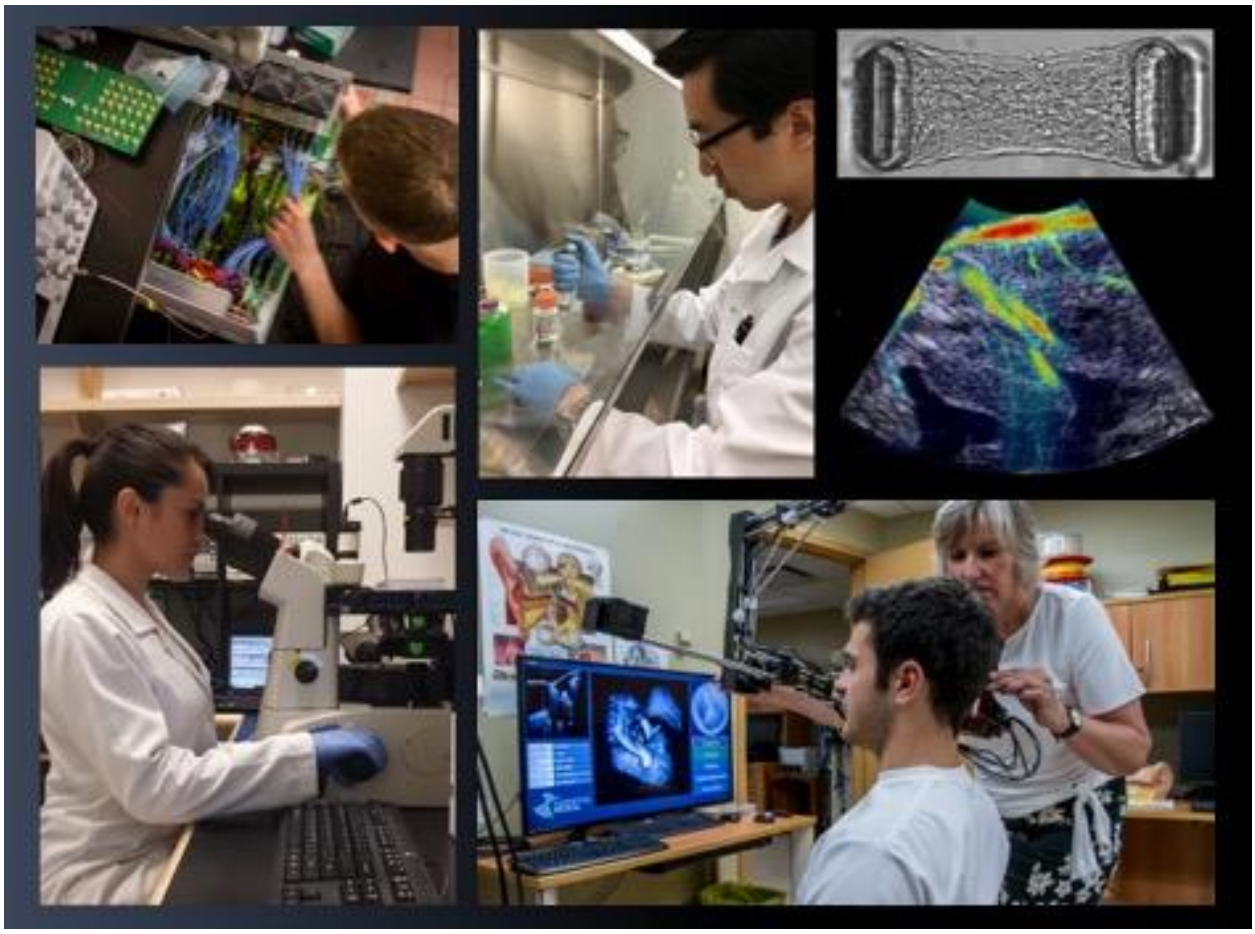
## School of Biomedical Engineering

# Research Day 2021



## Scientific Program

DALHOUSIE UNIVERSITY

DALHOUSIE UNIVERSITY

May 22, 2021

Dear Colleagues:

It is my pleasure to welcome you to the 19th Annual Research Day of the School of Biomedical Engineering at Dalhousie University! This year it is Research 'days', as we have spread it over two days as we hold the day online.

I am particularly proud of our students and faculty in SBME in making these months work so well as our year was almost entirely online. The DBES has been very active in thinking creatively how to bring our students together, with DBES socials online and when we were able in person with small dinners out with BMEeats and other activities, and they have more plans for our school coming up! Our seminar series is central to bringing us all together, where we each do deep dives of our research in progress, and the annual BME Research Day is the pinnacle event featuring the outstanding research conducted by our students, exciting seminars from our distinguished guest speakers and we are bringing back a career panel organized by the students and our School.

This year I have the pleasure to announce our distinguished academic speaker, Professor Elizabeth Gillies from the University of Western, Ontario who will present "Functional Polymers for Biomedical Applications" our distinguished industry speaker, Katherine Crewe, ICD.D, FCAE, P Eng, CHAIR, TEC Canada who will present a talk about "Look How Far We Have Come but oh Such a Long Way to Go". Please find their abstracts and brief bios in the program. They will also be participating in our career panel joined by BME alum Caitlin Pierlot, PhD, COO of Covina Biomedical a start-up company led by another BME alum Brett Dickey. Covina develops novel injectable biomaterials for minimally invasive orthopaedic procedures such as glass-based bone cements to provide long lasting stability more safely for patients with vertebral fractures.

The SBME Research Day is an important experience both for the presenters and for the audience. It's a chance to practice the conference format, engage in discussion with peers, and think about the big picture why is this research important, what does it mean right now and where does it point for the next steps. I encourage our students to ask questions, to clarify, to suggest a new experiment, to understand more deeply, and to challenge constructively.

