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Introducing 4-D Printing and Other Nanomedicine Advances: Controlling Materials in the Body from the Outside

Thomas J. Webster*

Interstellar Therapeutics and Northeastern University, USA

Abstract

Nanotechnology has revolutionized medicine in a number of ways, from improving disease detection to greater treatments. However, a particular growing concern to our healthcare system is to improve personalized medicine, which can be achieved through implantable nanosensors. This talk will cover advances in implantable nanosensors and barriers that remain before their widespread use. It will highlight current implantable sensors that can be used to sense tissue growth, infection, and inflammation sending such information to a handheld device to in turn release, on-demand, molecules to reverse adverse events. Further, this talk will introduce how 4D printing is being implemented into medicine where material geometry, drug delivery, and sensing can be remotely controlled from outside the body.

Biography

Thomas J. Webster's (H index: 100) degrees are in chemical engineering from the University of Pittsburgh (B.S., 1995) and in biomedical engineering from RPI (Ph.D., 2000). He currently serves as the Art Zafiropoulo Endowed Professor of Chemical Engineering at Northeastern University. Prof. Webster has formed over a dozen companies who have numerous FDA approved medical products currently improving human health. Prof. Webster is a fellow of numerous societies and is a SCOPUS highly cited researcher (top 1% citations for materials science and mixed fields) and a World Top 2% Scientist by Citations (PLOS).

Clinical Translation of a PLG Nanoparticle-Based Delivery System for the Induction of Immune Tolerance

Stephen D. Miller, Ph.D.

Northwestern University Medical School, Chicago, IL 60611 USS

Abstract

The utility of antigen-encapsulating carboxylated poly(lactide-co-glycolide) (PLG) nanoparticles (Ag-PLG) for tolerance induction in treatment of autoimmune and allergic diseases will be discussed. Data supporting the critical role of Ag-PLG uptake by tolerogenic spleen and liver APCs via the MARCO scavenger receptor and for activation of antigen-specific regulatory T cell subsets in tolerance induction and maintenance in Th1/17-driven animal models of MS and T1D, and Th2-driven allergic airway disease will be presented. Lastly, the ability gliadin-encapsulating PLG nanoparticles to safely and effectively prevent the activation of gliadin-specific IFN-gamma producing T cells and prevent intestinal inflammation in celiac disease patients undergoing oral gluten challenge in a recent Phase 1/2a proof-of-concept clinical trial will be discussed.

Biography

Stephen D. Miller completed his PhD in Immunology at the Pennsylvania State University and postdoctoral

studies at the University of Colorado Medical Center. He is the Judy E. Gugenheim Research Professor of Microbiology-Immunology and Director of the Interdepartmental Immunobiology Center at Northwestern University Feinberg School of Medicine and co-founder of Cour Pharmaceuticals Development Co. His research focuses on the pathogenesis and regulation of immune-mediated inflammatory diseases. He has published more than 425 papers and holds research grants from the NIH, the JDRF and multiple foundations and biotech companies.

Monitoring the growth of HUVECs under Electrical Stimulation using an Electrical Cell Stimulation and Recording Apparatus (ECSARA)

Anthony Guiseppi-Elie[1,2,*]

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Abstract

Ubiquitous, endogenous electric fields in the body, particularly streaming potentials, suggest the importance of this factor in controlling cellular process. Electroceuticals, locally produced changes in biochemical activities or biomolecular fluxes under the influence of an electric field (EF), is an example of harnessing electrification as an external cue to treat ailments. Here, the effect of EF on human umbilical vein endothelial cells (HUVECs) was studied with attendant real-time monitoring using electrical impedance spectroscopy (EIS) in a novel electroculture system, ECSASA. HUVECs on cell culture inserts were exposed to a perpendicular EF of 162 mV/mm at 1.2 Hz and pulse width of 0.25% and compared with non-stimulated cells. The viability was measured using alamarBlue assay. The EIS data collected every 12 h was modeled using an $R_S(Q_{CELL}R_{CELL})(Q_{OX}R_{OX})(Q_{DL}R_{CT})$ equivalent circuit and changes in R_{CELL} monitored.

Viability test showed that in the first 24 h, EF stimulated cells were smaller in number than control (85%) but outnumbered the control after 72 h (125%). EF stimulation initially inhibited growth but eventually supported the proliferation of HUVECs. EIS monitoring showed a ten-fold increase in R_{CELL} of EF stimulated cells after 54 h which gradually increased to a constant level after 72 h. The R_{CELL} of the control group increased after 78 h and continued to increase until it reached to a constant level after 108 h. R_{CELL}, a measure of TEER, corresponded to the formation of tight junctions that impede movement of ions between cell monolayer. The application of electrical stimulation promoted cell growth and proliferation and induced early formation of tight junctions in endothelial cells.

Biography

Anthony Guiseppi-Elie is TEES Professor of Engineering, Professor of Biomedical Engineering, Professor of Electrical and Computer Engineering and Director of the Center for Bioelectronics, Biosensors and Biochips at Texas A&M University. He is a fellow of IEEE, AIMBE, and the RSC. His interests are in bionanotechnology, BioMEMS, the interfacing of biology and engineering from the molecular through tissue levels, the application of semiconductor fabrication techniques to biomedical engineering and entrepreneurship to address opportunities in cardiovascular, neuroregeneration, chronic wound healing, and traumatic hemorrhage. He has been associated with three startups, most recently as founder and scientific director of ABTECH Scientific, Inc.

The Rise of Modern Genetic Engineering Tools: and our Responsibility to Introduce the Ethical and Societal Implication to our Students and the Public

Temple F. Smith

Boston University, MA

It is clear that tools such a CRISPR/cas 9, have immense potential, in medicine, agriculture and biotechnology. Along with this are the associated ethical and societal challenges. Therefore, not only do those of us who are developing and using such tools have an obligation to understand those challenges, but to help the general public and our students understand them. One of the initial steps is to be sure that we expose our students to these issues and challenges, and do that in the full historical context. Here I outline just such a university course recently devolved and taught within Boston University. That experience exposed the unanticipated need to discuss religious beliefs, current legal systems and the distinction between communal ethics and personal moral sensitivities, in some detail. In particular, we must not be insensitive to the real concerns these tools present. All of this requires the expanded education of our selves, the biomedical research community, and preparation to become more involved in the wider public discussions.

Multiphoton microscopy for imaging deeper, wider, and faster

Chris Xu

School of Applied and Engineering Physics, Cornell University, Ithaca, NY 14853

Abstract

Multiphoton microscopy has changed how we visualize neurons by providing high-resolution, non-invasive imaging capability deep within intact brain tissue. Multiphoton imaging will likely play a major role in understanding how the brain works at the level of neural circuits. In this talk, in vivo structural and functional imaging of mouse brain using long wavelength excitation and three-photon microscopy will be presented. By quantitative comparison to two-photon microscopy, the application space where 3-photon microscopy outperforms conventional 2-photon microscopy will be defined. In addition, a number of interesting directions, including new laser sources, new spectral windows, optimum illumination schemes, etc., will be presented, and their impact on further improving the imaging depth, volume, or speed in biological tissues will be quantified.

Biography

Chris Xu is the IBM Professor of Engineering, the Director of School of Applied and Engineering Physics at Cornell University, the founding co-director of Cornell Neurotech, and the director of Cornell NeuroNex Hub. Prior to Cornell, he was a member of technical staff at Bell Laboratories. His current research areas are fiber optics and biomedical imaging, with major thrusts in multiphoton microscopy for deep brain imaging, multiphoton microendoscopy for clinical applications, and fiber-based devices and systems for telecommunications and optical imaging. He is a fellow of the Optical Society of America and a fellow of the National Academy of Inventors.

Translating Big Data and AI for Biomedicine and Healthcare

May Dongmei Wang, Ph.D.

Director of Biomedical Big Data Initiative, Georgia Cancer Coalition Cancer Scholar, Kavli Fellow, FAIMBE, FIAMBE, Carol Ann and David D. Flanagan Faculty Fellow, Petit Institute Faculty Fellow, Professor, Departments of Biomedical Engineering, Electrical and Computer Engineering, IBB, IPaT, Winship Cancer Institute. Georgia Institute of Technology and Emory University, Atlanta, GA 30332-0535, USA

Abstract

Rapid advancements in biotechnologies such as wearable sensors, –omic (genomics, proteomics, metabolomics, lipidomics etc.), next generation sequencing, bio-nanotechnologies, and molecular imaging etc. accelerate the data explosion in biomedicine and health wellness. Multiple nations around the world have been seeking novel effective ways to make sense of "big data" for evidence-based, outcome-driven, and affordable 5P (Patient-centric, Predictive, Preventive, Personalized, and Precise) health care. The goal is develop multi-modal and multi-scale (i.e. molecular, cellular, whole body, individual, and population) biomedical data analytics research for discovery, development, and delivery in biomedical research. Ultimately, the goal is to promote healthy aging, improve quality of patient care, and reduce healthcare cost.

In this talk, I will discuss fasting growing research directions such as emerging HL7 Fast Health Informatics Resource (FHIR) for harmonizing data for integrated genomics, imaging, physiological, and clinical EMR for improving 5P health. I will highlight the current challenges, progresses in medical genomics, especially the next generation sequencing for precision medicine, and share multi-modality –omic integration for clinical decision making. I will summarize opportunities and challenges of advanced AI for translational medicine including wearable sensor informatics for improving patient-centric health monitoring in preventive medicine; next generation sequencing for improving predictive medicine, histopathological imaging informatics for improving precision in clinical decision, and Electronic Health Record data quality control and mining for personalized care quality. There is shortage of biomedical data scientists and engineers capable of handling Biomedical Big Data to meet the need of healthcare stakeholders such as patients, physicians, payers, and hospitals. I will share opportunities for practitioners to get trained in AI for Healthcare and Medicine.

Bio-Sketch

Dr. May Dongmei Wang is a full professor in the Departments of Biomedical Eng. and Electrical and Computer Eng. at Georgia Institute of Technology and Emory University. She is the Director of Biomedical Big Data Initiative, a Kavli Fellow, a Georgia Cancer Coalition Distinguished Scholar, a Carol Ann and David D. Flanagan Faculty Fellow, a Petit Institute Faculty Fellow, an AIMBE Fellow, and an IAMBE Fellow. She earned BEng from Tsinghua University China, and MS/PhD from Georgia Institute of Technology. Her research is in Biomedical Big Data Analytics with a focus on Biomedical and Health Informatics (BHI) for predictive, personalized, and precision health (pHealth). In FDA-organized MAQC international consortium, she led the comprehensive RNA-Seq analytics pipeline investigation. Dr. Wang published over 250 peer-reviewed articles in referred journals and conference proceedings with google scholar citations class to 12,000. She delivered more than 220 invited and keynote lectures. She is a recipient of Georgia Tech Outstanding Faculty Mentor Award for Undergraduate Research and a MilliPub Award (for a high-impact paper that has been cited over 1,000 times) from Emory University.

Dr. Wang was 2015-2016 IEEE Engineering in Medicine and Biology Society (EMBS) Distinguished Lecture and an Emerging Area Editor for PNAS. She serves as Senior Editor for IEEE Journal of Biomedical and Health Informatics, an Associate Editor for TBME, a standing panelist for NIH BCHI, a panelist for NSF, and a reviewer for panels in multiple countries. She has been helping organize ACM Bioinformatics, Computational Biology, and Health Informatics Conferences, and IEEE International Conference on Biomedical and Health Informatics from 2012-Present, co-organized 2016 and 2018 Gordon Research Conference (GRC) on Advanced Health Informatics, and co-chaired 2016 IEEE EMBS Annual Conference of 2,600+ people. She served in IEEE Big Data Initiative (BDI) Steering Committee, and was Vice President of Finance in IEEE EMBS, and has been AIMBE Nomination Committee Chair 2017-2019.

Dr. Wang is Director of Biomedical Big Data Initiative after serving as Georgia Tech Biomedical Informatics Program Co-Director in Atlanta Clinical and Translational Science Institute (ACTSI) and Co-Director of Georgia-Tech Center of Bio-Imaging Mass Spectrometry. Her research has been supported by NIH, NSF, CDC, Georgia Research Alliance, Georgia Cancer Coalition, Shriners' Hospitals for Children, Children's Health Care of Atlanta, Enduring Heart Foundation, Coulter Foundation, Microsoft Research, HP, UCB, and Amazon.

Navigating the risks and opportunities in bioengineering and regenerative medicine product development

Scott P. Bruder, MD, PhD

Bruder Consulting & Venture Group, LLC, USA and Case Western Reserve University, USA

Abstract

Since the time of Robert Langer and Joseph Vacanti's landmark paper on "Tissue Engineering" in 1993, thousands of biologists, clinicians and engineers have sought to develop Regenerative Medicine products to address some of the most challenging and pervasive problems in clinical medicine. As we evolved from the "Age of Chemistry", through the "Age of Engineering" and now into the "Age of Biology", the pace at which our knowledge expands has grown exponentially. While this has created a wide array of incredible laboratory-based solutions that hold promise for treating patients, industrialization of these concepts and navigation of the evolving regulatory landscape represents a formidable challenge. The process of Product Development is very different from the work typically done in university settings, and most early-stage companies are not been equipped to overcome the myriad challenges necessary to garner regulatory approval of these products in the United States or elsewhere. In response to the growing sophistication, complexity and growing demand for such products, the US FDA has crafted a series of Guidance Documents and other policies to help provide a roadmap for those seeking to commercialize products. Naturally, there is some controversy surrounding the interpretation of these rules, led primarily by those who are currently not following them, or those who wish the rules were different. At the close of the discussion, participants will have a greater understanding of the multi-year, multi-step, interactive process required to commercialize new products, with an emphasis on understanding the new paradigm for regulatory approval by the FDA.

Biography

Dr. Bruder is the Founder and CEO of the Bruder Consulting & Venture Group, providing product development, regulatory, compliance and commercialization support for companies and investors focused on tissue repair and regeneration. He is the former CMSO of Stryker and held other C-Suite roles at BD and J&J prior to that. Over the last 25 years he has launched dozens of products, published over 125 papers, abstracts and chapters, received numerous awards and has been elected to the National Academy of Inventors. Dr. Bruder maintains his academic ties as an Adjunct Professor of Orthopaedic Surgery and Biomedical Engineering at CWRU.

Crosslinking of Receptors as a Design Principle for Smart Nanomedicines

Jindřich Kopeček[1,2*], Jiyuan Yang[1], Lian Li[1], Jiawei Wang[1], D. Christopher Radford[2], Michael Gambles[1]

[1]Department of Pharmaceutics and Pharmaceutical Chemistry, [2]Department of Biomedical Engineering, University of Utah, Salt Lake City, Utah 84112, USA

Abstract

Receptor crosslinking can considerably enhance the rate of internalization and/or manipulate the subcellular fate of receptor-bound ligands. A recycling receptor, following crosslinking, may change its subcellular fate and carry the cargo to the lysosomal compartment[1].

The lecture will present two examples of new nanomedicines where the receptor crosslinking was an important design principle:

a) Drug-free macromolecular therapeutics[2] – a new paradigm in nanomedicine where crosslinking of slowly internalizating receptors results in apoptosis of Raji B cells in vitro, in Non-Hodgkin lymphoma animal models, and in cells from patients diagnosed with a variety of B cell malignancies[3].

b) Combination therapy of breast cancer using backbone degradable HPMA copolymer – epirubicin conjugate (KT-1) with a multivalent polymer-anti-PD-L1 peptide antagonist (MPPA). The rationale for this design is that KT-1 converts immunologically "cold" tumors to 'hot' via inducing immunogenic cell death, and then MPPA enhances T cell-mediated anti-tumor immunity by switching the recycling pathway of PD-L1 to lysosomal degradation via multivalent receptor crosslinking[4].

1. Moody P.R., Sayers E.J., Magnusson J.P., et al., Mol. Therapy 23, 1888-1898 (2015).
2. Yang J., Li L., Kopeček J., Biomaterials 190-191, 11-23 (2019).
3. Wang J., Li L., Yang J., et al., Nanomedicine: NBM 16, 217-225 (2019).
4. Li L., Li Y., Wang J., Radford D.C., Kopeček J., Yang J., Adv. Funct. Mater. 30, 1908961 (2020).

Biography

Professor Kopeček is currently Distinguished Professor of Biomedical Engineering and Distinguished Professor of Pharmaceutical Chemistry at the University of Utah. He is an elected member of the US National Academy of Engineering (2011) and elected fellow of the US National Academy of Inventors (2018). Kopeček's research interests are focused on biorecognition of macromolecules, bioconjugate chemistry, drug delivery systems, and self-assembled biomaterials. Hydrogels from his laboratory have been in clinical use and HPMA copolymer - anticancer drug conjugates in clinical trials. Kopeček's Hirsch index is 97; his publications have been cited 33,005 times (GoogleScholar 081320).

Magnetic Gene Delivery: Rotational motion of nanoparticles triggers RNA release under magnetic fields

Mina Kang[1], Justin Fang[1], Daniela Yorkby[1], Hiroshi Matsui[1,2*]

[1]Hunter College of City University of New York, USA

[2]Weill Medical College of Cornell University, USA

Abstract

In recent years, RNA interference (RNAi), a novel technique that involves the regulation of gene expression, has been applied to various therapeutics. With the development of this method, however, carrier systems that could efficiently transfect RNA and release it at desired times and specific locations are becoming high demand. First time, we used cage-shaped iron oxide nanoparticles (nanocages) to release RNAs in melanoma cells as magnetic field triggers rotational motion of nanocages via Brownian relaxation. RNAs were

incorporated inside its cavity, thereby protecting the RNA from the release before hitting the target in body. However, when magnetic fields are applied as nanocages reach to target locations, these nanocages start spinning, and RNAs are released from the cavity with the centrifugation force. Because the size of magnetic nanocages is less than 20 nm, alternating magnetic fields do not induce heating, which can trigger RNA release without denaturing. Traditionally, conventional magnetic hyperthermia of magnetic nanoparticles has been used to induce cell death by heating, but in our knowledge, we demonstrated first time that nanoscale motion of nanoparticles triggers the gene delivery with magnetic fields. In this study, we demonstrated that Silencer Firefly Luciferase siRNA could be delivered to luciferase-expressing melanoma cells by nanocages, triggered by magnetic fields. The nanocages can controlled-release RNA to desired sites by modulating magnetic fields, and viscosity o ECMs, depending on normal or tumor cells, could alter the rotation speed so that the RNA release could be dependent on the cell types.

