Research Projects in the SMART BioSyM IRG
(September 1, 2015)

1. **Mesenchymal Stem Cell Isolation via Mechanical Signatures**
   This project will focus on mulitscale analysis of bone marrow-derived mesenchymal stem cells as a function of culture conditions with distinct chemical and mechanical cues. Researchers will leverage skills in cell culture, mechanics, atomic force microscopy, optical imaging, and microfluidics, and contribute to new solutions to separate functionally distinct cells with mechanical forces.

   MIT Principal Investigator(s):
   Krystyn VAN VLIET (Material Science and Engineering & Biological Engineering)
   Jongyoon HAN (Electical Engineering & Biological Engineering)

   Singapore Co-Investigator(s):
   Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)
   Jerry CHAN (Duke-NUS Graduate Medical School)

2. **Mesenchymal Stem Cell Expansion and Delivery via Biophysical Innovation**
   This experiment-based project will focus on unique mechanical identification and sorting of stem cell state, and new means to deliver and analyze those cells in vitro and in vivo. Researchers will leverage skills in cell culture, histology, in vivo experiments (when appropriate), mechanics, atomic force microscopy, and optical imaging.

   MIT Principal Investigator(s):
   Krystyn VAN VLIET (Material Science and Engineering & Biological Engineering)
   Jongyoon HAN (Electrical Engineering and Computer Science & Biological Engineering)
   Linda GRIFFITH (Biological Engineering)

   Singapore Co-Investigator(s):
   Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)

3. **Kinetics of Adhesive Ligand-Receptor Interactions Under Force**
   This project will use molecular-scale experiments and simulations to predict the lifetime of key ligand-receptor complexes between cells and between cells and extracellular matrices. Understanding of these forces, and how these forces are changed by local pH near the cell, is key to understanding migration of stem cells and vascular endothelial cells to sites of injury or tumors.

   MIT Principal Investigator(s):
   Krystyn VAN VLIET (Material Science and Engineering & Biological Engineering)

   Singapore Co-Investigator(s):
   Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)

4. **Characterizing the Bone Marrow Niche**
   Stromal cells within bone marrow can be used for tissue repair and immune modulation, but this is greatly aided if we can expand those cells outside the body in material environments that are similar to bone marrow. This project helps to quantify the structural, chemical, and mechanical characteristics of human bone marrow in order to provide that key data for new material design.

   MIT Principal Investigator(s):
   Krystyn VAN VLIET (Material Science and Engineering & Biological Engineering)

   Singapore Co-Investigator(s):
   Jerry CHAN (Duke-NUS Graduate Medical School)

5. **Cellular Automata Models of Cell Migration**
   The objective of this work is to develop cellular automata models of angiogenesis that incorporates experimentally verified knowledge about biological processes during angiogenesis and is capable of generating vessel networks that are visually similar to actual data from time-lapse images. These models are expected to be used to interpret and "decode" time-lapse images of cell migration as well as to be able to predict the effect of certain angiogenic factors and extra-cellular matrix properties.

   MIT Principal Investigator(s):
   Harry ASADA (Mechanical Engineering)

   Singapore Co-Investigator(s):
   Justin DAUWELS (NTU, School of Electrical and Electronics Engineering)

6. **Unravelling The Molecular Mechanisms Of Endothelial Cell Behavior And Angiogenic Pattern Formation Using A Microfluidic In Vitro Angiogenesis System**
   To investigate the molecular mechanisms that control endothelial cell behavior using a unique microfluidic in vitro angiogenesis system coupled with advanced technologies in bioimaging as well as molecular/cellular biology. The real-time dynamic observation and manipulation offered by this unique microfluidic angiogenesis system provide opportunities to unravel previously un-discovered fundamental mechanisms of angiogenesis.