As I encouraged last year, since it is online it is harder to 'feel the audience' during or after a talk, so show your appreciation - use the clap hands, or unmute your mic and clap, turn on your cameras for questions and discussion - it will be meaningful to those presenting. And if there is no time for your question during the session, or you had something you wanted to ask but thought of it later – please send it to the presenter afterwards. This would normally be easy to do as you encounter your peers naturally, but now it's important to try to reach out via email/phone/teams etc. – our community benefits from communicating!

I want to sincerely thank all those who put this day together. Thank you to Brendan Leung, Sam Veres for their help organizing the sessions today and online and as always, a big thank you to Sandra Pereira who helped us all and me tremendously with many of the details and particularly helping me prepare the awards.

After the presentations, I am looking forward to the opportunity to acknowledge members of the SBME community and announce our annual SBME awards. Please join me and congratulate our award winners.

And finally, we hope to have a celebratory event together outdoors, - originally planned for this Saturday, but now postponed until restrictions are lifted.

Welcome to all!

Geoffrey Maksym, Ph.D.
Professor and Director

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School of Biomedical Engineering

**Research Day 2021**

# *DISTINGUISHED ACADEMIC LECTURE*


## Elizabeth Gillies, PhD

Professor, Department of Chemistry; Department of Chemical and Biochemical Engineering and School of Biomedical Engineering, Western University.


## *"Functional Polymers for Biomedical Applications"*

# “Functional Polymers for Biomedical Applications”

**Elizabeth R. Gillies, PhD**

**Department of Chemistry, Department of Chemical and Biochemical Engineering, School of Biomedical Engineering, Western University**

**Biography:** Elizabeth Gillies is Professor in the Department of Chemistry, Department of Chemical and Biochemical Engineering, and School of Biomedical Engineering at Western University, and former Canada Research Chair in Polymeric Biomaterials. She obtained her B.Sc. degree in Chemistry from Queen's University, Kingston, Canada in 2000. She then moved to the University of California, Berkeley where she completed her Ph.D. degree in 2004 working under the guidance of Jean Fréchet. After postdoctoral work at the University of Bordeaux with Ivan Huc, she joined Western in 2006. Her research interests are in the development of biodegradable polymers, stimuli-responsive polymers, phosphorus-containing polymers, and polymer assemblies. Her team is applying these polymers via multidisciplinary collaborations to a range of applications including drug delivery, tissue engineering, and agriculture. Dr. Gillies is currently the Director of the Centre for Advanced Materials and Biomaterials Research at Western. She has received a number of awards including Tier 1 and 2 Canada Research Chairs, E. W. R. Steacie Memorial Fellowship, Early Researcher Award (Ontario), and Fallona Interdisciplinary Science Award (Western).

**Abstract:** Over the past couple of decades, transformative advancements in polymer chemistry have enabled the widespread preparation of well-defined polymers with specifically tailored functionalities, degradation properties, and molecular architectures. These advancements are enabling new applications of polymers in a range of fields and in particular biomedical areas, where polymer structure and function are key for the development of drug delivery vehicles, tissue engineering scaffolds, and a wide range of other functional biomedical devices. This presentation will describe recent work from our group in two main areas. First, a class of polymers, termed “self-immolative polymers” (SIPs), which are designed to depolymerize end-to-end upon the cleavage of stimuli-responsive end-caps from the polymer termini will be presented. The development of these polymers, as well as their application in drug delivery nanoparticles and in coatings will be described. In addition, recent work on phosphonium polymers will also be presented. The use of phosphonium polymers as soluble and surface-active antibacterials will be presented.

## School of Biomedical Engineering

**Research Day 2021**

# *DISTINGUISHED INDUSTRY LECTURE*

**Katherine Crewe, ICD.D, FCAE, PEng**

CHAIR, TEC Canada

## *"Look How Far We Have Come but oh Such a Long Way to Go"*

# “Look How Far We Have Come but oh Such a Long Way to Go”

**Katherine Crewe, ICD.D, FCAE, P Eng**

**CEO and key Chair of TEC CANADA, MONTREAL, QC**

**Biography:** Taking the road less travelled for women 40 years ago, Katherine has a Masters in Biomedical Engineering, where medicine and engineering intersect, making her a pioneer at the time. Katherine had a successful career in Medical Device and Pharmaceutical Operations, where she worked in a variety of organizations from angel start up to Global Pharmaceuticals. Rising from entry level to leading Canadian operations she learned life lessons along the way always fortunate to leverage her engineering education. Now in her role on corporate boards she is living the dream of helping business leaders exceed beyond their wildest expectations. She is a Fellow of the Canadian Academy of Engineers and Certified Corporate Director. Katherine is pleased to be on the program today to inspire the next generation of Biomedical Engineers.

**Abstract:** Biomedical Engineering, where medicine and engineering intersect from an industrial perspective. When she studied biomedical engineering at McMaster 40 years ago, she was not sure she could have a relevant career in Canada as the medical device industry was in its infancy. This proved untrue and the depth and breadth of opportunity has only increased from then. By sharing her industrial experience, she hopes to illuminate the opportunities that exist beyond academia. With the current reality of the pandemic and the science renaissance resulting, she will also argue that we can take a leadership position to educate and garner societies respect for the contribution biomedical engineering makes to our standard of living

