Poster-30

Single-Molecule Rectifier Composed of DNA with High Rectification Ratio Enabled by Structure Modification

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The goal of molecular electronics is to functionally incorporate molecular components in electronic devices. The predictability, diversity, and programmability of DNA make it a leading candidate for the design of functional electronic devices using single molecules. The conductivity of DNA was recently found to be sensitive to subtle changes in DNA conformation caused by alterations in the ionic environment2 or by its modification with methylation3 or with metal ions.4 Remarkable in their own right, these achievements hint at the fascinating possibility that the electronic transport properties of DNA can be fine-tuned via structural modification for the development of a diversity of DNA-based electronic devices, especially an applicable DNA molecular rectifier.

Here we demonstrate a DNA-based single-molecule rectifier constructed by site-specific intercalation of small molecules (coralyne) into a custom-designed 11-base pair DNA duplex. Measured current-voltage curves of the DNA-coralyne molecular junction showed unexpectedly large rectification with a rectification ratio of about 15 at 1.1V, a counter-intuitive finding considering the junction's seemingly symmetrical molecular structure. A non-equilibrium Green's function-based model - parameterized by density functional theory calculations - revealed that the coralyne-induced spatial asymmetry in electron state distribution caused the observed rectification. This asymmetry inherently leads to changes in the coupling of the molecular HOMO-1 level to the electrodes when an external voltage is applied, resulting in an asymmetric change of the transmission. This approach provides a route for DNA-based single molecule electronic device development.

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Poster-31

Pili-Mediated Metal Acquisition – a Physiological Probe for Protein-Mediated Electron Transport?

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Cyanobacteria have a high demand for iron. In many environments iron is complexed and forms insoluble iron oxides that render the iron not readily bioavailable. Several indications exist that electron donation to extracellular iron oxides has a critical role in making iron accessible for the cell. We have investigated the role of pili, extracellular protein structures, in making iron that is complexed in iron oxides available for the cell. The genetic deletion of genes that form pili indicates that pili play a critical role in iron acquisition.

Poster-32

Cellular Electron Transfer: A New Direction in Controlling Cellular Electronic Talk

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The work presented will discuss the recent discovery that eukaryotic cells expel electrons directly to their external environment. The lack of progress in this area, until recently, may be explained by physiological hurdles posed by eukaryotic organisms because a majority of electron transfer occurs at the intracellular metabolic machinery. In addition, there has been a lack of technology capable of sensing these external electron transfer events. This lack of technology and understanding has been addressed by initially examining the redox interaction of soluble molecules with yeast cells. From these mediator studies unknown cell surface redox sites capable of transferring electrons externally were identified. Subsequently electrodes have been modified with an electrocatalyst that facilitated electron transfer across the yeast cell wall. Studies were then performed to develop nanostructured surfaces that could intracellularly sense electron transfer events via hydrogen peroxide production in immune cells. Molecular tailored surfaces were then fabricated in which immune cells-surface electronic interactions were modulated. The observed charge transfer observed in these investigations is thought to be facilitated by saccharide redox chemistry and these recent technological advancements suggest that cell-surface electronic interactions play an important role in cellular homeostasis. Importantly, the ability to modulate these bio-electrochemical events raises the opportunity of controlling the underlying biology that the cellular electrical talk underpins. Advancements in technology, coupled with a deeper understanding of the underlying biology will have an impact in electroceutical development and the invention of new electrochemical sensors and actuators to control and detect cellular events.

Poster-33

Tuning Electronic Transport via Hepta-Alanine Peptides Junction by Tryptophan Doping

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Biomolecules display great potential for future functional molecular electronic devices. Peptides are suitable as building blocks to bridge conductive electrodes of solid state electronic devices. To design and apply peptide junctions for solid state devices, the relations of peptide electron transport to their amino acid composition and structure need to be understood as well as the peptide electronic structures on electrode surface. Such information may also help understanding the electron transfer processes that occur in/with proteins in biological energy conversion, sensing and signaling systems.

Earlier we studied electron transport across self-assembled homopeptide monolayers of specific amino acids, length and structure, between gold contacts. Supported by high-level electronic structure calculations we found the nature of the amino acid, charge of its residue, length and secondary structure to determine the peptide conduction, which we suggested to be dominated by off-resonance tunneling[1].

We then used a series of heteropeptides, linear oligo-alanines with a single tryptophan substitution, which acts as "dopant", introducing a low-lying energy level. Trp doping markedly increases peptide conductance, especially if its location in the sequence is close to an electrode. Combining inelastic tunneling spectroscopy (IETS), ultraviolet photoelectron spectroscopy (UPS), advanced density-functional theory (DFT) electronic structure calculations, and current-voltage analysis, the role of Trp in ETp is rationalized by tunneling across a heterogeneous energy barrier, due to Ala and Trp electronic states, and Trp coupling to the electrodes. These results reveal a controlled way of modulating the electrical properties of molecular junctions by tailor-made "building block" peptides [2].

Electronic structure of a peptide molecule monolayer/electrode interface is directly related to the energy barrier and electrode-molecule coupling of the resulting junctions. In view of the results with Trp doping of poyl-Ala we compared the electronic structure of dipeptides (2Ala and 2Trp) in the gas phase and in a monolayer, bound via S-Au to a gold substrate, using UPS and advanced DFT. We find that amino acid residues on dipeptides are screened from the interaction to Au due to Au-S binding (via a mercapto-propionic acide linker), which are not directly

involved in the energy alignment with electrodes. The energy barrier of the peptide junctions between the electrode's Fermi level and the closest molecular level of the peptide are mainly determined by the types of amino acid that makes up the peptide, i.e., the side chains.[3]

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