   MIT Principal Investigator(s):
   Harry ASADA (Mechanical Engineering)

   Singapore Co-Investigator(s):
   Ruowen GE (NUS, Biological Sciences)

7. **Visualization of Angiogenic Pattern Formation Applying Hybrid Stochastic Dynamic Modeling to the Endothelial Cells Migration in the Microfluidic in vitro Environment**
   The dynamics of the tip cell and stalk cells migration in the gel matrix field are computationally modeled as a 3-dimensional stochastic agent. The objective of this project is to develop a computational tool that can visualize spation-temporal distribution of the multiple cells in the event of the angiogenic sprouting formation governed by novel hybrid stochastic dynamics based experimental observations.

   MIT Principal Investigator(s):
   Harry ASADA (Mechanical Engineering)

   Singapore Co-Investigator(s):
   Peter CHEN (NUS, Mechanical Engineering)

8. **Spatio-Temporal Image Analysis of Cell Sprouting with Bayesian Estimation**
   The aim of this work is to advance the understanding of cell behaviours and interactions with Bayesian estimation algorithms to provide more accurate interpretations of experimental data. The current focus is on analyzing the development of endothelial cell sprouts in "in vitro" experimentation. Results of this work would lead to closed-loop control of cell populations to a desired collective behaviour.

   MIT Principal Investigator(s):
   Harry ASADA (Mechanical Engineering)

   Singapore Co-Investigator(s):
   Justin DAUWELS (NTU, School of Electrical and Electronics Engineering)
   Marcelo ANG (NUS, Mechanical Engineering)

9. **Real-time Robust Phase Imaging for Applications in Biology**

Our objective is to develop novel optical systems for phase imaging, for a variety of applications in biology. When light propagates through a medium other than vacuum, the light amplitude and phase change as a result of interaction with the medium. Those amplitude and phase perturbations contain important information about the optical properties of that medium. However, only the intensity can be measured directly; the phase cannot be measured directly, but can be reconstructed computationally. We will derive novel statistical methods to estimate the phase from noisy intensity images. Those algorithms will then be implemented in hardware. Next we will use that system for studying cell migration, abnormal growth, and other phenomena in biology and beyond.

MIT Principal Investigator(s):
George BARBASTATHIS (Mechanical Engineering)

Singapore Co-Investigator(s):
Justin DAUWELS (NTU, School of Electrical & Electronic Engineering)

10. **3D In Vivo Imaging to Understand How the Intestinal Epithelium Migrates**

Regeneration of intestinal epithelial tissue is a complex dynamic process that involves division and differentiation of stem cells. To understand intestinal epithelium migration and the interactions between molecular motors and structural proteins, this project targets to develop new 3D imaging techniques with improved spatio-temporal resolution.

MIT Principal Investigator(s):
George BARBASTATHIS (Mechanical Engineering)

Singapore Co-Investigator(s):
Paul MATSUDAIRA (NUS, Biological Sciences)

11. **Integrated Waveguide Based Particle Actuation and Imaging**

A new concept for simultaneous manipulation and imaging of particles in an opto-fluidic platform. The main motivation is to enable cell and tissue manipulation and measurement functions while avoiding the mechanical complication of free-space optics surrounding the fluidic channel that plague traditional opto-fluidic systems. Our concept replaces the free space optics with a multimode waveguide where light localization for trapping and imaging is achieved through interference between field modes including reflections.

MIT Principal Investigator(s):
George BARBASTATHIS (Mechanical Engineering)

Singapore Co-Investigator(s):
Nanguang CHEN (NUS, Bioengineering)

12. High Throughput Raman Imaging Characterization of Non-Alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease is a precursor to disease such as hepatic liver cancer. We are recently developing a novel mouse model for this disease. Since lipid metabolism clearly play a role and the formation of lipid droplet is an important histological feature of disease progression. To improve the efficacy of this study, the development of high throughput Raman microscopy techniques are important. We are developing two novel microscopy techniques with one system based on light-sheet excitation of spontaneous Raman signal and a second system based on wide field stimulated Raman scattering.