# Previous Winners of the Community Builder Prize in Biomedical Engineering

**2008**

**Marianne Ariganello**

**2011**

**Adrian West**

**2013**

**J. Michael Lee**

**2015**

**Eleanor Seaman-Bolton**

**2017**

**Rishima Agarwal**

**2018**

**Kristin Robin Ko**

**2019**

**Tyler Herold**

**2020**

**Meghan Martin**

# Previous Winners of the Annual Teaching Prize in Biomedical Engineering

**2008**

**Geoff Maksym**

**2009**

**J. Michael Lee**

**2010**

**Jeremy Brown**

**2011**

**Paul Gratzer**

**2010**

**Rob Adamson**

**2013**

**Janie Astephen-Wilson**

**2015**

**Daniel Boyd**

**2016**

**Sarah Wells**

**2017**

**Jeremy Brown**

**2018**

**John Frampton**

**2020**

**Jeffrey Woodacre**

# Previous Winners of the George W. Holbrook Prize in Biomedical Engineering

**2010**
**Richard Roda**

**2011**
**Graeme Harding**

**2013**
**Matthew Walker**

**2014**
**Pouya Amiri**

**2015**
**Lauren Kiri**

**2016**
**Brandon Scott**

**2017**
**Kristin Robin Ko**

**2018**
**Rishima Agarwal**

**2020**
**Nicky Tam**

# Previous Winners of the Allan E. Marble Prizes in Biomedical Engineering

**2002**
**Sean Margueratt**

**2003**
**Anna Dion**

**2005**
**Doctoral: Mark Glazebrook**
**Pre-doctoral: Carolyn Lall**

**2006**
**Doctoral: Scott Landry**
**Pre-doctoral: Scott MacLean**

**2007**
**Doctoral: Janie Astephen**
**Pre-doctoral: Andrew Moeller**

**2008**
**Doctoral: Marianne Ariganello**
**Pre-doctoral: Vargha Talebi**

**2009**
**Doctoral: Jack Fairbank**
**Pre-doctoral: Jennifer Krausher**

**2010**
**Derek Rutherford**

**2012**
**Del Leary**

**2013**
**Andre Bezanson**

**2014**
**Caitlin Pierlot**

**2015**
**Arash Momeni Boroujeni**

**2016**
**Dan MacDougal**

**2017**
**Brett Dickey**

**2019**
**Alyne Teixeira**

**2020**
**Katherine Latham**

# School of Biomedical Engineering

## Research Day 2021 Scientific Program

### Thursday, June 3rd, 2021

**via Zoom**

| Morning Session | |
|---|---|
| **8:35 am to 8:40 am** | **Welcome: Dr. Geoff Maksym, Director, School of Biomedical Engineering** |
| **8:40 am to 8:45 am** | **Opening Remarks: Dr. John Newhook, Dean of Engineering** |

| Scientific Session 1 Chairs: Mady Thompson and Mireya C. Gonzalez | |
|---|---|
| **8:45 am to 9:00 am** | ***"Real-time volumetric middle-ear optical coherence tomography imaging using task-based parallelism and GPU acceleration"*** **Josh Farrell (PhD Student), R. Adamson** |
| **9:00 am to 9:15 am** | ***"Vaccine formulation screening in aqueous two-phase system microreactors"*** **Alyne G. Teixeira (PhD Student), J. Wang and J.P. Frampton** |
| **9:15 am to 9:30 am** | ***"Single collagen fibril degradation by MMP-1 in functionally distinct tendons"*** **Kelsey Y. Gsell (PhD Student), S.P. Veres, and L. Kreplak** |
| **9:30 am to 9:45 am** | ***"An efficient delay & sum beamforming algorithm to optimize memory usage on a field programmable gate array"*** **Nicolas A. Campbell (PhD Student), J.A. Brown** |

***Break (9:45 am – 10:00 am)***

| Scientific Session 2 Chairs: Christine Andrea and Bernadette McCann | |
|---|---|
| **10:00 am to 10:15 am** | ***"Age-related trends in the cortical sources of transient beta bursts during a sensorimotor task"*** **Lindsey N. Power (PhD Student), T. Bardouille** |
| **10:15 am to 10:30 am** | ***"Assembly and characterization of 3-D smooth muscle tissue rings for the study of asthma"*** **Jonathan Tjong (PhD Student), T.A. Quinn, G.N. Maksym and J.P. Frampton** |
| **10:30 am to 10:45 am** | ***"A dual frequency endoscopic histotripsy transducer"*** **Matthew Mallay (PhD Student), J. Woodacre, T. Landry, N. Campbell, and J. Brown** |

| | |
|---|---|
| **10:45 am to 11:00 am** | ***"Comparative Study of Potential Crosslinking in CS-Sodium Polyphosphate Beads Using DSC/TGA Analysis"*** **Sajjad Fanae (PhD Student), M. Filiaggi** |

## Distinguished Academic Lecture

| | |
|---|---|
| **11:00 am to 12:00 pm** | **Dr. Elizabeth Gillies, Ph.D.**<br>**Professor in the Department of Chemistry, Department of Chemical and Biochemical Engineering, and School of Biomedical Engineering, Western University**<br><br>***"Functional Polymers for Biomedical Applications"***<br>**Introduction: Dr Brendan Leung** |

## Friday, June 4th, 2021
**via Zoom**

## Scientific Session 3 Chairs: Nick Dawe and Sarah Spencer

| | |
|---|---|
| **8:45 am to 9:00 am** | ***"The use of optical clearing agents to improve the transparency of cartilage tympanoplasties for post-operative optical coherence tomography (oct) imaging"*** **Junzhe Wang (MASc Student), G. Chawdhary, X. Yang, D. Morris and R. Adamson** |
| **9:00 am to 9:15 am** | ***"PVA-based scaffolds for controlled release of neuroprotective compounds"*** **Zachary Visser (MASc Student), J.K. Rainey and J. Frampton** |
| **9:15 am to 9:30 am** | ***"Investigating the origin of the frequency dependence of respiratory resistance in disease - a modelling study"*** **Anas Tahir (MASc Student) and G. Maksym** |
| **9:30 am to 9:45 am** | ***"Composition-structure-property relationships in mixed alkali and alkaline earth borate glasses"*** **Remington .A. Manchester (MASc Student), T. Todorova U. Werner-Zwanziger, E. Tonkopi B. Kelly, J. Gosse, C. Davis, K. Brewer and D Boyd** |
| **9:45 am to 10:00 am** | ***"Examining radiologists' confidence in identification of stroke for retrospectively accelerated MR images acquired via a head-only point-of-care 0.5 t MRI system"*** **Michelle Pryde (MASc Student), T. Bouchie, S. Reeve, E.A. Cora, D. Volders, M. Schmidt, C. Bowen, J. Rioux and S. Beyea** |

