Index-Description

The Material Interactions with Biological Systems Laboratory focuses on improving the biocompatibility of biomaterials and biomedical devices, specifically for the ocular and circulatory systems. With the increasing utilization and invention of biomedical devices, the lives of countless individuals have been improved significantly. To maintain and maximize this improvement, the potentially life-threatening side-effects of such innovations, including infection, thrombosis, and fibrosis must be understood, and through this understanding, prevented, to ensure each patient’s safety and satisfaction. Hence, this laboratory studies the interactions that occur between biomaterials and biological systems to identify the mechanisms behind these negative outcomes along with those that could theoretically arise from a biomedical device or therapeutic measure. To do so, our laboratory studies biological systems’ responses to biomedical devices and therapies on a cellular level to comprehend and identify these processes and use this to quantitatively evaluate their biocompatibility. By understanding these mechanisms, and recognizing areas ripe for improvement in the industry, our laboratory innovates by developing materials, therapeutics and devices with improved biocompatibility, independently and alongside biomedical companies. To justify the value of our conceptions, we often develop or work with in vitro models to closely represent the biological systems we study to negate the necessity of testing on humans and animals. Overall, MIBS is dedicated to the improvement of therapeutics, and biomedical devices for the sake of innumerable patients worldwide.

CPB Model Description

Cardiopulmonary bypasses (CPB) frequently result in excessive bleeding, and consequently this surgery contributes to 10-15% of the national blood demand. This is caused by convoluted mechanisms, and is patient-variable, necessitating complex prediction methods. However, the main causes are believed to be platelet dysfunction, hyperfibrinolysis and coagulopathy. Coagulopathy specifically, is associated with the duration and complexity of the surgery, hemodilution, anti-platelet therapies, shear stress induced by the CPB flow conditions, blood-air and biomaterial interfaces, comorbidities, heparin and protamine doses, and genetics. The prediction of this phenomenon is essential as it could potentially be utilized to inform treatment decisions, signal the need for prophylactic and preventative measures, ensure the necessary blood for transfusion is prepared, and overall, improve the patient’s care. Currently, platelet function testing (PFT) is the technique used to coordinate surgeries for patients on antiplatelet therapy, and to improve transfusion algorithms since CPB-induced coagulopathy is not observed by other assays. Unfortunately, this test’s predictive sensitivity is merely 70%, generating a high rate of false positives, diminishing its clinical value. This is a consequence of the fact that these tests are conducted under resting conditions and that platelets experience changes during surgery which preoperative testing does not account for. Consequently, a prototype was designed to mimic the stresses that blood experiences during CPBs in vitro and in the future will be used on the blood of volunteers. After comparing these results with post-operative CPB results the device will be modified to more accurately predict patient-based outcomes. If this is successful, a point-of-care testing device will be designed.

Investigation of Latanoprost Release from Contact Lens Material

In this study research was conducted to evaluate the ability of contact lenses to uptake and release glaucoma drugs in vitro. This experiment was conducted by allowing different contact lenses to soak in solutions of glaucoma drugs for 24 hours. Afterwards, the lenses were placed on one of three models, a monolayer with human corneal epithelial cells (HCECs), a multilayer with HCECs, or a PET insert without any cells. Over 48 hours, the drug diffusion was calculated periodically for each of the contact lens types and was repeated in different mediums. Previous literature has demonstrated that this method has a low potential for drug administration, and that hydrophobic interactions between the drug and the contact lens material are the determining factor for adsorption. However, most of these studies have only been conducted on deionized water, phosphate buffered saline, and artificial tear solutions. Sources also state that the amount of drug released is also significantly greater in vivo than in vitro. In total, the results demonstrated that in cell-based in vitro models, the drug release is significantly higher than models without cells even when using different media in the no-cells model, and a dead-cell model. Regardless, only 2-3% of the drug adsorbed by the contact lens was released after 24 hours. Nonetheless, more drug may possibly be released from silicon hydrogels making them potentially useful for an ocular drug delivery system in the future. Overall, this research exemplifies the importance of using cell models for studying drug release in instances where the drug must be metabolized before being diffused within the tissue. In the future, a Tear Replenishment System will be deployed in our studies to more accurately simulate the dynamic environment characteristic to the front of the eye.

