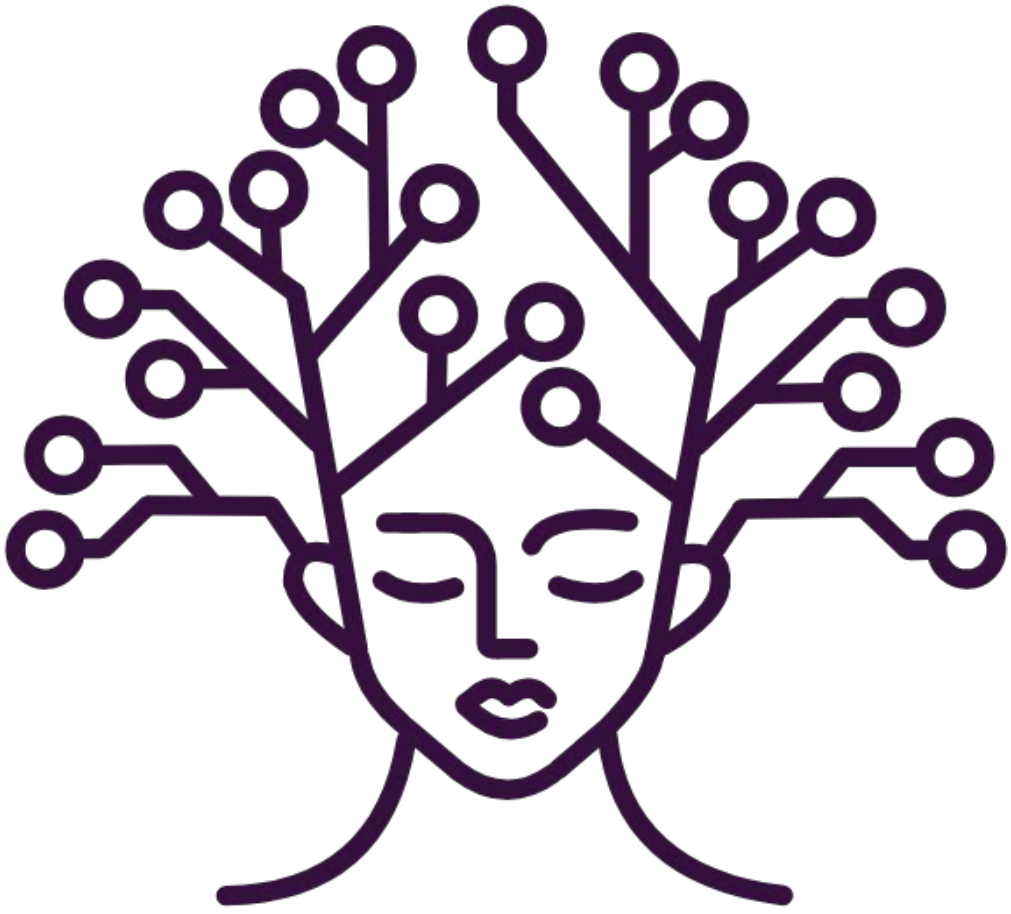
2024

ENGINEERING FOR WOMEN'S HEALTH

Conference

September 16, 2024 | Northeastern University, Boston



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Schedule of Events

8:00 AM – 9:00 AM Registration and Breakfast

8:15 AM – 8:45 AM *Speed Mentoring Session*

9:00 AM – 9:15 AM Welcome
Jackie Isaacs
Vice Provost for Faculty Affairs and Professor of Mechanical & Industrial Engineering, Northeastern University, Boston, MA

9:20 AM – 9:50 AM Engineering for Everyone – Engineering for Health
Gilda Barabino
President of Olin College, Professor of Biomedical and Chemical Engineering
Olin College of Engineering, Needham, MA

9:55 AM – 10:25 AM Tissue-Inspired Synthetic Biomaterials to Study Breast Cancer
Shelly R. Peyton
Chair of the Department of Biomedical Engineering
Tufts University, Medford, MA

Break

10:40 AM – 11:00 AM A New Model to Study Menstruation in Health and Disease
Çağrı Çevrim
Post-Doctoral Research Fellow at the Department of Stem Cell and Regenerative Biology
Harvard University, Cambridge, MA

11:05 AM – 11:25 AM Sex and Hormones Influence Tendon Extracellular Matrix Remodeling
Brianne Connizzo
Assistant Professor of Biomedical Engineering & Mechanical Engineering
Boston University, Boston, MA

11:30 – 1:00 PM **Poster Session**

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2:00 PM – 2:30 PM When the Technical is the Political: Bringing our Whole Selves to Engineering Design
Catherine M. Klapperich
Professor of Biomedical Engineering
Boston University, Boston, MA

2:35 PM – 2:55 PM Environmental Contamination and Adverse Pregnancy Outcomes in Puerto Rico

Akram Alshawabkeh
Senior Associate Dean for Research and Graduate Education, College of Engineering
Northeastern University, Boston, MA

Break

3:15 PM – 3:35 PM Modeling Menopause: Mechanistic Insights into Female Aging Trajectories of the Musculoskeletal System

Fabrisia Ambrosio
Associate Professor of Physical Medicine and Rehabilitation
Harvard University, Cambridge, MA

3:40 PM – 4:00 PM Multi-Scale Assessment of Biomechanics and Mechanobiology of Cardiovascular Tissues During Late Gestation

Rouzbeh Amini
Associate Professor of Mechanical and Industrial Engineering and Bioengineering
Northeastern University, Boston, MA

4:10 PM – 5:00 PM Panel Discussion: Unveiling Sex Differences in STEM Research

Soha Ben Tahar – Moderator
PhD Candidate, Mechanical and Industrial
Engineering Northeastern University, Boston, MA

Rosalia Rabinovsky - Panelist
Research Specialist, Ann Romney Center for Neurologic Diseases
Brigham and Women's Hospital, Boston, MA

Henriette Coetzer - Panelist
Chief Medical Oficer at Blue Health Intelligence
Boston, MA

Rupal Patel - Panelist
Professor of Speech Language Pathology and Audiology
Bouvé College of Health Sciences and the College of Computer and Information Science
Northeastern University, Boston, MA

Sarah Ostadabbas - Panelist
Director of the Women in Engineering Program Associate Professor of Electrical and Computer Engineering
Northeastern University, Boston, MA

5:00 PM – 7:00 PM Networking Happy Hour

Welcome

We are thrilled to welcome you to the 2024 Engineering for Women's Health Conference.

This gathering brings together leaders and emerging talents dedicated to advancing women's health through research, engineering, and interdisciplinary collaboration. Today, you'll have the chance to engage with experts in women's health through scientific sessions and a panel discussion featuring change-makers in research, healthcare delivery, and public policy. We invite you to explore cutting-edge research during the poster session and participate in our Speed Mentoring program, designed to inspire and connect the next generation of innovators.

Thank you for being part of this event—we look forward to the impactful discussions and connections that will shape the future of women's health.

