

Small Conferences. BIG Ideas.



horizons.aip.org



Small Conferences. BIG Ideas.

Targeted Nucleic Acid Detection and Delivery

Presented by *Biomicrofluidics*
APL Bioengineering • *Biointerphases*

July 23-24, 2018

Morris Inn, University of Notre Dame

Targeted Nucleic Acid Detection and Delivery

July 23 – 24, 2018

University of Notre Dame, Notre Dame, Indiana, USA

Conference Program Organizing Committee

Hsueh-Chia Chang

University of Notre Dame
Editor-in-Chief, *Biomicrofluidics*

Leslie Yeo

RMIT University
Editor-in-Chief, *Biomicrofluidics*

Justin Cooper-White

University of Queensland
Editor-in-Chief, *APL Bioengineering*

Sally McArthur

Swinburne University of Technology
Editor, *Biointerphases*

Anna M. Belu

Medtronic
Associate Editor, *Biointerphases*

Katharina Maniura

Empa, Swiss Federal Laboratories
for Materials Science and Technology
Associate Editor, *Biointerphases*

Stefan Zauscher

Duke University
Associate Editor, *Biointerphases*

Local Organizing Committee

Arnie Phifer

Associate Director, Advanced
Diagnostics and Therapeutics Initiative
University of Notre Dame

Heidi Deethardt

Center Coordinator, NDNano
University of Notre Dame

Corrine Hornbeck

Administrative Assistant, Advance
Diagnostics and Therapeutics Initiative
University of Notre Dame

Sunny Shah

Assistant Director, ESTEEM Program
University of Notre Dame

Dawn Boulac Howard

Senior Events Specialist
Morris Inn/Notre Dame Conference Center
University of Notre Dame

Ryan Spurr

Event Specialist/Event Management
VenueND
University of Notre Dame



Targeted Nucleic Acid Detection and Delivery is an AIP Publishing Horizons conference presented by *Biomicrofluidics*, *APL Bioengineering*, and *Biointerphases*. This conference is designed to facilitate conversation between leading scientists working on fundamental and applied research in the targeted sensing and delivery of nucleic acids. This forum will promote the cross-pollination of novel ideas that will catalyze future work in this area.

Please contact Matt Kershish or Fred Kontur at bmf-journalmanager@aip.org with any questions or concerns throughout and after the conference.

horizons.aip.org

PROGRAM

All talks will be held in the Morris Inn with specific rooms indicated below. Meals will be held in the Morris Inn in Salon A & B.

Sunday, July 22

4:00PM – 8:00PMRegistration & Check-in (*Morris Inn*)

Monday, July 23

7:30AM – 8:20AM Breakfast

INVITED SESSION I

CHAIR: LESLIE YEO – SALON C

8:20AM – 8:30AM Welcome Remarks

8:30AM – 9:00AM L. James Lee (The Ohio State University) | Nanoprotected Cell Transfection and Vesicle Secretion for Nucleic Acid Delivery – Cancer Therapy, Immune Disease Treatment and Regenerative Medicine

9:00AM – 9:30AM Shuichi Takayama (Georgia Tech/Emory University) | Micro- and Nanofluidic DNA and Chromatin Delivery and Analysis

9:30AM – 10:00AM Annelise Barron (Stanford University) | A New Type of Silicon NanoFET Detector with Single-Nanoparticle Sensitivity

10:00AM – 10:30AM Break

INVITED SESSION II

CHAIR: JUSTIN COOPER-WHITE – SALON C

10:30AM – 11:00AM Angus Johnston (Monash University) | Nanoescapology: Understanding Nanoparticle Trafficking in Cells

11:00AM – 11:30AM Steven A. Soper (University of Kansas) | New Tools for Liquid Biopsies: Microfluidic Platforms for the Efficient Isolation and Molecular Profiling of Circulating Tumor Cells (CTCs), Cell Free DNA (cfDNA) and Nanovesicles (Exosomes)

11:30AM – 12:00PM Gwo-Bin Lee (National Tsing Hua University) | Screening of ss-DNA Aptamers on Integrated Microfluidic Systems and Their Applications for Fast Diagnosis

12:00PM – 1:00PM Lunch

1:00PM – 3:00PM Contributed Talks in Parallel Sessions

CONTRIBUTED SESSION: GENE DELIVERY

CHAIR: GWO-BIN LEE – SALON C

1:00PM – 1:20PM Justin Cooper-White (The University of Queensland) | Targeted, Non-Viral Nanoparticle-Based Direct Reprogramming of Fibroblasts for Improved Tissue Function Post Injury

1:20PM – 1:40PM Soojung Hur (Johns Hopkins University) | Integrated Microfluidic Multi-gene Delivery for Genome Editing of Immune Cells

1:40PM – 2:00PM Leslie Yeo (RMIT University) | Acoustic Enhancement of Intracellular Delivery for Ex Vivo Therapeutics

2:00PM – 2:20PM Junfeng Shi (The Ohio State University) | High-throughput Precise Gene Delivery on a Microfluidic Biochip Platform

2:20PM – 2:40PM Y. Elaine Zhu (Wayne State University) | Multi-responsive Macromolecular Coacervate Complexes for Efficient Biomolecular Encapsulation and Controlled Release