## *Break (10:00 am – 10:15 am)*

| Distinguished Industry Lecture | |
|---|---|
| **10:15 am to 11:00 am** | **Ms. Katherine Crewe, CEO and Key Chair of TEC**<br>***"Look How Far We Have Come but oh Such a Long Way to Go"***<br>**Introduction: Dr. J. Michael Lee** |

| Career Panel Q&A | |
|---|---|
| **11:00 am to 12:00 pm** | **Student Questions and Answers and Career Advice with our Distinguished Speakers and one of our BME Alumni**<br>**<u>Panelist:</u>**<br>**Dr. Elizabeth Gillies, Professor, Western University**<br>**Ms. Katherine Crewe, CEO and Key Chair of TEC Canada**<br>**Dr. Caitlin Pierlot, COO of Covina Biomedical**<br>**<u>Moderators:</u>**<br>**Dr. Daniel Boyd, Associate professor, Dalhousie University**<br>**Ms. Kelsey Gsell, SBME Ph.D. student, Dalhousie University** |

| Awards and Closing | |
|---|---|
| **12:00 pm to 12:15 pm** | **Presentation Judging** |
| **12:15 pm to 12:30 pm** | **School of Biomedical Engineering Awards and Closing Remarks**<br>**Director: Dr. Geoff Maksym** |

# School of Biomedical Engineering
# Research Day 2021 Abstracts

## *SCIENTIFIC SESSION 1*

# REAL-TIME VOLUMETRIC MIDDLE-EAR OPTICAL COHERENCE TOMOGRAPHY IMAGING USING TASK-BASED PARALLELISM AND GPU ACCELERATION

J.D. Farrell[1], R. Adamson[1,2]

[1]School of Biomedical Engineering, Dalhousie University
[2]Department of Electrical and Computer Engineering, Dalhousie University

**Introduction:** We demonstrate a highly scalable heterogeneous software framework capable of real-time volumetric middle-ear optical coherence tomography (ME-OCT) imaging through utilization of task-based parallelism and general-purpose graphics processing unit (GP-GPU). By combining task-based parallelism with GPU acceleration we can achieve real-time interactive data rates without sacrificing software maintainability and extendibility. We cover how these two acceleration techniques can be combined and applied to ME-OCT imaging and discuss common implementation pitfalls.

**Methods:** Task-based parallelism is a form of multithreading that abstracts away low-level threading details by providing a high-level interface on how related work items or 'tasks' are to be distributed. We use this high-level interface to construct flowgraphs consisting of interconnected nodes where each node maps directly to a task. By specifying the relationships between each node, we can have the system optimize low-level threading resources automatically. This reduces development time and provides hardware scalability without extra developmental effort. Task-based parallelism is best suited for low-latency acceleration of complex control flow. In contrast the GPU is designed to processes large blocks of data concurrently using only a single instruction. Applying both acceleration techniques to ME-OCT imaging, we map each flowgraph node to one or more ME-OCT processing steps and accelerate each ME-OCT processing step using the GPU. This results in a heterogenous pipeline capable of real-time volumetric ME-OCT imaging while exposing a high-level interface that is easy to control, modify and fine-tune.

**Results and Discussion:** Profiling results from three different GPU accelerated ME-OCT image processing pipelines using single, multi and tasked-based threading strategies will be compared. Besides profiling, the maintainability and extensibility of each different pipeline implementation will be examined alongside each of their shortcomings.

**Conclusion:** We demonstrate a highly scalable heterogeneous software framework utilizing state-of-the-art acceleration techniques to achieve real-time volumetric ME-OCT imaging. Profiling and architectural analysis show that the architecture achieves very high throughput processing in a versatile and extensible framework.

# VACCINE FORMULATION SCREENING IN AQUEOUS TWO-PHASE SYSTEM MICROREACTORS

Alyne G. Teixeira[1], Jun Wang[2] & John P. Frampton[1,3]

[1]School of Biomedical Engineering, Dalhousie University
[2]Department of Microbiology and Immunology, Dalhousie University
[3]Department of Biochemistry and Molecular Biology, Dalhousie University

**Introduction:** To effectively screen vaccine formulations *in vitro*, a cell-based assay must be designed to evaluate cellular responses to an antigen, an adjuvant, and an antigen combined with one or more adjuvants. However, there is a lack of simple and cost-effective *in vitro* assays to evaluate vaccine formulations. Here, we developed an innovative platform for *in vitro* evaluation of vaccine formulations that conserves vaccine components in the gold standard enzyme-linked immunospot (ELISpot) assay. This platform uses an aqueous two-phase system (ATPS) to confine immune cells and reagents in microdroplet reactors, enabling the efficient screening of antigens and adjuvants using only a fifth of the amounts required by conventional ELISpot.

**Methods:** A previously characterized ATPS composed of 7% polyethylene glycol (PEG) and 10% bovine serum albumin (BSA) was used to reduce the reaction volume required for the ELISpot assay. The optimal concentration of the influenza antigen hemagglutinin (HA) was identified by serial dilution in the ATPS-based ELISpot and conventional ELISpot assays using primary peripheral blood mononuclear cells (PBMCs). Next, we screened vaccine formulations containing HA alone or combined with one of five toll-like receptor (TLR)-agonists (adjuvants) by measuring the number of interferon-gamma (IFN-γ)- secreting cells in the ATPS-based ELISpot. For the adjuvant screening experiments, HA concentration was fixed at 10 μg/mL, and the concentration of five TLR-agonists (pam3CSK4 (TLR1/TLR2), polyinosine-polycytidylic acid (poly(I:C)) (TLR-3), lipopolysaccharide (LPS) (TLR-4), imiquimod (TLR-7) and CpG oligonucleotide (TLR-9) were varied between 62.5 ng/mL and 100 μg/mL.

