Research highlights from BEES Lab, IISc, 2019

Dr. Hardik J. Pandya's Lab (Biomedical and Electronic (10^{-6}-10^{-9}) Engineering Systems Laboratory) at the Department of Electronic Systems Engineering, Indian Institute of Science, Bangalore focuses on developing novel biomedical devices and healthcare solutions by combining expertise in microengineering, biomedical engineering, electronic system design, additive manufacturing and sensor interfacing and calibration to solve unmet problems in biology and medicine. The research work in the lab broadly focuses on technologies for early detection, screening and diagnosis of breast, oral, brain, and other solid tumor cancers, smart catheter technologies for cardiac ablation and neonatal intubation, portable systems for auditory screening of infants and neonates using biopotentials, blue-sky research in bioresorbable devices for recording bio-potentials, microsystems for rapid antibiotic susceptibility screening, to name a few. In the year 2019 the lab published several review articles and a research article in these domains. The details of these publications follow:

1. ***"Electronic-nose: A non-invasive technology for breath analysis of diabetes and lung cancer patients"***

Journal: Journal of breath research

Publication date: 6/3/2019

About the publication: Non-invasive technologies for screening non-communicable diseases such as diabetes and cancer are the need of the hour owing to its inherent advantages. This article reviews the state-of-the-art and recent emerging trends in technologies employed for analyzing the breath samples from potential diabetes and lung cancer patients. Machine learning approaches for improving the sensing parameters is also presented.

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Journal of Breath Research

TOPICAL REVIEW

Electronic nose: a non-invasive technology for breath analysis of diabetes and lung cancer patients

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Keywords: electronic nose, non-invasive technologies, breath signals, volatile organic compounds, diabetes, lung cancer

Abstract

In human exhaled breath, more than 3000 volatile organic compounds (VOCs) are found, which are directly or indirectly related to internal biochemical processes in the body. Electronic noses (E-noses) could play a potential role in screening/analyzing various respiratory and systemic diseases by studying breath signatures. An E-nose integrates a sensor array and an artificial neural network that responds to specific patterns of VOCs, and thus can act as a non-invasive technology for disease monitoring. The gold standard blood glucose monitoring test for diabetes diagnostics is invasive and highly uncomfortable. This contributes to the massive need for technologies which are non-invasive and can be used as an alternative to blood measurements for glucose detection. While lung cancer is one of the deadliest cancers with the highest death rate and an extremely high yearly global burden, the conventional diagnosis means, such as sputum cytology, chest radiography, or computed tomography, do not support wide-range population screening. A few standard non-invasive techniques, such as mass spectrometry and gas chromatography, are expensive, non-portable, and require skilled personnel for operation and are again not suitable for large-scale screening. Breath contains markers for both diabetes and lung cancer along with markers for several diseases and thus, a non-invasive technique such as the E-nose would greatly improve analysis procedures over existing invasive methods. This review shows the state-of-the-art technologies for VOC detection and machine learning approaches for two clinical models: diabetes and lung cancer detection.

2. ***"Engineering approaches for characterizing soft tissue mechanical properties: A review"***

Journal: Clinical Biomechanics

Publication Date: 16/7/2019

About the publication: From cancer diagnosis to detailed characterization of arterial wall biomechanics, the elastic property of tissues is widely studied as an early sign of disease onset. The article we have published details state of the art advancements in probing strategies and associated challenges toward quantitative characterization of tissue biomechanics both from an engineering and clinical standpoint.