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Conference Organizing Committee

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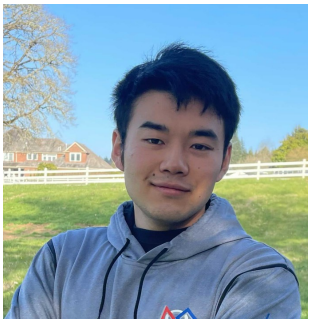

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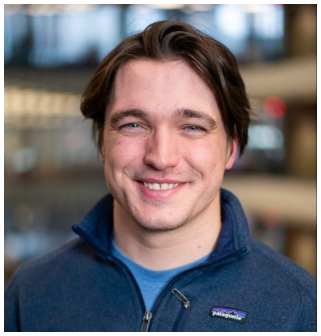

Sean Harrington
Member at Large

Invited Speakers Abstracts

Engineering for Everyone – Engineering for Health

Gilda Barabino
President and Professor of Biomedical and Chemical Engineering, Olin College, Needham, MA

Abstract: Through the lens of an African American woman engineering educator and researcher with career long interests in human health and health equity, this presentation explores engineering approaches to improved health and the elimination of inequities.

Tissue-Inspired Synthetic Biomaterials to study Breast Cancer

Shelly R. Peyton

Chair of the Department of Biomedical Engineering, Tufts University, Medford, MA

Abstract: Early-stage breast cancer has high cure rates, up to 70%, but frontline treatment for metastatic breast cancer demonstrates progression-free survival of only 15-20. Treatment regimens that ultimately fail patients do so because tumors become resistant to therapy via both intrinsic and acquired mechanisms. Our preliminary data suggests that the microenvironment of tumors (the extracellular matrix, ECM) promotes drug resistance to varying degrees depending on the anatomical location and ECM composition. Breast cancer commonly metastasizes to the bone, lung, liver, and brain, which span a broad diversity of ECMs. Understanding both the microenvironmental and genetic mechanisms of how these tissues promote drug resistance in metastatic breast cancer could lead to new treatment options and strategies for patients with metastatic disease. Improved experimental model systems are critically needed to better understand cancer progression and bridge the gap between lab bench proof-of-concept studies, validation in animal models, and eventual clinical application. Many methods exist to create biomaterials, including hydrogels, which we use to study cells in contexts more akin to what they experience in the human body. Our lab has multiple approaches to create such biomaterials, based on combinations of poly(ethylene glycol) (PEG) with peptides and zwitterions. In this presentation, I will discuss our synthetic approaches to building life- like materials, how we use these systems to grow cells and understand how a breast cancer cell's environment, particularly the extracellular matrix, regulates cancer cell growth, dormancy, and drug sensitivity.

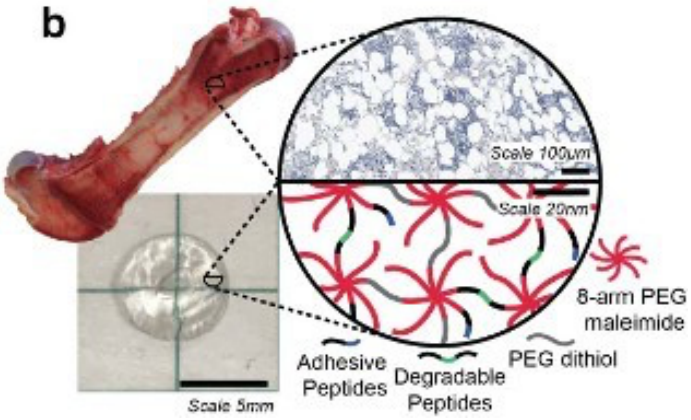

Figure:(Example of bone marrow-mimicking hydrogel) *we use a combination of mechanical characterization and tissue mass spectrometry to analyze real tissues (bone marrow example shown). Then we approximate those tissue characteristics with combinations of synthetic polymers and peptides for a variety of applications in cancer, tissue engineering, and TBI.*

A New Model to Study Menstruation in Health and Disease

Çağrı Çevrim
Post Doctoral Research Fellow at the Department of Stem Cell and Regenerative Biology, Harvard University, Cambridge, MA

Abstract: Menstruation is a complex physiological process found only in a few mammalian species, including humans, where the inner lining of the uterus (endometrium) undergoes cyclic shedding and subsequent regeneration. Despite its clinical significance and relevance to various disorders, like endometriosis, our understanding of menstruation and endometrial regeneration remains limited since no established menstruating model organism exists.

In menstruating species, the endometrium undergoes a major transformation, characterized by massive cell proliferation and tissue growth, in response to rising progesterone levels after ovulation. This newly formed tissue, the decidua, is shed and discarded upon the fall of progesterone secretion towards the end of the menstrual cycle, a process accompanied by bleeding. Non- menstruating mammals, including Mus, also form decidua, but only during pregnancy, as their natural ovarian cycle does not lead to decidualization. These observations suggest that decidua formation without pregnancy is a prerequisite for menstruation. Furthermore, if decidualization is induced in non-pregnant mice, it leads to menstruation-like bleeding. This mouse model has been the state-of-the-art approach to dissect menstruation in the field for decades. Although this mouse model is a valuable tool, induction of decidualization often requires surgery, which limits its use.

To overcome this hurdle, we developed a new, non-surgical transgenic mouse model to induce decidualization on demand. Characterization of this model revealed that these animals have a cycle mimicking human menstruation when progesterone levels decline, including endometrial bleeding and subsequent regeneration. We are now performing cross-species comparisons of assess cellular architecture and cell type diversity in this model and to compare it to human menstruation. We are currently characterizing the applications of this model for menstrual disorders, including endometriosis.

Our novel mouse model of menstruation offers a unique platform for studying the intricate processes involved in endometrial shedding and regeneration, with important implications for advancing reproductive health and improving the quality of life for millions of women worldwide.

Sex and Hormones Influence Tendon Extracellular Matrix Remodeling

Brianne Connizzo

Assistant Professor of Biomedical Engineering & Mechanical Engineering, Boston University, Boston, MA

Abstract: Biological sex is a clear factor in an individual's ability to repair and regenerate tissue. Females are at higher risk for soft tissue injuries compared to age-matched males, and exhibit higher rates of degenerative diseases such as osteoporosis, sarcopenia, osteoarthritis, and carpal tunnel syndrome. One common hallmark of these degenerative diseases is the disruption in homeostasis of the extracellular matrix (ECM). A delicate balance in tissue production and breakdown is essentially to healthy function in every single tissue. Production of too much matrix can lead to fibrosis, while excessive matrix breakdown results in weakened tissue function. Our work is defining the sex-specific programming involved in ECM remodeling, and the influence of sex hormones on these tightly regulated processes. In doing this, we have discovered coordinate, yet distinct functions of estrogen and progesterone in maintaining tendon ECM. Importantly, we have developed an in vitro simulation of the murine estrous cycle, demonstrating a critical role for hormone fluctuations in tissue health. Ultimately, we aim to harness this information to establish sex-specific prevention or treatment strategies for tendon injury.

When the Technical is the Political: Bringing our Whole Selves to Engineering Design

Catherine M. Klapperich
Professor of Biomedical Engineering, Boston University, Boston, MA

Abstract: Since the emergence of gynecology as a medical specialty in the United States, the design of medical devices has been influenced by political factors. From the vaginal speculum, to birth control, to abortion access and assisted reproduction, technology development and politics are intertwined. In this talk, I will use several examples to illustrate why we as biomedical engineers must use our own lived experiences and those of affected patient communities to inform the design and implementation of emerging technologies.