**Results and Discussion:** The ATPS-based ELISpot allowed us to determine the optimal concentration of HA with comparable performance characteristics to conventional ELISpot. However, the ATPS-based ELISpot requires 1/5 of the amounts of reagents in comparison with the conventional method. The ATPS-based ELISpot enabled screening of immune responses from PBMCs exposed to HA in combination with the TLR-agonists at five different concentrations. The optimal HA-specific IFN-gamma response was achieved when PBMCs were incubated with 2.5 ng/mL pam3CSK4, 10 ug/mL poly (I:C), 5 ug/mL imiquimod, 50 ug/mL CPG, or 1 ug/mL LPS.

**Conclusions:** We demonstrated that the PEG-BSA system can be employed to screen vaccine formulations by ELISpot using minimal amounts of antigen and adjuvant reagents, which may facilitate the cost-effective discovery of new vaccines and accelerate their availability in the market.

# SINGLE COLLAGEN FIBRIL DEGRADATION BY MMP-1 IN FUNCTIONALLY DISTINCT TENDONS

K.Y. Gsell[1], S.P. Veres[1,2], and L. Kreplak[1,3]

[1]School of Biomedical Engineering, Dalhousie University
[2]Division of Engineering, Saint Mary's University
[3]Physics and Atmospheric Science, Dalhousie University

**Introduction:** Bovine forelimb flexor and extensor tendons serve as a model for examining energy-storing and positional tendons, respectively. Previous research has shown that the structures of these functionally distinct tendons differ. The nanoscale collagen fibrils of flexor tendons are smaller in size, more heavily crosslinked, and respond differently to mechanical loading. Energy-storing tendons also have less collagen turnover compared to positional tendons. Therefore, structural and mechanical differences may underpin this, potentially by limiting access of collagenases to constituent collagen molecules. Here I examine the ability of matrix-metalloprotease (MMP)-1 to degrade bovine flexor and extensor fibrils in addition to rat tail tendon fibrils (positional), as a comparison to existing literature.

**Methods:** Atomic force microscopy was used to image dry collagen fibrils before and after 5-hour exposure to MMP-1 to detect changes in size measured through height and cross-sectional area (CSA). Nine tendons were harvested from 6 animals with sample preparation and treatment done simultaneously for groups of 3: one bovine flexor and extensor tendon from the same animal, and one rat tail tendon.

**Results and Discussion:** A significant decrease in fibril CSA following MMP-1 exposure was observed for fibrils from all three tendon types, with larger fibrils experiencing a greater magnitude of CSA decrease ($p<0.0001$, $R2=0.486$). This, along with visual evidence of degradation 'hot spots' confirmed that the enzyme was active and capable of degrading collagen fibrils prepared in this way. The buffer also seemed to affect the shape and possibly size of the fibrils; further work is underway to complete negative control trials from each tendon to better distinguish changes due to the buffer vs. enzyme. Our preliminary comparison suggests that the enzyme alone may have less of an effect on bovine flexor fibrils than on extensor or rat tail fibrils.

# AN EFFICIENT DELAY & SUM BEAMFORMING ALGORITHM TO OPTIMIZE MEMORY USAGE ON A FIELD PROGRAMMABLE GATE ARRAY

N.A. Campbell[1], J.A.Brown[1]

[1]Department of Biomedical Engineering, Dalhousie University, Halifax, Canada

Medical ultrasound imaging uses reflected acoustic energy to image tissue. An ultrasound transducer receives these reflected signals from an array of transduction elements. Using this set of spatially distributed signals, the acoustic energy can be focused through a process known as 'beamforming.' A widely used beamforming technique called 'Delay & Sum' aligns the received signals from all the sensors in time using fine delay control, and subsequently coherently sums the channels together to form a focused line in the image. For our in-house developed imaging system, a 64 element phased array was used to generate 128 steered lines, each with 512 pixels in depth. Each of 8 field-programmable gate arrays (FPGAs) in our system digitizes and inserts the delays of 8 signal channels in parallel. This theoretically requires each FPGA to store 4.2 million delays on board the microchips. To obtain enough delay precision, the delay values required a bit depth of 16, and therefore, 67Mb of memory is needed. This creates an issue since each FPGA has a maximum of 11.7Mb of memory. We have developed a new method of compressing beamforming delays to store them in memory effectively. By calculating the slope of time-delay per pixel for each element, it was discovered that the change in beamforming delays is approximately a constant for regions sufficiently far away from the transducer. Storing an integer approximation of the slope simplifies the beamforming delays down to two integer values, approximating the beamforming delay between each pixel. Therefore, the memory required to store the beamforming delays was reduced to approximately one bit per delay, reducing the required memory on each FPGA to only 4.2Mb. The firmware developed enabled the generation of ultrafast frame rates (~1kHz) using this approach.

# School of Biomedical Engineering
# Research Day 2021 Abstracts

## *SCIENTIFIC SESSION 2*

# AGE-RELATED TRENDS IN THE CORTICAL SOURCES OF TRANSIENT BETA BURSTS DURING A SENSORIMOTOR TASK

L.N. Power[1], T. Bardouille[2]

[1]School of Biomedical Engineering, Dalhousie University
[2]Department of Physics & Atmospheric Science, Dalhousie University

**Introduction:** Interpreting neurophysiology recordings as a series of transient bursts with varying temporal and spectral characteristics provides meaningful insight into mechanisms underlying neural networks. Previous research has revealed age-related changes in the time-frequency dynamics of sensorimotor beta bursts, but to date, there has been little focus on the spatial localization of these beta bursts or how the localization patterns change with normal healthy ageing. The objective of the current study is to implement existing source localization algorithms for use in the detection of the cortical sources of transient beta bursts, and to uncover age-related trends in the resulting source localization patterns.

**Methods:** Two well-established source localization algorithms (minimum-norm estimation and beamformer) were applied to localize beta bursts detected over the sensorimotor cortices in a cohort of 561 healthy participants between the ages of 18 and 88 (CamCAN open access dataset). Age-related trends were then investigated by applying regression analysis between participant age and average source power within several cortical regions of interest.