Biography

Hiroshi Matsui is a well-established nanotechnology scientist with expertise in development of nanoparticle synthesis, biological nanobots, and programmed biomimetic self-assembly systems, and nanobiotechnology, supported by various sources including DOE, NIH, and NSF. His high impact studies in these fields were recognized through his election as a frontier member of the National Academy of Engineering. He is a tenured professor at Hunter College of the City University of New York and also holds an appointment as an Adjunct Professor at Weill Cornell Medicine.

Bioinspired Synthetic Nanobiomaterials for Immunotherapy

Sijia Yi[1,2], Fanfan Du[1], Nicholas Karabin[1], Sharan Bobbala[1], Xiaohan Zhang[1], Hussain Sangji[1,2], Yugang Liu[1], Sean D. Allen[3], Baofu Qiao[4],Baixue Xiao[1], Ha-Kyung Kwon[4], Lei Cai[10], Peter I. Hecker[10,11], Mathew DeBerge[8,9], Edward B. Thorp[8,9], Ryan E. Temel[10,11], Samuel I. Stupp[1,4,5,6,7], Kenneth Shull[4], Monica Olvera de la Cruz[2,3,4,5], Evan A. Scott[1,2,3,7]*

[1]Department of Biomedical Engineering, [2]Chemistry of Life Processes Institute, [3]Interdisciplinary Biological Sciences, [4]Department of Materials Science and Engineering, [5]Department of Chemistry, Northwestern University, IL 60208

[6]Department of Medicine, [7]Simpson Querrey Institute, [8]Department of Pathology, [9]Feinberg Cardiovascular Research Institute, Northwestern University Feinberg School of Medicine, IL 60611, USA

[10]Saha Cardiovascular Research Center, [11]Department of Pharmacology and Nutritional Sciences, University of Kentucky, KY 40536, USA

Abstract

Self-assembled nanobiomaterials that are engineered to achieve specific biodistributions and mechanisms of degradation hold great promise for controlled stimulation of the immune system. Taking advantage of the morphological flexibility of self-assembled systems, we aim to mimic various structures and biochemical mechanisms of pathogens to enhance cell-selective intracellular delivery and treatment efficacy during immunotherapy. We specifically approach this by synthesizing, assembling and optimizing in vitro and in vivo a range of nanostructures loaded with strategically selected combinations of immunostimulants to achieve controlled activation or suppression of the immune system. Here, we will present several novel synthetic platforms for enhanced targeting of immune cell subsets, sustained delivery of drug loaded nanocarriers, and highly efficient multi-drug encapsulation of water-soluble payloads such as proteins, peptides and nucleic acids. Applications in the areas of vaccine delivery, theranostics and anti-inflammatory immunotherapy will be discussed.

Biography

Evan Scott, Ph.D. is an Associate Professor of Biomedical Engineering and Microbiology-Immunology at Northwestern University. He respectively received a B.S. and Ph.D. in Biomedical Engineering from Brown University and Washington University in St. Louis and completed his postdoctoral training at the EPFL in

Switzerland. He is a recipient of the NIH Director's New Innovator Award, National Science Foundation CAREER Award and American Heart Association Scientist Development Grant. He was selected as a BMES Young Innovator of Cellular and Molecular Bioengineering, Nano Research Young Innovator in Nanobiotechnology, National Academy of Engineering Frontiers of Engineering speaker, and a Biomaterials Science Emerging Investigator.

Pulsed Focused Ultrasound Lowers Interstitial Fluid Pressure and Improves Nanoparticle Delivery in Solid Tumor Xenografts

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[5]University of Maryland Greenbaum Comprehensive Cancer Center, Baltimore, MD

[6]Department of Neurosurgery, University of Maryland School of Medicine, Baltimore, MD

[7]Department of Pharmacology, University of Maryland School of Medicine, Baltimore, MD

Abstract

Advancements in nanotechnology provide a promising approach for enhanced delivery of anticancer drugs. The relatively large size of drug-loaded nanoparticles however limits their transport, especially to deeper regions in the tumor core. The delivery of therapeutics is impeded by factors in the tumor microenvironment (TME), including high interstitial fluid pressure (IFP) and fibrillar collagen in the extracellular matrix. Our earlier studies demonstrated how pretreatment of solid tumor xenografts with pulsed focused ultrasound (pFUS) can facilitate the delivery of various agents for improved therapeutic efficacy. These studies also found enlarged extracellular spaces (ECS), reduced tissue stiffness and an increase in hydraulic conductivity. The current study demonstrates an inverse relationship between nanoparticle penetration and increased IFP; the latter being higher at the tumor center. We also show that pFUS pretreatment can decrease the IFP gradient and subsequently increase NP penetration. Using quantitative polarized light microscopy, we show these results to be correlated with effects generated in the fibrillar collagen network microstructure in the ECS. The changes in the ECS were nondestructive and did not alter the tumor cross-sectional area, aspect ratio, collagen area fraction or collagen feature solidity. Based on these and earlier results, we present a biophysical model where pFUS-induced cytoarchitectural changes enhance hydraulic conductivity for improved redistribution of interstitial fluid, leading ultimately to a reduction in IFP for improved delivery and penetration of therapeutics. These results support those of our earlier therapeutic studies, and may facilitate the clinical translation of this procedure for treating cancer patients.

Biography:

Dr. Ali Mohammadabadi received his Ph.D. degree in Mechanical Engineering in 2019 from the University of Maryland Baltimore County. In 2016 he joined the University of Maryland School of Medicine; Department of Diagnostic Radiology and Nuclear Medicine. He is currently working as a postdoctoral researcher at the Translational Focused Ultrasound Laboratory. His research interests include the effects of pulsed focused ultrasound in tissues and the enhanced delivery of therapeutic agents using ultrasound.

Spatial Bioengineering of Single Cells for Visually Encoded Precision Medicine

Ahmet F. Coskun[1]*

[1]*Wallace H. Coulter Department of Biomedical Engineering, Georgia Institute of Technology and Emory University, Atlanta, GA, USA*

Abstract

Spatial organization of cells and subcellular variations in tissues can be considered as a quantitative metric in determining the health and disease states. Single cell analyses of molecular profiles with in-situ detection methods dissect spatial heterogeneity of distinct cell types. Such detailed cellular maps shed light on spatial regulation mechanisms of diseases.

In this talk, I will introduce multiplex imaging modalities to quantify up to hundred markers at macromolecular resolution in single cells. First, we have devised a "spatial genomics" method (seqFISH) to visualize 3D gene expression profiles in single cells. An application of this platform to reveal source-specific heterogeneity in mesenchymal stem cells toward regenerative medicine will be presented. Second, a "subcellular 3D metabolomics" approach to quantify time-encoded 4D dynamics of chromatin, replication, and transcription at 25-nm lateral and 5-nm axial resolution will be discussed. Extension of this platform to 4D spatially resolved metabolic distributions in immune organs has provided tissue compositions. Lastly, a "subcellular proteomics" scheme to determine 5D profiles of nuclear markers in immune/cancer cells within archival patient samples will be demonstrated. Super-resolved protein maps at 100-nm isotropic (x-y-z) resolution in FFPE tissues have suggested spatial hierarchical ordering of epigenetics markers and cellular phenotypes in blood and lung cancers.

Together, image-based molecular profiling, when combined with advanced mathematical theories and computation, has the potential to decode high-dimensional dynamics at the subcellular and molecular level in complex tissues and organs. Automated machine learning algorithms in this single cell big data impact the biomedical practice and clinical care.

Biography

Dr. Coskun is currently an Assistant Professor of Biomedical Engineering at Georgia Tech & Emory Medicine. Dr. Coskun directs an interdisciplinary research team at the Single Cell Biotechnology Laboratory and at the BioEngineering Media Laboratory. He is a recipient of the National Institutes of Health K25 Career Award (2018) and the Burroughs Wellcome Fund CASI Award (2016). Previously, Dr. Coskun was an Instructor at Stanford University School of Medicine. Dr. Coskun is an alumnus of the Ignite Entrepreneurship Program at the Stanford University. Dr. Coskun received his postdoctoral training from the Caltech and holds a Ph.D. degree from UCLA.

Mammalian Synthetic Biology: Foundation and Therapeutic Applications

Ron Weiss

Massachusetts Institute of Technology

Abstract

Synthetic biology is revolutionizing how we conceptualize and approach the engineering of biological systems. Recent advances in the field are allowing us to expand beyond the construction and analysis of small gene networks towards the implementation of complex multicellular systems with a variety of applications. In this talk I will describe our integrated computational / experimental approach to engineering complex behavior in a variety of cells, with a focus on mammalian cells. In our research, we appropriate design principles from electrical engineering and other established fields. These principles include abstraction, standardization, modularity, and computer aided design. But we also spend considerable effort towards understanding

what makes synthetic biology different from all other existing engineering disciplines and discovering new design and construction rules that are effective for this unique discipline. We will briefly describe the implementation of genetic circuits and modules with finely-tuned digital and analog behavior and the use of artificial cell-cell communication to coordinate the behavior of cell populations. The first system to be presented is a multi-input genetic circuit that can detect and destroy specific cancer cells based on the presence or absence of specific biomarkers in the cell. We will also discuss preliminary experimental results for obtaining precise spatiotemporal control over stem cell differentiation for tissue engineering applications. We present a novel approach for generating and then co-differentiating hiPSC-derived progenitors with a genetically engineered pulse of GATA-binding protein 6 (GATA6) expression. We initiate rapid emergence of all three germ layers as a combined function of GATA6 expression levels and tissue context. We ultimately obtain a complex tissue that recapitulates early developmental processes and exhibits a liver bud-like phenotype that includes haematopoietic and stromal cells, as well as a neuronal niche. This complex organoid can be used for drug development and potentially for tissue transplantation.

Inertial Sensing for Transfemoral Amputee Gait Detection

Elissa Ledoux

Middle Tennessee State University, USA

Abstract

While conventional microprocessor-controlled prosthetic knees use a multitude of sensors for gait detection and control, this array of electronics could ideally be reduced to one, simplifying both control and mechatronic design while reducing cost. As revealed through experimentation and data analysis, it is possible to accurately detect walking gait events using a single inertial measurement unit mounted on the shank. Experiments were conducted on 10 healthy subjects and 5 transfemoral amputees to detect heel strike and toe off while walking at various speeds and slopes on an instrumented treadmill. Three different algorithms (thresholding, linear discriminant analysis, and quadratic discriminant analysis) were used to process the data with reliable indication of both timing and frequency of gait events, although the thresholding algorithm performed the most accurately (100% event frequency detection within 2% stride time). Furthermore, universal parameters within each demographic could be used on all speeds and slopes. This results in a robust, simple, and inexpensive method of gait event detection using a single inertial sensor that could be easily implemented in a transfemoral prosthesis and the possibility of methodological extension to pathological gait detection for other lower-limb orthotic applications.

Biography

Despite beginning as a preschool dropout, Elissa found her passion for academics and graduated from Lousisiana State University in 2013 with a B.S. in Mechanical Engineering. She earned her M.S. in Mechanical Engineering from Vanderbilt University in 2016, with a focus on robotic prosthetics research as part of the NSF GRFP. After working at an industrial robotics startup for a time, she joined the Engineering Department at Middle Tennessee State University in 2018. Her research interests include design and control of rehabilitation robotics and robotic end effectors.

Surface Area to Volume Ratio of Electrospun Polydioxanone Templates Regulates the Adsorption of Soluble Proteins from Human Serum

Allison E. Fetz[1], Cristina A. Fantaziu[1], Richard A. Smith[2], Marko Z. Radic[3] and Gary L. Bowlin[1*]

[1]Department of Biomedical Engineering, University of Memphis, Memphis, TN, USA

[2]Department of Biomedical Engineering, College of Medicine, University of Tennessee Health Science Center, Memphis, TN, USA

[3]Department of Microbiology, Immunology, and Biochemistry, College of Medicine, University of Tennessee Health Science Center, Memphis, TN, USA

Abstract

Upon implantation of a biomaterial for guided tissue regeneration, neutrophils swarm to the site of inflammation where they interact with surface-adsorbed proteins on the biomaterial and can respond through the release of neutrophil extracellular traps (NETs). Because NETs are associated with inflammation and fibrosis, acute release on the surface of biomaterials may function as a significant adverse preconditioning event for in situ tissue regeneration. Recently, our group demonstrated that the surface area to volume ratio (SAVR) of electrospun polydioxanone (PDO) regulates the release of NETs with high SAVR (i.e. small diameter (SD) fibers) significantly up-regulating NET release compared to low SAVR (i.e. large diameter (LD) fibers). In this study, we quantified the in situ adsorption of abundant human blood serum proteins on SD and LD templates to begin understanding how protein adsorption may be linked to the strikingly different release of NETs. The results indicate that albumin and IgG adsorbed readily and increased significantly over time with SD templates adsorbing significantly more protein ($p < 0.05$) compared to LD templates. However, compared to albumin, IgG adsorption was 100- to 200-times greater, indicating its dominant adsorption on the biomaterial surface. By half an hour, nearly 4-times more IgG adsorbed on the SD templates compared to the LD templates, suggesting that the SAVR-dependent adsorption of IgG may be linked to the differential modulation of NET release. Future work includes evaluating the interaction of neutrophils with adsorbed IgG through their Fcč receptors and investigating their involvement in NET release. Ultimately, understanding the neutrophil response to electrospun biomaterials as a preconditioning event may enhance the design of immunomodulatory biomaterials for biomaterial-guided in situ tissue regeneration.

Biography

Dr. Bowlin is a Professor and Herbert Herff Chair of Excellence at The University of Memphis in the Department of Biomedical Engineering. He received his Ph.D. from the University of Akron in Biomedical Engineering. His collaborative research has and continues to focus on the application of electrospun templates for tissue regenerative applications. Dr. Bowlin's laboratory has published extensively with over 140 peer-reviewed, highly-cited manuscripts. He is a Fellow of the National Academy of Inventors and the American Institute for Medical and Biological Engineering.

Modeling Diseases in Human Vascular Microphysiological Systems

George A. Truskey*, Xu Zhang, Ellery Jones, and Nadia Abutaleb

Duke University, Department of Biomedical Engineering, Durham, NC USA

Abstract

Human microphysiological systems using cells derived from individual with various genetic or acquired

diseases hold great promise to model these diseases in vitro and thereby provide more accurate systems to evaluate promising therapeutic approaches. Towards this end, we have developed models for the rare, accelerated aging disease Huntington-Gilford Progeria Syndrome (HGPS) and early-stage atherosclerosis. For HGPS, tissue engineered blood vessels (TEBVs) are fabricated with endothelial cells and smooth muscle cells differentiated from patient-derived induced pluripotent stem cells (iPSCs). These TEBVs replicate the disease pathology including reduced smooth muscle cell content, greater vessel wall thickness, altered vasoactivity and calcification. A novel observation is that the HGPS endothelium is proinflammatory which could exacerbate disease conditions. These disease processes can be reversed by treatment with the farnesyltransferase inhibitor (FTI) lonafarnib and the rapamycin analog everolimus, with functional restoration. In modeling early atherosclerosis, we can reproduce steps in endothelial dysfunction, monocyte and foam cell formation induced by modified forms of low-density lipoprotein (LDL). Fabricating TEBVs with chondroitin sulfate glycosaminoglycans in the extracellular matrix leads to further increases in monocyte accumulation. Initial results suggest that elevated levels of branched chain amino acids, which are associated with increased risk of type 2 diabetes and cardiovascular disease, act in concert with modified LDL to cause endothelial dysfunction and lead to increased monocyte accumulation. These results demonstrate that these model systems can identify key factors influencing disease progress that can then be targeted for drug development.

Biography

George A. Truskey, PhD, is the R. Eugene and Susie E. Goodson Professor of Biomedical Engineering at Duke University. He has made major contributions to understanding endothelial cell adhesion to biomaterials and cell mechanical properties measured by atomic force microscopy. His current research interests focus on the development of human microphysiological systems for disease modeling. He is Editor-in-Chief of Current Opinion in Biomedical Engineering and is a Fellow of the American Association for the Advancement of Science, Biomedical Engineering Society, American Institute of Medical and Biological Engineering, the American Heart Association, and the International Academy of Medical & Biological Engineering.

Biopolymer Hydrogels for Articular Cartilage Repair and Regeneration

Alyssa Panitch[1]*, Clair Kilmer[2], Nelda Vazquez[1,2] and Julie Liu[2]

[1]University of California, Davis, USA and [2]Purdue University, USA

Abstract

Osteoarthritis (OA), a debilitating condition defined by degradation of the extracellular matrix in articular cartilage, affects over 27 million people in the United States alone. While several treatment options are available, there is no cure for OA, and most options aimed at cartilage repair promote the growth of fibrocartilage, which is inferior to the mechanical properties of native cartilage. Here, we describe a tissue engineering approach to repair. Collagen hydrogels are an attractive scaffold option since collagen is biocompatible and can take on any desired defect shape. Collagen type I continues to be the most utilized type of collagen in tissue engineered scaffolds even though collagen type II is the most abundant type of collagen produced by chondrocytes and is prevalent in hyaline cartilage. In addition, collagen type II has been shown to promote the secretion of ECM molecules specific to cartilage by mesenchymal stem cells (MSCs) but exhibits poor mechanical properties when forming a hydrogel without chemical crosslinking. Taking advantage of the ability of collagen types I and II to copolymerize into gels that exhibit mechanical properties similar to those of collagen type I and biological properties including those of collagen type II, we prepared hydrogels composed of types I and II collagen to investigate cartilage repair. We seeded rabbit mesenchymal stem cells into the hydrogels and evaluated chondrogenesis in vitro, and the ability to support hyaline cartilage repair in an in vivo rabbit cartilage defect model. Gels incorporating collagen type II showed improved structure, cellularity and tissue integration.