Environmental Contamination and Adverse Pregnancy Outcomes in Puerto Rico

Akram Alshawabkeh

Senior Associate Dean for Research and Graduate Education, College of Engineering, Northeastern University, Boston, MA

Abstract: Adverse pregnancy outcomes (APOs) such as preterm birth (delivery at <37 weeks gestation) are a major, costly health problem. Exposure to environmental chemicals contributes to APOs. Reproductive and child health has been at the forefront of Puerto Ricans' health concerns as rates of PTB and infant mortality in Puerto Rico (PR) are among the highest of all U.S. states and territories. Contamination is extensive in PR: there are 19 Superfund sites contaminated with a myriad of chemicals including Chlorinated Volatile Organic Compounds (CVOCs), phthalates, Polycyclic Aromatic Hydrocarbons (PAHs), pesticides, and metals; evidence of contamination of the drinking water is extensive. There are also extreme weather events (Extreme weather events, e.g. hurricanes, flooding) that may result in elevated exposures to environmental pollution. In addition, the population is, on average, significantly poorer than the general US population.

Supported with funding from the National Institute of Environmental Health Sciences' Superfund Research Program, the PROTECT Center was established in 2010 to study exposure to environmental contamination in Puerto Rico and its contribution to adverse pregnancy outcomes, including preterm birth. PROTECT work has documented significant contamination in the study area in Puerto Rico, and compelling epidemiologic and mechanistic toxicology associations between Superfund chemicals and APOs. These exposures, toxicity mechanisms, and mitigation strategies are significantly modified and impacted by the complexities of environmental (e.g., high vulnerability to climate change) and psychosocial (e.g., substantial poverty and health disparity) realities of disadvantaged, highly-exposed and lower income communities.

Modeling Menopause: Mechanistic Insights into Female Aging Trajectories of the Musculoskeletal System

Fabrisia Ambrosio

Associate Professor of Physical Medicine and Rehabilitation, Harvard University, Cambridge, MA

Abstract: As indicated by the 2019 Global Burden of Disease Study, although women, on average, have a longer lifespan than men, women typically experience worsened health outcomes as they age. Notably, postmenopausal women have a higher incidence of knee osteoarthritis (KOA) and present with more severe disease progression over time. Osteoarthritis is major contributor to the loss of physical mobility for our aging population, affecting more than 60% of individuals aged 65 and older. However, the sex-specific aging trajectory of KOA is poorly understood, partly because conventional aging animal models fail to recapitulate human menopause phenotypes. In her talk, Dr. Ambrosio will discuss recent work from her laboratory that uses a chemically-induced menopause model in middle-aged (14-16 months) female mice together with a series of in vitro, in silico, and in vivo assays to interrogate molecular and cellular mechanisms underlying menopause-induced KOA. The long-term goal of this work is toward the development of effective interventions that consider sex-specific variables to the benefit of our aging population.

Multi-Scale Assessment of Biomechanics and Mechanobiology of Cardiovascular Tissues During Late Gestation

Rouzbeh Amini

Associate Professor Mechanical & Industrial Engineering and Bioengineering, Northeastern University, Boston, MA

Abstract: The maternal mortality rate in the United States was 20.1 deaths per 100,000 live births in 2019, more than double that of other developed countries. Cardiovascular disease remains the leading cause of maternal mortality, responsible for one in four pregnancy-related deaths. Our recent research shows that pregnancy induces significant biomechanical changes in large blood vessels. This mechanobiological remodeling likely helps maintain vascular homeostasis as cardiac demands increase during late gestation, requiring a 50% rise in blood volume to support the fetus and placenta. Complicated pregnancies, such as those involving preeclampsia, significantly increase the risk of future cardiovascular disease, including heart disease and stroke.

To further investigate pregnancy-induced remodeling, we measured the biaxial mechanical response of the murine thoracic aorta during a normotensive late-gestation pregnancy. Non-invasive hemodynamic measurements confirmed a 50% increase in cardiac output in pregnant mice, with no change in peripheral blood pressure. Pregnancy was associated with a 14% increase in wall thickness, a 6% increase in luminal diameter, and material softening in both circumferential and axial directions. This expansive remodeling reduced tensile wall stress and intrinsic tissue stiffness, suggesting that vessel geometry adapts to accommodate the increased cardiac output and blood flow during pregnancy. These changes, including wall thickening and increased luminal diameter, without a rise in blood pressure, may help lower tensile wall stress and prevent complications following late gestation.

Panel Discussion: Unveiling Sex Differences in STEM Research

Moderator: Soha Ben Tahar

PhD Candidate in Mechanical & Industrial Engineering
Northeastern University, Boston, MA

Rosalia Rabinovsky

Research Specialist

Department of Neurology, Brigham and Women's Hospital, Boston, MA

Henriette Coetzer

Chief Medical Officer

Blue Health Intelligence, Boston, MA

Rupal Patel

Professor of Speech Language Pathology and Audiology

Bouvé College of Health Sciences and the College of Computer and Information Science Northeastern University, Boston, MA

Sarah Ostadabbas

Director of the Women in Engineering Program & Associate Professor in Electrical and Computer Engineering

Northeastern University, Boston, MA

Abstract: Despite significant advancements in science and medicine, the fields of research—public and private—clinical practice, and policy have historically overlooked women's health. This panel brings together experts from all these domains to explore the ongoing challenges and opportunities in addressing sex differences. We will discuss how biases in scientific research, healthcare delivery, and public policy have shaped the landscape of women's health and what strategies can be employed to correct these disparities.

By examining the intersection of research, clinical practice, and policymaking, we aim to understand how these fields can collaborate to promote gender equity in healthcare. How can research more effectively account for sex differences? How can clinical trials and diagnostics better include women as subjects? What role do policies play in creating a more inclusive and equitable future? Together, we'll explore these questions with the goal of fostering a cultural shift that integrates women's health at every stage of scientific inquiry and medical care.

Poster Presentation Abstracts

The Influence of Fibrotic Stiffness on Lung Endothelial Glycocalyx

Chinedu Okorafor (1), Sanjana Shastri (2), Yu Chen (1), Eno E. Ebong (1, 3)

(1) Chemical Engineering, Northeastern University, Boston, MA, USA
(2) Behavioral Neuroscience, Northeastern University, Boston, MA, USA
(3) Bioengineering, Northeastern University, Boston, MA, USA

Problem Statement: Smoking, radiation treatment, etc. can induce fibrosis in lungs, increasing susceptibility to various pathological conditions like breast cancer metastasis. The lung's transformed mechanical environment, specifically the heightened wall stiffness of the blood vessels through which metastatic cancer and other pathogens travel, may vitally contribute to susceptibility to disease. A key barrier in this process is the endothelial cell (EC) surface glycocalyx (GCX), primarily made up of heparan sulfate (HS), hyaluronic acid (HA), and negatively charged sialic acid (SA). This GCX structure is understudied for lungs under mechanical conditions.

