Project S151: Characterization and Demonstration of OSTE+Neuronal Probes *in vivo*

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Location of Project

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Possible Project Terms: Summer 2015

Introduction:

Implantable neuronal probes are commonly made with silicon, using microfabrication techniques that have become widely available in the last two decades. Recently there has been interest in using softer materials than silicon for implantable probes to reduce the mechanical mismatch between the hard probe material and the soft brain tissue. However, specific material properties are required for a material to be compatible with conventional microfabrication techniques, and therefore the fabrication of flexible implantable probes has proved challenging. A new material, off-stoichiometry thiol-ene-epoxy, or OSTE+, demonstrates many promising properties for use in flexible probes, and is also curable by UV light, and therefore compatible with many photo-lithographic processes. Use of a direct UV laser has been employed by our lab to begin to fabricate neuronal probes using this new material. The design, fabrication, characterization, and testing of these neural probes is the current Master's thesis topic for one student in our lab.

Student's Role:

Initially, the summer student will be expected to evaluate, test, and characterize the OSTE+ probes as they are manufactured in the McGill clean room. This would include material characterizations such as mechanical stability and thermal responses, possibly through the use of atomic force microscopes, dynamic mechanical-thermal analysis (DMTA), thermogravimetric analysis (TGA), or differential scanning calorimetry (DSC), as well as dimension characterization with a profilometer, and with microscopes. In particular, this portion of the project is expected to generate some SEM images of fabricated probes, of high enough quality to be used in publications. In addition, electrical impedance spectroscopy of the electrode sites on the fabricated probes will be performed.

Once the initial characterizations are complete, and the probes deemed acceptable for further use, the student will continue to the next stage of the project, which is aimed at demonstrating OSTE+ as an acceptable material for implantable neural probes. Initially, Peltier cooling elements will be researched and purchased by the student, and probes will be implanted into 0.5% agar gel of various temperatures. The summer student will have to troubleshoot the setup and communicate with the Master's student manufacturing the probes, such that the probe design may be optimized until it can be successfully implanted into 0.5% agar gel at 37 degrees, which has a stiffness similar to brain tissue. This will demonstrate that these probes are ready to be implanted in vivo.

At this point the manufactured OSTE+ probes, as well as silicon probes and possibly SU8 probes, will be implanted into rat brains in vivo. This may be done at the MNI by a trained surgeon, who is a contact of the project team. Additionally, various surface treatments will be used for each type of probe, including the PEM coatings developed in the Barrett lab. This section of the project will rely heavily on collaborations with surgeons and neuroscientists at the MNI, and in particular in Tim Kennedy's lab, as the next step is to get brain sections from the rats with implanted probes. These brain sections will be stained for reactive astrocytes and the immune response of OSTE+, silicon, and SU8 probes may be evaluated with several different surface chemistries. The student will assist in this section of the project by helping to plan experiments, communicate clearly with interdisciplinary contacts, and ultimately assisting the primary Master's student in executing these experiments. It is not expected that these experiments will be complete by the end of the summer, as in vivo tests will take time. However, if the experiments progress well and in a timely fashion, the student will help in imaging and analyzing brain sections to generate data and draw conclusions from this study.

Project S152: Rapid Prototyping of Capillaric Circuits For Bacteria Detection

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Possible Project Terms: Summer 2015

Introduction:

Capillaric circuits enable pre-programmed and equipment-free delivery of multiple liquids using only surface tension forces. These devices are assembled from capillary microfluidic elements and designed using electrical analogies. However, the most commonly used microfluidic prototyping material – Poly-dimethylsiloxane, a silicone rubber – is not inherently wettable and when plasma-treated to make it hydrophilic, gradually reverts to its hydrophobic form. The goal of this project is to fabricate capillary microfluidic devices with polymeric materials that have stable hydrophilic surfaces and can be rapidly prototyped in a laboratory setting. In addition, we will rapidly prototype molds for the capillaric circuits using a 3D printer followed by replica molding in polymers. This will require work on soft lithography and surface chemistry. We are seeking a student with a physics/chemistry or a chemical/mechanical/ material engineering background and that has expertise in one or several of the above research areas.