2:40PM – 3:00PM Stefan Zauscher (Duke University) | Enzymatic Synthesis of Aptamer-Targeted Polynucleotide Drugs for Cancer Therapy

CONTRIBUTED SESSION: EXOSOMES AND miRNAs

CHAIR: SIVA VANAPALLI – PRIVATE DINING ROOMS

1:00PM – 1:20PM Yong-Ak Song (NYU Abu Dhabi) | Electrokinetic Preconcentration of DNA/RNA and Exosomes for Enhancing Detection Speed and Sensitivity in Liquid Biopsy

1:20PM – 1:40PM Eduardo Reategui (The Ohio State University) | Microfluidic Isolation and Molecular Profiling of Circulating Tumor Cells and Extracellular Vesicles

1:40PM – 2:00PM Zeinab Ramshani (University of Notre Dame) | Accurate PCR-free MicroRNA Quantification for Early Stage Cancer

2:00PM – 2:20PM Mei He (University of Kansas) | Microfluidic Exosome Analysis for Understanding in Vivo Cellular Communication

2:20PM – 2:40PM Kwang Joo Kwak (The Ohio State University) | Biochip for Subgroup Capture and Characterization of Extracellular Vesicles in Cancer Patient Plasma

POSTER SESSION AND BANQUET

4:00PM – 8:00PM CORBETT HALL, 7th Floor • Downes Ballroom

PROGRAM

Tuesday, July 24

8:00AM – 9:00AM Breakfast

9:00AM – 10:20AM Contributed Talks in Parallel Sessions

CONTRIBUTED SESSION: CELLS/TISSUES AND CTCs

CHAIR: SOOJUNG HUR – SALON C

9:00AM – 9:20AM Jeremiah Zartman (University of Notre Dame) |
Stress Dissipation During Organ Growth Through Calcium Signaling

9:20AM – 9:40AM Loan Bui (University of Notre Dame) | Microfluidic Hydrogel-Based
Platform to Study Breast Cancer Cell and Lymphatic
Capillary Interaction

9:40AM – 10:00AM Gongchen Sun (Georgia Institute of Technology) | An Open-surface
Microdroplet Generator for High-throughput Screening of *C. elegans*

10:00AM – 10:20AM Siva Vanapalli (Texas Tech University) | Label-free Approaches
for High Throughput Phenotyping of Cancer Cells

CONTRIBUTED SESSION: MOLECULAR SENSING

CHAIR: L. JAMES LEE – PRIVATE DINING ROOMS

9:00AM – 9:20AM Kenry (National University of Singapore) | Highly Selective
and Sensitive Diagnosis of Malaria Using MoS₂ Nanosheet-mediated
Fluorescence Aptasensors: From Solution- to Paper-based Nanosensors

9:20AM – 9:40AM Larry Cheng (Oregon State University) | Rapid Highly
Sensitive Nucleic Acid Detection Using Quantum Dot-Fullerene
Enabled Molecular Beacons

9:40AM – 10:00AM Yunshan Wang (University of Utah) | Label Free Biosensing Enabled
by UV Plasmonic Fluorescence Enhancement

10:00AM – 10:20AM Henrich H. Paradies (Jacobs University Bremen) | Lipid-A Phosphate
Phases for Harnessing Antimicrobial Resistance

10:20AM – 10:50AM Break

10:50AM – 12:00PM Contributed Talks in Parallel Sessions

CONTRIBUTED SESSION: CELLS/TISSUES AND CTCs

CHAIR: SOOJUNG HUR – SALON C

10:50AM – 11:10AM Diya Li (University of Notre Dame) | A Shear-Enhanced
CNT-DEP Nanosensor Liquid Biopsy for Screening and Subtyping
Metastatic Breast Cancer

11:10AM – 11:30AM Larry Cheng (Oregon State University) | Ultrasensitive DNA
Detection Using Plasmonic Open-Ring Nanoarrays

CONTRIBUTED SESSION: MOLECULAR SENSING

CHAIR: L. JAMES LEE – PRIVATE DINING ROOMS

10:50AM – 11:10AM Shau-Chun Wang (National Chung Cheng University)
Using Membrane Micro-concentrators to Enhance Ultrasensitive
Fluorescence Detections of Nucleic Acids and Proteins without
Using Confocal Optics

11:10AM – 11:30AM Sagnik Basuray (New Jersey Institute of Technology)
Shear-enhanced Electrochemical Platform (ESSENCE) for
Multiplexed Detection of Cancer Biomarkers

12:00PM – 1:00PM Lunch

1:00PM – 3:30PM Contributed Talks in Parallel Sessions

CONTRIBUTED SESSION: NANOPORES AND LIQUID BIOPSY

CHAIR: LARRY CHENG – SALON C

1:00PM – 1:20PM Xiyun Guan (Illinois Institute of Technology)
Label-free Detection of DNA Mutations by Nanopore Analysis

1:20PM – 1:40PM Yaning Li (Institute of Modern Physics, Chinese Academy of Sciences)
Ion Transportation and Charge Inversion in Single Conical Nanopores

