Department of Biomedical Engineering
Graduate Seminar

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Subject: Non-Invasively Predicting Function and Identity of a Tissue Engineered Therapy for Macular Degeneration and the Development of a New Data Science Platform to Enable It

Abstract:

Progressive increases in the number of retinal cell therapies in the preclinical and clinical phases has prompted the need for reliable and non-invasive assays to validate transplant function in clinical biomanufacturing. I will discuss the development of a robust characterization platform composed of a newly developed light microscopy technique called quantitative bright-field absorbance microscopy (QBAM) and deep neural networks (DNNs) to non-invasively predict tissue function and induced pluripotent stem cell (iPSC) donor identity. The platform was validated using clinical-grade iPSC derived retinal pigment epithelial cells (iRPE). QBAM images of iRPE were used to train DNNs that predicted iRPE monolayer transepithelial resistance, polarized cytokine secretion, and matched iRPE monolayers to the iPSC donors. DNN predictions were supplemented with traditional machine learning algorithms that identified shape and texture features of single cells that were used to predict tissue function and iPSC donor identity. The above work was accomplished using three different image acquisition software packages, four different programming languages, more than 20 software libraries/packages, and generated over 1 TB of data (>200,000 images and 12M cells) obtained across three labs and four microscopes. Information technology (IT) challenges such as powerful enough computers to do the data processing, keeping all data organized and meta-data appropriately linked, and maintaining data provenance throughout the analysis was every bit as challenging to overcome as the science. Thus, I will also cover my Group's work to help overcome some of these hurdles in a unified, open-source, data analysis platform called Polus that we are developing in collaboration with the National Institute of Standards and Technology.

Bio:

Dr. Nathan Hotaling is the Vice President of Data Science at Axle Informatics and is a Senior Data Scientist within the Information Resources Technology Branch at NCATS where his group develops the next generation of artificially intelligent image analysis tools. He received his PhD in Biomedical Engineering in 2013 from the Georgia Institute of Technology. After his PhD, Nathan did post-doctoral research in a project led by the National Institute of Standards and Technology (NIST) in collaboration with the National Eye Institute (NEI)

where he developed software that could accurately assess nanofiber diameter from electron microscopy images.

Using this technology he helped develop and optimize a novel biodegradable nanofiber scaffold for use in a cell therapy for age-related macular degeneration. His post-doctoral work at NIST transitioned to his second post-doctoral position at the NEI where he further optimized the nanofiber scaffold for use in an Investigational New Drug application to the FDA. While pursing these projects he began to develop a platform to analyze high content image datasets collected for drug screening and cell bio-manufacturing. This work led to his transition to NCATS where he oversees the development of the next generation of image analysis tools for researchers in the high-throughput and high-content screening fields.

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