Untangling the Mysteries of the Tear Film Neutrophil

Polymorphonuclear neutrophils (PMNs) invade the cornea while the eye is closed. A closed-eye environment is also known to induce hypoxia, tear components, and interactions with corneal epithelial cells, which could be responsible for the difference between tear PMNs and blood-isolated PMNs. This study was conducted to determine if, by exposing blood-isolated neutrophils to this environment that they could mimic the tear-film neutrophils to develop improved in vitro models to more accurately study ocular inflammation. In this experiment, tear PMNs were collected from donors via having the volunteers wash the PMNs off their corneas immediately after waking up. Meanwhile, blood was also collected, and the neutrophils were isolated from these samples. The tear PMNs were immediately stimulated with LPS (known to induce inflammation), PMA (a synthetic endotoxin and inflammatory stimulant), and fMLP (a cytokine for activation) and analyzed with flow cytometry to determine certain gene expressions. Afterwards, the isolated neutrophils were exposed to FBS and ATS, followed by half of these neutrophils being exposed to hypoxia normoxia and interactions with human corneal epithelial cells for 6 hours. The first half was directly tested in the same manner as the tear PMNs, while the second half was tested immediately after the hypoxia and cell exposure. Once the cellular data was analyzed, it was clear that the experiment did not cause the isolated neutrophils to mimic the tear film neutrophils. However, it demonstrated that exposure to human corneal epithelial cells, incubation time, and different media do induce significant changes. Regardless of these results, future experiments will be conducted as the development of a robust tear film neutrophil model is essential to the accurate study of material interactions with the cornea in vitro.

The Effect of Substrate Elastic Modulus on CECs

It is known that chemical and mechanical signals such as stress and the properties of the substrate that the cells interact with can induce cellular proliferation, differentiation, and directional migration. These mechanical signals are especially interesting in the study of keratoconus, a corneal condition which involves mechanical changes such as corneal thinning and consequently decreased mechanical stability and elastic modulus. Hence, this study was conducted to determine if these mechanical alterations elicit changes in the cellular environment, specifically changes to the elastic modulus. To do so, human corneal epithelial cells were cultured on substrates with differing elastic moduli, and were subsequently studied regarding their viability, cytoskeletal structure, adhesion molecule expressions, apoptosis, and inflammatory responses. The variant elastic moduli were constructed via the use of differing concentrations of polyacrylamide. Afterwards, it was determined through analysis that this biomaterial was not toxic by conducting a cell viability test, while altering the elastic moduli affected the cytoskeletal structure of the cells. Specifically, the compliant substrate resulted in the crumbling of actin fibers and a disrupted overall structure, while the cells cultured on a stiff substrate expressed stretched and well-organized actin fibers. Through the video above, it was observed that the lack of organization and the deterioration of the actin fibers directly affected the migratory behavior of the cells in the softer substrate. Meanwhile, the apoptosis assay revealed that substrates with decreased mechanical properties had an increased rate of apoptosis, while the differing substrates did not change the levels of adhesion molecules or the molecules associated with an inflammatory response. Overall, this study determined that substrates with a relatively low stiffness induce apoptosis and disrupt actin fibers and as a result disrupted migration, which prompts further research involving the context of keratoconus.