1:40PM – 2:00PM Ceming Wang (University of Notre Dame) | PCR-free Absolute
Quantification of Sequence-specific microRNAs Using Nanopore
Single-molecule Sensors

2:00PM – 2:20PM Yanyi Huang (Peking University) | ECC Sequencing: Highly Accurate
DNA Sequencing with Information Theory-based Error Correction

2:20PM – 2:40PM Edmondo Battista (University of Naples Federico II)
Multifunctional Microgels for Liquid Biopsy

2:40PM – 3:00PM Zehao Pan (University of Notre Dame) | AC Electrospray Digital
Droplet PCR with Tunable and Scalable Droplet Generation

3:00PM – 3:20PM Matthew Libera (Stevens Institute of Technology) | Solid-Phase Nucleic Acid Amplification and Multiplexed Molecular Diagnostics

CONTRIBUTED SESSION: ELECTROKINETIC SENSORS/PRETREATMENT
CHAIR: YONG-AK SONG – PRIVATE DINING ROOMS

1:00PM – 1:20PM Wonseok Kim (Seoul National University) | In vivo Closed-loop Circulation of Peritoneal Dialysate Using a Nano-electrokinetic Purifier

1:20PM – 1:40PM Chenguang Zhang (University of Notre Dame) | On-Chip Ionic Transistor with Continuous Flow for High-Efficiency Nucleic Acid Extraction and Purification

1:40PM – 2:00PM Zdenek Slouka (University of Chemistry and Technology, Prague) | Electrokinetics of Ion-exchange Systems for Nucleic Acid Detection and Preconcentration

2:00PM – 2:20PM Gilad Yossifon (Technion – Israel Institute of Technology) | Microfluidic Immunoassay Platform Based on Combining Concentration-polarization Analyte Preconcentration and Dielectrophoretic Trapping of Functionalized Beads

2:20PM – 2:40PM Ze Yin (University of Notre Dame) | An Integrated Low-cost, Rapid and Non-optical Real-time PCR Chip

2:40PM – 3:00PM Jarrod Schiffbauer (Colorado Mesa University) | Overlimiting Current Due to Electro-diffusive Amplification of the Second Wien Effect at a Cation-anion Bipolar Membrane Junction.

3:00PM – 3:20PM Xiaoye Huo (Technion – Israel Institute of Technology) | Electrorheological Diode-like Effect in Funnel-shaped Microchannel Device

3:30PM – 4:00PM Break

INVITED SESSION III
CHAIR: HSUEH-CHIA CHANG – SALON C

4:00PM – 4:30PM Chang Lu (Virginia Tech) | Ultralow-input Microfluidic Assays for Epigenomic Analysis

4:30PM – 5:00PM Andrew de Mello (ETH Zurich) | Droplet Microfluidics for High Throughput Biology

5:00PM – 5:15PM Closing Remarks



ANNELISE BARRON

Stanford University

Presentation Title

A New Type of Silicon NanoFET Detector with Single-Nanoparticle Sensitivity

ABSTRACT

Current advances in bioanalysis take advantage of solid-state electronic detection, eliminating the need for UV or fluorescence signals and affiliated lasers, lenses, CCDs and dyes. Jumping onto this exciting bandwagon, we have designed, fabricated, and are testing a novel type of silicon Field Effect Transistor (FET) detection system for microfluidic devices. Our goal is to integrate this detector into a low-cost platform that will be beautifully applicable to the solid-state electronic analysis of electrophoresing biomolecules from low-volume samples. We created a planar sensor—and nanopore is necessary!—and fabricated the chips using conventional, scalable CMOS techniques. These sensors can be integrated into bioanalysis devices that, in their entirety, will be the size of a USB memory stick, and which will draw their power from and download their data to a laptop computer. Charged particles moving down a microchannel (hydrodynamically or electrophoretically) pass over a thinly insulated gate region. Charged proteins (e.g., BSA with a charge of -18) altered the gate potential by ~ 1 mV, to change the source-drain current by an easily detectable ~ 1 nA. This sort of electronic detection technology has inherent sensitivity up to one million times greater than electrode sensing or nanopore-current blockade measurements, because it measures perturbations to the flow of electrons through the silicon chip itself. Computational methods will translate high-speed electronic pulses into quantitative signals that encode specific information about the bioanalytes of interest. This technology has myriad exciting

applications in the fields of genomics, proteomics, biomarker discovery, and diagnostics by providing a label-free method to sensitively identify and quantify biological material (e.g., DNA, RNA, proteins, viruses, cells) at the single molecule/particle level. We are aiming to develop our detector for genetic analyses ("Slither Sequencing"), and will present experimental results for the analysis of anionic nano- and microspheres; and initial results for the detection of DNA molecules.