**Results:** Both methods revealed that beta bursts localized primarily to the sensorimotor cortex ipsilateral to the side of the sensor used for their detection. Region of interest analysis revealed that there were age-related changes in the beta burst localization pattern, with most substantial changes evidenced in frontal brain regions.

**Discussion:** These results show for the first time that source localization techniques can be implemented for the identification of the sources of transient beta bursts. The exploration of these sources provides us with insight into the anatomical generators of transient beta activity and how they change across the lifespan.

# ASSEMBLY AND CHARACTERIZATION OF 3D SMOOTH MUSCLE TISSUE RINGS FOR THE STUDY OF ASTHMA

J. Tjong[1], T.A. Quinn[1,2], G.N. Maksym[1], and J.P. Frampton[1,3]

[1]School of Biomedical Engineering, Dalhousie University, Halifax, NS, Canada
[2]Department of Physiology & Biophysics, Dalhousie University, Halifax, NS, Canada
[3]Department of Biochemistry & Molecular Biology, Halifax, NS, Canada

**Introduction:** Airway inflammation, bronchoconstriction, and extracellular matrix (ECM) remodeling are hallmarks of asthma that are present in the intact human airway but missing in many *in vitro* model systems used to better understand asthma pathophysiology and develop novel therapies. To better represent the structure and function of the small airways, one promising approach is to design contractile microtissues with dimensions that approximate those observed *in vivo*. Here, we present the assembly and characterization of airway microtissue rings for modeling asthma, which recapitulate some of the key structural and functional characteristics of the small airways.

**Methods:** Airway smooth muscle (ASM) cells were aggregated to form tissue rings in custom polydimethylsiloxane (PDMS) (Sylguard 184, Dow Corning, Midland, MI) conical molds pre-treated with a 1% w/v solution of Pluronic F-127. The tissue rings developed for up to 21 days in 1:1 DMEM/F-12 culture medium supplemented with 1% fetal bovine serum. At day 7, the culture medium was supplemented with insulin, transferrin, and selenium for 7 days prior to the administration of exogenous signaling factors, including TGF-β1 at 10 ng/ml. At set time points during ring development, rings were collected to examine cell viability, and to measure their physical dimensions by quantification of light microscopy images. To measure mechanical properties, live tissue rings were suspended between a linear motor and load cell, pre-stressed to 10-15% strain for 10 cycles, then pulled to rupture. The expression of ECM, contraction-associated proteins, and inflammation-associated factors was examined using semi-quantitative endpoint PCR.

**Results and Discussion:** ASM cells consistently formed tissue rings that were tunable in size (interior diameter and ring thickness) by varying mold dimensions and seeding densities. Cell metabolic activity decreased over time up to 7 days as the rings developed. Viable ASM cells with spindle-like morphology were observed along the surface of the tissue, axially aligned along the circumference of the ring for up to 21 days. Ring strength and elastic modulus increased over 14 days, but this was not accompanied by significant changes in ring size. PCR analysis indicated stable expression of genes coding for ECM proteins, including collagen I and laminins α1 and α4 over 21 days. TGF-β1 treatment at 10 ng/ml over 3 days induced the expression contraction-associated smooth muscle myosin heavy chain and α-smooth muscle actin genes.

**Conclusions:** In this work, we developed ASM tissue rings in custom PDMS wells for the study of ASM phenotype and function in a 3D cell culture environment. This study demonstrates the ability to examine ASM cell mechanics and gene expression in a physiologically relevant format. This system may better facilitate the study of airway pathologies *in vitro*.

# A DUAL FREQUENCY ENDOSCOPIC HISTOTRIPSY TRANSDUCER

M. Mallay[1], J. Woodacre[1], T. Landry[1], N. Campbell[1], and J. Brown[1,2]

[1]School of Biomedical Engineering, Dalhousie University, Halifax, Canada
[2]Department of Electrical Engineering, Dalhousie University, Halifax, Canada

**Introduction:** Histotripsy is a therapeutic ultrasound technique for non-invasively ablating tissue. Typically, a piezoelectric transducer is focussed using an acoustic lens to generate high pressures. We hypothesize that an endoscopic histotripsy transducer could potentially replace traditional surgical aspirators because of the inherent advantages, such as higher precision and improved ability to avoid nerves or vessels. Reducing the device aperture to an endoscopic size makes it challenging to generate the peak negative pressure required for cavitation. In this work, a dual frequency transducer is used to increase peak negative pressure by summing the pressure generated by each transducer individually.

**Methods:** Four lens designs, each with an f-number of approximately 1, were evaluated in a 5 MHz PZT5A composite transducer. A dual frequency device was created by bonding a 1.2 MHz (pump) transducer to the back face of a 5 MHz transducer incorporating the best performing lens.

**Results and Discussion:** The measured peak negative pressure was 0.150, 0.124, 0.160, and 0.160 MPa/V for the resin conventional, resin Fresnel, silicone conventional, and silicone Fresnel lenses, respectively. For the dual frequency device, the 5 MHz (therapy) transducer had a measured peak negative pressure of 0.136 MPa/V for PZT5A composite and 0.163 MPa/V for PMN-PT composite. The 1.2 MHz (pump) transducer had a measured peak negative pressure of 0.028 MPa/V.

**Conclusions:** The pump transducer significantly lowered the cavitation threshold of the therapy transducer. The dual frequency device was tested on an ex vivo rat brain, ablating tissue at up to 4 mm depth, with lesion sizes as small as 500 μm.

# COMPARATIVE STUDY OF POTENTIAL CROSSLINKING IN CS-SODIUM POLYPHOSPHATE BEADS USING DSC/TGA ANALYSIS

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**Introduction:** Chitosan (CS) is a biopolymer derived from chitin that bears a positive charge when dissolved in acid. For CS biomedical applications, physical rather than chemical crosslinking is preferred as it typically involves milder processing conditions. Polyelectrolyte complexation via crosslinking with negatively-charged sodium polyphosphate inorganic polymers (PP) is one possible approach, but little is known about CS-PP interactions involving longer PP chains. Thermal analyses (DSC/TGA) may provide insight into the extent of crosslinking possible.