MIT Principal Investigator(s):
Peter SO (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Hanry YU (NUS, Physiology)
Lisa TUCKER-KELLOGG (Duke-NUS Graduate Medical School)
Zhiwei HUANG (NUS, Bioengineering)

13. Three-Dimensional Image Cytometry for High-throughput Drug Screening Against Liver Cancer

In vitro cell-based models with a few cell layers are increasingly used in high content screen for compound safety and efficacy against various diseases. Morphological information about large populations of cells can be extracted using high-throughput high-content microscopy in combination with automated image processing. This technology is commonly known as image cytometry. In our group we have developed one of the fastest 3D imaging cytometers existing today. The system can image about 800 cells/sec in 3D with subcellular resolution enabling it to perform high-content drug screening limited by processing speed. In this project we propose to design and develop novel image segmentation and quantification algorithms that support parallel implementation on GPUs for enhanced speed. This is combined innovative high content molecular probes to develop a powerful 3D assay for high content high throughout screen that is validated with paradigm compounds.This project will focus on mulitscale analysis of bone marrow-derived mesenchymal stem cells as a function of culture conditions with distinct chemical and mechanical cues. Researchers will leverage skills in cell culture, mechanics, atomic force microscopy, optical imaging, and microfluidics, and contribute to new solutions to separate functionally distinct cells with mechanical forces.

MIT Principal Investigator(s):
Peter SO (Mechanical Engineering & Biological Engineering)

Singapore Co-Investigator(s):
Hanry YU (NUS, Physiology and A IBN)*

14. Does Repetition of Injury Cause Impairment of Stem Cell Regeneration In Vivo?

Skeletal muscle regeneration is a highly regulated process consisting of an inflammation, proliferation and remodeling phase. After a single injury the process is very efficient, however, in diseases where repeated injuries occur regeneration fails and eventually muscle tissue is replaced by fibro-fatty tissue. The aim of this project is to determine whether signaling from adjacent injuries, which are in different phases of the regeneration process, impairs regeneration. To achieve this we will use a mouse model that expresses four fluorescent colors in the muscle stem cells, and perform laser micro-dissection to make simultaneous and a-synchronous pairs of injuries in the skin muscle, followed by in vivo imaging.

MIT Principal Investigator(s):
Peter SO (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Lisa TUCKER-KELLOGG (Duke-NUS Graduate Medical School)

15. **Optical and Electron Microscope Tissue Imaging over Seven Orders of Magnitude in Length Scale**

Structured-light image cytometry enables high throughput quantifications of 3D morphology of cells in 2D culture. With the advent of optical clearing techniques for ex vivo tissues, we will explore the extension of this methodology for tissue studies. Combining with super-resolution imaging techniques, organ structures may be imaged spanning length scales from centimeters down to 100 nm level. In order to access nanometer scale structures, we will explore synthesizing optical and electron microscopy data potentially providing tissue morphological information across seven orders of magnitude. Since the tissue volumes that can be imaged by these two modalities are very different, novel algorithms for information synthesis will need to be developed. We will first apply this approach to study the renewal process of cells in mouse intestinal crypts.

MIT Principal Investigator(s):
Peter SO (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Paul MATSUDAIRA (NUS, Biological Sciences)
Lisa TUCKER-KELLOGG (Duke-NUS Graduate Medical School)

16. **Quantitative Phase Microscopy for the Quantification of Cell and Tissue Rheology**