Biography

Dr. Panitch completed her Ph.D. in Polymer Science and Engineering at the University of Massachusetts, Amherst and her postdoctoral fellowship at the Swiss Federal Institute of Technology (ETH) and University of Zurich. She is the Edward Teller Professor of Biomedical Engineering and the Executive Associate Dean at the University of California, Davis. Dr. Panitch specializes in biopolymer design and controlled release. Her research interests include the design and synthesis of biomaterials for drug delivery and the development of biomimetic therapeutics for vascular, cartilage, dermal, neural and fibrotic diseases.

Eggshell microparticle-reinforced biomaterials for bone regeneration

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Abstract

More than two million bone graft procedures are performed each year to treat patient defects due to aging, degeneration, cancer, accidents, diseases, and war injuries. We hypothesized that incorporation of eggshell microparticles (ESP) into protein-based hydrogels will enhance osteogenic differentiation and bone regeneration due to the superior biophysical properties of calcium carbonate. Although they are readily available, sustainable, and cost-effective, the potential of eggshells in bioengineering applications remains greatly understudied.

In this work, we developed ESP-reinforced gelatin-based hydrogels to obtain mechanically stable and biologically active 3D scaffolds that can differentiate pre-mature cells into osteoblasts. We investigated the physical properties including swelling ratio, degradation, porosity, and mechanical properties of the composite hydrogels. Pre-osteoblasts were encapsulated within these hydrogels to study their differentiation and mineral deposition by the cells. The ESP-reinforced gels were then subcutaneously implanted in rats to determine their biocompatibility and degradation. Finally, these scaffolds were implanted into critical size cranial defects in rats and bone regeneration was evaluated after 6 and 12 weeks.

The ESP-reinforced composite hydrogels have shown outstanding tunability in physical and biological properties holding substantial promise for engineering mineralized tissues. The composite gels exhibited significant enhancement in mechanical properties and mineralization. These 3D scaffolds were osteoinductive and osteoconductive. The in vivo experiments exhibited biodegradation of the ESP-reinforced hydrogels and indicated no inflammatory response. The implants were easily accepted by the host, allowed for cellular migration and infiltration in 3D, and highly vascularized. We achieved near complete regeneration of the critical size cranial defects after 12 weeks.

Biography

Gulden Camci-Unal is a fourth-year Assistant Professor in the Department of Chemical Engineering at the University of Massachusetts Lowell. Her multidisciplinary work in biomaterials, bioengineering, and diagnostics has made important contributions in generation of engineered platforms for cardiovascular and bone tissue engineering, wound healing, and disease detection including bacterial and viral conditions. Her current research interests include design and implementation of engineered constructs for regeneration of tissues, paper-based biomaterials and medical devices for personalized medicine, and low-cost POC diagnostics. Her research has been supported by the US Army, Congressionally Directed Medical Research Programs (CDMRP), and the American Heart Association (AHA).

Cardiac-Specific Nanofibrous Scaffold for Cardiac Tissue Engineering

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Abstract

Natural extracellular matrix (ECM) possesses immunoregulatory and regenerative properties due to its conjugated paracrine factors, matrix-bound nanovesicles, and degradation peptides. Tissue-engineered cardiac patches with cardiac specific ECM and mature cardiomyocytes (CMs) have great potential to promote cardiac remodeling after myocardial infarction (MI). In the native myocardium, cardiac fibroblasts (CFs) regulate ECM deposition and cell communication. In addition, they display a unique molecular profile with CM ontogenesis associated cardiogenic transcription factors, compared to non-CF fibroblasts. However, the application of primary CFs (Pri-CF) has been limited by their resources and slow proliferation rate. Human pluripotent stem cell (hPSC) derived CFs (hPSC-CFs) can potentially overcome these limitations. Another unmet challenge of cardiac tissue engineering is the differentiation and maturation of human induced PSC-derived CMs (hiPSC-CMs), due to their inferior action potential and contractile force generation compared to native CMs. We expect that a CF-derived ECM will provide a cardiac tissue-specific microenvironment to enhance iPSC-CM's structural and functional maturation. The objective of this study was to develop a completely biological, anisotropic, nanofibrous ECM scaffold carrying cardiac-specific bioactive components by the decellularization of highly aligned hPSC-CF sheets. We have successfully created such a highly aligned nanofibrous ECM scaffolds by decellularizing both hPSC-CF and Pri-CF cell sheets. hiPSC-CMs cultured on both of these decellularized ECM sheets exhibited enhanced alignment following ECM anisotropy and matured organization of structural proteins. Such a highly biomimetic cardiac-specific scaffold holds great promise for cardiac tissue regeneration.

Biography

Dr. Feng Zhao is an associate professor in the Department of Biomedical Engineering at Texas A&M University. Her lab seeks to address the challenges associated with engineering cardiovascular, lymphatic and skin tissues for regenerative medicine applications. Dr. Zhao's research has been well supported by NIH, NSF, and other funding agencies. She has published more than 80 peer-reviewed journal papers and book chapters. Her research products have been highlighted by various national and international news agencies, newspapers, and scientific publishers.

Resorbable Scaffolds of Polybutylene Succinate for Soft Tissue Repair and Support

David Martin*, Skander Limem, Jeffrey Scott, Michael Bache, Kai Guo, Simon Williams and Said Rizik

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Abstract

Resorbable scaffolds are an attractive alternative to permanent materials to support soft tissue in hernia, sports medicine, urogynecology and plastic and reconstructive surgeries. Porous scaffolds that can provide initial support, allow tissue in-growth and eventually degrade and remodel into healthy living tissue may overcome some of the long-term problems associated with permanent materials such as infection, encapsulation and chronic foreign body reaction. Polymeric devices are also much less expensive than human or animal derived biological alternatives such as acellular dermal matrices.

Polybutylene succinate (PBS) is a biodegradable polyester that has not been used in implantable medical devices. High purity PBS was melt-extruded into monofilament fibers and knitted into resorbable scaffolds.

The PBS scaffolds passed all required ISO 10993 standards testing for biocompatibility. In vitro degradation testing in phosphate buffered saline solution demonstrated predictable Mw and strength degradation profiles. A rabbit model for subcutaneous implantation was used to determine the in vivo strength and Mw retention profiles. The strength retention of the scaffolds was similar to that of the class-leading competitive scaffolds based on poly-4-hydroxybutyrate. Histopathology of the peri-implant tissue demonstrated a minimal tissue reactivity. The hydrolytic degradation products of PBS are degraded via 4-hydroxybutyrate and succinate and eliminated through the Krebs cycle as carbon dioxide and water. Long-term studies are underway to confirm the functionality of the PBS scaffolds in a porcine model of hernia repair.

The development of novel PBS-based devices will be presented and discussed with an eye towards developing scaffolds for applications in soft tissue reconstruction.

Human organ-on-a-chip models for predictive drug screening to determine anti-tumor efficacy and cardiac safety

Alan Chramiec[1*], Diogo Teles[1,2,3], Keith Yeager[1], Alessandro Marturano-Kruik[1,4], Joseph Pak[1], Timothy Chen[1], Luke Hao[1], Miranda Wang[1], Roberta Lock[1], Daniel Naveed Tavakol[1], Marcus Busub Lee[1], Kacey Ronaldson-Bouchard[1], and Gordana Vunjak-Novakovic[1,5]

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Abstract

Traditional drug screening models used in preclinical research are unable to faithfully recapitulate human physiology, leading to inefficiencies in clinical trials. Organ-on-a-chip (OOC) platforms have since been developed to more accurately mimic native human tissues. Unfortunately, these integrated OOC systems have thus far been limited by their complexity, size, and dependence on polydimethylsiloxane (PDMS). In this study, we report the design and utilization of a novel, integrated, open setting, PDMS-free, imaging and sampling accessible, polysulfone-based platform uniquely featuring minimal hydrophobic compound binding that allows for simultaneous assessment of a drug's anti-tumor efficacy and cardiotoxicity. Previously, we had published bioengineered models of Ewing sarcoma (ES) and iPSC-derived cardiac tissues: the former recapitulated critical tumor phenotypes within a native bone tissue milieu, while the latter demonstrated adult-like cardiac physiology and function. The two bioengineered OOCs were treated in isolation and in the integrated platform with linsitinib, an anti-cancer drug currently in phase II clinical trials for ES, according to the 3 week-long clinical regimen. Overall, the responses to drug treatment of non-metastatic and metastatic tumors, and of the cardiac tissue, were much more in line with clinical observations than those observed with conventional culturing. Moreover, the inclusion and treatment of the tissues within the integrated platform yielded more accurate predictability for both the direct and off-target effects of linsitinib. Therefore, our novel platform addresses several of the practical challenges of translating OOC platforms into workable systems for drug screening, with more efficient data collection and clinically relevant interpretation.

Biography

I received my bachelor's degree cum laude from Cornell University in 2013, with an honor's thesis on bacterial genetic engineering. I was subsequently a research technician in Dr. Scott Armstrong's lab at Memorial Sloan Kettering Cancer Center, where I acted as a founding member of the Center for Epigenetics Research by establishing an automated epigenetics core facility. Currently I am pursuing my PhD in Dr. Gordana Vunjak-Novakovic's laboratory, where I am focused on the development of novel multi-tissue platforms for the evaluation of chemotherapeutic target and off-target tissue toxicities, as well as on the modeling of breast cancer metastatic progression.

Protein Therapeutic Manufacturing at the Point of Care

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Abstract

Funded by DARPA's "Biologically-derived Medicines on Demand (Bio-MoD) Program," we demonstrated the feasibility of protein therapeutics manufacturing at the point-of-care. Protein therapeutics, also known as biologics, are currently manufactured at centralized facilities according to rigorous protocols collectively referred to as Current Good Manufacturing Practices (cGMP). Since such facilities require multiple years to design, build, activate, and qualify, they are unsuited to respond to rapid changes in demand. The Bio-MOD technology combines in vitro protein expression (IVT) from lyophilized cell lysates with microfluidic purification methods to produce highly purified products in a few hours using an automated platform with built-in diagnostics to monitor process consistency. Essentially, this manufacturing technology reduces a large GMP facility into the size of a box. To demonstrate the potential of IVT in the production of biologics, His-tagged granulocyte-colony stimulating factor (G-CSF) produced by IVT was subjected to rigorous product characterization and validation. Our results demonstrate that the structure and potency of IVT-generated G-CSF-His are comparable to those of reference products generated by the biotechnology industry. The Bio-MOD technology establishes a new paradigm for dosage level, point-of-care manufacturing of biologics with consistent control in the end-to-end production of a pure and potent protein product.

Biography

Dr. Leah Tolosa Croucher is Research Professor and Assistant Director of the Center for Advanced Sensor Technology at the University of Maryland Baltimore County. She obtained her BS and MS in Chemistry from the University of Santo Tomas in Manila, Philippines and her PhD in Biological Chemistry from the University of Connecticut in Storrs. Her expertise is in fluorescent sensors and biosensors, training under Drs. Vijay Kumar and Joseph Lakowicz. Dr. Tolosa has worked as Project Manager and Principal Investigator for 18 years in the academe-industry hybrid, Center for Advanced Sensor Technology, by initiating study investigations and projects to their successful completion. She has instigated collaborative research in engineering, chemistry, and biotechnology, enabling scientific achievements in multidisciplinary projects, creating methods, products, and devices for biomedical, biotechnological and bioprocessing applications under GLP and GMP.

Efficacy of engineered skin grafts prevascularized with skin-specific and non-specific endothelial cells

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[2]Columbia University, Department of Biomedical Engineering, USA

Abstract

In light of the growing evidence for organotypic vasculature, there is a need for further research into recapitulating endothelial cell (EC) heterogeneity in bioengineered organs. As we previously showed, vascularization of human skin constructs (HSCs) greatly improves survival of engineered skin and hair follicles on mice. The insufficient availability of human dermal blood ECs (HDBECs), often led researchers to utilize human umbilical vein ECs (HUVECs) to vascularize skin models, regardless of tissue-specificity of endothelium. Induced pluripotent stem cell-derived endothelial cells (iECs) also feature a promising autologous cell source to generate bioengineered vasculature in HSCs. Yet, it is uncertain whether iECs and HUVECs can equate HDBECs vascularization efficiency in HSCs, and represent an alternative cell source for skin replacement therapy. We assessed HDBECs, HUVECs, and iECs by quantitative comparison of gene expression and vas-

culature generation within HSCs in vitro and engrafted onto mice. HSCs vascularized with HDBECs in vitro developed a thin and elongated network; HUVECs generated larger and branched vessels; and iECs formed short rudimentary structures. In immunodeficient mice, HSCs with HDBECs and HUVECs exhibited a similar neovascularization and maintained the proliferative state of basal keratinocytes. HSCs vascularized with iECs also developed a good quality epidermis, despite a lower number of proliferative basal keratinocytes. Globally our data suggests that HUVECs and iECs may be a suitable alternative to HDBECs to support graft viability in mice. Nevertheless, the significant differences showed in autonomous vascular development in HSCs in vitro may affect their long-term outcome and realistic use in skin replacement therapy.

Biography

Dr. Hasan Erbil Abaci is a tenure-track Assistant Professor at Columbia University, Department of Dermatology, focusing on the recapitulation of skin and tissue-specific vascular microenvironments using state-of-the-art microfabrication tools. He received his Ph.D. degree from the Johns Hopkins University in Dr. Sharon Gerecht's lab and postdoctoral trainings in Drs. Michael Shuler and Angela Christiano's labs, working on tissue engineering of blood-brain-barrier and skin, as part of the NCATS Microphysiological Systems consortium. Dr. Abaci recently received the Ines Mandl Fellowship and K01 grant from NIAMS. His current research includes understanding of skin-specific vasculature and engineering improved skin and hair follicle substitutes.

Engineered models to study the role of innervation in cancer

Thanh Le & Madeleine J. Oudin*

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Abstract

Metastasis, the dissemination of cells from the primary tumor, is the leading cause of death in breast cancer patients. Peripheral nerves are present in the tumor microenvironment and associated with poor outcome in breast cancer, although their role in breast tumor progression and metastasis remains poorly studied, largely due to the lack of models available to study innervation in cancer. Our goal was to characterize the types of nerves breast in breast tumor tissue, develop in vitro 2D and 3D models to co-culture nerves and cancer cells, and evaluate the impact of nerves on cancer progression. First, we analyzed gene expression data from publicly available data sets and found markers of sympathetic, parasympathetic and sensory neurons, and confirmed their presence by immunostaining of human samples. Second, we set out to optimize a co-culture system of invasive breast cancer cells and primary neurons to study the interaction between nerves and cancer. We used peripheral nerves isolated from different ganglia of female adult mice to obtain populations enriched for the three neuronal subtypes identified and human neural stem cells differentiated to different lineages. Our data show that co-culture with sensory neurons enhances invasive breast cancer cell migration and proliferation, while sympathetic nerves had no effect. Finally, we repurposed microfluidic devices to study how cancer cells regulate nerve axon extension to better understand the mechanisms of tumor innervation. Through building novel engineering models of cancer, we are working to elucidate the role of nerve-cancer crosstalk in cancer progression.

Biography

Madeleine Oudin is an Assistant Professor in the department of Biomedical Engineering at Tufts University. She completed her PhD in Neuroscicence at King's College London, UK under the supervision of Prof. Patrick Doherty working on neuronal cell migration and her post-doctoral research with Prof. Frank Gertler at the Koch Institute for Integrative Cancer Research at MIT trying to understand how mechanisms of cancer metastasis and drug resistance. Currently, research in her lab lies at the intersection of cell biology, translational research, and bioengineering where we investigate the role of the tumor microenvironment in driving cancer metastasis and drug resistance.

3D Models to Study Tumor and Immune Cell Recruitment Following Normal Tissue Radiation Damage

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[2]Department of Biomedical Engineering, Vanderbilt University, USA

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Abstract

Triple negative breast cancer (TNBC) recurrence rates remain high despite aggressive therapeutic intervention, including surgery, chemotherapy, and radiotherapy (RT). Recent studies suggest that circulating tumor cell re-seeding of primary tumors may enable recurrence rather than persistent tumor cells in the irradiated surgical bed. However, the role of the microenvironment in recurrence is not well understood. We studied the influence of the immune system in tumor cell recruitment to radiation-damaged sites. We characterized the effects of normal tissue irradiation on tumor and immune cell migration. We found that RT stimulates tumor cell recruitment in immunocompromised mice and that CD8+ T cells inhibit tumor cell migration to normal tissues. Tumor cell recruitment was shown to be coupled with excess macrophage infiltration. Using 3D mammary epithelial organoids and extracellular matrix hydrogels, we determined that radiation facilitates normal tissue damage that enhances immune cell infiltration as well as tumor cell proliferation and invasion. Taken together, these results indicate that irradiation of normal tissues may produce a microenvironment suitable for tumor cell recruitment, retention, and proliferation, especially under immunosuppressed conditions. Our work suggests that the tumor stroma may enable TNBC cell recruitment and regrowth following RT in immunocompromised patients. This study represents an important step toward elucidating the contribution of stromal cells and immune status to local recurrence following therapy in breast cancer. Future studies will utilize these results to engineer improved in vitro tumor microenvironment models to probe the complex physical, chemical, and biological cues that promote TNBC recurrence and metastasis.

Biography

Dr. Marjan Rafat received her undergraduate degree in Chemical Engineering at the Massachusetts Institute of Technology. She earned her PhD at Harvard University where she focused on fabricating injectable and multi-functional biomaterials for modulating cell behavior. During her postdoc in Radiation Oncology at Stanford University, she studied how normal tissue damage alters tumor and immune cell behavior. Dr. Rafat currently applies chemical and biomedical engineering concepts toward understanding the mechanisms driving breast cancer recurrence and metastasis. Her interdisciplinary laboratory at Vanderbilt University examines and models the tumor and tissue microenvironment.