BIOSKETCH

Dr. Barron's diverse projects juxtapose polymer science, biophysics, medicine, and biotechnology. Her training is in Chemical Engineering (B.S., Ph.D.), biotechnology and pharmaceutical chemistry. Projects diversely span bioinspired design, chemical synthesis and in vitro and in vivo biophysical testing of precisely defined biomimetic molecules designed as biostable analogues of therapeutic proteins; the development of novel strategies, devices, materials and bioconjugates to expand the capabilities of microfluidic genetic analysis devices; and the creation and elaboration of hybrid protein/polymer-based hydrogel systems for medical applications. She has received the Presidential Early Career Award for Scientists and Engineers (NIH), Beckman Young Investigator Award, Camille and Henry Dreyfus Teacher-Scholar Award, and served as the youngest member ever of the NIH's 20-member Advisory Council to the Director (Elias Zerhouni). With ~ 200 publications, her ISI H-index is currently 43.



ANDREW DEMELLO

ETH Zurich

Presentation Title

Droplet Microfluidics for High Throughput Biology

ABSTRACT

The past 25 years have seen considerable progress in the development of microfabricated systems for use in the chemical and biological sciences. Interest in such microfluidic technologies has been driven by concomitant advances in the areas of genomics, proteomics, drug discovery, high-throughput screening and diagnostics, with a clearly defined need to perform rapid measurements on small sample volumes. At a basic level, microfluidic activities have been stimulated by the fact that physical processes can be more easily controlled when instrumental dimensions are reduced to the micron scale.¹

The relevance of such technology is significant and characterized by a range of features that accompany system miniaturization. Such features include the ability to process small volumes of fluid, enhanced analytical performance, reduced instrumental footprints, low unit costs, facile integration of functional components within monolithic substrates and the capacity to exploit atypical fluid behaviour to control chemical and biological entities in both time and space.

My lecture will discuss how the spontaneous formation of droplets in microfluidic systems can be exploited to perform a variety of complex analytical processes and why the marriage of such systems with optical spectroscopies provides a direct route to high-throughput and high-information content experimentation.

Droplet-based microfluidic systems allow the generation and manipulation of discrete droplets

contained within an immiscible continuous phase.² They leverage immiscibility to create discrete volumes that reside and move within a continuous flow. Significantly, such segmented-flows allow for the production of monodisperse droplets at rates in excess of tens of kHz and independent control of each droplet in terms of size, position and chemical makeup. Moreover, the use of droplets in complex chemical and biological processing relies on the ability to perform a range of integrated, unit operations in high-throughput. Such operations include droplet generation, droplet merging/fusion, droplet sorting, droplet splitting, droplet dilution, droplet storage & droplet sampling.³⁻⁴ I will provide examples of how droplet-based microfluidic systems can be used to perform a range of experiments including nanomaterial synthesis,⁵ cell-based assays⁶ and DNA amplification.⁷

The considerable advantages that are afforded through the use of microfluidic systems are in large part made possible by system downscaling and the associated improvements in mass and thermal transfer. Nonetheless, handling and processing fluids with instantaneous volumes on the fL-nL scale represents a critical challenge for molecular detection, and still defines one of the key limitations in the use of a microfluidic system in a given application. To this end, I will also describe recent studies focused on the development of novel imaging flow cytometry platform that leverages the integration of inertial microfluidics with stroboscopic

illumination to allow for high-resolution imaging of cells at throughputs approaching 105 cells/second.⁸

BIOSKETCH

Andrew is currently Professor of Biochemical Engineering in the Department of Chemistry and Applied Biosciences at ETH Zürich. Prior to this he was Professor of Chemical Nanosciences and Head of the Nanostructured Materials and Devices Section in the Chemistry Department at Imperial College London. He obtained a 1st Class Degree in Chemistry and PhD in Molecular Photophysics from Imperial College London in 1995 and subsequently held a Postdoctoral Fellowship in the Department of Chemistry at UC Berkeley working with Professor Richard Mathies. His current research interests cover a broad range of activities in the general area of microfluidics and nanoscale science, including the development of microfluidic devices for high-throughput biological and chemical analysis, ultra-sensitive optical detection techniques, microfluidic reaction systems for chemical

and nanomaterial synthesis, the exploitation of semiconducting materials in diagnostic applications and the processing of living organisms. Andrew has given approximately 350 invited lectures at conferences and universities in North America, Europe, Africa and Asia (including over 75 plenary/keynote lectures), has published over 300 papers in refereed journals, and co-authored two books. He currently sits on the Editorial Boards of *Analytical Chemistry*, *The Journal of Flow Chemistry*, *Advanced Materials Technology and Chem*. He is also co-founder of Molecular Vision Ltd, an Imperial College spin-out company developing low-cost diagnostic devices and Drop-Tech Ltd. Science originating from the deMello group has been recognized through the award of the 2002 SAC Silver Medal (RSC), the 2009 Clifford Paterson Medal (The Royal Society), the 2009 Corday Morgan Medal (RSC) and the 2007 Clark Memorial Lectureship (California State University). In 2012, Andrew was awarded the Pioneers of Miniaturization Lectureship by Dow Corning and the Royal Society of Chemistry.

