Addressing Challenges in Blood Multi-Omics Data Optimization and Analysis: A Call for AI Solutions

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Abstract

As an integral component of the SC ADAPT program, Thrust I is dedicated to leveraging multimodal, longitudinal, and cross-sectional data obtained from experimental sources and existing clinical databases. Our primary objective entails harnessing explainable artificial intelligence (XAI) methodologies to pioneer the development of a biomedical device for informed decision-making. In this presentation, I will provide a brief overview of our strategy for advancing the development of XAI-enabled biomedical devices. Our approach involves the integration of XAI principles into two innovative devices currently under development by the Thrust I team: one designed for impedance-based wound assessment and the other tailored for microchamber-based antibiotics analysis.

I will discuss our ongoing efforts in devising novel methodologies for identifying protein biomarkers within human blood samples. This endeavor entails the utilization of cutting-edge nanomaterials to selectively enrich low-abundance biomarker proteins, coupled with metabolomics techniques. It is noteworthy that the utilization of blood plasma for biomarker testing holds immense promise due to its cost-effectiveness, accessibility, and minimally invasive nature. We envision that our ultimate methodology will yield a comprehensive understanding of signature patterns, enabling more sensitive, specific, and robust predictions for various diseases. A paramount challenge we face is establishing an efficient feedback loop to expedite the optimization process of our methodologies and devices, while concurrently correlating our multiomics dataset with clinical data obtained from patients. We hope that the collaboration between engineers and data scientists will help solve this challenge.

Biomedical Imaging Through Tissue with a micro-LED Display

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Implant infection results in local acidosis, where the bacterial activities and immune system responses change the pH level. The pH is reportedly spatially heterogeneous at the micrometer level in biofilms near an implant. Thus, imaging these spatially heterogeneous regions through implantable pH-sensitive sensors can help detect infection early, monitor during treatment, and elucidate the local environment to help design effective treatment strategies. This study focuses on imaging pH variations on orthopedic implants inside a body using microlight-emitting diodes (μLEDs). The μLEDs are bright and more cost-effective compared to X-rays used in the X-ray excited luminescence chemical imaging (XELCI) systems for pH imaging. In this work, we used a flexible OLED display array as a local light source to image optical absorption from pH indicator dyes. The OLED array enabled us to raster scan different targets through porcine tissues of varying thicknesses (~1-4 cm). The light that passed through the tissues and optical reference targets was captured either using a Nikon camera or a photomultiplier tube (PMT). The imaged targets consisted of a colored arrow printed on A4 paper and a pH reference strip. Successful reconstruction of the images of these targets showed color sensitivity and fine resolution, limited only by the pixel size of the μLED. This technique enabled us to image different pH sensors through tissues of thickness as thick as ~4 cm. These combined results showed that μLED can be appropriate for non-invasive, effective imaging of implant-associated infections.

Measuring chondrocyte viability of articular cartilage with two-photon microscopy and deep learning image analysis

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Keywords Cell Viability, Label-free imaging, Nonlinear Optical Microscopy, Deep Learning, Instance Segmentation

Introduction/Background: Articular cartilage has a limited healing capacity. Traumatic and degenerative lesions eventually progress to osteoarthritis (OA), a leading source of disability worldwide. Among various surgical resurfacing treatments, osteochondral allograft transplantation has been proven to have good clinical outcomes, especially for relatively large lesions. Osteochondral allografts have become increasingly popular due to the improvement and standardization in allograft storage. As the chondrocyte is the only cell type in articular cartilage, chondrocyte viability (CV), the ratio between populations of viable cells and all cells at the time of implantation, is believed to be a critical factor in ensuring long-term allograft survival in vivo. However, viability assessment usually requires dye labeling; tissues are not unusable after the evaluation. Label-free, nondestructive methods to measure CV is desired.

Goal of Study: The purpose of this study is to develop a label-free method for measuring CV of articular cartilage with two-photon microscopy imaging and deep learning image analysis.

Methods and Results: Autofluorescence of intracellular fluorescent coenzymes, such as reduced forms of nicotinamide adenine dinucleotide (NADH) or nicotinamide adenine dinucleotide phosphate (NADPH) and oxidized flavoproteins (FPs), have been long used as a label-free means to study metabolic states of cells. We previously found that viable and nonviable cells had different appearances when imaged with two-photon excitation autofluorescence (TPAF) and second harmonic generation (SHG) microscopy on rat and porcine cartilage samples. In this study, we acquired TPAF/SHG images with a homebuilt two-photon microscope on porcine cartilage samples and merged three-channel images to RGB color images by assigning red, green, and blue to FPs, NAD(P)H, and collagen signal channels, respectively. To count the viable and total number of cells, we developed a deep learning neural network for cell segmentation and classification based on Mask R-CNN algorithms. The new network is a single integrated architecture that can identify individual cells and, at the same time, classify them with cell status. Using training (300 images) and test (120 images) datasets from rats and porcine cartilage, we have demonstrated that Mask R-CNN based networks provide integrated segmentation and classification of individual cells with high accuracy as indicated by F1 scores of ~0.9. The accuracy of the Mask R-CNN based CV measurement has reached over 95%. Moreover, image preprocessing with the Wiener Deconvolution filter significantly improves the accuracy of the CV measurement using Mask R-CNN.

Discussion/Conclusions: The new network is a single integrated architecture that can identify individual cells and, at the same time, classify them with live or dead status. This integrated architecture only needs a single annotated training and test dataset, making the learning and viability analysis more efficient. Secondly, the new network performs instant segmentation, which identifies each chondrocyte as a distinct object with the category that it belongs to and the boundary that separates it from the rest of the pixels in an image. Instant segmentation improves the accuracy of both segmentation and classification. Moreover, we have found that Wiener deconvolution preprocessing can significantly improve the accuracy of CV measurement. Taken together, we have demonstrated a novel CV measurement method that offers a label-free, nondestructive assessment of allografts.

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