Organs-On-Chips: Next Generation Platforms for Toxicological Studies of Engineered Nanomaterials

Herdeline Ann M. Ardoña,[1*] Seungkuk Ahn,[1] Feyisayo Eweje,[1] John F. Zimmerman,[1] Blakely O' Connor,[1] George J. Touloumes,[1] Evan K. Casalino,[1] Christophe O. Chantre,[1] Thomas Grevesse,[1] Johan Lind,[1] Dimitrios Bitounis,[2] Philip Demokritou[2] and Kevin Kit Parker[1]

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Abstract

While engineered nanomaterials (ENMs) have emerged as important components in various consumer products, human exposure to ENMs has been associated with negative health outcomes such as respiratory and

cardiovascular diseases. To completely understand the mechanisms related to such ENM-induced diseases, there is a pressing need to develop physiologically relevant models in vitro that faithfully recapitulate the native form and function of an organ or tissue. Moreover, it is also important to accurately model the uptake, transport, and systemic distribution of nanomaterials through pertinent biological barriers models. Organs-on-chips (OOC) offer a potential solution to many of these challenges, by providing a platform that can be rationally designed and built from the ground up to mimic the native target organ and barrier functions. This talk will highlight our work on this area, showing particular advances on developing chip-based cardiac models for toxicology screening. The design criteria for building these platforms include cellular organization, fiber topography and alignment, substrate stiffness, and the capability of a device to non-invasively deliver electrical cues. Our chip-based analytical platforms can measure contractile stress and beat rates, which can serve as a metric of tissue function. By having access to testing platforms that mimic organ-specific drug or toxicant delivery, we allow for high throughput screening in vitro under physiologically relevant conditions that can be standardized.

Biography

Herdeline Ardoña is originally from Valenzuela City, Philippines. She received her B.S. in Chemistry from the University of the Philippines (UP) Diliman in 2011. In 2017, she completed her Ph.D. in Chemistry at Johns Hopkins University. Her dissertation is focused on developing optoelectronic peptide assemblies towards bioscaffolding applications. Currently, Herdeline is a postdoctoral researcher in the Disease Biophysics Group at the Wyss Institute for Biologically Inspired Engineering at Harvard. As the 2018-2020 ACS Irving S. Sigal Postdoctoral Fellow, she is investigating the structural and functional impacts of multiple engineered nanomaterials through microphysiological platforms and biohybrid models.

Designing Microenvironments for Cardiovascular Disease Investigations

Renita E. Horton*

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Abstract

Cardiovascular diseases (CVDs) are the leading cause of death globally. Central to CVDs is inflammation which contributes to tissue damage, fibrosis, and vascular and endothelial dysfunction. Current challenges with in vitro CVD models include recapitulating the architecture of ventricular and vascular tissue, quantifying contractile function, and tissue dysfunction. Creating in vitro systems capable of mimicking both structural and functional properties of the cardiovascular system can be beneficial in mechanistic and drug efficacy studies. We have utilized angiotensin II (ANG II) to elicit pathological responses in a CVD chip platform. ANG II, an octapeptide of the renin-angiotensin system, is important in cardiovascular homeostasis and pathogenesis, contributing to pathophysiological cardiac remodeling, endothelial dysfunction, and ultimately, heart failure. The goal of this study was to demonstrate that our system could effectively recapitulate features of CVD, specifically cardiac and endothelial dysfunction, by testing the effects of ANG II on the pathological remodeling of engineered cardiac and endothelial tissues. We found that ANG II exposure led to functional decline in cardiac tissues, evident in arrhythmias and decreased contractile stress generation. Further, we found that ANG II contributed to elevated reactive oxygen species levels in our system. Results from this study can be used to design mechanistic studies to better characterize receptor contributions to physiological or pathological states and identify novel pathways for ANG II induced CVDs. We assert that this in vitro model is a suitable tool for disease studies and has the potential to serve as a testbed for drug treatment strategies.

Biography

Dr. Renita Horton joined the Cullen College of Engineering at the University of Houston in January 2019. Her research focuses on understanding the factors that lead to heart disease and sickle cell anemia. She is the Principal Investigator of the Cardiovascular Tissue Engineering Laboratory (CTEL) that focuses on developing tools and techniques to investigate cardiovascular disease development and progression. She received

her BS in Chemical Engineering from Mississippi State University and her MS and PhD in Engineering Sciences with an emphasis in Biomedical Engineering from Harvard University.

Circadian Control of Organoid Physiology

Juan R. Alvarez-Dominguez[1*], Julie Donaghey[1], Niloofar Rasouli[1], Jennifer H. R. Kenty[1], Aharon Helman[1], Jocelyn Charlton[1,2], Juerg R. Straubhaar[1], Alexander Meissner[1,2], Douglas A. Melton[1]

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Abstract

Stem cell-derived tissues could transform disease research and therapy, yet most methods generate functionally immature products. We investigate how human pluripotent stem cells (hPSC) differentiate into pancreatic islets in vitro by profiling DNA methylation, chromatin accessibility, and histone modification changes. We find that enhancer potential is reset upon lineage commitment, and show how pervasive epigenetic priming steers endocrine cell fates. Modeling islet differentiation and maturation regulatory circuits reveals genes critical for generating endocrine cells and identifies circadian control as limiting for in vitro islet function. Entrainment to circadian feeding/fasting cycles triggers islet metabolic maturation by inducing cyclic synthesis of energy metabolism and insulin secretion effectors, including antiphasic insulin and glucagon pulses. Following entrainment, hPSC-derived islets gain persistent chromatin changes and rhythmic insulin responses with a raised glucose threshold, a hallmark of functional maturity, and function within days of transplantation. Thus, hPSC-derived tissues are amenable to functional improvement by circadian modulation.

Biography

Juan joined the Melton lab in the summer of 2015. His work aims to build a systems-level understanding of the development and maturation of human stem cell-derived islet organoids, with a view to finding ways to grow lab-matured organoids for diabetes modeling and treatment.

Juan received his PhD in Biology from the Massachusetts Institute of Technology, where he studied the modulation of lineage-specific cell differentiation by long non-coding RNAs, and his A.B. in Molecular Biology from Princeton University, where he studied the role of DNA self-catalytic depurination in site-specific mutagenesis.

Having trained many undergraduate and master's students, Juan is devoted to undergraduate science education and mentoring.

Microvasculature on chip for cancer models

Zhengpeng Wan (Jason) [1]* and Roger D. Kamm[1,2]

[1]Department of Biological Engineering, Massachusetts Institutes of Technology, Cambridge, MA, USA;

[2]Department of Mechanical Engineering, Massachusetts Institutes of Technology, Cambridge, MA, USA

Abstract

Microvasculature is essential for oxygen delivery and nutrient/waste exchange, plays an important role in tumor pathophysiology and prognosis. Over the past two decades, our ability to realistically model the critical biological steps in development and disease has dramatically improved, due in part to advances in microfluidic technologies. Microfluidics is invaluable for studying microvasculature, incorporation of microvasculature into engineered organs or microtissues and development of disease on-chip models. These techniques recapitulate many key features of 3D microenvironments, including microvascular perfusion and multiple cell

types interactions, have led to in vitro models offer considerable advantages over in vivo experiments. This presentation will address some recent advances in creating microvascular networks by different sources of endothelial cells in vitro and using these to model the vascularized organoids, cancer metastasis, as well as tumor vascularization.

Biography

Zhengpeng Wan (Jason) is currently a postdoc working with Dr. Roger D. Kamm, the Cecil and Ida Green Distinguished Professor of Biological and Mechanical Engineering at MIT. Before joining Kamm lab, he trained as an immunologist working on B lymphocyte mechanobiology in Dr. Wanli Liu's lab and graduated from Tsinghua University, China. A primary objective of his research in Kamm lab is vascularization in tumor models, in particular, long-lasting microvascular networks formation, molecular mechanisms of emerging vasculature and immunotherapy in cancers.

Vibrational Optical Coherence Tomography

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[3] Department of Pathology and Laboratory Medicine, Robert Wood Johnson Medical School, Rutgers, The State University of New Jersey, USA

Abstract

Numerous methods have been used to evaluate the mechanical properties of materials both in vitro and in vivo, including three-point bending, uniaxial tensile testing, Magnetic Resonance Elastography (MRE), Ultrasound Elastography (UE) and Optical Coherence Elastography (OCE). In vitro methods of measurement are mostly destructive in nature, while in vivo techniques are expensive, provide a lower spatial resolution or are in nascent stages of development. Biological tissues exhibit a nonlinear mechanical behavior and have a rapidly rising stress-strain curve. This makes it arduous to determine an accurate slope for the tangent to the curve and the modulus changes as a function of strain.

The purpose of this article is to present the results of a low-cost methodology to evaluate the mechanical properties of soft tissues and polymeric materials in-vivo, non-destructively. This novel method utilizes the characteristic resonant frequency of each sample and computes an elastic modulus for each major component of composite materials. The results presented in this talk summarize our lab's research on skin, cornea, vessel wall, cartilage, tendon, nerve, and muscular tissues. This method employs both OCT and vibrational testing and serves as a tool to improve implant design, detect skin and other cancers, and determine the efficiency of skin aesthetic treatments.

Keywords

Vibrational Optical Coherence Tomography, Mechanical Properties, Resonant Frequency, Implant Design, Skin Cancer, Cartilage, Tendon, Nerve, Muscle, Cornea

Biography

Nikita Kelkar received her Master's in Biomedical Engineering from Rutgers, The State University of New Jersey. She is now a Biomedical Engineer at the OptoVibronex, LLC. Her interests include Medical Device Development, Biomechanics, and Cancer Research.

Innovative Non-Invasive Technology for Detecting Bone Fragility in Osteoporosis

Amit Bhattacharya[12*], Nelson B Watts[3], Kim Dietrich[1], Jun Ying[1], Cyndy Cox[1], Lorenna Altman[1], Rachel Zeiler[1], Chi Wei[1], Ayat Almomani[4] and Christopher Dicesare[5]

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Osteoporosis (OP) common and costly. Bone mineral density (BMD) measured by dual energy x-ray absorptiometry (DXA) can identify patients at risk of OP-related fractures but is a poor predictor. Drugs reduce fracture risk by 50-80% but who should receive them is problematic. The Unmet Clinical Need results from poor performance of DXA-measured BMD -- insufficient accuracy to identify patients most likely to suffer OP-related fractures. Bone Shock Absorption (BSA) (US patent Serial No. 12/402,586; 2014) offers a potential remedy could have transformative impact. BSA not only measures fracture risk-related properties of bone not captured in DXA but also is done under dynamic conditions. Since most fractures occur under dynamic conditions, BSA is a better reflection of the risk than a static measure such as DXA. BSA does not involve radiation, and is quick, easy and non-invasive. A structure's ability to resist fracture depends on its ability to effectively dampen and dissipate external loading. So far, BSA has been successfully tested in a variety of populations: healthy teenagers, young adults, pediatric patients with osteogenesis Imperfecta and older patients with OP with and w/o fracture. ROC Analysis results: BSA: 0.72 to 0.91 vs BMD: 0.52 to 0.63. Impact of BSA Technology for Early Detection of Bone Fragility : Preliminary results based from our NIH project ["Early and Non-invasive detection of lead-associated risk of bone fragility later in life among African American (AA) women",] BSA identified over 8%of AA women at mean age 32.7 years having bone damping values [mean č (SEM)=14.04 (±1.82) in OP vs 16.85 (±0.63) in Pb subjects] comparable to those found in OP without fracture at mean age of 72.2 years. Potential: BSA could be used to identify patients who are in a borderline category of fracture risk and then only those patients would need a DXA study.

Rylar™ a Bioresorbable polymer for Congenital Heart Disease

Tré Raymond Welch*[1], Jamie Wright[1], Surendranath Veeram Reddy[1], Robert Jaquiss

[1]*University of Texas at Southwestern Medical Center, USA*

Abstract

We have developed a bioresorbable radiopaque material, Rylar, for pediatric use either as a structural conduit to battle airway malacia or as a drug delivery material in combination with a bioresorbable stent to treat coarctation of the aorta. Rylar can be heat-cured into a bioresorbable conduit to provide temporary structural support while encouraging native tissue repopulation. These conduits would replace permanent synthetic grafts like Teflon (ePTFE) that are not bioresorbable, foster compliance mismatch with native tissue, and fail to allow somatic growth in pediatric patients. In this study, we examined the fabrication of Rylar into films by thermal curing and characterizing the thermal and mechanical properties of Rylar to ePTFE and polyglycerol sebacate. Rodent implant studies investigated the inflammation after implantation confirming the relative bio-inertness of Rylar compared to ePFTE. Bioresorbable stents provide an alternative to permanent metal stents that do not grow with the patient, have to be serially dilated as the patient grows, and suffer from early or late restenosis caused by neointimal hyperplasia. We have examined, Illusicor™, a bioresorbable stent over the past 10 years in animal model studies showing complete degradation over 5 years and vessel growth. Rylar has shown promise as a drug delivery alternative that could be coupled with a bioresorbable stent as a coating to target lesions. In the second phase of this work polymer blending of Rylar with PLGA at different ratios was tailored to form nanoparticles for controlled drug delivery of therapeutic agents to be used on a bioresobable stent.

Biography

Dr. Tré Raymond Welch is a Professor at the UT Southwestern Medical Center of Dallas where he works in pediatric cardiovascular and thoracic surgery. His research is investigating bioresorbable stents for adult and pediatric cardiovascular disease. He founded a company, Tremedics Medical Devices, and received his Ph.D. degree in Biomedical Engineering from UT Arlington in 2009. He is a member of American Society of Mechanical Engineers, Biomedical Engineering Society, and Society for Biomaterials, and American Heart Association. His accomplishments are publications on bioresorbable stent, formulation of bioresorbable polymers, patents, and funding from American Heart Association and National Institutes of Health.

EFFECTS OF ENDOGENOUS AND EXOGENOUS AGENTS ON PLATELET ADHESION

Sowjanya Dokku[1], Steven A. Jones[2].

[1,2]Louisiana Tech University, USA

Abstract

Platelet adhesion is regulated by both activators, such as adenosine diphosphate, and inhibitors, such as nitric oxide (NO). Both agents are released on platelet activation, so that platelets initiate both positive and negative feedback systems. In vivo platelet adhesion models generally consider the effects of platelet activators and inhibitors separately. The goal of this study was to create an environment in which interplay between positive and negative feedback can be observed together and in which the roles of endogenous and exogenous platelet activators are distinguishable. The results are expected to be applicable to the design of stents, which are susceptible to thrombus formation and which provide multiple adjacent regions where platelet-released agents can interact with one another.

To distinguish between the role of exogenous and endogenous agents, microchannels were produced that had multiple thrombogenic (fibrinogen) regions separated by non-thrombogenic (BSA-coated) regions. This geometry reveals the effect of agents released from different thrombogenic regions on one another. Adhesion was quantified by percent platelet surface area coverage.

Surface area coverage differed between the upstream and downstream sides of the thrombogenic regions. Positive and negative feedback effects were enhanced by increased platelet production of activator and inhibitor. In contrast, when the NO donor DPTA was added, with the intent to overwhelm the endogenous feedback, a more uniform spatial distribution of adhesion was obtained.

Biography

Sowjanya Dokku is a Ph.D. student in Biomedical Engineering in Louisiana Tech University, Louisiana. Her research focuses on platelet adhesion mechanisms and their impact on thrombus formation on a microfabricated channel.

Modeling and experimental approaches to understand Tenascin-C production in lung cancer

Rebecca Goldstein[1, 2], Keith Carney[2, 3], and Michelle Mendoza[2, 3]

[1]Department of Biomedical Engineering, University of Utah

[2]Huntsman Cancer Institute

[3]Department of Oncological Sciences, University of Utah

Lung cancer invasion is the major cause of lung cancer death, but remains poorly understood and untargeted. Invasion is a cellular process, in which cancer cells sense and adapt to mechanical and chemical

signals in their extracellular matrix (ECM) environment. The ECM protein Tenascin-C is a candidate LUAD invasion driver in lung adenocarcinoma. Tenascin-C is upregulated in lung adenocarcinoma, portends poor prognosis, and promotes metastasis. However, the mechanisms of Tenascin-C upregulation are unclear. Prior research suggests that Tenascin-C is produced by tumor cells in advanced high-grade cancers due to genetic alterations. We present data that Tenascin-C is also expressed in the earliest lesions by cancer-associated fibroblasts. Because strain is a stimulus for fibroblast Tenascin-C production, we tested a model that small tumors create a stiffened area within the alveolar lattice that increases strain in the surrounding area during lung respiration. Simulations of the mechanical properties of the collagen-elastin fibers under 130% stretch show that indeed, isolated stiffening increases local lattice energy and strain. Future studies aim to test this model experimentally with cell lines and in situ tumor cultures. Finding that fibroblasts under strain produce Tenascin-C in LUAD would suggest that tension receptors could be targeted to block progression. As fibroblasts are less genomically plastic than tumor cells, they present an opportunity to circumvent tumor resistance mechanisms.