Quantitative phase microscopy (QPM) allows measurement of important quantities in biological specimens that greatly aid in quantifying their physiological state. QPM method also provides the capability to measure cellular plasma membrane fluctuation with resolutions on the scale of nanometres and milliseconds, and used for staging of malaria parasite infection of red blood cells (RBCs). The developed QPM methods are mainly transmission based and have good sensitivity and speed but these methods lack three-dimensional (3D) resolution. In this project, we are developing next generation QPM with 3D resolution and sufficient sensitivity and speed to study biomechanics of complex eukaryotic cells and tissue rheology. One potential application is to use this system in developing the biophysical marker for mesenchymal stromal cells (MSCs) by using the nuclei membrane fluctuations analysis. This system brings a new advance in QPM method for inspection, monitoring, and analysis for cell biology studies. New mathematical models development will relate the plasma and nuclei membrane fluctuations to the intracellular level viscoelastic properties of the cell. Further, investigation of the interaction of 3D cytoskeletal structured with the plasma membrane help to describe the mechanism and interaction of intracellular structured under various cellular biophysical conditions.

MIT Principal Investigator(s):
Peter SO (Mechanical and Biological Engineering)
Roger KAMM (Mechanical and Biological Engineering)
Krystyn VAN VLIET (Material Science and Engineering & Biological Engineering)

Singapore Co-Investigator(s):
Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)
Thai TRAN (NUS, Physiology)

17. In Vivo Deep Brain Imaging Beyond 2 mm Based on Multiphoton Focal Modulation Microscopy

Large scale mapping efforts by research centers, such as the Allan Institute, have provided wiring information on the regional connectivity of the brain for many physiological and pathological states in small animal models. While this wiring diagram is important, dynamic functional imaging of the brain on the neuronal level remains a major challenge. One difficulty lies in the limited imaging depth of conventional optical microscopy. Recent works in multiphoton imaging with infrared radiation at 1300-1800 nm range have demonstrated imaging beyond 2 mm in the mouse cortex. While this is an impressive achievement, the imaging of cortex-hippocampus coupling and studying larger animals will require even deeper penetration. We propose to develop two-photon and three-photon microscopes with novel focal modulation technology that can provide high-resolution images (better than 2 micron) of neuronal morphology down to a depth of approximate 4 mm.

MIT Principal Investigator(s):
Peter SO (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Nanguang CHEN (NUS, Bioengineering)

18. Imaging Zebra Fish Neuronal Circuit Dynamics Using Two-Photon Temporal Focus Microscopy

Behavior and cognition result from dynamic processes in highly complex neural networks. An understanding of how the brain functions involves several approaches, such as manipulation of specific circuits, recording neural activity during defined behavior and analysis of large data sets. Traditional methods of recording, such as electrophysiology, only allow limited sampling. Optical methods, in contrast, allow large populations to be recorded. Multi photon microscopy has emerged as an important technique, as it utilizes and invisible laser and has good penetration. Conventionally, the excitation region is localized to a diffraction-limited focal point of a high numerical aperture objective lens, and requires raster scanning to produce a 3D image. To overcome the inherent slowness of this method, we are developing an advanced wide field two photon imaging system capable of imaging multiple axial planes simultaneously. With temporal focusing, a 3D resolved plane is generated without the need for lateral scanning. The femtosecond laser is chirped to generate wide field two photon excitation at multiple planes, and detection of multiple axial planes is performed using volume holographic methods. To test this system, imaging will be carried out on larval zebrafish, a powerful model for systems neuroscience. This is a vertebrate and all neurons in the brain are optically accessible. Imaging can be combined with behavior and genetic manipulation. One potential goal will be to establish how the whole brain responds to stimuli with emotional value, including the alarm pheromone, in different situations such as where escape is possible or impossible.

MIT Principal Investigator(s):
Peter SO (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Suresh JEYARAJ JESUTHASAN (A IMCB and Duke-NUS Graduate Medical School)*

19. Elucidating the Role of ECM Degrading Enzymes in Cancer Cell Extravasation

This project will focus on profiling invasive cancers in terms of their ECM degrading enzyme expression. The aim is to identify enzymes that play a unique role in cancer cell extravasation and might therefore be suitable therapeutic targets to prevent metastasis formation. This project will work at the interface of molecular biology, biochemistry, and microfludics. 3D microfluidic cell culture systems can be employed to study the effect on transendothelial migration of cancer cells upon inhibition or knockout of these enzymes. Cancer cell lines can be profiled by mRNA arrays or RT-PCR methods to gain insights into the expression level of ECM degrading enzymes. Biochemical methods such as zymography, immuno cyto chemistry and others will be employed to further characterize the action of identified enzymes.