Student's Role:

The role of the student will be to work closely with a PhD student in the Juncker group and develop expertise in the following areas:

- **Evaluate different polymeric materials for device fabrication including: Polydimethylsiloxane (PDMS), Norland Optical Adhesive (NOA), and Off-Stochiometric Thiolene Polymer (OSTE).**
- **Investigate methods for modifying surface chemistry of polymers to obtain stable hydrophilic surface.**
- **Soft-lithography and rapid prototyping.**
- **Microfabrication and CAD design.**
- **3D printing of capillaric circuits**
- **Perform immunoassays to detect bacteria using capillaric circuit**

Student Requirements:

- **Some background in chemistry and surface chemistry would help.**
- **Experience working with polymers, soft lithography, and rapid prototyping is an asset.**
- **Strong ability to design experiments and work in a laboratory setting.**
- **Some background and theory in fluid mechanics (and microfluidics) is helpful.**

Project S153: Multiplex immunoassays of single-cells using trap-arrays

Supervisor: Prof David Juncker

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Location of Project

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Possible Project Terms: Summer 2015

Introduction:

Cell-to-cell heterogeneity leads to difficulties in analyzing ensemble cell-based assays. This evokes the need for immunoassay techniques that can resolve data from single-cells. Current methods for single-cell analysis such as flow cytometry sacrifice cells (fixing) in order to reveal the intracellular/secreted protein levels. Furthermore, the number of targets that can be detected simultaneously is limited due to the overlap of the excitation/emission spectra of fluorochromes. In this project we will design and implement a microfluidic device which allows multiplex protein detection on live, isolated single-cells. An important aspect of this project will be the integration of cell-encapsulation and protein detection on a single chip, thereby minimizing the workflow in cell-based assays. For this, 2D or 3D trap arrays of cell-encapsulating microparticles will be used to allow for live fluorescent imaging of the cells.

Student's Role:

The student will be in charge of designing, fabricating, and operating the microfluidic device. The microfluidic device will be streamlined with multiple modules aimed at (1) encapsulation of single-cells in water-in-oil (W/O) droplets, (2) gelation of the aqueous solution, (3) collection into culture media, and (4) automated trapping within the arrays. 3D printers will be utilized initially to fabricate prototype devices before realizing the device using typical soft lithography. After a successful completion of this step which yields single-cells encapsulated in gel microparticles arrayed on the PDMS, beads will be co-encapsulated within the microparticles to capture secreted proteins from the cells. Finally, live fluorescent imaging will be utilized to run time-course measurements of secreted proteins on a single-cell basis.

As such the project requires a multidisciplinary effort throughout which the student will learn techniques in microfluidics, fluorescent imaging, and surface-based immunoassays. The project is expected to take 4 months, and will result in a publication of the work in an appropriate journal such as Lab on a Chip.

Project S154: Multiplexed micro-immunohistochemistry using a snap chip

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Possible Project Terms: Summer 2015

Introduction:

Profiling of proteins in tissue has great potential to discover new biomarkers that can be used in breast cancer diagnosis, subtyping, prognosis, and treatment selection. It has been well accepted that single biomarkers are not clinically useful, and a panel of multiple proteins is required for accurate diagnosis and subtyping. Immunohistochemistry (IHC) has been one of the major technologies to identify biomarkers in breast cancer tissues and subclassify patients. However, the multiplexing capability of conventional IHC is very limited; therefore multiple tissue samples and long assay time is required for the detection of tens to hundreds proteins. Microfluidic technologies have been used to develop miniaturized IHC by flowing reagents across the tissue through microchannels, but the multiplexing capability is still limited to a few targets. In Prof. Juncker's laboratory, we have developed an easy-to-use snap chip technology for transferring an array of reagents from chip-to-chip without cross contamination, thus allowing for scalable multiplexed bioassays in a microarray format using minute amount of reagents. Collaborating with Prof. Peter Siegel's Breast Cancer Metastasis Research Group, we aim to develop a novel multiplexed micro-IHC platform using snap chip technology. Assay conditions will be optimized and 20 cancer-related proteins will be analyzed on human breast cancer tissues.