Hybrid laser platform for printing 3D multiscale multi-material hydrogel structures

Pranav Soman*, Puskal Kunwar, Zheng Xiong, Yin Zhu, Haiyan Li, and Alex Filip

Department of Biomedical and Chemical Engineering, Syracuse University, Syracuse NY

Abstract

Over the course of billions of years, biological evolution has created and refined numerous elegant processes to build multifunctional structures that suit specific structural, mechanical and physiologic demands. Modern fabrication techniques, however, are unable to build complex multiscale multimaterial structures using biological materials. Few research groups have utilized the ability of ultrafast lasers to shape biomimetic hydrogel materials into complex 3D structures. However, current laser based methods, limited by scalability, types of materials, and incompatible laser and materials processing requirements, are unable to match complexities found in biological structures. Our group has designed and built a versatile hybrid laser platform (HLP) that utilized the unique nonlinear multiphoton absorption property of ultrafast lasers to process photosensitive hydrogels. HLP technology synergistically combines additive continuous liquid interphase printing (CLIP), additive multiphoton polymerization (MPP) and subtractive multiphoton ablation (MPA), three methods that are generally considered as mutually exclusive due to differences in their material processing conditions. HLP's fabrication versatility, unmatched by existing methods, can print 3D multi-material structures of complex hierarchical design architecture within minutes. Using several proof-of-concept studies, we have demonstrated that HLP can print 3D structures that are either (i) technically challenging to print, and/or (ii) extremely time consuming to manufacture, and/or (iii) not possible with current technologies. We believe that HLP technology can potentially offer a unique fabrication opportunity for a range of biological applications.

Biography

Pranav Soman is an Associate Professor in the Department of Biomedical and Chemical Engineering at Syracuse University. The central research focus of his research group is to develop new, advanced manufacturing technologies to engineer cellular and tissue models that could capture key aspects of in vivo physiology to address challenges in the fields of developmental biology and tissue regeneration. Toward this goal, his group has built machines capable of printing sophisticated structures using thermoplastics, hydrogels, and living cells. In 2019, Prof. Soman has authored and coauthored 8 articles in peer-reviewed journals such as Advanced Optical Materials, Biofabrication, among others.

Computational network models of the human immunome in cancer

Yongsheng Li[1], Brandon Burgman[1,2], Daniel J. McGrail[3], Bo Li[4], Nidhi Sahni[5,6], and S. Stephen Yi[1,2,7,8]*

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[2]*Institute for Cellular and Molecular Biology (ICMB), College of Natural Sciences, The University of Texas at Austin, Austin, TX 78712, USA*

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[8]*Oden Institute for Computational Engineering and Sciences (ICES), The University of Texas at Austin, Austin, TX 78712, USA*

Abstract

Alterations in immune-related pathways are common hallmarks of cancer. A comprehensive understanding of how cancer mutations rewire immune signaling networks and functional output across cancer types is instrumental to realize the full potential of immunotherapy. Herein we computationally interrogated somatic mutations involved in immune signaling that alter immune responses in cancer patients. To do so, we developed a Network-based Integrative model to Prioritize Potential immune respondER genes (NIPPER). Identified mutations were enriched in essential protein domains and the genes identified by NIPPER were associated with responsiveness to multiple immunotherapy modalities. Using these genes, we devised an interactome network propagation framework integrated with drug associated gene signatures to identify potential immunomodulatory drug candidates. Together, our systems-level informatics analysis results help interpret the heterogeneous immune responses among patients, and serve as a resource for future functional studies and targeted therapeutics.

Biography

S. Stephen Yi is Director of Bioinformatics, Developmental Therapeutics Lab at Livestrong Cancer Institutes of the University of Texas at Austin. He is a faculty member in the Department of Biomedical Engineering, and the Oden Institute for Computational Engineering and Sciences. He received his Ph.D. with distinction from the University of Iowa, and completed a postdoctoral fellowship at Harvard. Dr. Yi has received Komen Scholar award, NIH Outstanding Investigator Award, NIH Early Career Development Award, and Dean's Distinguished Dissertation Award. Dr. Yi's research is at the interface of biomedical engineering and informatics in the modern era of precision medicine.

Intensive Care in the Age of Artificial Intelligence (AI)

Parisa Rashidi

University of Florida, United States

Abstract

Today's ICUs face many critical barriers to achieve continuous monitoring of the patients. First, essential information such as functional status is not captured automatically but repetitively assessed by overburdened ICU nurses. Second, critical severity-of-illness scores for predicting patient trajectory are sparsely assessed

and have limited accuracy, leading to alarm fatigue, and missing early interventions.

This presentation will explore solutions to these issues using AI techniques customized to the critical care setting. More specifically, this presentation will examine how pervasive sensing technology and machine learning can be used for monitoring patients and their environment in the ICU. Additionally, this presentation will explore how AI techniques can analyze the wealth of data in the ICU, including clinical data, lab results, and physiological signals. Finally, it will discuss the issues and challenges remaining in this space and will point to future opportunities for novel research directions.

Biography

Dr. Parisa Rashidi is an associate professor at University of Florida (UF). She is the director of the "Intelligent Health Lab" (i-Heal). Her research aims to bridge the gap between Artificial Intelligence (AI) and patient care. Dr. Rashidi has received the National Science Foundation (NSF) CAREER award, National Institute of Health (NIH) Trail Blazer Award, Herbert Wertheim College of Engineering Excellence Award, and the UF term professorship. She is also a recipient of UF's Provost excellence award. To date, she has authored 120+ peer-reviewed publications, and has served on the program committee of 20+ national and international conferences.

Biomedical and Healthcare Data as a Service: A FHIR Approach

Rishi Saripalle[1]*

[1]*Illinois State University, USA*

Abstract

The FHIR interoperability standard, a new member of HL7, enables informatics experts to offer biomedical and healthcare data as a service - a modern way to access and save data. In this talk, I will present our recent work on leveraging the FHIR for representing semantic knowledge captured by UMLS. UMLS is a large medical vocabulary that plays a crucial role in many biomedical and healthcare informatics applications, specifically biomedical natural language processing. However, currently, accessing its captured knowledge requires the user to have a good understanding of relational databases, comprehend its complex knowledge structure, and use SQL to query the required knowledge - major obstacles for users with no or minimal technical knowledge. In this research, I demonstrate how FHIR's terminological resources, specifically ConceptMap, allow us to hide the UMLS complexity, normalize its knowledge structure to the standard, and offer the knowledge as a service. However, as it is, FHIR ConceptMap cannot completely represent the UMLS knowledge structure. As FHIR is extendable, I have designed multiple extensions that are attached to the ConceptMap to express the complete UMLS knowledge structure in an interoperable format.

Biography

I am Rishi Saripalle, Assistant Professor in the School of Information Technology at Illinois State University. My primary research focus is on easing structural and semantic interoperability issues in biomedical and healthcare by borrowing proven concepts from software engineering and secondary interest is on understanding what role and functionality virtual and augmented reality applications play in healthcare. I have received my Ph.D. in Computer Science from the University of Connecticut and worked as a software contractor in Information Access Division at the National Institute of Standards and Technology.

Cerebrospinal Fluid Interaction with Cerebral Cortex during Pediatric Abusive Head Trauma

Milan Toma[1,2]* and Hallie Zwibel[3]

[1]College Of Osteopathic Medicine, New York Institute of Technology, Old Westbury Campus, Northern Boulevard, Old Westbury, New York 11568-8000, USA; [2]Department of Mechanical Engineering, College of Engineering & Computing Sciences, New York Institute of Technology, Old Westbury Campus, Northern Boulevard, Old Westbury, New York 11568-8000, USA; [3]Department of Sports Medicine, College Of Osteopathic Medicine, New York Institute of Technology, Old Westbury Campus, Northern Boulevard, Old Westbury, New York 11568-8000, USA

Abstract

Abusive head trauma is a preventable and severe form of physical child abuse that results in a brain injury from forcefully shaking an infant or toddler. It occurs when a caregiver aggressively shakes a child in frustration or anger, usually because the child will not stop crying. Permanent brain damage may result, but even death in some extreme cases. The methods used in this work are a high-order finite element method with the most comprehensive to-date head/brain model and next-generation smoothed particle hydrodynamics, the combination of which makes it possible to analyze the interaction of cerebrospinal fluid with the brain under loading conditions typical of abusive head trauma. The interaction of cerebrospinal fluid with brain cortex is demonstrated during multiple shaking cycles. Our study helps doctors as well as caregivers understand why and how abusive head trauma can actually have severe long-term effects such as hearing loss, vision loss, motor disabilities or even premature death. By considering simulations (such as the one in this study) in medical practices and diagnoses, one could better predict the short- and long-term effects, as well as give a more accurate assessment concerning the health of the child after severe abuse (such as shaking). The study shows that the cerebrospinal fluid is only able to protect against one acceleration and one only.

Biography

With Ph.D. in Engineering Science, more precisely Structural Biomechanics, got the Marie Curie Fellowship for Experienced Researchers in France, moved to Japan for second post-doc developing Finite Element Fluid-Structure Interaction Solver, spent 8 months exploring the field of Computational Combustion in Saudi Arabia and then went back to Biomedical Engineering at Georgia Institute of Technology and Emory University; currently an assistant professor at the New York Institute of Technology.

Anchoring and Migration of Balloon in REBOA

S. Michelle, Y. Li, P. Sammarco, P. B. McBeth and C. C. Mei*

A mechanical theory is described for a phenomenon in the surgical procedure of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA), first introduced to treat battlefield injuries in Korea (Hughes, 1958). Trauma from intra-abdominal, pelvic, and groin hemorrhage cannot be effectively stopped by applying clamping or compression, This technique involves rapidly placing a flexible catheter into the femoral artery in the groin, maneuvering it into the aorta and inflating a balloon at its tip. This stops blood flow beyond the balloon, until the patient is transported to the operating room.

During the procedure arterial pressure and the balloon inflation should be maintained and the balloon position should be secured to prevent distal movement caused by cardiac pressure. So far the mechanics of such movement is not well understood to prevent balloon migration (Stannard et al. 2011) This work is a theoretical study of the physics of balloon anchoring and migration. A viscoelastic model is adopted for the aorta wall for the analysis of pressure waves between the left ventricle and the balloon. The theory incorporates the lubrication approximation for blood flow in the thin gap partially opened between the walls of balloon and aorta, and accounts for solid friction along the tightly contacting walls. Examples of quantitative predictions will be discussed for an idealized model of REBOA placed in Zone One from the left subclaven artery to the upper border of the aliac trunk. Secure anchoring is shown to depend on the

friction coefficient between the contacting walls, the dimensions, the initial distention as well as the position of the balloon. Balloon migration due to insufficient anchoring is also predicted by solving a nonlinear free-boundary problem numerically.

Biography

Chiang C Mei is Ford Professor of Engineering, Emeritus, Civil & Environmental Engineering, Massachusetts Institute of Technology. His primary research areas are fluid mechanics, ocean wave dynamics, and applied mathematics. His recent interests include effects of vegetation on shallow water waves, and blood flow in arteries. He was the founding editor of Journal of Applied Ocean Research, and editorial board members of Wave Motion and Journal of Fluid Mechanics. He is also Member of US National Academy of Engineering. His publications include four books: Theory and Applications of Ocean Surface Waves: vol. I, Linear Aspects, and vol. II, Nonlinear Aspects; Mathematical Analysis in Engineering and Homogenization Methods in Multiscale Mechanics.

Computational prediction of drug-eluting stent performance in patient-specific arteries – a virtual reality

Farhad Rikhtegar Nezami[1*], Rami Tzafriri[2], Elazer R. Edelman[1,3]

[1] Institute for Medical Engineering and Science, Massachusetts Institutes of Technology, USA; [2]CBSET Inc., Lexington, MA, USA; [3]Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, USA

Background: Computational modeling is revolutionizing device design and evaluation. While great progress has been made in virtual stent angioplasty and computational hemodynamics, drug delivery modeling in patient-specific geometries remains a grand challenge owing to its inherently-dynamic nature.

Methods: We developed a drug-delivery computational module for an everolimus-eluting stent with proximal and distal strut level malapposition. Patient-specific geometries were provided through automatic image processing and virtual angioplasty. All aspects of stent-based drug delivery were modelled, including drug release kinetics based on animal data, flow-mediated drug convection, and tissue diffusion and binding to nonspecific proteins and pharmacological receptors based on preclinically extracted parameters. Computational tractability was achieved combining verified model reduction techniques. Besides individual verification of preliminary steps, drug-delivery computations are being verified against benchtop experiments and in vivo immunohistology.

Results: Receptor saturation in the tissue and at the luminal interface exhibited strong spatial and time dependencies. By 1h receptor saturation was confined to peristrut sites. By 12h receptor saturation extended across the luminal interface and wall thickness of the apposed segment, and even stent downstream; while later significantly declined across the luminal interface, but not inside the wall.

Conclusion: Efficient computational modeling of stent implantation and drug delivery in patient-specific geometries paves the way for predicting clinical performance during preclinical development. Working towards greater realism, further validation, and computational efficiency, we require as a community of regulatory scientist to disuses a confidence-building framework in this virtual clinical approach.

Biography

Dr. Farhad Rikhtegar Nezami, is a Research Scientist at Harvard-MIT Biomedical Engineering Center at MIT. He received his PhD in Mechanical engineering from ETH Zurich, where he conducted research on hemodynamics and drug transport in stented coronary arteries. Dr. Rikhtegar Nezami's research interests revolve around human pathophysiology, successful translation of preclinical experiments to clinical practices, design and optimization of medical devices, and developing engineering platforms to drive progress from the laboratory bench and computational toolkit to the patient's bedside. His work embraces precision medicine and personalized therapy and developing predictive/prognostic tools incorporating clinical data, computational tools, and machine-learning algorithms.

Human models of the reflex arc for use in efficacy investigations in pre-clinical drug discovery for applications in neurological diseases

James J Hickman*

University of Central Florida, USA and Hesperos, Inc. USA

Abstract

One of the primary limitations in drug discovery and toxicology research is the lack of good model systems between the single cell level and animal or human systems. This is especially true for neurodegenerative diseases such as ALS and Alzheimer's as well as spinal cord injury. In addition, with the banning of animals for toxicology testing, using body-on-a-chip systems to replace animals with human mimics is essential for product development and safety testing. Our research focus is on the establishment of functional in vitro systems to address this deficit where organs and subsystems are created to model motor control, muscle function, myelination and cognitive function. The idea is to integrate microsystems fabrication technology and surface modifications with protein and cellular components, for initiating and maintaining self-assembly and growth into biologically, mechanically and electronically interactive functional multi-component systems. Our advances in culturing rat, mouse and human neuronal and other cells in a defined serum-free medium, suggest outstanding potential for answering questions related to maturation, aging, neurodegeneration and injury. A specific embodiment is the creation of a functional human NMJ system to understand ALS. We investigated four mutations found in ALS patients, SOD1, FUS, TDP43 and C9ORF72, for motoneurons, skeletal muscle and astrocytes. The models demonstrated variations of the disease phenotype compared to WT for NMJ stability and functional dynamics. Results of these studies will be presented as well as preliminary results for reversal of the deficits. Examples will also be given of some of the more advanced human-on-a-chip systems being developed for CNS and PNS disease applications.

Biography

James J. Hickman is the Founding Director of the NanoScience Technology Center and a Professor of Nanoscience Technology, Chemistry, Biomolecular Science, Material Science and Electrical Engineering at the University of Central Florida. Previously, he was the Hunter Endowed Chair in the Bioengineering Department at Clemson University. Dr. Hickman has a Ph.D. from MIT in Chemistry. For the past thirty years, he has been studying the interaction of biological species with modified surfaces, first in industry and in the latter years in academia. He has worked at NSF and DARPA in the area of biological computation. He is also the founder and current Chief Scientist of a biotechnology company, Hesperos, that is focusing on cell-based systems for drug discovery and toxicity. He has 155 publications and 20 book chapters, in addition to 28 issued patents out of 49 total patent applications. He is a Fellow of the American Institute of Medical and Biomedical Engineers (2004), the American Vacuum Society (2007) International Academy of Nanobiotechnology (2019) and the National Academy of Inventors (2020).

Nanomeshing Adds Multifunctionality to Conventional Neuroelectrodes

Hui Fang*

Northeastern University

Abstract

The Fang research group is committed to innovating scalable nanotechnologies to address various grand challenges facing our society. In this talk, I will introduce the concept of nanomeshing microelectronics that we recently conceived to develop next-generation neuroelectrode arrays. Notably, by stacking individu-

al layers of polymer, metal, and low impedance coating reliably in a same nanomeshed pattern, the final multilayer multifunctional nanomeshes achieved system-level performance from all individual layers, in addition to nanomesh advantages. Neuroelectrodes from multifunctional nanomeshes achieve simultaneous, on-demand electrochemical impedance, mechanical flexibility/stretchability and optical transparency, with scalability down to a single neuron. We envision that this unique approach will shift the neuroelectrode paradigm from the current rigid, opaque electrode arrays towards ultrasoft transparent ones, and produce transformative impacts in both biology and medicine.

Biography

Hui Fang received his B.S. degree in 2009 from Tsinghua University and his Ph.D. degree in 2014 from the University of California, Berkeley, both in Materials Science and Engineering. He was then a postdoctoral fellow at the University of Illinois, Urbana-Champaign from 2014 to 2016. He joined Northeastern University in August 2016 where he is currently an Assistant Professor in Electrical and Computer Engineering, with affiliate appointments in Bioengineering and Mechanical & Industrial Engineering. Fang's research has been recognized by an NSF CAREER Award (2019), and a CDMRP Epilepsy Risk Factors Award (2018).

Understanding DRG stimulation to enhance management of visceral pain

Bin Feng, Longtu Chen, Tiantian, Guo

University of Connecticut, Storrs, USA

Abstract

Chronic visceral pain is the cardinal symptom of patients with irritable bowel syndrome (IBS) affecting up to 15% of the U.S. population. Efficacious and reliable therapeutic intervention is still unavailable despite the tremendous economic burden imposed by visceral pain. Pharmacological treatments of IBS-related visceral pain are largely unsatisfactory with side effects outweighing therapeutic benefits. We hypothesize that stimulation of the dorsal root ganglions (DRG) can alleviate visceral pain by blocking action potential transmission in visceral afferent axons. In this study, we implement ex vivo single-unit recordings from split dorsal roots to assess the neuromodulatory effect of DRG stimulation on action potential transmission in mouse visceral afferent axons. From C57BL/6 mice, we harvested in continuity the distal colon and rectum (colorectum), L6 spinal nerve, DRG and L6 dorsal root. We evoked action potential from peripheral endings either by mechanical colorectal distension or electrical stimulation and recorded the single-unit action potentials from individual axons at split L6 dorsal root. We then modulated action potential transmission in afferent axons by DRG stimulation at a wide range of frequencies (10, 50, 100, 500, 1000 Hz). Our results indicate the optimal frequency of 50 Hz to block unmyelinated C-fibers and 100-500 Hz to block thinly myelinated Ač-fibers. This study reveals the frequency-dependent blocking of action potential transmission in mouse L6 afferent axons by DRG stimulation. Outcomes of this study strongly suggest the therapeutic potential of DRG stimulation at optimal frequency range to attenuate nociceptive pain by blocking afferent neural transmission.