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Review

Engineering approaches for characterizing soft tissue mechanical properties: A review

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ARTICLE INFO

Keywords:
Indentation
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Catheters
Elastic modulus
Machine learning

ABSTRACT

From cancer diagnosis to detailed characterization of arterial wall biomechanics, the elastic property of tissues is widely studied as an early sign of disease onset. The fibrous structural features of tissues are a direct measure of its health and functionality. Alterations in the structural features of tissues are often manifested as local stiffening and are early signs for diagnosing a disease. These elastic properties are measured *ex vivo* in conventional mechanical testing regimes, however, the heterogeneous microstructure of tissues can be accurately resolved over relatively smaller length scales with enhanced spatial resolution using techniques such as micro-indentation, microelectromechanical (MEMS) based cantilever sensors and optical catheters which also facilitate *in vivo* assessment of mechanical properties. In this review, we describe several probing strategies (qualitative and quantitative) based on the spatial scale of mechanical assessment and also discuss the potential use of machine learning techniques to compute the mechanical properties of soft tissues. This work details state of the art advancement in probing strategies, associated challenges toward quantitative characterization of tissue biomechanics both from an engineering and clinical standpoint.

3. ***"Futuristic medical implants using bioresorbable materials and devices"***

Journal: Biosensors and Bioelectronics

Publication Date: 2/7/2019

About the publication: The article discusses the clinical applications of bioresorbable devices including real-time monitoring of physical parameters (temperature, pressure, and biopotentials), bioresorbable materials and the fabrication of such devices. The bioresorbable devices can be a potential alternative to the conventional implantable clinical devices owing to its resorbability in biofluids eliminating the retrieval surgery of the implant.

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Futuristic medical implants using bioresorbable materials and devices

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ARTICLE INFO

Keywords:
Bioresorbable materials
Sensor fabrication
Bioresorbable devices
Implantable devices
Clinical applications

ABSTRACT

Implantable medical devices have been used for real-time monitoring of physical parameters (temperature, pressure and biopotentials), sustained drug release, cardiovascular and pulmonary stents and other clinical applications. Several biocompatible materials (titanium and its alloys, aluminium, cobalt-alloys, stainless steel, poly-ethylene, polyurethanes, polyglycolide and polylactides) have been commercially used for fabricating implantable devices. However, these devices require retrieval operations after a certain period. Bioresorbable materials disintegrate gradually *in vivo* and their derivatives get absorbed completely in the body fluid with no residue and with minimal toxic effects, thus, eliminating the need for retrieval operations. In this article, state-of-the-art advances in materials, fabrication techniques and clinical applications of bioresorbable implantable devices are reviewed. We first discuss the bioresorbable materials (e.g., magnesium, molybdenum, tungsten, silicon, germanium, silicon dioxide, silicon nitride, silk and synthetic polymers) used in the fabrication of implantable devices. Later, an overview of processes to fabricate pressure, temperature, electrical and chemical sensors are discussed, followed by their applications as implantable devices in biomedical engineering.

4. "***Emerging technologies for antibiotic susceptibility testing"***

   Journal: Biosensors and Bioelectronics

   Publication Date: 09/08/2019

   About the publication: Clinical complications arising from antibiotic resistance is already an important healthcare challenge across medical science. This article reviews the emerging technologies that are being employed to profile the antibiotic resistance of bacteria from clinical samples and cultures while also discussing the classical techniques that serve as gold standard presently. The focus is on the technology per se and its suitability for translation as a rapid, cost-effective, clinically relevant platform.

Biosensors and Bioelectronics 142 (2019) 111552

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Emerging technologies for antibiotic susceptibility testing