Project Overview: This study aims to understand how matrix stiffness regulates GCX structure and its role in mediating cancer metastasis in fibrotic lungs. We hypothesize that fibrotic stiffness decreases overall GCX expression on human pulmonary microvascular ECs by downregulating HS-, HA-, and SA-synthesizing enzymes, thereby increasing GCX barrier permeability. We replicated fibrotic conditions via mechanically tunable gelatin methacrylate hydrogels of 5 kPa (healthy) and 34 kPa (fibrotic) stiffness. These hydrogels serve as substrates for EC culture. Results so far show that fibrotic stiffness reduces whole GCX, suggesting increased vascular permeability to various pathogens. However, individual GCX components showed differentially behavior. HA reduction in fibrotic stiffness conditions may create an inflammation gradient that attracts cancer cells to the endothelium. Conversely, increased SA expression may provide more binding sites for pathogens. HS expression showed no change. These results suggest that GCX is a potential future therapeutic target.

Fields: Bioengineering, Chemical Engineering

Keywords: Lung Fibrosis, Endothelial Glycocalyx, Matrix Stiffness

Evaluations and optimization of STING agonist implants for ovarian and breast cancer

Yulei Xu (1), Xiaoheng Lyu (1), Khadijah Zai (2), Shicheng Yang (2), Needa Brown (2, 3), Srinivas Sridhar (1, 2, 4)

(1) Department of Bioengineering, Northeastern University, Boston, MA, USA
(2) Department of Physics, Northeastern University, Boston, MA, USA
(3) Department of Materials Science and Engineering, University of Central Florida, Orlando, FL, USA
(4) Department of Chemical Engineering, Northeastern University, Boston, MA, USA

Anti-tumor immunity activated by the cyclic GMP-AMP synthase (cGAS)-stimulator of interferon genes (STING) pathway is emerging as a promising treatment for BRCA-deficient cancers like ovarian and breast cancers. Specifically, our idea is to combine conventional therapy of Poly (ADP-ribose) Polymerases (PARP) inhibitor with ADU-S100, a synthetic cyclic dinucleotide that could activate the STING pathway. PARP inhibitors are known to disrupt the DNA repair in BRCA mutated cancer cells leading to cell death. Although effective, PARPi therapy is not sustainable, and resistance develops with limited alternatives for patients. Recent work has shown that STING pathway activated by ADU-S100 can trigger tumor-specific immune activation and enhance treatment efficacy. However, due to systemic inflammatory concerns, STING agonists are currently limited to intratumoral delivery. Here, we have developed a solvent evaporation method to fabricate ADU-S100 PLGA-based sustained-release implants as an alternative. As a first step to characterization, a bio-mimic release study of ADU-S100 was performed in phosphate-buffered saline (PBS) at 37oC, pH 7.4 and pH 6, respectively, to mimic physiologic and tumoral pH. Then, the drug release kinetics of ADU-S100 implants were evaluated by HPLC. The results showed sustained release of ADU-S100 over 21 days, echoing our hypothesis. Additionally, to confirm bioactivity, THP-1 ISG-Blue IRF reporter cells, which produce secreted embryonic alkaline phosphatase (SEAP) upon IRF pathway activation, were utilized as a surrogate for STING activation. The optimized results of drug dosage formulation of the implant would lay a foundation for future in vivo model experiments and clinical translation.

Fields: Bioengineering

Keywords: Sustained delivery, BRCA-deficient cancers, PARP inhibitor, STING pathway, ADU-S100 loaded implant

Sex-based computational analysis of estrogen impact on microglia during progression of AD

Anagha Deepak (1), Christina Velez (2)

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(2) Department of Bioengineering , Northeastern University, Boston, MA

Alzheimer's disease, a common neurodegenerative disease is caused by the formation of amyloid-β plaques and tau tangles within and around neurons, results in marked cognitive decline, memory loss, and changes in behavior in aging individuals. Microglia are the primary resident immune cells of the brain that act as the inherent response systems to address the impact of these formations and maintain homeostasis in the central nervous system. The onset and progression of AD have been directly linked to microglia function which is markedly different in males and females due to underlying differences in inflammatory responses and hormonal influences. Women account for two-thirds of prevalent AD cases and yet most of the research on the cause, effects, and progression of the disease has been focused on the male population, leading to a gap of knowledge in understanding how fluctuating estrogen concentrations and menopause play a role in AD. The purpose of this research is to create a computational tool that will allow us to predict differences in the microglial effects of the brain based on sex, age, and APOE genetics. We aimed to simulate an agent-based computational model to analyze the microglial efficiency in clearing the degenerated neurons in both women and men. The key variables required for simulation come from scientific data published by research work within PubMed and the National Institute of Health's data collection. The simulations are generated from an open-source agent-based modeling tool, NetLogo, with the computational model described here openly available online at https://github.com/teenie3/ SexEffect_Microglia_AD.

Fields: Bioengineering

Keywords: Neuroscience, Computational Modeling, Alzheimer's Disease, microglia, Sex-Based research

Mucus-inspired therapies for recurrent vaginal infections

Kelsey Wheeler (1), Liubov Yakovlieva (1), Caroline Werlang (1), Caroline Mitchell (2), Katharina Ribbeck (1)

(1) Department of Biological Engineering, MIT, Cambridge, MA
(2) Department of Obstetrics & Gynecology, Massachusetts General Hospital, Boston, MA

Vaginitis, a common women's health condition characterized by discharge, odor, and discomfort, is responsible for 10 million office visits annually in the US. The two most common causes of vaginitis are bacterial vaginosis or vulvovaginal candidiasis. Antibiotics and antifungals can cure these infections temporarily, but these infections often return and become recurrent problems. In the case of bacterial vaginosis, up to 80% of people suffer a recurrence within nine months. There are currently no reliable solutions for preventing these infections. To meet this need, we have leveraged insights from the natural mucus barrier, which domesticates microbes by suppressing their virulence while providing a livable habitat, thereby maintaining the microbial homeostasis vital to health. The microbe-taming function of mucus stems from the complex sugars that densely coat the mucin polymers that give mucus its gel-like properties. We have developed technology to deliver infection- fighting sugars via mucin-inspired therapeutic polymers to treat and prevent infectious vaginitis. Moreover, the immense water-holding capacity of mucin-inspired polymers will have the added benefit of providing hydration to the vaginal epithelium to further ease discomfort associated with infections.

Fields: Bioengineering

Keywords: Mucus, Vaginitis, Mucin, Gardnerella, Lactobacillus

In-silico Models of In-vivo Cervical Stiffness Measurements for Improving Preterm Birth Prediction

Abigail Laughlin (1), Adriana Delagarza (2), Erin Louwagie (3), Jacqueline C. Hairston (4), Mirella Mourad (3), Michael House (4), Kristin Myers (1)

(1) Mechanical Engineering, Columbia University, New York, NY, USA
(2) Obstetrics and Gynecology, Northwestern Medicine, Chicago, IL, USA
(3) Obstetrics and Gynecology, Columbia University Irving Medical Center, New York, NY, USA
(4) Obstetrics and Gynecology, Tufts Medical Center, Boston, MA, USA

Globally, the incidence of preterm birth (PTB, delivery before 37 weeks) is approximately 1 in every 10 live births [1]. Despite its clinical importance, PTB is difficult to predict. A novel device for PTB prediction is the Pregnolia system, which tests the stiffness of the cervix via aspiration [2]. The goal of this study is to determine patient-specific cervical material properties using simulation of cervical aspiration, which could be used to enhance PTB prediction.