1. A.J. deMello, *Nature*, 442 (2006) 394-402.

2. X. Casadevall-i-Solvas & A.J. deMello, *Chemical Communications*, 47 (2011) 1936-1942.

3. X. Niu, S. Gulati, J.B. Edel & A.J. deMello, *Lab Chip*, 8 (2008) 1837-1841.

4. X. Niu, F. Gielen, J.B. Edel & A.J. deMello, *Nature Chemistry*, 3 (2011) 437-442.

5. I. Lignos et al., *Nano Letters*, 16, (2016) 1869-1877.

6. Soongwon Cho et al., *Analytical Chemistry*, 85 (2013) 8866-8872.

7. Yolanda Schaerli et al., *Analytical Chemistry*, 81 (2009) 302-306.

8. Rane et al., *Chem*, 3 (2017) 588-602.

INVITED SPEAKERS



ANGUS JOHNSTON

Monash University

Presentation Title

Nanoescapology: Understanding Nanoparticle Trafficking in Cells

ABSTRACT

Efficient delivery of siRNA, DNA and proteins has the potential to significantly improve the treatment of many diseases. These biological molecules are highly susceptible to degradation by the body, and current treatments are limited by high doses. Immobilizing these therapeutics inside a nanoparticle can prevent the molecules from being degraded by the body and also improves their bioavailability. However, a significant challenge remains to control where the therapeutics are trafficked to once they are taken up into the cell.¹ Nanoparticles are typically taken up by endocytosis into endosomes and then trafficked into acidic lysosomal compartments. The highly degradative environment of the lysosome can result in significant degradation of the therapeutic cargo.

We are developing tools to understanding how these materials interact with cells,^{2,3} so we can engineer materials that respond better to the biological conditions they encounter.^{4,5} In particular, we are interested in understanding the internalisation, processing and trafficking of nanoparticles in cells. This presentation will

focus on understanding the internalisation of polymer nanoparticles into cells, and their subsequent fate once they are inside the cell. It will also outline the progress we are making towards understanding how nanoparticles can induce transport of drugs from the endosomal compartments into the cytoplasm.

BIOSKETCH

Dr Angus Johnston is an NHMRC Research Fellow and head of the Nanomaterials for Biology group at the Monash Institute of Pharmaceutical Sciences. His current research focuses on developing drug delivery systems and engineering molecular sensors for tracking proteins, nucleic acids and nanoparticles in cells. He received his PhD in 2006 from the University of Queensland and worked at the University of Melbourne as a research fellow and Australian Postdoctoral Fellow until 2013. Angus has received a number of awards for his research, including the 2017 Grimwade Prize for Industrial Chemistry, Young Tall Poppy Award and he was a finalist for the Eureka Award for Outstanding Young Researcher.

1. Selby, L. et. al. *WIREs Nanomed Nanobiotechnol*, 2017, e1452
2. Liu, H. et. al. *Angew Chem Int Edit* 2013, 52, 5744–5748
3. Selby, L. et. al. *Advanced Healthcare Materials* 2016, 5, 2333–2338.
4. Wong, A. S. M. et. al. *Soft Matter*. *Soft Matter* 2015, 11, 2993–3002.
5. Mann, S. K. et. al. *Pharmaceut Res* 2016, 33, 2421–2432.

INVITED SPEAKERS



GWO-BIN LEE

National Tsing Hua University

Presentation Title

Screening of ss-DNA aptamers on Integrated Microfluidic Systems and Their Applications for Fast Diagnosis

ABSTRACT

Systematic Evolution of Ligands by Exponential Enrichment (SELEX), which is based on selection of target-specific single-stranded DNA (ssDNA) aptamers through repeated incubation, isolation and amplification, has attracted considerable attention in the last decade. However, the benchtop protocol for ssDNA aptamers screening is relatively lengthy and labor-intensive. Furthermore, it requires well-trained laboratory personnel and consumes a relatively large amount of expensive samples and reagents, which may hinder its practical applications. Our team has exerted much effort to establish nanofluidic and microfluidic platforms to automate the SELEX screening processes using proteins, viruses, bacteria, cancer cells and even tissue samples as the targets in the past decade. These automatic screening platforms offer several advantages over the existing bench-top systems in the aspects of sample and reagent consumption and processing time. Furthermore, they have a better chance to identify affinity reagents since the “dead-volume” issues have been properly addressed in the integrated microfluidic systems and non-specific contaminants can be significantly reduced. In this talk, I will introduce the state-of-the-art process on this platform and its applications for fast diagnosis of infectious diseases, cardiovascular diseases and cancers. Similar microfluidic technology could be also used for screening of peptides specific for molecular targets by using phage display techniques. I will also briefly introduce this technique to screen peptides for a variety of biomedical applications.

BIOSKETCH

Gwo-Bin Lee received his B.S. and M.S. degrees in Department of Mechanical Engineering from National Taiwan University in 1989 and 1991, respectively. He received his Ph.D. in Mechanical & Aerospace Engineering from University of California, Los Angeles, USA in 1998. Dr. Gwo-Bin Lee is currently a Chair Professor in the Department of Power Mechanical Engineering at National Tsing Hua University. His research interests lie on nano-biotechnology, micro/nanofluidics and their biomedical applications. He is Directors of “MEMS Design and Microfabrication Lab” and “Microfluidic Biochips Lab”. Dr. Lee has been very active in the field of micro/nanofluidic systems, and has developed integrated micro/nano systems incorporated with nano/biotechnology for biomedical applications. He has developed several micro/nano-scale platforms for cell, protein, and DNA manipulation and detection. Dr. Lee has published over 290 SCI journal papers, 380 conference papers, and filed 154 patents (108 patents granted) in the past 20 years. His works have been highly cited in Google Scholar, citations of all Dr. Lee's papers are 14,000 times with an h-index of 65. He also published 8 book chapters. He was Chair of International Steering Committee for IEEE MEMS 2015 and General Co-chair of IEEE NEMS 2014, IEEE MEMS 2013, IEEE NEMS 2011, and IEEE NANOMED 2013. He will be the General co-chair of Micro TAS 2018. He was an elected Fellow of ASME RSC, IET, IEEE and AIMBE.