Biography

Dr. Feng is an Assistant Professor at the Department of Biomedical Engineering in the University of Connecticut (UConn). Dr. Feng received a B.S. from Tsinghua University in Precision Instruments, an M.S. from the University of Oklahoma in Mechanical Engineering, and a Ph.D. from Purdue University in Biomedical Engineering. He completed his postdoctoral training at the University of Pittsburgh in visceral pain-related neuroscience. Dr. Feng currently leads a multi-disciplinary research team that brings in engineering approaches to advance the management of chronic pain. Dr. Feng received the NSF CAREER award and multiple research grants from the NIH.

UHPLC-QqQ-MS/MS Method Development and Validation with Statistical Analysis: Determination of Raspberry Ketone Metabolites in Mice Plasma and Brain

Bo Yuan[a, b], Danyue Zhao[a], Dushyant Kshatriya[c], Nicholas T. Bello[c], James E. Simon[a], Qingli Wu[a, b,*]

[a]*New Use Agriculture and Natural Plant Products Program, Department of Plant Biology, School of Environmental and Biological Sciences, Rutgers University, 59 Dudley Road, New Brunswick, NJ 08901, USA*

[b]*Department of Food Science, School of Environmental and Biological Sciences, Rutgers University, 65 Dudley Road, New Brunswick, NJ 08901, USA*

[c]*Department of Animal Sciences and Nutritional Sciences, School of Environmental and Biological Sciences, Rutgers University, 84 Lipman Drive, New Brunswick, NJ 08901, USA*

Raspberry ketone (4-(4-hydroxyphenyl)-2-butanone) is used commercially as flavoring agent and weight loss supplement and is responsible for the characteristic aroma and flavor of red raspberries. A targeted ultra-high performance liquid chromatography – triple quadrupole tandem mass spectrometry (UHPLC-QqQ-MS/MS) method was developed and validated for analysis of raspberry ketone (RK) and 25 identified RK metabolites in mouse plasma and brain. Dispersion and projection analysis and central composite design were used for method optimization. Random effect analysis of variance was applied for validation inference and variation partition. Within this framework, repeatability, a broader sense of precision, was calculated as fraction of accuracy variance, reflecting instrumental imprecision, compound degradation and carry-over effects. Multivariate correlation analysis and principle component analysis were conducted, revealing underlying interlinkage and mechanisms among the manifold of method traits. R programming was engaged in streamlined statistical analysis and data visualization. Two particular phenomena, the analytes' background existence in the enzyme solution used for phase II metabolites deconjugation, and the noted liability of analytes in pure solvent at 4 ℃ vs. elevated stability in biomatrices, were found critical to method development and validation. The approach for the method development and validation provided a foundation for experiments that examine RK metabolism and bioavailability.

Understanding DRG stimulation to enhance management of visceral pain

Bin Feng, Longtu Chen, Tiantian, Guo

University of Connecticut, Storrs, USA

Abstract

Chronic visceral pain is the cardinal symptom of patients with irritable bowel syndrome (IBS) affecting up to 15% of the U.S. population. Efficacious and reliable therapeutic intervention is still unavailable despite the tremendous economic burden imposed by visceral pain. Pharmacological treatments of IBS-related visceral pain are largely unsatisfactory with side effects outweighing therapeutic benefits. We hypothesize that stimulation of the dorsal root ganglions (DRG) can alleviate visceral pain by blocking action potential transmission in visceral afferent axons. In this study, we implement ex vivo single-unit recordings from split dorsal roots to assess the neuromodulatory effect of DRG stimulation on action potential transmission in mouse visceral afferent axons. From C57BL/6 mice, we harvested in continuity the distal colon and rectum (colorectum), L6 spinal nerve, DRG and L6 dorsal root. We evoked action potential from peripheral endings either by mechanical colorectal distension or electrical stimulation and recorded the single-unit action potentials from individual axons at split L6 dorsal root. We then modulated action potential transmission in afferent axons by DRG stimulation at a wide range of frequencies (10, 50, 100, 500, 1000 Hz). Our results indicate the optimal frequency of 50 Hz to block unmyelinated C-fibers and 100-500 Hz to block thinly myelinated Ač-fibers. This study reveals the frequency-dependent blocking of action potential transmission in mouse L6 afferent axons by DRG stimulation. Outcomes of this study strongly suggest the therapeutic potential of DRG stimulation at optimal frequency range to attenuate nociceptive pain by blocking afferent neural transmission.

Biography

Dr. Feng is an Assistant Professor at the Department of Biomedical Engineering in the University of Connecticut (UConn). Dr. Feng received a B.S. from Tsinghua University in Precision Instruments, an M.S. from the University of Oklahoma in Mechanical Engineering, and a Ph.D. from Purdue University in Biomedical Engineering. He completed his postdoctoral training at the University of Pittsburgh in visceral pain-related neuroscience. Dr. Feng currently leads a multi-disciplinary research team that brings in engineering approaches to advance the management of chronic pain. Dr. Feng received the NSF CAREER award and multiple research grants from the NIH.

Non-Genetic "Optogenetics": Silicon Based Bio-Interfaces for Multi-scale Optical Modulation

Menahem Y. Rotenberg

Faculty of Biomedical Engineering, Technion - Israel Institute of Technology, Israel.

Abstract

Traditional methodologies for bio-electrical interrogation are associated with interconnected leads and substrate bound electrodes, which are mechanically invasive and lack intra-volumetric access. Optogenetics, however, requires genetic modification, which limits its translational applications. Here we describe optically sensitive silicone-based materials to perform leadless, minimally invasive non-genetic photo-electrical modulation from the organ to the sub-cellular level. For whole heart optical pacing, we used ultrathin (~1μm) single crystalline silicon membranes. These thin and flexible membranes were able to confirm and wrap around the contractile heart. We then performed photo-pacing of the heart and achieved 1:1 capture using ~95mW/cm2 and 10ms laser pulses. We photo-paced the heart from both the right and left ventricles, which demonstrates its feasibility for cardiac resynchronization therapy applications.

For sub cellular modulation, we hybridized myofibroblasts and oligodendrocytes with silicon nanowires by spontaneous internalization. Then, we performed local stimulation with sub cellular resolution by illuminating the nanowires. We then show that these cell-silicon hybrids (myofibroblasts or oligodendrocytes) were capable of coupling to cardiomyocytes or neurons, respectively in vitro. Thereafter, we used these cell-silicon hybrids to address the long-standing debate of weather myofibroblasts electrically couple with cardiomyocytes in vivo. When hybrids were injected into the left ventricular wall, they establish a seamless integration with the native heart in vivo. We then harvested the heart and applied local, cell specific photo-stimulation of the pre-hybridized cells. Surpassingly, we found that hetero-cellular electrical coupling did not occur in vivo, as no calcium propagation was observed from the stimulated myofibroblasts to the native tissue.

Biography

Hemi (Menahem) Rotenberg is a newly appointed assistant professor at the Faculty of Biomedical Engineering at the Technion, Israel. He is leading the laboratory of Bioelectrical and Biomechanical Interfaces, developing new methodologies for electrical and mechanical multiscale interrogation of cells and tissues. He graduated from Ben Gurion University in Israel where he did his PhD with profs Smadar Cohen and Yoram Etzion. He recently finished his postdoctoral training with prof Bozhi Tian at the University of Chicago.

Novel Cytotoxicity and Broad-Spectrum Genotoxicity Platforms

Lizzie Ngo[1], Tze Khee Chan[1], JingGe[1], John Winters[2], Carol Swartz[2], Les Recio[2], Leona Samson[1,3] and Bevin Engelward[1]*

[1]Department of Biological Engineering and [3]Department of Biology, Massachusetts Institute of Technology

[2]Toxicology Program, Integrated Laboratory Systems, Inc., Research Triangle Park, NC

Abstract

Toxicity and Genotoxicity testing are fundamental to drug safety and drug development. Here, we leverage cell microarray technology to create a robust and highly sensitive cytotoxicity platform and a broad-spectrum genotoxicity platform. Quantification of cell viability is one of the most fundamental and broadly used endpoints in the life sciences. The gold standard is the colony forming assay, which has an impressive dynamic range, but is low-throughput (10-21 days), laborious and requires large dishes/high volumes of media (thus requiring large amounts of test compounds). To overcome these limitations, we developed the MicroColonyChip (uCC), which directly measures the ability of cells to divide, but with the scale and speed of microtiter assays. Microcolonies grow in a microarray and toxicity is derived using a novel metric (distribution of microcolony sizes). The result is an exquisitely sensitive and robust assay. For genotoxicity testing, we recently developed a higher throughput version of the comet assay that exploits a cell microarray. The "CometChip" is more than 1000X faster and image analysis is automated. Further, we broadened the spectrum of detectable lesions to include bulky lesions, a class of DNA damaging agents that has the potential to cause cancer. Accurate cytotoxicity and genotoxicity testing hold a central role in drug development. Having reliable and sensitive assays enables identification of untoward deleterious effects of drug candidates, providing immense savings by narrowing the candidate pool. Further, cytotoxicity and genotoxicity assays are also pivotal for development of novel DNA damaging chemotherapeutics, the mainstay of cancer treatment today.

Biography

Bevin Page Engelward graduated from Yale University in 1988 and from the Harvard School of Public Health in 1996. She joined the faculty at the Massachusetts Institute of Technology in 1997. She is Professor of Biological Engineering and Director of the MIT Superfund Research Program. Prof. Engelward's work focuses on DNA damage and repair, and development of novel technologies relevant to cancer etiology and drug development. She leads efforts to exploit cell microarrays that serve as a platform for novel toxicity and genotoxicity assays.

Tissue Oxygen Concentration Sensing from the Bench to the Bedside

Conor L. Evans

Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School

Abstract

Oxygen is a crucial metabolite in the cellular respiration pathway. Without adequate oxygen, cells and tissues can enter hypoxic states; when starved of oxygen cells and tissues can die. A large portion of the body is devoted to the delivery of oxygen to tissues, from the lungs and heart to the capillaries that travel throughout distal limbs. Abnormal tissue oxygenation is linked to numerous diseases and conditions, from diabetic and pressure ulcers to the failure of tissue transplants.

The central importance of tissue oxygenation makes its measurement paramount, yet there are few tools to directly measure oxygen concentration within tissues. There are numerous tools that measure indirect tissue oxygenation information, such as perfusion and the binding of oxygen to hemoglobin. The current standard-of-care to measure tissue oxygen concentration is the TcPO2 device, which heats the skin and uses a polarigraphic electrode. This tool has limited use and sensitivity; for example it cannot be placed directly

on wound beds.

We have developed a set of tissue oxygen concentration sensing tools based on oxygen-sensing sensing phosphorescence. The measurement of tissue oxygenation can be carried out via a simple color change even under room or sunlit conditions. Our porphyrin chemistry has been developed into films, bandages, wearable devices, and needle-based probes to address specific medical and surgical needs. We have recently finished a successful clinical trial, where an oxygen-sensing bandage was tested against the standard-of-care in breast reconstruction surgeries. New tools, incorporating circuits and wireless transmission, are now entering clinical studies.

Biography

Dr. Conor L. Evans is an Associate Professor at the Harvard Medical School, an Affiliated Faculty member of the Harvard University Biophysics Program, a Faculty member of the Laser Biomedical Research Center, and leads his lab at the Wellman Center for Photomedicine at Massachusetts General Hospital. Dr. Evans received his Bachelors of Science in Chemical Physics from Brown University and his PhD in Chemistry from Harvard University. His research is focused on the development and clinical translation of optical microscopy and spectroscopy tools, with specific interests in label-free imaging of drugs and the imaging and quantification of tissue oxygenation.

Cognitive-based motor rehabilitation with computerized interfaces

Raviraj Nataraj[1]*, Sean Sanford[1], Mingxiao Liu[1], Noam Y. Harel[2,3], Soha Saleh[4]

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Abstract

Physical rehabilitation after neurological traumas traditionally relies on repetitive practice of movement to reformulate neuromotor connections and improve functional abilities. It is critical to ensure patients are cognitively engaged in the rehabilitation process to maximize training effects, thereby optimizing outcomes relative to therapeutic dosage. Our laboratory has investigated how systematic presentation of virtual avatars can generate covariation in cognitive agency (perception of control) and movement performance. Among our recent findings is positive correlation between agency and performance for both grasp and reach tasks performed with a computerized interface. We have also observed that disproportionately positive feedback, without consideration of reinforcement, during training can be an enhancer of both agency and performance. Finally, we have demonstrated how learning movement commands over a computerized interface depends on visual feedback characteristics, including complexity and body representation. The sum of our findings suggests how intelligent sensory feedback from devices can leverage cognition for movement learning.

Our current focus is the development and clinical testing of sensory-driven rehabilitation platforms that utilize instrumented glove and bracing technology with virtual reality. Our 'cognition' glove system facilitates grasp training in mixed-mode reality using a custom-developed glove instrumented with force- and flex-sensors. The glove includes onboard processing to run machine algorithms in real-time synchrony with commercial hardware and software modules for virtual reality. We have also created a multi-sensory training brace system for rehabilitating upper-arm muscle control. This brace system includes visual, audio, and vibro-haptic modalities for feedback during myoelectric control of virtual avatars.

Biography

Dr. Nataraj is an Assistant Professor in the Department of Biomedical Engineering at Stevens Institute of Technology. His laboratory (est. 2017, www.mocorelab.com) has research focus in the development of methodologies that leverage cognition through computerized interfaces to accelerate motor rehabilitation. The lab has created platforms that incorporate instrumented wearables and virtual reality to improve grasp

and reach function for persons with neurological traumas. These platforms are currently being tested with persons having brain and spinal cord injury in partnership with clinical research collaborators at the Kessler Foundation and the Bronx VA Medical Center.

An NCATS Perspective: Progress, Challenges and Future Applications of Organs-on-Chips

Passley Hargrove-Grimes[1]

National Center for Advancing Translational Sciences, National Institutes of Health, Bethesda, MD, USA[1]

Abstract

Microphysiological systems (MPS) or tissue chips/organs-on-chips (OoCs) are promising in vitro models that emulate human physiology at the most basic functional level. In the last decade there has been a large expansion in the OoC field due to the convergence of many technologies, including microfluidics, sophisticated cell sensors, induced pluripotent stem cells (iPSCs) and expanded cell culture capabilities, genome editing, microfabrication engineering and 3D printing. OoC's could substantially improve the drug development process, particularly for underserved patient populations such as those with rare diseases, neural disorders, and diseases impacting pediatric populations. Currently, one of the main goals of the National Institutes of Health MPS program, led by the National Center for Advancing Translational Sciences (NCATS), is to demonstrate the utility of this emerging technology for preclinical drug safety and toxicity studies, disease modeling of both common and rare diseases, and for personalized medicine applications. In this presentation, I will discuss the NIH MPS Program's major aims, as well as our ongoing initiatives, including the newest 'Clinical-Trials'-on-a-Chip initiative. I will discuss how NCATS is supporting the path to community adoption of OoC technology through funding of independent tissue chip testing centers, as well as promotion of data sharing through funding of a central MPS Database Center. In addition to these validation efforts, NCATS in partnership with the National Aeronautics and Space Administration (NASA), is funding the Tissue Chips in Space Program, where developers are creating robust, miniaturized, and automated MPS platforms that will help catalyze adoption of the technology.

Biography

Passley Hargrove-Grimes is a scientific program manager for the trans-NIH Tissue Chip for Drug Screening program, where she serves as a liaison between funded investigators, NIH administrative and program management staff, and external stakeholders, including the Food and Drug Administration and members of the pharmaceutical industry. She manages more than 20 teams in both the Tissue Chips for Disease Modeling and Efficacy Testing and "Clinical Trials" on a Chip initiatives, under the direction of Danilo A. Tagle, Ph.D. Her work focuses on translating NIH-funded basic research into creation of potentially transformative tissue-chip technology to counter systematic challenges in drug development.

Injectable Microscale Optoelectronically Transduced Electrodes (MOTEs)

Sunwoo Lee[1]*, Alejandro Cortese[1], Aaron Mok[1], Chunyan Wu[1], Tianyu Wang[1], Conrad Smart[1], Yanxin Ji[1], Jesse H. Goldberg[1], Chris Xu[1], Paul L. McEuen[1], Alyosha C. Molnar[1]

[1]Cornell University, USA

Abstract

Decades of brain research have provided us with a sound insight into how neurons function, though small numbers. On the other hand, functional magnetic resonance imaging provides knowledge of brain activities over large volumes at second-to-minute time scales. Naturally, there is a strong interest in bridging this gap in understanding by recording from large populations of neurons in awake, behaving animals chronically.

Although multi-electrode probe shanks are widely employed, they often too invasive as the subject's relative motion against the implant constantly causes damage. Therefore, recent efforts have focused on building micro-scale, tetherless neural implants. While microscale RF and ultrasonic systems have shown promises, their scaling below a millimeter challenging. On the other extreme, optical imaging techniques based on calcium/voltage sensitive dyes/proteins allow noninvasive imaging of larger numbers of neurons' activities with a cell-scale resolution, but often are limited to subsets of neurons in an organism, are impeded by scattering, and have a low temporal resolution.