**Methods:** CS-PP beads were prepared at different concentrations of PP (15, 50, 150, 500 mg/ml). After freeze drying, beads were ground and 20 mg of the resultant powder was used for DSC/TGA (NETZSCH STA 409 PC/PG) studies from room temperature to a final temperature of 670℃.

**Results and Discussion:** Analysis of the DSC graphs showed two separate peaks for all the samples, an endothermic peak at ~100℃ and an exothermic peak in the 200-320℃ range due to water evaporation and thermal dissociation, respectively. The endothermic peak shifted to higher temperatures for samples with higher [PP] possibly due to consumption of amine groups during crosslinking and the subsequent interaction of water molecules with -OH groups (a stronger bond) instead of amine groups. Higher [PP] also shifted the exothermic peak to lower temperatures indicating lower thermal stability and a sign of crosslinking, in agreement with the literature; however, the underlying reason for this shift is not obvious. TGA indicated initial weight loss associated with water evaporation (~ 2-4%), with an additional loss of 5-16% at the exothermic peaks. The inorganic residue at final temperature was higher for samples with higher [PP], suggesting higher phosphorous content and better diffusion in the structure with increasing [PP].

**Conclusions:** Thermal analysis may offer insight into crosslinking in CS-PP polyelectrolyte systems, though additional complementary techniques are needed to fully describe this interaction.

# School of Biomedical Engineering
# Research Day 2021 Abstracts
# *SCIENTIFIC SESSION 3*

# THE USE OF OPTICAL CLEARING AGENTS TO IMPROVE THE TRANSPARENCY OF CARTILAGE TYMPANOPLASTIES FOR POST-OPERATIVE OPTICAL COHERENCE TOMOGRAPHY (OCT) IMAGING

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**Introduction:** Optical coherence tomography (OCT) is an emerging technology for diagnosing the middle ear. Patients who undergo tympanoplasty for conductive hearing loss receive a tympanic membrane graft. This graft is optically opaque and limits the ability of OCT to be used for post-operative visualization of middle ear. In this ex vivo study, we investigate the use of glycerol, a hyperosmotic, non-toxic optical clearing agent (OCA), to increase the transparency of cartilage tympanoplasties to allow for OCT imaging. We measure OCT signal through a set of human tragal cartilage samples. Second, we simulate a post-surgical ear in a fresh-froze cadaveric temporal bone and exam the impact of glycerol on the detectability of a partial ossicular replacement prosthesis (PORP).

**Methods:** Tragal cartilage samples were harvested from fresh-frozen temporal bones (N=1) and as surplus material from patients undergoing middle surgery (N=2). The cartilage was prepared by removal of perichondrium and thinning to 0.4mm. A custom-built swept-source OCT system was used to acquire the relative optical transmission through the cartilage samples as a function of time following treatment. Separately, a temporal bone was prepared with a PORP and a graft to simulate ossiculoplasty surgery and imaged before and after glycerol was applied to the graft.

**Results:** OCT signal increased by an average of 48dB within 7 mins with glycerol treatment. In the simulated ossiculoplasty ear the prosthesis reflection was below the noise floor prior to glycerol treatment and could be clearly visualized following treatment.

**Conclusion:** We have demonstrated that cartilage grafts can be cleared within 7 minutes following treatment of glycerol and that clearing produced clinically significant improvement in the ability to visualize the middle ear with OCT imaging.

# PVA-BASED SCAFFOLDS FOR CONTROLLED RELEASE OF NEUROPROTECTIVE COMPOUNDS

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**Introduction:** Over 320,000 North Americans live with a spinal cord injury, with an additional 18,000 new cases every year. To restore function lost by damage to the nerve fibers in the spinal cord, nerve regeneration must take place. This process occurs only sparingly, in part due to neuroinflammation and scarring. Unfortunately, existing experimental therapies such as growth factor treatment show less than desirable levels of neuronal regeneration. Stem cell therapies have also attracted interest; however, the safety and efficacy of these treatments have not yet been determined. Due to the limited efficacy of existing treatment options, biomaterial scaffolds have been explored for their ability to release biologic and small molecule compounds that suppress inflammation and promote neurite outgrowth. We have designed, characterized, and performed *in vitro* testing to identify a novel fiber-based biomaterial scaffold for controlled release of the model anti-inflammatory compound quercetin with the ultimate goal of developing a surgical material for suppressing inflammation associated with spinal cord injury.

**Methods:** Fibers were contact-drawn from viscous solutions of 205 kDa poly(vinyl alcohol) (PVA) at 10.0-17.5%wt in $H_2O$. Glyoxal was incorporated as a crosslinking agent to decrease water solubility, therefore increasing resistance to degradation of the resulting fibers in aqueous environments. The glyoxal cross-linking reaction was characterized by infrared spectroscopy. Failure analysis was conducted to elucidate the effects of glyoxal concentration, cross-linking time, PVA concentration and contact drawing speed on the fiber formation process and the fiber diameter. Quercetin (a model neuroprotective and anti-inflammatory agent) was incorporated into the fiber-forming solution to demonstrate the potential for controlled scaffold degradation and cumulative drug release in artificial cerebrospinal fluid.

**Results and Discussion:** Glyoxal efficiently crosslinked fibers, leading to stability in aqueous solvents for up to 10 days. PVA concentration, quercetin loading, glyoxal concentration and cross- linking kinetics were all shown to play a role in fiber formation. Increasing glyoxal resulted in decreased free hydroxyl stretching in the IR spectrum (~3280$cm^{-1}$). Increasing PVA concentration and glyoxal concentration allowed formation of fibers at slower pulling speeds. Furthermore, the introduction of glyoxal and quercetin resulted in increased fiber diameter. Quercetin could be loaded into the scaffolds at concentrations of 50-200 μM and displayed a modest burst release followed by sustained release over 10 days, achieving a maximum cumulative release in artificial cerebrospinal fluid of 56%. Preliminary experiments using PC12 cells cultured in the presence of glyoxal cross-linked, quercetin-loaded PVA fibers demonstrated that drug-releasing scaffold materials were not cytotoxic.