MIT Principal Investigator(s):
Roger KAMM (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)

20. Developing a Microfluidic Platform for Screening Anti-metastatic Drugs

The aim of this project is to develop a microfluidic platform technology that enables screening for anti-metastatic drugs. A microfluidic platform will provide an assay to screen in parallel several drugs for their ability to prevent transendothelial migration of cancer cells. Inhibitory effects of potential drugs will be tested using a 3D microvasculature based cancer cell extravasation assay. The developed system will facilitate semi-automated analysis of cancer cell extravasation medium throughput studies.

MIT Principal Investigator(s):
Roger KAMM (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)

21. Interactions between Engineered HBV-specific T Cells and Hepatocellular Carcinoma Cells in a 3D Microfluidic Platform

Hepatocellular carcinoma (HCC) cells often have hepatitis B virus (HBV)-DNA integration and can be targeted by T cells engineered to express HBV-specific T-cell receptors (TCR) as a means of therapy. However, pre-clinical in vitro characterizations of the engineered T cells were usually performed in artificial conditions that stray far from the physiologic or diseased liver setting. The aim of the project is to investigate how these engineered T cells behave in conditions that mimic the intra-hepatic environment. Influence of inflammatory cytokines and the role of different oxygen levels have to be investigated in live time-lapse confocal imaging experiments.

MIT Principal Investigator(s):
Roger KAMM (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Antonio BERTOLETTI (Duke-NUS Graduate Medical School)

22. Blood Brain Barrier on-a-chip

The project aims to develop a novel three-cell culture system with primary neurons and astrocytes isolated from rats and brain microvascular endothelial cells for mimicking blood-brain barrier (BBB) functions and to study the interactions among the three cell types involved in various neurological disorders.

MIT Principal Investigator(s):
Roger KAMM (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Eyleen GOH (Duke-NUS Graduate Medical School)

23. Macrophage-assisted Extravasation of Pancreatic Cancer Cells

This project investigates the role of human primary monocyte-derived macrophages in the extravasation of pancreatic cancer cells in a 3D microfluidic device. The altered metabolic profile in early pancreatic lesions and its effect on macrophage polarization toward a pro-metastatic phenotype will also be studied.

MIT Principal Investigator(s):
Roger KAMM (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Siew Cheng WONG (NUS, SIgN/Department of Microbiology)

24. Organ-specificity in Cancer Cell Extravasation and Recolonization

Here we aim to mimic organ-specific microenvironments to which different types of cancers cells metastasize. In particular, human liver sinusoidal microvascular endothelial cells (HLSMECs) will be used to mimic the endothelial monolayer and human liver epithelial cells (THLE-3) to mimic the liver tissue that will host the extravasated cancer cells.

MIT Principal Investigator(s):
Roger KAMM (Mechanical and Biological Engineering)

Singapore Co-Investigator(s):
Siew Cheng WONG (NUS, SIgN/Department of Microbiology)

25. Single-Strand Binding Protein Binding to Single Stranded DNA

Such proteins are involved DNA replication and in DNA damage repairing process. This research aims to study the mechanical properties of DNA-SSB complexes. Two major experimental methods will be involved: (1) Magnetic tweezer manipulation of DNA-SSB co-polymer, (2) AFM imaging of DNA-SSB co-polymers.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Jie YAN (NUS, Physics)

26. Single Molecule Based Biosensors

Single molecule based biosensors will be developed to explore probe-field interactions upon force activation. A single molecule platform with optical force manipulation and simultaneous fluorescence spectroscopic monitoring will allow for systematic validation and development of various probe strategies. The interactions of various analytes (or drug molecules) and biomacromolecules will be investigated on the molecular level and eventually adapted to the cellular systems.