Infrared Therapy for Healthy and Diabetic Conditions

While corneal epithelial and other epithelial tissues are similar, they are certainly not identical. Unfortunately, corneal epithelial tissue heals significantly slower, leading to seemingly everlasting visual complications. To make things worse, 2% of natural, complete wound healing processes lead to corneal abnormalities. While there are therapeutic technologies currently available, many patients are reluctant to utilize them as they are invasive, expensive, and inconvenient. This is especially regrettable for diabetics as they experience even slower corneal wound healing, and an increased rate of post-surgical complications. Thus, one of our current projects has been to study an alternative method of wound healing therapy, infrared radiation. In the past, studies have demonstrated that certain wavelengths of infrared radiation can stimulate the mitochondria of different tissues, leading to an increase in ATP production, reactive oxygen species, nitric oxides, and calcium ions, which overall lead to an increase in cellular proliferation, and consequently wound healing. Therefore, we are determining whether these effects can be observed in the corneal epithelium as well to improve the wound healing rate of diabetic, and otherwise healthy patients alike. Through our experiments we have been studying the physical and chemical properties of scraped human corneal epithelial cells that have either been exposed to a standard growth environment, or an environment with increased glucose to reflect diabetic conditions, along with different fluencies and wavelengths of infrared radiation. In total, we hope our results, using a more complex in vitro corneal model will be successful, and eventually in vivo to improve the corneal wound healing process for everyone, including diabetics.

Assessing OcuCell for Realistic In Vitro Testing

For the general population, contact lenses are merely pieces of plastic that correct eyesight. However, engineers are attempting to achieve a paradigm shift in the way contacts are seen by the public as they are working to develop contact lenses with diagnostic, therapeutic, and monitoring capabilities. However, for these technologies to be approved they must be biocompatible. Hence, there is a growing demand for advanced in vitro models capable of assessing ocular surface toxicity and the biocompatibility of these future innovations. The objective of this study was to develop an in vitro cell culture system to replicate the tear flow between the eyeball and the eyelid with OcuCell. The experiment was conducted by first synthesizing a silicone eyelid and eyeball on which cells were grown for a period of 4 days. Next, the OcuCell was assembled and the silicone pieces were added. Once the device was prepared, the cellular response was characterized with flow cytometry after, 0, 2, 4, and 6 hours of running the device. After MTT and XTT testing, it was discovered that the cells were able to grow to an even confluence on the silicone eyelid pieces, and that the device does not lead to cell death. Furthermore, the use of flow cytometry to evaluate cellular expressions demonstrated upregulated integrin a3­­ and b1 expressions, which was believed to be the result of the low shear stress induced by the flow of the artificial tear fluid. After further testing the apparatus with contact lenses soaked in PBS, no contact lenses, and a positive control contact lens designed to kill cells, it was determined that the OcuCell system is a formidable in vitro testing device for contact lenses as it mimics the essential ocular parameters of cells and tear flow, generating more meaningful results.

Maud Gorbet

With a Ph.D. in Biomedical/Medical Engineering, and expansive research experience as seen through her wealth of research papers and innovations, Dr. Gorbet is well equipped for her position as the Material Interaction with Biological Systems laboratory director. Dr. Gorbet is dedicated to aiding millions of people by solving biocompatibility complications between biomaterials and biomedical devices, as well as therapeutics. Through her research, she has published a series of papers which have benefitted the biomedical community by providing the information and insight necessary to develop novel biomaterials, biomedical devices, and therapeutics, and has provided them with improved in vitro models, which more accurately mimic biological systems to ensure that innovations are successful when implemented in the industry. Meanwhile, as biomedical engineering department director and associate professor at the University of Waterloo, Dr. Gorbet is dedicated to ensuring that the future of biomedical engineering is worth being optimistic about, and that her legacy of biocompatibility will be maintained for years to come.

Parisa Hamilton

Through a bachelor’s degree in chemical engineering at the University of Tehran, a master’s degree in chemical engineering, and a PhD in nanotechnological chemical engineering at the University of Waterloo, Doctor Hamilton has acquired the knowledge necessary to excel at the MIBS lab. Not only that, she has procured wisdom through working as a research assistant and associate at the University of Waterloo, completing numerous projects. For instance, for her doctoral thesis, she developed self-assembling peptide based nanocarriers for anticancer drug delivery to stabilize hydrophobic drugs such that a low immune response was induced, while maximal anticancer properties were maintained. Currently, Doctor Hamilton is the liaison between Penta Medical and the MIBS lab and has developed the photo biomodulation device, which she is currently utilizing to study the therapeutic effect of infrared radiation on corneal epithelial cells to improve the rate of wound healing for both healthy and diabetic patients.