**Conclusions:** Glyoxal cross-linked PVA fibers show resistance to hydrolytic degradation. Quercetin release from these fibers indicates neuroprotective capacity of the novel biomaterial approach. The novel biomaterials produced by our approach have potential to provide improved scaffolds for nerve regeneration.

# INVESTIGATING THE ORIGINS OF THE FREQUENCY DEPENDENCE OF RESPIRATORY RESISTANCE IN DISEASE – A MODELING STUDY

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**Introduction:** Lung disease leads to heterogeneity in small airways where unfortunately standard spirometry is insensitive. Oscillometry using small pressure oscillations over a range of frequencies $f$, is sensitive to heterogeneity via the frequency dependence of resistance $R(f)$. $R(f)$ can also arise from time-varying lung stiffness during breathing in disease. Here we developed a model to assess the contribution from time-varying lung stiffness.

**Methods:** We used the single compartment Constant Phase Model (CPM) and adapted it to include the exponential nonlinear stress-strain behavior of lung tissue making stiffness time-varying creating the Quasi-Linear CPM (QLCPM). Using published lung tissue data and changes in nonlinearity in the pressure-volume relationship, we modeled lung tissue and whole lung pressure-volume behavior. We explored 3 different operating points, 3 amplitudes, as well as 3 different exponents $\alpha$ mimicking emphysema and assessed $R(f)$ over the low-frequency ventilation range (0.1-3 Hz) and the clinical oscillometry range (5-37 Hz).

**Results & Discussion:** Striking $R(f)$ was observed to occur at higher operating points and disease models. $R(f)$ exceeding 500% was found for the ventilation range. Time-varying stiffness was associated with modest $R(f)$ in the ventilation range for lower $\alpha$, normal operating points and amplitudes. Importantly these results show that $R(f)$ can arise from changes in time-varying stiffness due to excessive nonlinearity in the lung tissue from disease. However, the effect of this non-linearity influencing that $R(f)$ was negligible in the oscillometry frequency ranges.

**Conclusions:** $R(f)$ can arise from nonlinear tissue behavior in the ventilation range but in the oscillometry range it is more likely due to heterogeneity. This is important for interpreting research and pharmaceutical studies.

# COMPOSTION-STRUCTURE-PROPERTY RELATIONSHIPS IN MIXED ALKALI AND ALKALINE EARTH BORATE GLASSES.

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**Introduction:** Soluble borate glasses are interesting materials for a range of biomedical applications. At present however, less than 2% of the glass literature is focussed on borate glasses. Within this literature, binary borate glass systems have been characterized in the range of 0-31 mol% alkali *or* alkaline earth network modifier. Contrastingly, glasses with mixed alkali *and* alkaline earth cations, are poorly understood and their properties and structures are difficult to predict. The objective of this work was to establish the composition-structure-property relationships for borate networks modified with $K_2O$ and SrO using design of mixtures.

**Methods:** 16 compositions were produced using design of mixtures (DoM) for subsequent characterization ($^{11}$B MAS NMR, differential scanning calorimetry, and pycnometry in addition to computed tomography (CT) and magnetic resonance imaging (MRI) imageability) to assess the role of $K_2O$ and SrO on the composition-structure-property relationships in borate glass.

**Results and Discussion:** $^{11}$B MAS NMR data showed that both $K_2O$ and SrO had a similar effect on the % B3 and B4 units within the networks. SrO was found to have the largest positive effect on $T_g$ despite it similarly influencing the % B3 and B4, contrary to existing literature. These results indicate that SrO may act as a network cross-linker and $K_2O$ may behave as a B4 stabilizer. SrO also had the largest positive effect on density and CT radiopacity, over $K_2O$ and $B_2O_2$.

**Conclusions:** By modeling the change in properties using DoM the authors were able to establish statistically significant models to better understand the role of both $K_2O$ and SrO in the borate glass network. These models will enable users to modulate and tailor these unique glass compositions to best meet design inputs for a variety of applications.

# EXAMINING RADIOLOGISTS' CONFIDENCE IN IDENTIFICATION OF STROKE FOR RETROSPECTIVELY ACCELERATED MR IMAGES ACQUIRED VIA A HEAD-ONLY POINT-OF-CARE 0.5 T MRI SYSTEM

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**Introduction:** Accelerated MR image acquisition is key for emergency medicine situations, such as acute ischemic stroke, but yields degraded image quality. However, this reduction in quality may not impact a radiologist's ability to identify stroke. Therefore, the aim was to understand the trade-off between acceleration factor and radiologists' confidence in identifying acute and chronic stroke, using a head-only point-of-care 0.5 T MRI system to investigate this problem.

**Methods:** Data were acquired from 15 patients with suspected stroke and 2 healthy volunteers who were recruited and scanned on the 0.5 T MRI system under a NSH REB-approved protocol. The protocol included an axial T2 FLAIR (scan time: 266 seconds) and DWI sequence. T2 FLAIR images were degraded by retrospectively undersampling k-space data at various acceleration factors (R), followed by compressed sensing reconstruction. All T2 FLAIR images, alongside corresponding DWI images and ADC maps, were shown to three board-certified radiologists who were individually asked to identify acute and chronic stroke, ranking their confidence in these identifications on a Likert scale (1 = 0 % confidence, 5 = 100 % confidence).

**Results and Discussion:** Preliminary results show that, for a range of acceleration factors from R = 1-7X, radiologists' confidence in identifying acute stroke remains high, while radiologists' confidence in identifying chronic stroke begins to decrease at higher R within the given range.

**Conclusions:** Reduced acquisition time is clearly beneficial for acute stroke scenarios, but valuable information on chronic stroke can also be gained from these accelerated scans. Overall, since our aim is to one day move this to the truly acute phase of ischemic stroke then imaging needs to be both as fast as possible and remain diagnostically useful.