L. JAMES LEE

The Ohio State University

Presentation Title

Nanoporated Cell Transfection and Vesicle Secretion for Nucleic Acid Delivery – Cancer Therapy, Immune Disease Treatment and Regenerative Medicine

ABSTRACT

Nucleic acid therapeutics including small interfering RNA (siRNA), microRNA (miRNA), microRNA antagonists (antagomiRs), antisense oligonucleotides, messenger RNA (mRNA), and DNA plasmids have great potential for disease treatment. However, a major limiting factor is the ability to deliver well-defined amounts of these relatively large and negatively charged molecules into target tissues and cells. A variety of cell transfection techniques have been developed for in vivo gene delivery, including viral vectors and chemical methods (e.g. liposomal and polymeric nanoparticles). But they suffer from severe immunogenicity, poor efficacy, and/or high cost. Recently, cell-secreted vesicles that encapsulate genetic and proteomic materials have emerged

as promising therapeutic agents. However, only a few cell types such as multipotent stem cells are found to secrete high numbers of exosomes that exhibit immunosuppressive activity. Here we show the development of a new technology platform, nanochannel electroporation (NEP) for highly effective cell transfection and vesicle secretion. The potential of those transfected cells and their secreted vesicles is demonstrated in several frontier medical fields including non-viral generation of induced neurons (iNs) for stroke recovery and induced endothelial cells (IECs) for wound healing, therapeutic neutrophils for targeted rheumatoid arthritis (RA) treatment, and therapeutic exosomes for glioblastoma multiforme (GBM) treatment.

References:

- P. E. Boukany, A. Morss, W-C Liao, B. Henslee, X. Zhang, B. Yu, X. Wang, Y. Wu, H.C. Jung, L. Li, K. Gao, X. Hu, X. Zhao, Q. Hemminger, W. Lu, G. Lafyatis and **L.J. Lee**, "Nanochannel Electroporation Delivers Precise Amounts of Biomolecules into Living Cells", *Nature Nanotechnology*, 6, 747-754 (2011), research highlight in *Nature Methods*, 8, 996-997 (2011).
- D. Gallego-Perez, J.J. Otero, C. Czeisler, J. Ma, C. Ortiz, P. Gygli, F.P. Catacutan, H.N. Gokozan, A. Cowgill, T. Sherwood, S. Ghatak, V. Malkoc, X. Zhao, W-C Liao, S. Gnyawali, X. Wang, A.F. Adler, K. Leong, B. Wulff, T.A. Wilgus, C. Askwith, S. Khanna, C. Rink, C.K. Sen, **L.J. Lee**, "Deterministic Transfection Drives Efficient Nonviral Reprogramming and Uncovers Reprogramming Barriers", *Nanomedicine*, 12, 399-409 (2016).
- D. Gallego-Perez, L. Chiang, J. Shih, J. Ma, S. Kim, X. Zhao, X. Wang, P. Mao, K.J. Kwak, Y. Wu, L. Wu, G. Lafyatis, D.J. Hansford, I. Nakano, and **L.J. Lee**, "On-chip Clonal Analysis of Oligo RNAs on Glioma Stem Cell Motility and Drug Resistance", *Nano Letters*, 16(9), 5326-5332 (2016).
- D. Gallego-Perez, D. Pal, S. Ghatak, V. Malkoc, N. Higueta-Castro, S. Gnyawali, L. Chang, W-C Liao, J. Shi, M. Sinha, K. Singh, E. Steen, A. Sunyecz, R. Stewart, J. Moore, T. Ziebra, R.G. Northcutt, M. Homsy, P. Bertani, W. Lu, S. Roy, S. Khanna, C. Rink, V.B. Sundaresan, J.J. Otero, **L.J. Lee** and C.K. Sen, "Topical Tissue Nano-transfection Mediates Non-viral Stroma Reprogramming and Rescue", *Nature Nanotechnology*, :10.1038/nnano.2017.134 (2017).

BIOSKETCH

Dr. Lee is the Helen C. Kurtz Professor of Chemical and Biomolecular Engineering at The Ohio State University (OSU). He founded and serves as the Director of NSF Nanoscale Science and Engineering Center for Affordable Nanoengineering of Polymer Biomedical Devices (CANPBD) at OSU. He received a BS degree in chemical engineering from National Taiwan University and a Ph.D. degree in chemical engineering from University of Minnesota. Before joining OSU in 1982, he worked as a research scientist at General Tire and Rubber Company for 3 years. His research interest includes BioMEMS/NEMS, micro-/nanofabrication, and polymer and composite materials. He has more than 400 refereed

journal publications, 30 patents and patent applications, and 14 book chapters. He was elected as the Fellow of American Institute for Medical and Biological Engineering in 2006. Dr. Lee received the 2008 Malcolm E. Pruitt Award from Council of Chemical Research, 2010 International Award from the Society of Plastic Engineers, and 2016 Lifetime Achievement Award from the Society of Advanced Molding Technology.