We present tetherless, injectable microscale optoelectronically transduced electrodes (MOTEs) which combine the merits of optical and electronic modalities to enable extreme scaling and direct electrical measurement with a high temporal resolution. MOTEs are ~60 μm × 30 μm × 330 μm and weigh ~1 μg, and have noise floor ~10 μV_{RMS} with 20 KHz bandwidth. The MOTEs are optically powered and transmit the measured neural signals optically through pulse-position-modulation. MOTEs can survive in phosphate buffered saline for more than four months and inside mice brains for more than one month (and counting).

Biography

Dr. Sunwoo Lee is a postdoctoral researcher in Molnar Group at Cornell University. He received his B.S. in Electrical and Computer Engineering from Cornell University in 2010, and obtained M.S. and Ph.D. degrees in the Department of Electrical Engineering at Columbia University in 2012 and 2016 respectively. During his Ph.D., he had worked on chemical vapor synthesis of high-quality graphene, and signal processing and force-sensing based on graphene nano-electro-mechanical systems (GNEMS) resonators. Sunwoo is currently working on microscale opto-electronically transduced electrodes (MOTEs), heterogeneously integrated AlGaAs μLED on CMOS, for tetherless physiological monitoring.

Heart Rate Variability Analysis Using Neural Network Models for Automatic Detection of Lifestyle Activities

Sandy RIHANA[1]* and Sarah Christina MATTA[2] and Ziad SANKARI[3]

[1]*Holy Spirit University of Kaslik, USEK, Lebanon*

[2]*University of West Brittany, France*

[3]*Cardiodiagnostics, USA*

Abstract

Heart Rate Variability (HRV) is the difference in time between one heartbeat and the next. HRV primarily depends on the extrinsic regulation of the heart rate and so is believed to reveal the heart's ability to detect and rapidly adjust to promptly varying stimuli. HRV mirrors autonomic stability between the sympathetic and parasympathetic nervous systems. HRV measurement is simple, non-invasive and relatively not expensive which makes its use as an assessment tool for health very promising. The main aim of this work is to investigate the dynamics in the autonomic regulation of the heart rate by using frequency and temporal analysis to correlate between the HRV and these physiological patterns. Therefore, the recording of electrocardiogram (ECG) on free-moving subjects provides a useful tool to evaluate the autonomic states in the daily activities.

In addition to the applied frequency and temporal analyses, pattern recognition is also accomplished using Neural Networks which are further implemented and explored in this work. In the first place, the detection of the sleep/awake states is achieved. Next, a multiclassification of different types of activities such as sleeping, walking, exercising and eating is performed.

Biography

Sandy Rihanna is a results-oriented professional with a sound background covering multiple disciplines including engineering, technology, healthcare and management. A creative thinker, Sandy is multilingual and has presented at numerous international conferences and workshops. She is first-author and co-author

of more than 40 peer-reviewed articles in various domains in the medical and in the healthcare technology interdisciplinary journals.

A computer communications engineer, Sandy received her Master's degree and Ph.D. in Biomedical Engineering from the Technical University Of Compiegne, France. While there, she was awarded the Best Ph.D. Prize called the Guy Denielou Prize.

She is qualified to the 61th section: Computer Engineering, signal processing and control in France.

She is a Fulbright scholar at University Of South Florida, USA and an invited researcher at Ecole PolyTechnique Montreal.

She joined USEK in 2011 to establish the Biomedical Engineering Department, American Board of Engineering and Technology (ABET). She is currently a Professor and the Head of Department.

She has a proven track in French-tech, in international startups and in industrial applications. Currently, she also works as a consultant.

Real-time Optical Monitoring of Endotracheal Tube Displacement

Bing Yu[1,2,*], Ramzan Ullah[1,2], Karl Doerfer[2], Pawjai Khampang[2], Faraneh Fathi[1,2], Wenzhou Hong[2] and Joseph E. Kerschner[2]

[1]Marquette University, USA; [2]Medical College of Wisconsin, USA

Abstract

Endotracheal tubes (ETTs) are used to establish and maintain a patent airway for adequate O_2 and CO_2 exchange for patients undergoing surgery or with severe respiratory failure. Inadvertent extubation is a major risk following ETT placement, especially in children and patients with complex airway pathology or low cardiopulmonary reserve. In the operating room and critical care setting, hospital staffs rely on O_2, CO_2 and volume/pressure sensors to help monitor appropriate ETT function. However, such sensors do not provide exact information about ETT position and often trigger alarms only after placement has been compromised, leaving providers with little time to correct a scenario that may lead to severe anoxic injury or death. To address this problem, we have developed a cost-effective optical monitoring system for real-time tracking of an ETT after the initial placement. The system consists of a 850nm LED as the light source, a side-firing optical fiber attached along the ETT for light delivery, two photodetectors placed on the skin above the fiber tip for light detection, and an Arduino board with a LabVIEW program to display the position of the tube inside the windpipe. The system generates both visual and audible warnings if the ETT displaces over a preset distance. The minimum displacement that can be detected by the device is 1.2mm, and displacement prediction is made using a 2nd order polynomial fit on the voltages from each detector in a transimpedance mode. The system was tested on two pigs and piglets to mimic adult and pediatric subjects.

Biography

Bing Yu, PhD, is an Assistant Professor of Biomedical Engineering at Marquette University and Medical College of Wisconsin. He received his PhD in Electrical Engineering from Virginia Tech, in 2005 and postdoctoral training in Biomedical Engineering at Duke University in 2008. Dr. Yu's research focuses on optical imaging and spectroscopy, fiber optic endoscopy, biophotonic sensors, and their applications in cancer detection, cancer treatment evaluation, medical monitoring, and global health.

Systems and strategies for 3D intravascular ultrasound imaging of blood flow velocity fields using ultrasound

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Mechanical Engineering, Georgia Institute of Technology, Atlanta, GA, USA

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Division of Cardiothoracic Surgery, Joseph P. Whitehead Department of Surgery, Emory University School of Medicine, Atlanta, GA, USA

Abstract

>8 million people in the U.S. suffer from stable coronary artery disease (CAD). Currently, the decision to stent a patient is guided by fractional flow reserve (FFR), a guidewire-based technique measuring decrease in pressure across a coronary artery stenosis. 12% of patients who are not initially stented based on FFR require a stent within 2 years, resulting in a large number of repeated invasive procedures. In patients with stable CAD, elevated wall shear stress (WSS) has been associated with development of high-risk plaques, which increases the likelihood of major adverse cardiac events. While catheter-based interventions are common for imaging plaque morphology and assessing decrease in pressure across a stenosis via FFR, there is no approach for directly measuring hemodynamic-derived quantities such as WSS in these patients. We present the development of a catheter-based 3D intravascular forward-viewing ultrasound system for direct estimation of velocity fields and WSS. Initial proof-of-concept for real-time 3D imaging of all three velocity components (including components orthogonal to the beam) has been demonstrated in the femoral artery of a pig with a 4 mm, 5 MHz transducer. In addition, the effects of the catheter on blood flow dynamics have been experimentally quantified to drive development of catheter-based devices that are minimally-disruptive to blood flow dynamics. Ongoing work on instrumentation development and non-invasive measurement of 3D velocity fields using ultrasound-based approaches will also be discussed.

Biography

Dr. Lindsey is assistant professor of biomedical engineering at Georgia Institute of Technology and Emory University, where his lab develops systems for ultrasound imaging and image-guided intervention. He completed a PhD at Duke University and post-doctoral training at the University of North Carolina and held NIH fellowships at both career stages. His lab is currently funded by NIH and NSF. Dr. Lindsey is a member of the organizing committee for the 2020 IEEE International Ultrasonic Symposium and is an active member of IEEE, BMES, and the Ultrasonics, Ferroelectrics, and Frequency Control society.

Assessing fatty acid-induced lipotoxicity in glioblastoma using stimulated Raman scattering (SRS) microscopy

Yuhao Yuan[1]*, Niraj Shah[2], Mohammad I. Almohaisin[1], Soumit Saha[1], and Fake Lu[1]†

[1]Binghamton University, State University of New York, Department of Biomedical Engineering, Binghamton, NY 13902, USA

[2]Binghamton University, State University of New York, Department of Psychology, Binghamton, NY 13902, USA

Abstract

Glioblastoma multiforme (GBM) is the most aggressive primary tumor in the central nervous system. Conventional therapies for GBM have limited efficiency and new therapies are always desired. It is reported that targeting lipid metabolism may be a promising therapeutic strategy in GBM. This study assesses the therapeutic potential of free fatty acid-induced lipotoxicity for suppression of glioma growth with stimulated Raman imaging of label-free lipids. Three fatty acids (FAs), including palmitic acid (PA), oleic acid (OA), and eicosapentaenoic acid (EPA), are supplied to cultured U87 glioma cells. A lab-built stimulated Raman scat-

tering (SRS) microscope is used to track the FAs uptake and lipid droplets (LDs) formation quantitatively. Our results show that PA-, OA-, and EPA-treatment efficiently increases the LDs accumulation in U87 cells. We also find that the inhibition of triglycerides (TAGs) synthesis and depletion of LDs enhance lipotoxicity in OA and EPA treated cells, but on the contrary, rescue PA treated cells. Our results suggest that EPA treatment combined with depletion of LDs significantly reduces the survival rate of glioma cells by nearly 50%, which may be used as a potential therapeutic approach for GBM treatment.

Biography

Yuhao Yuan is a senior Ph.D. student in biomedical engineering at Binghamton University, the State University of New York (SUNY). He has earned a bachelor's degree in basic medical sciences at Southern Medical University in China. Currently, his research focuses on developing stimulated Raman scattering (SRS) microscopy technologies and exploring its biomedical applications.

Quantifying normal and cancerous breast temperatures: Results of a pilot clinical study

Adolfo Lozano III[1,2]*, Jody C. Hayes[3], Lindsay M. Compton[3], Fatemeh Hassanipour[1]

[1]The University of Texas at Dallas, USA; [2]Raytheon Intelligence & Space, USA; [3]The University of Texas Southwestern Medical Center, USA

Abstract

Infrared (IR) imaging is an imaging technique approved by the United States Food and Drug Administration (FDA) as an adjunct to mammography in the context of breast cancer detection. Fundamentally, IR imaging is based on detecting temperature changes in the breast potentially associated with cancer. Early clinical studies between 1960s-1990s investigated the screening and diagnostic capabilities of IR imaging with mixed findings. Here, we outline the results of a pilot, multi-institutional clinical study investigating high-resolution infrared imaging in a breast cancer detection environment. A total of eleven female subjects with radiologic breast abnormalities were enrolled in the study after obtaining Institutional Review Board (IRB) approval and informed consent. High-resolution static IR images were recorded for each subject. The Wilcoxon signed rank test was used to conduct paired comparisons between normal and cancerous breast temperatures among histologically-diagnosed breast cancer subjects (n=8). Two temperature data sets were considered: Localized temperatures at the site of the cancerous lesion and mean surface temperatures over the entire breast (i.e., generalized temperatures). Results indicated that localized temperatures were significantly warmer on cancerous breasts than corresponding regions on contralateral normal breasts ($p=0.0142$). In contrast, generalized temperatures of cancerous breasts were not significantly warmer than contralateral normal breasts ($p=0.0625$). Study data suggested that certain breast cancers may elevate temperatures locally at lesion sites (i.e., localized hyperthermia) but may not necessarily elevate temperatures over the entire breast (i.e., generalized hyperthermia). More data are needed to confirm these findings.

Biography

Adolfo Lozano is a Senior Mechanical Engineer and the Business Area Engineering Operations Manager at Raytheon Intelligence & Space in Dallas, TX. He has 9 years of industry experience in the thermal analysis, design, and management of electronic defense systems. He graduated with a Ph.D. in Mechanical Engineering from The University of Texas at Dallas in 2020, an M.S. in Mechanical Engineering from The University of Texas at Austin in 2011, and a B.S. in Mechanical Engineering from The University of Texas Rio Grande Valley in 2008. He is a registered Professional Engineer in Texas.

Endogenous Fluorescent Biomarkers Originate in Lipid Droplets of Adipose Tissues

[1]Yang Zhang, [2] Joseph M McEwen, [1, 3]Zhiyi Liu, [1] Dimitra Pouli, [2] Rebecca Scheck, [1, 4]Irene Georgakoudi*

[1]*Tufts University, Department of Biomedical Engineering, Medford, Massachusetts, United States*

[2]*Tufts University, Department of Chemistry, Medford, Massachusetts, United States*

[3]*Zhejiang University, State Key Laboratory of Modern Optical Instrumentation, College of Optical Science and Engineering, Hangzhou, Zhejiang, China*

[4]*Tufts University, Program in Cell, Molecular & Developmental Biology, Graduate School of Biomedical Sciences, Boston, Massachusetts, United States*

Abstract

Besides acting as an energy reservoir, adipose tissue is reported as one of the largest endocrine organs in the body. Thus, there is great interest in developing modalities that can assess adipose tissue function, especially in non-destructive ways and within thick specimens. Our goal is to establish label-free two-photon excited fluorescence (TPEF) microscopic imaging as a tool with some unique capabilities to achieve this goal. White and brown adipose tissues are two main classes of adipose tissue with distinct appearances, molecular origins and functions. We have imaged such depots in vivo using mice. We have observed that endogenous fluorescence is present in lipid droplets (LDs), with LDs from white and brown adipocytes exhibiting distinct fluorescence lifetimes. We also found that cold activation leads to further changes in the fluorescence lifetime characteristics of brown adipose depots. To identify the origins of the LD fluorescence, we performed spectroscopic TPEF and Coherent anti-Stokes Raman Spectroscopy (CARS) imaging. These indicate that differences in the unsaturation levels of the LDs are correlated with fluorescence lifetime differences between white and brown fat LDs. High pressure liquid chromatography (HPLC) and Q-TOF Mass spectrometry (MS) of the fluorescent components extracted from lipid extracts also support that lipids of different unsaturation levels may be the origin of the fluorescence lifetime differences we detect. Together, our studies highlight the potential of label-free two-photon fluorescence lifetime imaging to extract useful information regarding adipose tissue function with subcellular level resolution and in an in vivo setting.

Biography

Yang Zhang is a graduate student in biomedical engineering at Tufts University. In her research, she uses endogenous fluorescence and nonlinear optical imaging techniques to assess cell structure, metabolism, and function. She applies these techniques to the analysis of disease states such as breast cancer, osteoarthritis, wound healing, and traumatic brain injury.

Label-Free Optical Detection of Circulating Tumor Cell Clusters Using Back Scattered Flow Cytometry

Nilay Vora*[,1], Andrew Wishart[1], Madeleine Oudin[1,2], Irene Georgakoudi[1,2]

[1]*Department of Biomedical Engineering, Tufts University, Medford, MA, USA*

[2] *Cell, Developmental, and Molecular Biology Program, Tufts University, Boston, MA, USA*

Abstract

The majority of cancer related deaths can be attributed to tumors metastasizing to distal organs such as the brain, lungs, and bone. As tumors metastasize, circulating tumor cells (CTCs) and rare circulating tumor cell clusters (CTCCs), which can range in size from 2-20 cells, are introduced to the bloodstream. CTCCs, in particular, have shown an increased ability to survive in the bloodstream and are more likely to lead to a metastasis than individual CTCs. Due to CTCCs increased metastatic potential, there is a growing need to detect these rare events in the bloodstream for improved diagnosis, stratification, and treatment of cancer patients. This study utilizes a custom confocal back scatter and fluorescence flow cytometer (CBSFFC) designed to optically detect CTCCs in vitro and ultimately in vivo. Initial studies focus on determining sensitivity and specificity of the flow cytometer through in vitro experiments using CTCCs alone and blood spiked with

CTCCs. Samples are flowed through microfluidic devices with 30x30 čm channels at physiologically relevant speeds and back-scattered and fluorescent signals are detected using a combination of five confocal detectors. Initial studies performed with GFP-fluorescent breast cancer CTCCs mixed in media demonstrate a sensitivity of detection of over 99%, using the endogenous light scattering signal and comparing it to the GFP fluorescence peaks as a gold standard. Current studies focus on optimizing sensitivity and specificity of CTCC detection in blood samples to demonstrate performance that at least matches that of CTCC chips that rely on deterministic lateral displacement.

Biography

Nilay Vora is a second year Ph.D. Candidate at Tufts University as a member of the Georgakoudi Lab. Nilay received a Bachelor of Science degree from Rutgers University in New Brunswick, NJ. During that time, Nilay's work focused on the use of Ultrasound for scoliosis monitoring as an alternative to ionizing methods as a member of the CompAST lab. His current work focuses on designing a custom back-scatter fluorescence flow cytometer for in vivo detection of circulating tumor cell clusters.

3D-imaging of whole porcine cochlea using custom-built light-sheet microscopy

Adele Moatti*[1], Yuheng Cai[1], Chen Li[1], Tyler Sattler[1], Laura Edwards[2], Jorge Piedrahita[2], Frances S. Ligler[1], and Alon Greenbaum[1]

[1]Joint Department of Biomedical Engineering, North Carolina State University and University of North Carolina at Chapel Hill, USA

[2]Department of Molecular Biomedical Sciences, North Carolina State University, USA

Abstract

Hearing loss is a major health problem worldwide, with over 5% of the population being affected. Hearing-aids are the most common solution provided; however, the quality of perceived sound is still poor. Recently, gene therapy has gained attention among researchers for its potential to regenerate the mechanosensory hair cells and their neuronal innervations inside the cochlea. Although there are promising researches in the field of regeneration, studying and evaluating these regenerative therapeutics in a big animal model (like pigs) with similar anatomy, physiology, and organ size to a human is challenging. In big animal models, the cochlea is enormous and enclosed in the dense bony otic capsule. These facts complicate whole-tissue imaging that is critical in the cochlear research, where structure-function correlation is shown repeatedly.