Student's Role:

1. Pattern antibodies on a substrate with a microarray spotter.
2. Optimize the snapping protocol to ensure reliable transfer of the antibody microarray to the tissue chip.
3. Optimize IHC assay conditions.
4. Perform micro-IHC assay targeting ~20 proteins on human breast cancer tissue.
5. Compare the micro-IHC results with conventional IHC and analyze data.

Student Requirements:

1. Chemistry, biochemistry, or bio-related background.
2. Basic laboratory and computer skills.
3. Previous laboratory experience preferred.
4. Ready to work in a multidisciplinary team and learn new techniques.
5. Highly motivated and hard working.

Project S155: Characterization of Plasmonic Nanostructures for Biosensing

Supervisor: Prof Paul Charette

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Location of Project

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Possible Project Terms: Fall 2015

Introduction/Background

The research group led by professor Paul Charette at the Université de Sherbrooke develops biosensors for measuring biomolecular kinetics in fluids for medical and environmental monitoring applications. One of the sensing modalities used in these biosensors is known as "surface plasmon resonance" (SPR), whereby surface-based biomolecular reactions at a metal/dielectric interface can be monitored in real-time with great precision.

By nanostructuring the metal surface, the surface-bound electric field can be engineered with specific properties useful for biosensing. In particular, normally occurring "propagating" plasmons can be used to excite "localized" plasmons having unique properties for spatially-resolved sensing.

Student's Role & Student Requirements

Based on numerical modeling, SPR samples with a variety of nanostructured patterns will be fabricated by electron beam lithography in the University of Sherbrooke cleanrooms. These nanostructured samples will need to be characterized rigorously in terms of biosensing measurement sensitivity, noise level, and range.

Using an optical test bench, the student's role will be to work on sample characterization, under the supervision of a postdoctoral fellow in the research group. The student must be enrolled in an undergraduate electrical engineering or physics program.

PROJECT S156: Environmental monitoring system for beehives using IR imaging and audio analysis

Supervisor: Dr. Viacheslav Adamchuk

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Location of Project

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Term Available : Summer 2015

Introduction:

Honey bees are an essential crop pollinator which are responsible for over one-third of the global agricultural production and provide a multi-billion dollar ecosystem service. As such, pollinator activity is an important environmental health indicator. Unfortunately, many species of pollinators, including honeybees, have faced unprecedented losses over the past decade without a clear understanding of the cause. The phenomenon, known as Colony Collapse Disorder, may be attributed to mites, bacterial infections, pesticides, electromagnetic interference, or other factors. Although colony losses are a global issue, the problem is exacerbated by the difficulty of beehive management and the lack of integrated sensor systems in apiculture. Therefore, the development of innovative sensor systems is a promising way to expand honeybee and pollinator research.

In a partnership between the McGill Department of Bioresource Engineering and the McGill Apicultural Association (MAA), a distributed beehive monitoring network was developed over the summer of 2014. The network was designed for the purpose of conducting pollinator research at McGill University. Currently, the system provides the capability for researchers to collect and visualize real-time internal hive data for up to 10 hives; it records the temperature, relative humidity, barometric pressure, and sound amplitude/frequency of the colonies. Future applications of environmental sensor systems in beehives may provide the capability to predict swarms, identify hives at risk of infection, and minimize winter/thermal stress.

Student's Role and Requirements:

For this research project, the student will help expand the capabilities of a preexisting beehive monitoring system through the development of a computer-vision web application. A camera will be implemented alongside a microphone for the purpose of (a) quantifying the amount of hive activity and (b) categorizing hive behavior. To accomplish this task, the student will work closely with the MAA which will provide the hives and serve as the site for the research. Due to the nature of year-round monitoring in outdoor conditions, a necessary engineering component of this project will be the design of a rugged, weatherproof enclosure for the sensor systems which takes into consideration the biological attributes of an active honeybee colony. The student will also be encouraged to improve the research GUI by adding the ability to visualize the new computer-vision and audio data on the web application.