Matthew Robichaud

### Even before completing his bachelor’s degree in systems design engineering at UW, Matt began working as a research assistant at the MIBS lab, aiding in various research projects, while still being academically awarded with distinction. Through cooperative education, he was already a versatile worker when beginning at the MIBS lab, having worked in various engineering positions including at Cooper Lighting Controls where he automated the organization’s testing procedure, contributing to the deployment of smart lighting systems. As for his Capstone project, he worked as part of the Secure team to develop an instrument to minimalize the invasiveness of mitral valve repair by creating a device that automates repetitive and complex parts of the surgery. This project is related to his master’s degree research as he is testing a device he developed to predict the outcomes of open heart surgery. To accelerate his progress towards the creation of a point-of-care testing device, he recently went to the University of Technology of Compiegne where he established a research partnership and studied microfluidic design and fabrication techniques.

Dana Toameh

Dana has been working in the MIBS lab almost as long as she has been in post-secondary education and has since been involved in the assessment of material biocompatibility in vitro, the study of controlled drug release, and tests determining the sheer stress induced by blinking. Concurrently, she not only excelled in her health science classes at the University of Laurier, and acquired numerous academic awards, she also found time to be involved in a variety of associations and societies such as the Pre-Medical Society where she promoted and executed events designed to prepare students for medical school, and was the executive vice-president of the Faculty of Science Students’ Association where she sought to improve the academic, social, and professional experience for her fellow science students. Amidst all of this, she was even involved in another research project on neuromuscular physiology at Laurier where she designed a non-invasive experiment to test cortical inhibition and tested the validity of decomposition electromyography. Needless to say, Dana has played an important role in recent research at the Material Interaction with Biological Systems Lab.

Yutong Jin

Immediately after completing her Bachelor of Science in Biomedical Science in 2017 during which she continuously appeared on the Dean’s honor List, and completing her work as a laboratory assistant at the University of Waterloo in the department of biology, Yutong initiated her journey to acquire a master’s of vision science at the MIBS lab. Prior to her work here, her laboratory assistant position ensured she was well-appointed to her current research position as she has experience cell culturing since she grew the anaerobic microbe, Clostridium Beijerinckii which she analyzed using spectroscopy and gas chromatography to determine their alcohol dehydrogenase enzyme activity and fermentation end products respectively. Currently, she is studying different methods for the collection of closed-eye neutrophils from the ocular surface, examining their interactions with different types of contact lenses, and characterizing them with flow cytometry. Lastly, she is currently a teaching assistant at the School of Optometry and Vision Science which is only fitting as her cheery personality brightens up our lab.

Sadaf Mohsenkhani

While only recently starting at the Material Interaction with Biological Systems lab, Sadaf has been an important catalyst to new confidential research. Prior to her work here, she acquired plenty of research experience through her work as an undergraduate researcher, completing a project which modeled and optimized the membrane formation parameter with an artificial neural network, and afterwards her experience as a research assistant at the Babol University of Technology where she studied ligand immobilization on high density nanoporous kappa-carrageenan/zinc adsorbents and evaluated their potential for protein nanoparticle separation as part of the nanotechnology research institute. Simultaneously, she was acquiring her master’s degree in which her thesis was the fabrication and evaluation of high density nano porous adsorbents suitable for high flow rates in the expanded bed process. Through this research, Sadaf has become an expert in adsorbent composite synthesis and characterization, as well as expanded bed chromatography, and has expertise with a variety of lab instruments. Overall, with this knowledge Sadaf is an excellent addition to the MIBS lab.