To enable the 3D-imaging of an intact cochlea of pigs with a volume up to 250 mm^3, we utilized the Bone-Clear tissue clearing technique, which renders this bony tissue transparent. The transparent cochleae were imaged with cellular resolution using an adaptive custom-built light-sheet fluorescence microscope. This method is ten times faster compared to the conventional confocal microscopy leading to higher quality images since it prevents bubble formation and tissue degradation. The adaptive terms in light-sheet microscope comes from the adjustment of the illumination beam by changing the angles of the beam and translating it into the detection objective lens while acquiring images. The adaptive quality provides opportunity to compensate for the light deflection due to the tortuous structure of cochlea which in turns gives rise to better-focused images. The physical properties of the cochlea such as the density of hair cells and frequency maps were then extracted using semi-automated approach. The proposed pipeline could support the growing investigation to regenerate cochlear hair cells and assist with basic science to advance therapeutics for hearing impairments.

Biography

Adele Moatti received her PhD in Materials Engineering from North Carolina State University. She then joined the joint department of Biomedical Engineering at North Carolina State University and University of North Carolina at Chapel Hill as a postdoc. Currently her research focus is on the regenerative solution for hearing loss in big animal models with the emphasis on microscopy asset. In doing so, the viral gene therapy

and its delivery to the inner ear is being investigated. She has received multiple Young Scholar awards from Comparative Medicine Institute which are aligned with the goal of cochlear hair cell regeneration studies.

3D-imaging of whole porcine cochlea using custom-built light-sheet microscopy

Adele Moatti*[1], Yuheng Cai[1], Chen Li[1], Tyler Sattler[1], Laura Edwards[2], Jorge Piedrahita[2], Frances S. Ligler[1], and Alon Greenbaum[1]

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Abstract

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To enable the 3D-imaging of an intact cochlea of pigs with a volume up to 250 mm^3, we utilized the BoneClear tissue clearing technique, which renders this bony tissue transparent. The transparent cochleae were imaged with cellular resolution using an adaptive custom-built light-sheet fluorescence microscope. This method is ten times faster compared to the conventional confocal microscopy leading to higher quality images since it prevents bubble formation and tissue degradation. The adaptive terms in light-sheet microscope comes from the adjustment of the illumination beam by changing the angles of the beam and translating it into the detection objective lens while acquiring images. The adaptive quality provides opportunity to compensate for the light deflection due to the tortuous structure of cochlea which in turns gives rise to better-focused images. The physical properties of the cochlea such as the density of hair cells and frequency maps were then extracted using semi-automated approach. The proposed pipeline could support the growing investigation to regenerate cochlear hair cells and assist with basic science to advance therapeutics for hearing impairments.

Biography

Adele Moatti received her PhD in Materials Engineering from North Carolina State University. She then joined the joint department of Biomedical Engineering at North Carolina State University and University of North Carolina at Chapel Hill as a postdoc. Currently her research focus is on the regenerative solution for hearing loss in big animal models with the emphasis on microscopy asset. In doing so, the viral gene therapy and its delivery to the inner ear is being investigated. She has received multiple Young Scholar awards from Comparative Medicine Institute which are aligned with the goal of cochlear hair cell regeneration studies.

Understanding the causes and effects of temporal pitch distortion in cochlear implant users

Barry D. Jacobson

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Abstract

Cochlear Implants (CIs) have done a wealth of good for the profoundly deaf. In quiet environments, they allow for good speech perception and enable normal conversation, which significantly improves quality of life. However, in more complex environments, such as with significant background noise, or on pitch and music perception tasks, users often experience great difficulty, as numerous studies have shown. We argue that a common design practice may contribute to these problems. By taking a step-by-step tour through the block diagram of a prototypical CI processor, properly accounting for the input and output frequency components at each stage, we will uncover some surprising results that may explain the difficulties users have. These include frequency transformations, flattening of pitch contours, generation of output components that were non-existent at the input, and other problems that degrade the musical experience, such as inharmonicity and dissonance. A major culprit is the envelope processing scheme which has been widely adopted in some form or another by almost all contemporary manufacturers. We recommend that alternatives be sought that do not suffer from these issues. We endeavor to avoid any complex statistical models or particular assumptions that might engender controversy, but rather to stick to standard signal-processing theorems and straightforward, back-of-the-envelope calculations for utmost clarity. The results fully conform to our own experience as a CI user, and we believe are consistent with the many behavioral studies that have previously been published. Along the way, we will attempt to provide historical context as to current design philosophy, and to contrast temporal and spatial pitch, and the difficulties in making each of them effectively available to users.

Biography

Barry Jacobson holds a B.S. and M.S. in Electrical Engineering from Columbia University, and a Ph.D. from the Harvard-MIT Division of Health Sciences and Technology. His thesis work was on Neuromorphic Signal Processing for Audio Source Separation. His interests include Auditory and Visual Signal Processing, the Cocktail Party Effect and the Uncertainty Principle, Quantum Computing and Machine Learning, Dynamic DNA Processing and its relation to Cellular Differentiation, Cancer, Epigenetics, and Personalized Medicine.

Comparison of annulus tension between clip and edge-to-edge suture in mitral valve

Shadan Roumany[1]*, Abby Dumey[1], Nolan Knupp[1,] Shamik Bhattacharya[2] , Zhaoming He[3]

[1]Biology, Southeast Missouri State University, USA; [2]Engineering and Technology, Southeast Missouri State University, USA; [3] Mechanical Engineering, Texas Tech University

Abstract

Mitral valve (MV) regurgitation is a growing problem in the U.S. today. According to NCBI, mitral valve regurgitation affects approximately 2-3% of Americans which equates to about 7.8 million people in the United States. It is a heart valve condition in which the MV does not close in the way it should to where it opens up into the left atrium. Therefore, when blood is flowing through the heart and the mitral valve does not close properly it causes the blood to backflow into the left atrium which could cause a heart murmur. In order to fix this problem, patients can choose to have surgery to repair the valve; however, almost 77% of patients have a recurrence in about five years after their initial surgery. Edge to Edge repair (ETER) is a common technique to correct MV prolapse. MitraClip is a percutaneous technique based on ETER. However, the effect of MitraClip on the annulus mechanics is not well understood. In this study we compare the annulus tension for both techniques in vitro and evaluate the annual mechanics long term efficacy.

The experimental method is based on a previous study of annulus tension (Bhattacharya et al). A clip is used like MitraClip which will hold the leaflets together. First a clip will be used to measure the annulus tension (AT) and then the ETER suture will be incorporated and AT will be measured. Preliminary experiment has been performed. 10 valve experiments have been planned and then statistical analysis will be done.

Bhattacharya S, He Z. Annulus tension of the prolapsed mitral valve corrected by edge-to-edge repair. J Biomech. 2012 Feb 2;45(3):562-8. doi: 10.1016/j.jbiomech.2011.11.005. Epub 2011 Dec 5. PMID: 22153221

Biography

Shadan Roumany is an undergraduate student at Southeast Missouri State University. She is a Biomedical Sciences Major with two minors in Physics and Chemistry. She has worked at St. Francis Medical Center since the start of 2021 as a Patient Care Technician. Shadan is the Secretary of the Alpha Epsilon Delta Honor Society, a National Health Preprofessional Honor Society. She is conducting this heart valve research along with Abby Dumey and Nolan Knupp. Dr. Shamik Bhattacharya is an Associate Professor in the Department of Engineering and Technology who is helping to guide this research.

POSTERS

Low cost, Low foot-print, Fast Processing POC Glucose Meter

Senait Haileselassie[1*] and Mufeed MahD[1]

University of Massachusetts Lowell, MA, USA

Abstract

A low cost low foot print with extended battery life handheld impedance based biosensor system is proposed and designed. The real-time impedance measurement device is based on analog devices AD5933 integrated circuit.

The glucose meter will be equipped with on board user display unit with simple alarm sounds, lights, and characters to be used by patients with different abilities and backgrounds.

The device belongs to the class of noninvasive and label-free biosensors. The proposed design will adopt multi blood sugar biomarkers measuring algorithms optimally fused to improve signal to noise ratios, reduce false alarms and missed detections. Features such as improved sensitivity and selectivity are main characteristics of the device.

Additional features based on reported and complete research will include adjustments for the race, gender, physical activity level, stress level as well as skin condition are uniquely incorporated in the designed glucose meter, few if any, meter in the market have such features.

Biography

University of Massachusetts Lowell

Bachelor of Science in Electrical Engineering	June 2005
Masters of Science, in Electrical Engineering	May 2011
Doctoral Program, Electrical Engineering / Biomedical	(active)

Professional Staff Engineer, Electrical & Computer Engineering

University of Massachusetts Lowell College of Engineering, January 2005 to present

Novel tattoo electrode for High-density surface Electromyography

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Abstract

High-density surface electromyography (HDsEMG) enables recording of muscle spatial activity patterns distributed across the skin surface of a muscle. Because of its ability to provide non-invasive recordings with high spatial fidelity, HDsEMG is playing an increasing role in clinical and neuroscientific research (e.g. identifying neuro-muscular junction location, measuring fiber conduction velocity, Motor Unit discrimination).

With the growing demand for high-quality HDsEMG recordings in clinical applications, dry epidermal electrodes are of increasing interest. However, conventional metallic electrode arrays and gel-based electrodes are impractical because of long-term skin irritation, inadequate electrode-skin contact, and limited layout configurability. Because of such constraints, the HDsEMG in its current form is not yet well accepted in clinical settings.

We demonstrate here a novel tattoo electrode that addresses these limitations. We fabricated a 4cm×3cm tattoo HD electrode grid on a deformable electronics membrane incorporating 64 electrodes (2mm diameter). Our dry HDsEMG grid exhibits easy layout programmability, skin breathability, remarkable "stretchability" and superior skin conformity, while faithfully recording signals during different levels of isometric contraction of the biceps brachii**.** The recordings were found to be provide accurate reproduction of the EMG spectrum, signal to noise ratio> 32, and spectral power order of magnitude higher than the commercial electrode across the relevant spectrum.

The tattoo grid electrode can potentially be used for recording high-density sEMG from skin overlying superficial muscles. This tattoo electrode will potentially facilitate HDsEMG application in clinical scenarios, especially in tracking severe neuromuscular disorders, such ALS and Spinal muscular atrophy.

Biography

Sourav Chandra has received his biomedical engineering at the undergraduate level. He has Obtained his doctoral training at the Indian Institute of Technology Madras. Since 2017 he is working as a Postdoctoral Fellow at Single Motor Unit Laboratory at Shirley Ryan Ability Lab and Northwestern University.

Diagnostic performance of a deep learning-based voice analysis for diabetes screening

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[2]Division of Endocrinology and Metabolism, Department of medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand;

[3]Department of Communication Science and Disorders, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Thailand;

[4]Division of Endocrinology, Metabolism and Lipids, Department of medicine, Emory University school of Medicine, USA;

Abstract

Background: Deep learning has been applied successfully in the field of medical imaging. The utility of artificial intelligence-aided audio classification of the human voice for diabetes screening has never been reported. We explored this method with the hypothesis that high blood glucose levels would cause laryn-

geal soft tissue swelling and lead to change in certain voice characteristics.

Objective: To develop non-invasive method for screening of diabetes using spectrogram of voice recording for classification of diabetes and normal voice.

Methods: A prospective matched control study was performed in subjects recruited from the Endocrinology Clinic and individuals working at Ramathibodi Hospital from January 2017 to January 2018. We extracted spectrogram via Mel frequency cepstral coefficient from 3-second samples of a sustained /a/ vowel and designed convolutional neural network (CNN) architecture for classification.

Results: There were a total 139 subjects consist of 76 diabetes and 63 healthy included in this study. The mean age of diabetic participants was significant older than healthy participants (54.14 years vs 48 years, p-value <0.001). The average duration of being diabetes is 9.23±7.91 years. The VGG model CNN classifier achieved 99.7% and94.59% accuracy on training and validation datasets, respectively. On the test dataset, the model achieved 83.15% sensitivity 50.91% specificity and 70.83% accuracy.

Conclusions: A Convolutional neural network algorithm has high sensitivity and specificity to adequately differentiate between normal and diabetic voice samples for screening purpose. Base on this pilot study, deep learning-based voice analysis holds promise in identifying patients who may have undiagnosed diabetes.

Biography

Dr. Pichatorn Suppakitjanusant is a research fellow at Division of Endocrinology, Metabolism and Lipids, Emory university school of medicine. She received her M.D. degree from faculty of Medicine Ramathibodi hospital, Mahidol university in 2019. She obtained Prince Mahidol Award Youth Program Scholarship 2018 for voice analysis research using machine learning in patients with diabetes. She is interested in audio classification using deep learning.

Studies of polystyrene nanoparticles penetration efficiency in PLGA hydrogel of different hardness

Mingze Sun

Department of Biomedical Engineering, University of Connecticut, CT

As a biologically adaptable biomaterial, hydrogels have been widely used in biomedical engineering in recent years. Nanoparticles or drug delivery penetration efficiency in hydrogel model in vitro has been always the focus of attention in tissue engineering field. Several factors could affect the diffusion process of nanoparticles in the hydrogel, such as the pore size that should be compared to the size of nanoparticles, polymer chain mobility, polymer concentration and crosslink density. Latex microspheres (polystyrene) are easy to produce and surface-modify, have good biocompatibility, and are easy to attach fluorescence molecules. A variety of products are commercially available and are widely used in the study of nanoparticle penetration.

In this work, we changed PLGA hydrogels with different physical properties by changing different preparation conditions (concentration and UV exposure time). The self-customized force sensor is used to characterize the physical properties of hydrogels under different conditions. At the same time, the relationship between physical properties and polystyrene nanoparticles penetration was established by tracking the diffusion efficiency of fluorescent nanoparticles in the hydrogel.

Deep learning classification model for atrial fibrillation from multichannel ECG and validation on synthetic and clinical databases

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[1]University of Zagreb, Faculty of Electrical Engineering and Computing, Croatia

Abstract

The deep learning approach for improved disorder classification is increasingly used in clinical decision support systems as databases have become more accessible and representative. In this study, we implemented a deep learning model for classifying atrial fibrillation (AF) and normal sinus rhythm (NSR) from multichannel ECG records.

Following previous work, we chose the feedforward neural network model consisting of seven dense layers, which has been shown to be effective in classifying AF. A publicly available 12-lead ECG database, the Physionet/Cinc 2020 Challenge, was chosen because it contains clinical data from multiple sources. A balanced dataset of 2603 patients with AF and 3000 subjects with NSR were selected. Additionally, 240 synthetic AF ECG records were used for comparison. The dataset was split patient-wise into training (60%), validation (20%) and test (20%) sets. 10-second records were preprocessed by filtering, removing DC component, normalizing, and extracting R peaks using the Pan-Tompkins algorithm. RR segments were extracted and resampled to equal size and used as inputs for the deep learning model. Total number of segments was 69698 from clinical and 222644 from synthetic database. To take advantage of the multichannel ECG, the voting for majority class was applied to the model.

The best F1-score was 95.8% (aVR lead) using the clinical database. For the synthetic database, the best F1-score was 99.8% (II lead). By applying voting to all leads, test results on clinical database were improved by 1.1%. Training the model on the clinical database showed good results (F1-score = 98.3%) when tested on the synthetic database. However, training on the synthetic database gave poor results (F1-score = 64.3%) when tested on clinical database.

This study showed that we can achieve better results using multichannel classification. We also showed limitations of using the synthetic database in generalizing ECG changes in morphology during AF episodes.

Biography

Mr. Krešimir Friganovič is a PhD student at the University of Zagreb, Faculty of Electrical Engineering and Computing in Croatia. He received the M.Sc. degree in electrical engineering and information technology from the Faculty of Electrical Engineering and Computing in 2016. Krešimir is currently employed as a Research Assistant with the University of Zagreb. His research interests include biomedical signal processing, EEG and ECG signal analysis, and machine learning applications in biomedical and clinical decision support systems.

A semi-autonomous, multi-zone, microfluidic platform to measure transendothelial electrical resistance

Priya P. Vijayakumar[1]*, Roberto Falcón-Banchs[2], and Lydia L. Sohn[1,2]

[1]UC Berkeley Mechanical Engineering Department, USA; [2]UC Berkeley-UCSF Graduate Program in Bioengineering, USA

Abstract

A transendothelial electrical resistance (TEER) measurement of a cell monolayer can quantify its permeability and reveal important information about a cancer cell's invasive potential. The Transwell Assay is the gold standard for measuring TEER, but it requires frequent manual handling and only provides one-time, averaged measurements. This presentation describes a semi-autonomous, multi-zone, microfluidic TEER platform that

has improved spatial resolution of measurements and a drastically reduced need for physical handling.

The microfluidic TEER platform features a central channel, in which an endothelial monolayer is cultured, intersected by four orthogonal channels. This particular design provides both apical and basal access to the endothelial monolayer through the central and orthogonal channels, respectively. A multi-zone electrode interface is mated to the microfluidic TEER platform to enable measurements from multiple zones along the monolayer. Consequently, the multi-zone, microfluidic TEER platform increases spatial resolution by an order of magnitude as compared to Transwell Assay measurements from cell culture plates. Furthermore, the platform features continuous, automated data collection, minimizing interruptive manual manipulation between measurements. Reference experiments verified the microfluidic TEER platform's accuracy when measuring the expected range of resistance for endothelial monolayers. Measurements of 1000 kΩ and 10,000 kΩ resistors exhibited less than a 0.25 and 1.25 percent error, respectively. A TEER measurement was performed uninterrupted for three hours in a cell culture incubator and, no significant time-based variation occurred, demonstrating reliable performance without manual adjustment.

The multi-zone, microfluidic TEER platform accurately measures the electrical resistance across an endothelial monolayer over long, uninterrupted intervals and demonstrates greatly enhanced spatial resolution as compared to a Transwell Assay approach. This platform can be utilized to further understand cancer cell extravasation and to explore potential cancer drug delivery applications.

Biography

Priya P. Vijayakumar is an undergraduate senior pursuing a Bachelor of Science in mechanical engineering at UC Berkeley. She has been an undergraduate researcher in Dr. Lydia Sohn's lab since 2018 and is interested in novel biomedical technologies for point-of-care diagnostics. She hopes to pursue an MD-PhD in the future.

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