Using TVUS images of patient cervices and their corresponding aCS values, measurements were recorded to create a high fidelity (HF, ~60 measurements), mid-fidelity (MF, ~20 measurements), and low-fidelity (3 measurements) model for three high-risk (CL < 25 mm, no PTB history) and three low risk (screened against known PTB risk factors) patients. Models were meshed and imported to FEBio Studio for finite element analysis. The cervix was modeled as a passive fiber composite material with a compressible neo-Hookean ground substance fit to existing mechanical tissue tests [9]. Inverse finite element analysis was performed to find the computed fiber stiffness (cCS) value. cCS values for HF, MF, and LF models were compared to understand how geometric fidelity affected the numerical outcomes of the simulations.

When examining LF results, the patient with the lowest cCs value corresponded to the only patient who delivered extremely preterm (24 weeks). No clear trend in cCS values were found, with some high cCS values correlating with lower aCS values, etc. Additionally, there was no direct correlation between CL, aCS, and cCS values.

References

[1] World Health Organization, “Preterm Birth”, 2023.
[2] Kyvernitakis, I et al., PLOS One, 18(4):e0283944, 2023.
[3] Shi, L et al., J Biomech Eng, 141(9): 0910171–09101713, 2019."

Fields: Bioengineering, Mechanical Engineering

Keywords: Preterm Birth, Pregnancy, Cervix, Predictive Tools

Relaxin is Necessary for Normal Cervical Remodeling in Murine Pregnancy

Serena Russell (1), Nicole Lee (1), Sudeshna Tripathy (2), Mala Mahendroo (3), Kristin Myers (1)

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(2) Oregon National Primate Research Center, Beaverton, OR, USA
(3) University of Texas Southwestern Medical Center, Dallas, TX, USA

Introduction: Cervical remodeling is crucial to preterm birth and is characterized by increased tissue compliance allowing the cervix to stretch. Relaxin is a peptide hormone that reduces fibrosis, affecting parturition in mice. We performed a biomechanical test and inverse finite element analysis to determine material parameters to inform cervical relaxin function.

Methods: We tested wild-type (WT) and relaxin-receptor knockout (RKO) mice at three timepoints (d12, 15, 18, n=5). Tension tests were implemented to determine altered cervical performance. Bulk modulus κ, initial stiffness ξ and locking-stretch N (fiber extensibility), were found using an objective function with measurements from these tests. Material parameters were found using a genetic algorithm. Statistical analysis was performed to compare parameters across groups.

Results: Constitutive material modeling showed no significant change in ξ between RKO and WT models. κ is significantly reduced in RKO models at d12 ($p < 0.05$). N increases significantly in RKO mice at d12, with differences between d15 mice, and RKO and WT models having no significant difference in N by d18.

Conclusions: Relaxin is necessary for cervical remodeling in mice, and has distinct effects at each gestational age. The loss of the relaxin receptor generally softens and makes the cervix more pliable at gestation d12 and d15. By d18, changes are resolved. Changes in material properties may indicate premature ripening of the cervix in RKO models, implying the necessity of relaxin for normal cervical remodeling.

Fields: Mechanical Engineering

Keywords: preterm birth, cervical remodeling, cervix, biomechanics, pregnancy

Sialidase enzymes derived from bacterial vaginosis associated bacteria may impair sperm function by remodeling the sperm glycocalyx

Sarah Dohadwala (1), Purna M Shah (1), Maura K Farrell (1), Joseph A Politch (2), Kevin Whaley (3), Deborah J Anderson (1, 2), Catherine E Costello (1)

(1) Boston University, Boston, MA, USA
(2) Boston University Medical School, Boston, MA, USA
(3) ZabBio Inc., San Diego, CA, USA

Bacterial vaginosis (BV), a dysbiosis of the vaginal microbiome, affects approximately 23 to 29 percent of women worldwide and is associated with several adverse health outcomes including preterm birth, subfertility, and sexually transmitted infections (STI). BV-associated bacteria, such as Gardnerella vaginalis, are known to cause epithelial damage and degradation of the vaginal mucosa through the activity of sialidase enzymes that remodel the epithelial glycocalyx and metabolize mucin glycoproteins. This damage to the vaginal glycocalyx creates an inflammatory environment which likely contributes to adverse health outcomes. However, whether BV-associated glycolytic enzymes can also damage sperm during their transit in the reproductive tract has not yet been determined. Here, we show that sialidase-mediated glycocalyx remodeling of human sperm increases sperm susceptibility to innate immune damage within the female reproductive tract. In particular, we report that upon exposure to physiologically relevant amounts of sialidase enzymes, desialylated human sperm demonstrate increased susceptibility to complement lysis (~2.5-fold) and agglutination (~2-fold). Our results demonstrate a potential mechanism by which BV glycolytic enzymes may affect sperm survival and function and thereby contribute to adverse reproductive outcomes such as subfertility.

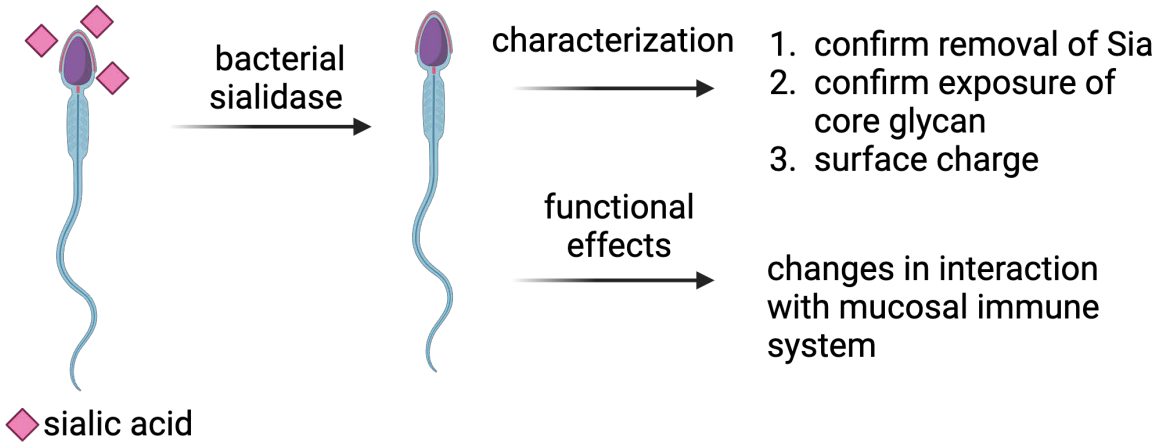

Figure: Sialidase enzymes derived from bacterial vaginosis associated bacteria may impair sperm function by remodeling the sperm glycocalyx

Fields: Immunology

Keywords: fertility, bacterial vaginosis, sperm, glycans, complement

Actomyosin fibers in the spermatheca are under tension

Fereshteh Sadeghian (1), Erin Cram (1, 2)

(1) Bioengineering, Northeastern University, Boston, MA, USA
(2) Biology, Northeastern University, Boston, MA, USA

Regulating contractile and relaxation processes is crucial for the functionality of tubular structures in organisms. In C. elegans, the spermatheca, the site of fertilization, consists of smooth muscle-like cells. As oocytes pass through the spermatheca, they undergo multiple cycles of stretching and contracting.
We utilized laser ablation to assess fiber tension. Using a SpectraPhysics Spirit laser, operating at 1040 nm, with 400 fs pulses at a frequency of 1 kHz and approximately 500 mW power, we severed the fibers in animals expressing ACT-1::GFP to monitor retraction rates.