MIT Principal Investigator(s):
Matthew LANG (Biological and Mechanical Engineering)

Singapore Co-Investigator(s):
Qing-Hua XU (NUS, Chemistry)

27. Single Molecule Microscopy of the Biophysics of DNA

The goal of this project is to understand single DNA physics in confinement and subject to electric fields. Recently, we have found that a moderate electric field strongly compresses isolated DNA polymer coils into isolated globules. Insight into the nature of these compressed states is gained by the expansion of the molecules back to equilibrium after halting the electric field. Additionally we have demonstrated that large DNA molecules and low ionic strength favor such compression.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Jie YAN (NUS, Physics)

28. Single-Molecule Studies of DNA Intercalators

Many ligands bind to DNA by intercalation. Famous examples are some commonly used DNA dyes and anti cancer compounds. This research investigates the interaction between DNA and DNA intercalators using a magnetic tweezer. Applying tensile force to the DNA enhances intercalation that results in DNA elongation. By monitoring the real time elongation of a single DNA, the kinetics and equilibrium properties of the interactions can be obtained with high accuracy.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Jie YAN (NUS, Physics)

29. Magnetic Tweezing of Single DNA

The goal of this project is to develop magnetic tweezers for studying DNA-protein and DNA-crowder interactions. A magnetic-tweezer setup with ingenious temperature controller has been built. The DNA overstretching transition through both of the “B-to-S" transition pathway and the strand-unpeeling pathway has been studied with the tweezers. The entropy change and enthalpy change during both transition pathways are determined. Based on these experiments, we have revealed for the first time that the DNA overstretching transition through the “B-to-S” transition pathway leads to a highly ordered double-stranded structure without melting of DNA base pairs.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Jie YAN (NUS, Physics)

30. Displaying DNA for Mapping Nanofluidic Devices

The goal of this project is to understand how a combination of nanoconfinement and DNA-binding peptides can be used to elongation DNA for direct mapping of single molecules.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Johan VAN DER MAAREL (NUS, Physics)
Jeroen A. VAN KAN (NUS, Physics)
Jie YAN (NUS, Physics)

31. Microrheology to Study DNA-Topoisomerase Interaction and the Role of Anti-cancer Drugs

Topoisomerases are of special interest due to their involvement in a large number of biological activities including unlinking DNA catenates, resolving intertwined chromosomes etc. Topoisomerases are also the target of some anti-cancer drugs, because its inhibition impedes the division of cells. This can be due to the blocking of the double strand passage reaction and/or the formation of cross-linking protein clamps between different DNA segments. We specifically wanted to understand how anticancer drugs affect this process. We employ multiple particle tracking microrheology for this effort. The technique allows us to follow in real-time the change in the structure and rheology of these small, precious samples.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Johan VAN DER MAAREL (NUS, Physics)

32. Micromechanics of Biofilms Studied with Active Microrheology

In this project we are interested in leveraging our expertise in magnetic tweezing to understand the micromechanics of biofilms. By locally pulling and pushing on the biofilms, we wish to understand local mechanics and how this varies with matrix components.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Staffan KJELLEBERG (NTU, School of Biological Sciences)
Jie YAN (NUS, Physics)

33. Sequencing Single DNA Molecules with Graphene Nanopores

The goal of this project is to develop nanopore technologies for the sequencing of single DNA. Strategies will be pursued to couple nanofluidic devices and other materials with nanopores to control the physics of DNA passage in these pores.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Slaven GARAJ (NUS, Physics)

34. Microfluidic Generation of Artificial Cells

The goal of this project is to use microfluidic devices to produce soft particles with controlled stiffness and surface chemistry. These synthetic cell mimics will be used to understand cell sorting with respect to size and physical properties.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Saif KHAN (NUS, Chemical Engineering)

35. Ecomechanics of Biofilms under Microfluidic Flows

In this project we are interested how biofilms respond to flow. We will use microfluidic devices to construct model flows to study streamer formation. Streamers are prevalent in many settings, such as water processing.