INVITED SPEAKERS



CHANG LU

Virginia Tech

Presentation Title

Ultralow-input Microfluidic Assays for Epigenomic Analysis

ABSTRACT

Epigenome dictates turning on and off genes in a highly dynamic fashion during normal development and diseases, forming another layer of regulation on top of gene sequence. In this talk, I will discuss our efforts on using microfluidics as a versatile platform for profiling epigenomes based on a low number of cells in the context of precision medicine.

BIOSKETCH

Dr. Chang Lu is the Fred W. Bull professor of chemical engineering at Virginia Tech. Dr. Lu obtained his B.S. in Chemistry with honors from Peking University in 1998 and PhD in Chemical Engineering from University of Illinois at Urbana-Champaign in 2002. He then spent 2 years as a postdoctoral associate in Applied Physics of Cornell University. His research has been in the general area of developing microfluidic technologies for molecular/cellular manipulation and analysis, with recent focus on profiling epigenomes using tiny amounts of samples. These technologies have been useful for understanding disorders and processes such as cancer, stem cell differentiation, and brain development. His lab has published in leading journals such as *Nature Methods*, *Nature Biomedical Engineering*, *Science Advances*, and *Nature Protocols*. Dr. Lu received Wallace Coulter Foundation Early Career Award, NSF CAREER Award, and VT Dean's award for research excellence among a number of honors.

INVITED SPEAKERS



STEVEN A. SOPER

University of Kansas

Presentation Title

New Tools for Liquid Biopsies: Microfluidic Platforms for the Efficient Isolation and Molecular Profiling of Circulating Tumor Cells (CTCs), Cell Free DNA (cfDNA) and Nanovesicles (Exosomes)

ABSTRACT

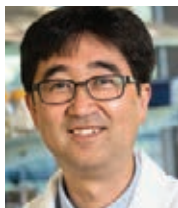
Liquid biopsies are generating great interest within the biomedical community due to the simplicity for securing important biomarkers to manage complex diseases, such as many of the cancer-related diseases. These circulating markers consist of CTCs, cfDNA and exosomes. We are developing a suite of microfluidic devices that can process whole blood directly. The microfluidics are engineered to efficiently search for a variety of disease-associated liquid biopsy markers from divergent subpopulations comprising the tumor microenvironment that can supply complementary clinical information. Each microfluidic device can isolate the target with recovery >90% and sufficient purity (>80%) to enable downstream molecular analysis of the particular biomarker. The microfluidic devices are made from thermoplastics via injection molding to allow for mass-production with tight compliancy to accommodate clinical implementation. In this presentation, information will be shared on the operational parameters of these devices for the selection of liquid biopsy markers, and the downstream molecular information that can be garnered from the isolated markers in diseases such as colorectal, ovarian, breast, pancreatic and prostate cancers as well as some of the liquid-based cancers (acute myeloid leukemia).

BIOSKETCH

Prof. Soper is currently a Foundation Distinguished Professor in Chemistry and Mechanical Engineering at the University of Kansas, Lawrence. Prof. Soper also holds an appointment at Ulsan National Institute of Science and Technology in Ulsan, South Korea, where he is an Adjunct Professor. He is also serving as a Science Advisor for a number of major worldwide companies. Prof. Soper is currently the Editor of the Americas for the *Analyst*. Prof. Soper is the Director of a NIH sponsored biotechnology center (Center of BioModular Multi-scale Systems for Precision Medicine).

As a result of his efforts, Prof. Soper has published over 245 peer-reviewed manuscripts (h index = 64) and authored 14 patents. He is also the founder of a startup company, BioFluidica, which is marketing devices for the isolation and enumeration of circulating tumor cells. His list of awards includes Chemical Instrumentation by the American Chemical Society, the Benedetti-Pichler Award for Microchemistry, Fellow of the AAAS, Fellow of Applied Spectroscopy, Fellow of the Royal Society of Chemistry, R&D 100 Award, Distinguished Masters Award at LSU and Outstanding Scientist/Engineer in the state of Louisiana in 2001. Finally, Prof. Soper has granted 44 PhDs and 6 MS degrees to students under his mentorship. He currently heads a group of 17 researchers.

INVITED SPEAKERS



SHUICHI TAKAYAMA

Georgia Tech/Emory University

Presentation Title

Micro- and Nanofluidic DNA and Chromatin Delivery and Analysis

ABSTRACT

This presentation will give an overview of efforts in our laboratory to develop microfluidic systems to control cell microenvironments and to perform high precision biochemical measurements with a focus on nucleic acids and chromatin. For example, chromatin is known to be important in both regulating genetic information as well as modulating the body's immune response. The presentation will start with a motivation to develop in vitro models of disease, some of the challenges and opportunities, and micro- and nanofluidic solutions. Specific topics include micropatterned nucleic acid delivery to cells using aqueous two phase systems, microfluidic cell cultures that incorporate immune response stimulating chromatin materials, and analysis of DNA and chromatin that uses fracture-fabricated nanofluidic devices.