Additionally, to understand the mechanical forces during ovulation, we employed the strain sensor STReTCh to measure tension on the actin fibers within the spermatheca. The STReTCh system is composed of SpyTag and SpyCatcher, which interact when the mechanosensitive domain is unfolded. We adapted this method by integrating the sensor into mechanosensitive regions of DEB-1/vinculin and FLN-1/filamin in C. elegans. Our observations revealed that SpyCatcher paired with DEB-1/vinculin::SpyTag and FLN-1/filamin::SpyTag coincides in the spermatheca under mel-11/MYPT RNAi treatment and plc-1/phospholipase C RNAi treatment, respectively, indicating their role in fiber tension regulation.

Our ongoing research aims to map tension distribution throughout the spermatheca and related proteins' regulatory role in contractility.

Fields: Bioengineering

Keywords: Actomyosin contractility, Tension, STReTCh sensor, Laser ablation, C. elegans

Cardiac-induced Brain Tissue Motion in Chiari Malformation Type 1 and Its Relationship to Surgery, Crowding, and Symptomatology

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Chiari Malformation type 1 (CMI), a condition characterized by the descent of the cerebellar tonsils below the foramen magnum, is more common in females and can lead to a range of debilitating symptoms. Understanding brain tissue motion during the cardiac cycle is critical in CMI research because abnormal motion may contribute to symptom severity and could be a key factor in the disease's pathophysiology. This study utilized Phase Contrast MRI (PCMRI) to measure brain tissue displacement in 48 adult CMI patients, including 22 who underwent posterior fossa decompression (PFD) surgery. Significant reductions in cerebellar and medullary tissue displacement were observed post-surgery, yet no correlation was found between tissue motion and symptoms such as cough-associated headaches and neck pain. Additionally, no significant differences in displacement were detected between surgical and non-surgical groups. These findings suggest that brain tissue motion may not be directly related to CMI symptoms, challenging existing perspectives on the condition's pathophysiology. While PCMRI is effective for assessing tissue motion, further research is necessary to clarify its role in CMI management and to identify more reliable diagnostic markers and treatment strategies.

Fields: Bioengineering

Keywords: Chiari Malformation, Phase Contrast MRI, Cardiac Brain Tissue Motion

Label-free Microscopy to Evaluate MSC Metabolism and Osteogenic Differentiation

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Mesenchymal Stem Cells (MSCs) are pivotal in regenerative medicine due to their therapeutic potential, yet the lack of standardized potency metrics hinders FDA-approved applications. Traditional methods for assessing MSC differentiation, such as Western blots and PCR, are destructive and fail to capture the dynamic processes of differentiation and metabolism. This study introduces a label-free approach using differential phase-contrast microscopy and multi-photon fluorescence microscopy to non-invasively evaluate MSC metabolism and osteogenic differentiation. We exploit the optical redox ratio, derived from the autofluorescence of oxidized flavin adenine dinucleotide (FAD) and reduced nicotinamide adenine dinucleotide (NADH), alongside third harmonic generation (THG) imaging to assess cellular changes.

MSCs were induced to differentiate using osteogenic media, and their metabolic activities and differentiation status were monitored over time. Phase imaging and alizarin red S staining confirmed successful MSC differentiation. Autofluorescence imaging revealed that differentiated MSCs exhibited higher metabolic activity compared to undifferentiated counterparts, as indicated by a higher redox ratio (0.51 for osteogenic media vs. 0.38 for basic media). THG signals, associated with calcium mineralization, were present in differentiated MSCs but absent in undifferentiated cells.

These findings demonstrate the efficacy of using non-invasive imaging techniques to assess MSC differentiation and metabolic activity, providing valuable insights into MSC therapeutic potential. Future research will expand on these methods to optimize MSC function and explore the manipulation of metabolic pathways to enhance regenerative outcomes.

Fields: Bioengineering, Electrical & Computer Engineering

Keywords: microscopy, label-free, health

Morphometric Analysis of Pediatric Female Chiari Malformation: Age-Related Changes and Comparative Study with Adult Female Populations

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Purpose: This study aims to determine the differences in craniospinal morphology between pediatric and adult female Chiari Malformation Type I (CM) patients and assess age-related changes in pediatric cases.

Methods: We analyzed 87 girls aged 0 to 18 years diagnosed with CM. Six craniospinal morphometric parameters were assessed: McRae Line, Tonsillar position, Clivus length, Wackenheim angle, Anterior CSF area, and Posterior CSF area. These parameters were compared between pediatric CM (12-18 years old) and adult CM, as well as between pediatric CM (9-11 years old) and healthy controls. Linear regression was used to determine the slope of morphological changes with age (1-8 years old) in pediatric CM.

Results: Among pediatric CM patients (12-18 years old), Tonsillar position and anterior CSF area were 32% and 57% larger, respectively, compared to adult CM, with other parameters showing <10% differences. Comparing pediatric CM (9-11 years old) with healthy controls revealed no significant differences in McRae Line, Clivus length, and Wackenheim angle, but tonsillar position, anterior CSF area, and posterior CSF area showed significant variations. Age-related analysis showed significant changes in McRae Line ($p = 0.007$) and Clivus length ($p = 4.2E-06$).

Conclusion: Pediatric CM patients exhibit distinct morphometric differences, particularly in tonsillar position and CSF areas, compared to adult CM patients and healthy pediatric controls. Significant age-related changes were also observed in McRae Line and Clivus length.

Fields: Bioengineering, Mechanical Engineering

Keywords: Chiari malformation type I, Pediatric Brain morphometrics, Age-related changes, Brain MRI

On the Pressure-induced Nuclear Deformation of Murine Vascular Cells: The Effects of Pregnancy induced Remodeling

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Significant changes in a woman's cardiovascular system during pregnancy may influence the morphology of the cells ensconced within the aortic wall. Here, we examine such alterations by measuring the nuclear aspect ratio (NAR) of fibroblasts and smooth muscle cells in the aorta of female mice, to understand the biomechanical effects of pregnancy on cells and their role in vascular remodeling. Computational methods were employed to analyze 3D image stacks from pregnant and sex- and age-matched nulligravida control mice, focusing on the media and adventitia layers of the aortic wall. Gaussian smoothing and Otsu's thresholding were used to segment the cells, and distinct cell types were identified based on their geometry and spatial positioning. To account for the natural curvature of the aortic wall, the cells were flattened using polar coordinates. NAR, defined as the ratio of the longest to the shortest axis of the cell nucleus, was calculated for each cell type at varying pressure levels. We found minimal changes in NAR within physiological pressure ranges, suggesting that nuclear shape is preserved despite varying mechanical stresses in both pregnant and nulligravida mice (Figure 1). The lack of significant differences in NAR between pregnant and control groups suggests that cellular adaptations during pregnancy may aim to maintain nuclear homeostasis despite significant differences in luminal diameter and tissue mechanics between pregnant and nulligravida groups. These findings provide insights into how mechanical forces affect cellular morphology and highlight the importance of maintaining nuclear integrity for vascular health during pregnancy, offering valuable implications for maternal cardiovascular health and therapeutic strategies for pregnancy-related vascular complications.