MIT Principal Investigator(s):
Patrick DOYLE (Chemical Engineering)

Singapore Co-Investigator(s):
Staffan KJELLEBERG (NTU, School of Biological Sciences)
Jie YAN (NUS, Physics)

36. High throughput Microfluidic Cell Separation

The goal of this project is to develop and apply microfluidic tools for sorting cells utilizing various inertial microfluidics concepts. So far, we have been applying the inertial microfluidics system for sorting circulating tumor cells (CTCs), bacteria, and leukocytes directly from a relatively large volume (1mL or more) of raw blood. We will continue to develop new ways of sorting cells using inertial microfluidic interactions, as well as engineer even higher flow rate capacity.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science & Biological Engineering)

Singapore Co-Investigator(s):
Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)
Peter CHEN (NUS, Mechanical Engineering)

37. Biomechanical Study of Biofluids and Biofilms Using Micro/Nanofluidic Channels

To explore and study the rheological properties of various biofluids (e.g. mucus) and biofilms. The goal here is to identify useful physical biomarkers that can be correlated with the physiological/biochemical properties of these fluids. At the same time, using microfluidic systems we will develop in vitro methods to study these complex fluids in more detail.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science & Biological Engineering)

Singapore Co-Investigator(s):
Yee Cheong LAM (NTU, Mechanical & Aerospace Engineering)

38. On-Chip Magnetic Resonance Device for Portable Disease Diagnostics

In this pilot project, we will design, fabricate and test such a microfluidic magnetic resonance spectroscopy system, with the intention of applying the tool to the magnetic, non-invasive cell monitoring and profiling. The two potential application modes for disease diagnostics (malaria and blood anomalies) are currently being pursued, but more diagnostic modalities with different diseases are possible and will be explored.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science & Biological Engineering)

Singapore Co-Investigator(s):
Peter PREISER (NTU, Biology)

39. High-Throughput Microfluidic Single Cell Analysis of Intracellular Compounds

We aim to develop an integrated microfluidic system for precise, high-throughput single-cell analysis of intracellular enzyme activities to establish accurate disease models. The integrated microfluidic platform combines the droplet generator, picoinjectors and micro-concentrators, which allows us to run multiplexing enzyme activity assay with high sensitivity in the micro-droplets. Thousands of droplets with individual cell encapsulations with different chemical sensing are generated for high-throughput screening. The ability to collect the statistical measurement data of different enzyme reactions effectively from the individual cells will revolutionize the current analytical methods for the biomarker detections. Therefore our device can be used as a diagnosis system for personal medicine purposes, which the commercially available devices are unable to.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science, Biological Engineering)

Singapore Co-Investigator(s):
Chia-Hung CHEN (NUS, Bioengineering)
Chwee Teck LIM (NUS, Bioengineering)

40. Nanoarchitected Surfaces for Multiplex Detection of Biomolecules

The detection of DNA hybridization and protein recognition event (immunoassay) is very important for the diagnosis and treatment of genetic diseases, for the detection infectious agents and for reliable biomedical analysis. The aim of proposed project is to develop nanostructured biosensor based on rationale design for ultra trace dynamic detection of disease related biomarkers.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science & Biological Engineering)

Singapore Co-Investigator(s):
Martin PUMERA (NTU, School of Physical and Mathematical Sciences)

41. Mechanical Property based Acoustic Cell Sorter

This project will explore and study the response of cells with varying mechanical property (e.g. deformability) when exposed to acoustic waves in both travelling field and standing field. The ultimate goal is to develop a novel cell sorting technology based on the cellular mechanical property using acoustic waves. The proposed technology will provide new cell sorting capability for cancer and stem cell research.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science, Biological Engineering)