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ARTICLE INFO

Keywords:
Bacteria
Antibiotics
AST
Emerging technologies
Microfabrication

ABSTRACT

Superbugs such as infectious bacteria pose a great threat to humanity due to an increase in bacterial mortality leading to clinical treatment failure, lengthy hospital stay, intravenous therapy and accretion of bacteraemia. These disease-causing bacteria gain resistance to drugs over time which further complicates the treatment. Monitoring of antibiotic resistance is therefore necessary so that bacterial infectious diseases can be diagnosed rapidly. Antimicrobial susceptibility testing (AST) provides valuable information on the efficacy of antibiotic agents and their dosages for treatment against bacterial infections. In clinical laboratories, most widely used AST methods are disk diffusion, gradient diffusion, broth dilution, or commercially available semi-automated systems. Though these methods are cost-effective and accurate, they are time-consuming, labour-intensive, and require skilled manpower. Recently much attention has been on developing rapid AST techniques to avoid misuse of antibiotics and provide effective treatment. In this review, we have discussed emerging engineering AST techniques with special emphasis on phenotypic AST. These techniques include fluorescence imaging along with computational image processing, surface plasmon resonance, Raman spectra, and laser tweezer as well as micro/nanotechnology-based device such as microfluidics, microdroplets, and microchamber. The mechanical and electrical behaviour of single bacterial cell and bacterial suspension for the study of AST is also discussed.

5. ***"Force sensing technologies for catheter ablation procedures"***

Journal: Mechatronics

Publication date: 1/12/2019

About the publication: This article discusses several advancements in force sensor designs that could be potentially integrated with ablation catheters. Their sensing principles, design specifications and their need for interfacing with cardiac catheters are also elaborated.

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Review

Force sensing technologies for catheter ablation procedures ☆

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ARTICLE INFO

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Force Sensor

ABSTRACT

Cardiac Arrhythmia, a condition of abnormal activation and conduction of electrical impulses in the heart is observed in a large proportion of the world population. Radio frequency (RF) ablation catheters have revolutionized the treatment of cardiac arrhythmias. Over the years, researchers have been extensively working towards developing a more promising catheter technology that ensures definitive treatment. Since RF energy is based on the principle of resistive heating, to optimize effective lesion formation, a catheter to adequately sense tissue contact force becomes vital. The review focuses on state-of-the-art advancement in force sensors, design specification and their need for interfacing with cardiac catheters. Minimally invasive medical procedures for cardiac ablation followed by various controlling methods used for providing quality lesion have been overviewed. Several design prototypes and variants of force sensors that can potentially be integrated with ablation catheters are reviewed with their sensing principles and implementation.

6. ***"A smart tele-cytology point-of-care platform for oral cancer screening"***

Journal: PLOS One

Publication date: 15/11/2019

About the publication: The article discusses an automated oral cancer staging tool to analyze cytology images developed in collaboration with Mazumdar Shaw Medical Centre (MSMF), Bangalore, India. The work resulted in the development of an algorithm that predicts the most likely stage of oral cancer from cytology images. The algorithm could achieve 90% overall accuracy over manual tele cytology (60% accuracy) in predicting the oral cancer stage when compared with histopathology as the gold standard.

PLOS ONE

RESEARCH ARTICLE

A smart tele-cytology point-of-care platform for oral cancer screening

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Abstract

Early detection of oral cancer necessitates a minimally invasive, tissue-specific diagnostic tool that facilitates screening/surveillance. Brush biopsy, though minimally invasive, demands skilled cyto-pathologist expertise. In this study, we explored the clinical utility/efficacy of a tele-cytology system in combination with Artificial Neural Network (ANN) based risk-stratification model for early detection of oral potentially malignant (OPML)/malignant lesion. A portable, automated tablet-based tele-cytology platform capable of digitization of cytology slides was evaluated for its efficacy in the detection of OPML/malignant lesions (n = 82) in comparison with conventional cytology and histology. Then, an image pre-processing algorithm was established to segregate cells, ANN was trained with images (n = 11,981) and a risk-stratification model developed. The specificity, sensitivity and accuracy of platform/ stratification model were computed, and agreement was examined using Kappa statistics. The tele-cytology platform, Cellscope, showed an overall accuracy of 84–86% with no difference between tele-cytology and conventional cytology in detection of oral lesions (kappa, 0.67–0.72). However, OPML could be detected with low sensitivity (18%) in accordance with the limitations of conventional cytology. The integration of image processing and development of an ANN-based risk stratification model improved the detection sensitivity of malignant lesions (93%) and high grade OPML (73%), thereby increasing the overall accuracy by 30%. Tele-cytology integrated with the risk stratification model, a novel