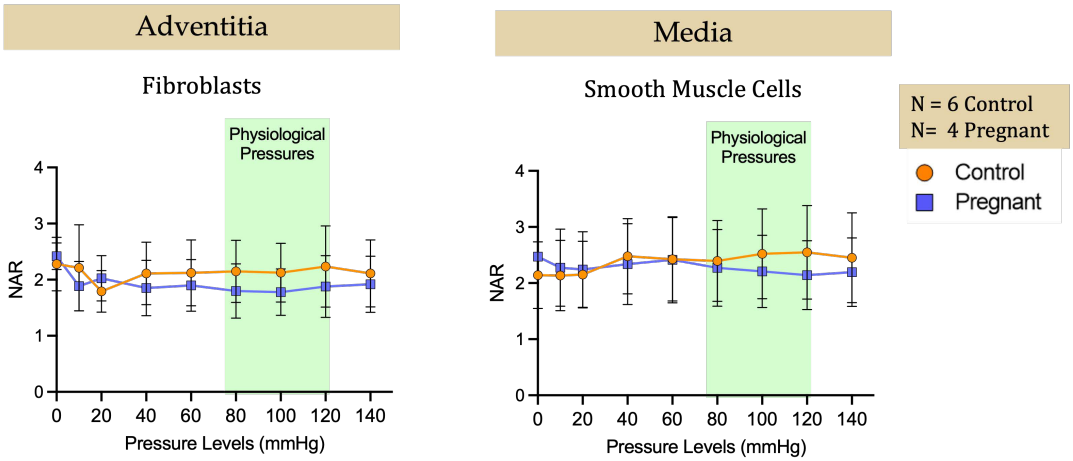

Figure 1: Effects of luminal pressure on the nuclear aspect ratio (NAR) for fibroblasts and smooth muscle cells. In both cell types, we observed minimal changes in nuclear shape within the physiological pressure, and no differences in nuclear shape between the pregnant and control groups.

Fields: Bioengineering

Keywords: Nuclear Aspect Ratio, Cellular Deformation, Pregnancy, Vascular Remodeling, Computational Imaging

A novel antibody based, on-demand contraceptive to prevent unintended pregnancies

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In the United States, nearly half of all pregnancies are unintended, causing negative health and socioeconomic outcomes for women and infants. Despite currently available contraception methods, an unmet need for additional effective contraception methods remains. Current birth control options have side effects, high costs and/or require visits to a healthcare provider. Here we show the development of the Human Contraception Antibody (HCA) which is an antisperm antibody targeting a male reproductive tract-specific glycan called CD52g. It functions as a contraceptive primarily by agglutinating sperm within seconds (30 seconds at 0.39 ug/ mL), and secondly by potent complement mediated sperm immobilization (100% at 0.1 ug/mL) and mucus trapping (25 ug/mL). Phase I clinical trial of the HCA film (ZB-06) was shown to be safe and effective. We currently deliver this antibody topically via a fast dissolving polyvinyl alcohol based film, and are exploring other approaches including mRNA delivery, a slow release film, and encapsulation in lubricants. In addition, we are developing multivalent and bispecific antibodies to further develop this contraceptive platform and pursue the development of concurrent protection from STIs and unintended pregnancy. These data indicate that HCA is a novel on demand contraceptive that is potent, low cost, and easy to access.

Fields: Immunology

Keywords: Unintended pregnancies, contraception, human contraception antibody

Early stages of EMT are not completely reversible in MCF10A cells

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In development and wound healing, typically non-motile cells gain migratory properties in a reversible biological process termed the epithelial to mesenchymal transition, or EMT. The genetic changes that drive EMT are exploited by cancer cells, allowing them to disseminate from the primary tumor and spread throughout the body. In order to effectively colonize a secondary location to form a metastatic site, the cells revert back to their original phenotype in the mesenchymal to epithelial transition, or MET. TGF-β, a common driver of EMT in breast cancer, can be used to stimulate EMT in vitro. Using MCF10A cells, a non-transformed mammary epithelial cell line, we sought to evaluate the extent of MET achievable when cells are treated with TGF-β and then given time to revert back. We allowed cells in early and late EMT, treated for 3 and 12 days with TGF-β, respectively, to have 12 days without exposure to TGF-β to go through MET, taking samples for RNA and protein analyses every 3 days. RT- PCR of 12 genes known to be either up or downregulated during EMT showed no difference between the early and late populations in their ability to go through MET. Although early EMT is generally considered to be completely reversible, half of the genes were unable to return to baseline mRNA expression in both the early and late EMT treatment conditions. The majority of these partially-reversible genes are involved in maintenance of cell-to-cell contacts, indicating cellular contacts could be weaker after MET irrespective of their EMT stage.

Fields: Bioengineering

Keywords: Breast Cancer, EMT

Developing a microbial biosensor for fertility hormone detection in whole blood

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Fertility hormone testing provides vital information for women undergoing In Vitro Fertilization, ectopic pregnancies, miscarriages, and polycystic ovary syndrome. However, the current methods of testing pose many accessibility barriers to women around the world. At-home urine tests lack the sensitivity and specificity of blood tests that healthcare providers desire. However, blood tests require the patient to rely on testing centers. At these centers, extensive sample preparation is required, and results can take days. The goal of our research is thus to devise a test that can detect fertility hormones in whole blood in the comfort of the patient's home. To achieve this goal, genetically engineered microbial cells will be used as a robust sensing platform. However, the function of microbial cells in blood has not yet been well established. In order to test both the survivability and sensing ability of engineered cells in blood, we synthesized four variants that would fluoresce in the presence of a model target molecule. Our experiments revealed successful designs of reporter action, with increased fluorescence in the presence of the target molecule. Now that these strains have been established, their behavior in whole blood may be explored. These results will inform the development of our fertility hormone sensors, and break down barriers to reproductive healthcare.

Fields: Immunology

Keywords: fertility, bacterial vaginosis, sperm, glycans, complement

Optimization of bubble detachment from electrode using machine learning method

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Water contamination poses a significant risk to public health, particularly affecting pregnant women, who are more vulnerable to pollutants in drinking water. Advanced Oxidation Processes (AOPs) have emerged as a highly efficient method for purifying water by generating reactive oxidizing agents through electrochemical reactions. Despite their effectiveness, the presence of bubbles in these processes can reduce the efficiency of contamination removal by decreasing the cathode's electroactive surface area. Understanding and optimizing bubble behavior in these systems is crucial for enhancing the performance of water treatment methods. This study investigates the dynamics of bubbles generated during AOPs and their impact on the efficiency of water treatment reactors, particularly in flow-through systems designed to remove persistent pollutants. We employ the Volume of Fluid (VOF) method, implemented through the CSECGEFoam solver, to model bubble behavior in a multiphase flow environment. Machine Learning (ML) techniques, specifically Artificial Neural Networks (ANNs), are then applied to analyze the data. This approach allows us to predict critical outputs such as bubble growth rate and the rate of bubble detachment from the electrode. By using ANN-based ML approaches, we aim to bypass the complexity of traditional models, making predictions more efficient and accurate.