Singapore Co-Investigator(s):
Ye AI (SUTD, Engineering Product Development)

42. Portable Imaging-based Cell Deformability Cytometer

Cell deformability has been identified as a promising label-free mechanical biomarker to determine the cell state for various biomedical applications, for example malaria diagnosis, blood storage, cancer and stem cell research. This project aims to develop a portable on-chip cell-imaging device capable of high-throughput deformability analysis.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science, Biological Engineering)

Singapore Co-Investigator(s):
Ye AI (SUTD, Engineering Product Development)

43. Application of Biophysically sorted Chondrocytes in Articular Cartilage Regeneration

Different depth-related zones of cartilage vary greatly in terms of density, morphology and metabolic activity, as well as the composition and structural arrangement of the extracellular matrix components. These zonal biochemical differences in turn lead to significant variations in strains and stresses experienced by the cells in different zones during joint loading. The approach to engineer a fully functional tissue based on zonal chondrocytes for treatment of cartilage defect to date presents many difficulties. Apart from the limited amount of cells that can be harvested from each zone, the lack of reliable and easy-to-handle zonal cell sorting protocols severely hinders the practicality. In this project, we will apply inertial microfluidics to separate different zonal chondrocytes from cartilage tissue, or from stem cell-derived tissue, based on the size-variation of zonal chondrocytes. These zonal chondrocytes will be transplanted to animals with artificial cartilage defects so as to validate the efficacy of restoring hierarchically-organized cartilage.

In this project, researchers will leverage skills in microfluidics, mechanics, cell culture, histology, molecular biology, in vivo experiments, and optical microscopy.

MIT Principal Investigator(s):
Jongyoon HAN (Electrical Engineering and Computer Science, Biological Engineering)

Singapore Co-Investigator(s):
Eng Hin LEE (NUS, Orthopaedic Surgery Department & NUS Tissue Engineering Program)
Chwee Teck LIM (NUS, Bioengineering and Mechanical Engineering)

44. Data Analytics for Understanding and Prediction in Biomedical Science

Many branches of science result in the creation of large data sets that we inherently believe contain generalizable information and specific findings of significant importance, but we lack tools that readily identify these large and important signals from among all the surrounding noise. The goal of this project is to design and implement tools for use in specific applications through the careful use of current advances in machine learning and information theory, as well as the development of new approaches where warranted. We are particularly interested in working with very high dimensional data sets, in the identification and compression of both redundant and irrelevant information, and in the extraction of key features and relationships with high statistical significance. Example applications include identification of adverse drug interactions, identification of predictive markers for cancer progression, and identification of signaling pathway connections from systems biology measurements.

MIT Principal Investigator(s):
Bruce TIDOR (Biological Engineering and Computer Science)

Singapore Co-Investigator(s):
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45. Advancing the Engineering of Complex Biological Systems

Synthetic biology is an emerging and rapidly developing field. It involves the design and construction of complex biological systems with novel functions to address important, challenging problems in many areas including health, energy and environment. For example, probiotics have been re-engineered to fight superbugs and cells have been engineered to become “cell factories” to produce drugs more efficiently. To achieve these goals we need experimental systems and tools, together with a modeling framework, that facilitates the assembly of individual pieces into larger wholes with prescribed properties, in a manner that is robust to uncertainties in individual behaviors and fluctuations in environmental conditions. Current constructions generally require a significant amount of “tinkering” to create seemingly arbitrary changes that eventually allow parts to work together in desired ways. The current project involves the development of combined experimental and computational systems that together control uncertainty and are robust to fluctuations to allow the design of systems whose operation is largely assured by an iterative design strategy, with a small number of iterations, rather than through arbitrary adjustments. Key features include using measurements in each iteration to reduce the uncertainty in future iterations and controlling the effect of both uncertainty and fluctuations through a proper statistical treatment of each. The outcome of the project will advance our ability to engineer complex biological systems in a more predictive and efficient manner.

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