In order to successfully complete this project, the student will be required to be proficient in computer programming (Python, JavaScript), electronics of sensor systems, as well as modern computer-vision and audio analysis methodologies. The student should also be familiar with computer networking since the platform used by the MAA consists of nodes (one per hive) which communicate via a centralized web application over Ethernet. Over the course of the project, the student will be expected to submit a bi-weekly log detailing his/her progress as well as a final summary report.

PROJECT S157: Single Molecule Detection on Planar Devices

Supervisor: Prof. Dan Nicolau

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Location of Project

Laboratories of the Department of Bioengineering

Term Available : Summer 2015

Background: Many advances in diagnostics and drug discovery were possible due to the development of *planar biomedical micro-devices*, or "biochips", of which protein-based ones are increasingly important. These biochips consist of surface-immobilized "targets", e.g., antibodies, which specifically bind to "probes", e.g., antigens. However, *protein-surface interaction* has two important side effects: *loss of sensitivity* and *slow reaction time*, both of which connect to three areas of applicant's research.

Proposed Study: The strategic intent of this line of research is to fabricate nanostructures that interact with *individual* protein molecules, for fundamental studies and for high sensitivity diagnostic devices. Polymer self-assembly, either triggered by laser micro-ablation or by UV radiation was, and will be used for the immobilisation of proteins on micro/nanostructured surfaces. It was found that the topography *and* physico-chemically heterogeneous, nano-structured surfaces preserve better the bioactivity of surface-immobilized proteins. Importantly, proteins have been immobilized on nano-sized objects (nanoparticles), calibrated to allow a precise number of protein molecules (from 1 to 6) per nanoparticle. This approach allows a very high sensitivity and specificity of molecular recognition, due to the perfect control and amplification of the fluorescence signal via Surface Plasmon Resonance (SPR) effects.

The information regarding the protein bioactivity on surfaces, especially the impact of nano-structures, will be used to design better surfaces that preserve protein bioactivity. The *central methodological concept of this module is that the immobilization of individual protein molecules on nanostructures matching their size will result in the preservation of bioactivity and (possibly) in increased reaction rates*. Because the proposed architecture has a smaller contact area of the surface with the individual protein molecule, the surface-induced denaturation and loss of bioactivity is expected to be minimal. An additional advantage of the Au nanoparticle-on-Si pillar is that separate chemistries can be applied for the functionalization of NP, for protein immobilization; and for the nano-pillar, for supressing non-specific binding, respectively. Consequently, the "protein crowding", as well as nonspecific binding will be minimized. It is also expected that the elevated position of the target will lead to an increased exposure of the protein and thus the increase of the rate of molecular events, leading to shorter reaction rates. Another advantage is that the fluorescent signal can be amplified, either by Fluorescence Interference Contrast (FLIC), or SPR effects.

Supervisor: The PI has degrees in Chem.Eng (PhD), Cybernetics (MS) and Polymer Sci. (MEng). Dan, who is the Chair of the Bioengineering Department at McGill University, published more than 100 scientific papers and was the PI of projects, many international, in excess of $15mil. Dan's work focuses the intelligent-like behaviour of microorganisms in confined spaces. Two postdoctoral researchers will focus on experimental and mathematical areas. The project will be hosted in the Bioengineering Department Laboratories with facilities for micro/nanofabrication, cell culture, advanced microscopy and computing.

Students' Roles: The students are expected to (i) fabricate the micro/nano-structures following pre-existing and new designs; (ii) immoblize proteins (and other biomolecules, e.g., DNA) on nanostrutured surfaces; (iii) operate the prototypes of the diagnostics devices ; and (iii) quantify the performance of the diagnostic devices and, if needed, start again the cycle from design, fabrication, etc.

Student Requirements: The candidates are expected to have a very good academic record and demonstrated ability to either perform complex experiments, or synthesize complex data in concise statistical reports - better both.