Our findings aim to contribute to the development of more efficient water treatment systems, ultimately improving water quality and benefiting women's health by reducing exposure to harmful contaminants. This research underscores the importance of optimizing water purification technologies, particularly in flow-through systems, to safeguard public health, especially for vulnerable populations like women and pregnant women.

Fields: Chemical Engineering, Civil & Enviromental Engineering

Keywords:Water treatment, advanced oxidation processes, bubble dynamics, machine learning

Impact of Wildfire Smoke Inhalation on Immune- Mediated Endothelial Dysfunction in Mice

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Wildfires have become increasingly frequent and intense due to rising temperatures and prolonged drought conditions. These fires emit a heterogeneous mixture of particulate matter, gases, and chemicals, contributing to deteriorating air quality across the United States and posing serious health risks. Recent studies have shown that wildland fire smoke (WFS) inhalation has adverse cardiovascular effects, prompting the need for evidence-based interventions. Previous studies have hypothesized that immune cell response to WFS inhalation is the main instigator of the chemical cascade that causes endothelial dysfunction in the aorta of mice. To determine the validity of this hypothesis, female ApoE -/- mice were exposed to similar conditions as wildland firefighters over a 7-day period. The immune system was characterized in the blood and lungs though the use of flow cytometry. From this study, we conclude that endothelial dysfunction in the aorta is driven by monocytes reaction in the lungs and blood rather than the current theory of a neutrophil driven response. Understanding the cardiovascular effects of WFS is crucial for guiding efforts to protect vulnerable populations from the health risks associated with wildfire exposure. This knowledge is vital for healthcare professionals, environmental justice advocates, and forest management authorities working to mitigate the impact of wildfires on public health.

Fields: Bioengineering

Keywords: Wildfire, vascular, health, heart, firefighters, women

Pregnancy-Induced Aortic Remodeling: Collagen Orientation and its Impact on Aortic Stiffness

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During pregnancy, significant hemodynamic changes impact the cardiovascular system, with cardiovascular disease being the leading cause of maternal mortality in the US. Despite the well-documented hemodynamic shifts, the mechanisms underlying the remodeling of elastic arteries like the aorta remain largely unexplored. In this study, we investigated pregnancy-induced aortic remodeling by examining collagen fiber orientation and distribution under mechanical loading, aiming to connect these microscale alterations with observed macroscale mechanical responses.

Descending thoracic aorta segments were collected from pregnant and control C57BL6 female mice. Samples were imaged using multiphoton microscopy to capture collagen, elastin, and cell nuclei across the aortic wall thickness. Image analysis were used to quantify in-plane collagen distribution via OrientationJ, while mechanical properties were assessed via stiffness tensor components derived from previous biaxial mechanical tests.

The results showed that pregnant samples exhibited a less organized collagen structure (Fig. 1A), indicated by lower κ values, and a faster shift towards circumferential fiber orientation under pressure (Fig. 1B), reflecting increased circumferential stiffness. This remodeling suggests a shift toward a more isotropic mechanical response during pregnancy. These microstructural and mechanical changes in the pregnant aorta, characterized by collagen reorientation and a more rapid gain in circumferential stiffness, may help accommodate the hemodynamic demands of pregnancy. However, they could also have implications for postpartum aortic function and maternal health.

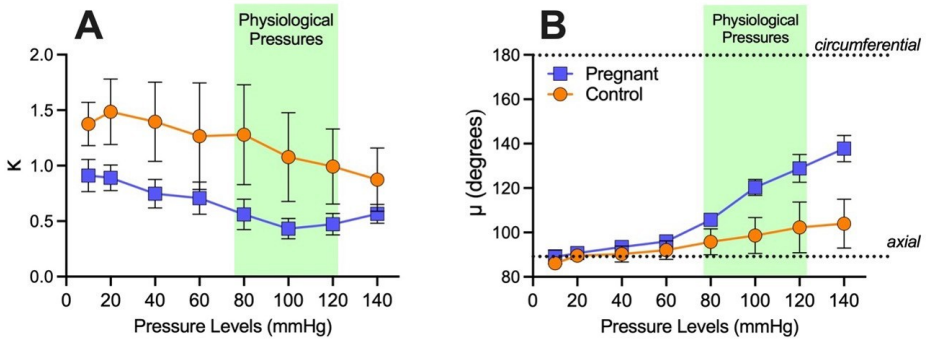

Figure 1: Collagen Fiber Organization at In Vivo Axial Stretch. (A) Concentration parameter (κ) and (B) primary orientation parameter (μ) plotted against pressure for control and pregnant groups.

Fields: Bioengineering, Mechanical Engineering

Keywords: late-gestation, pregnancy, vascular mechanics, collagen

Characterizing the Viscoelastic Properties of Murine Placental Tissues

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While studies aiming to characterize individual segments of the placenta and umbilical cord exist, our ability to develop new screening processes and treatments are severely hampered by the lack of a comprehensive biomechanical model for the umbilico-placental system.

This study aims to quantify the mechanical properties of murine placental tissues. Samples are taken from three litters of mice in late gestation (gestational day 13). The thickness and diameter of each placental sample is measured, and can be compared to the weight of the associated pup. The stress relaxation response of the placental tissues is then measured using spherical indentation methods.

To obtain the viscoelastic material properties, the experimental data is fitted to a two-term Prony series viscoelastic finite element model. This model has six terms to adjust to fit the experimental data: Young's Modulus, Poisson's ratio, two dimensionless viscoelastic loss parameters, and two relaxation time constants. The model is run iteratively until the finite element model, with its six material parameters, fits the experimental data.

Fields: Bioengineering, Mechanical Engineering

Keywords: Placenta, Viscoelastic, Finite Element Method

Sex Representation in Biomechanics and Bioengineering Research: A Meta-Analysis of SB3C 2023 Abstracts

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A balanced sex distribution in health care research is essential to enhance the accuracy of findings, particularly in biomechanics, bioengineering, and biotransport fields. We conducted a meta-analysis—extending from the work of Sebastian et al. (2023, J Biomech, 146(6):060906)—by analyzing 600 abstracts presented at the 2023 Summer Biomechanics, Bioengineering, and Biotransport Conference (SB3C). The focus was on whether the sex of study samples was reported, and if studies were limited to only one sex, whether such an approach was justified.
Of the 600 abstracts, only in 131 (21.8%) the sex of the samples were disclosed. Among these, in 48 (36.6%), the researchers confirmed the use of both sexes, but only 22 (45.8%) of those studies were balanced, while 10 (20.8%) were unbalanced, and 16 (33.3%) did not specify a male-to-female ratio. Most concerning, 93 (71%) studies were unbalanced, with only 31 (33.3%) of these being gender-specific. In 62 (66.7%) abstracts, the choice of a single sex was unjustified. The data showed a predominance of male-only study samples (69.4%) of the unjustified unbalanced studies.

These findings reveal persistent sex imbalances in research, underscoring the need for better inclusion of diverse sex samples to address the biomechanical and physiological needs of all individuals, especially women.

Fields: Bioengineering, Mechanical Engineering

Keywords: Biomechanics, Mechanobiology, Sex, Study Sample, Biotransport