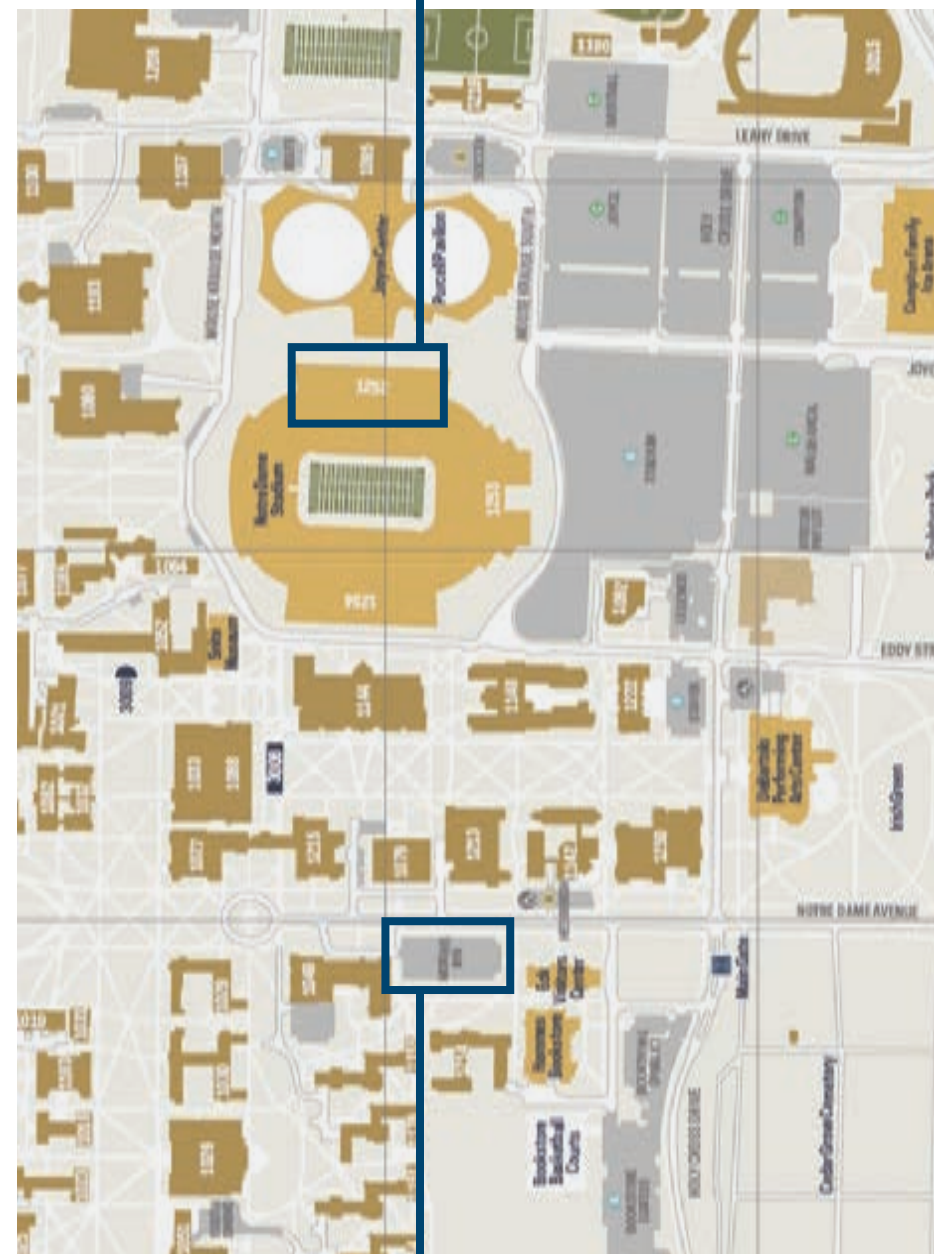
BIOSKETCH

Prof. Shuichi Takayama's research interests (B.S. & M.S. from the University of Tokyo, Ph.D. from the Scripps Research Institute) started with organic synthesis of enzyme inhibitors. Subsequently he pursued postdoctoral studies in bioengineered microsystems at Harvard University as a Leukemia and Lymphoma Society Fellow with goal of developing microsystems to perform bioevaluations of the inhibitor molecules he synthesized. He spent 17 years at the University of Michigan in the Biomedical Engineering Department and Macromolecular Science and Engineering Program, then moved to the Wallace H. Coulter Department of Biomedical Engineering at the Georgia Institute of Technology and Emory School of Medicine in the summer of 2017. He is an associate editor of *Integrative Biology* and on the board of several other journals. Awards and honors include the NSF CAREER award, Pioneers of Miniaturization Prize, and AIMBE Fellow

CONFERENCE MAP

CORBETT HALL (Downes Ballroom)

Poster Session and Banquet



MORRIS INN

Registration, all talks and meals