

Phasor-Based FLIM Imaging and Mitometer: Linking ECM Mechanics to Metabolic Signatures and Mitochondrial Dynamics



PRESENTED BY

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SCHEDULE

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Metabolic alterations, particularly increased glycolysis (Warburg effect), and atypical extracellular matrix (ECM) structure contribute to tumor aggressiveness and drug resistance. While tumor cells stiffen the ECM during progression, the direct relationship between ECM stiffness and altered metabolism remains poorly understood. We apply phasor-based fluorescence lifetime imaging microscopy (FLIM) to measure metabolic changes as a function of ECM mechanics. Comparing triple-negative breast cancer (TNBC) cells to non-cancerous cells on substrates of varying stiffness, we found that TNBC exhibits decreased bound NADH fraction (indicative of glycolysis) with increasing substrate stiffness, while other cell lines showed minimal changes. To investigate mitochondrial dynamics, we developed "Mitometer" (available on GitHub), an unbiased algorithm for automated segmentation and tracking of mitochondria in live-cell 2D and 3D time-lapse images. Mitometer reveals that mitochondrial motility and morphology in breast cancer—but not normal breast epithelia—correlate with bound NADH fractions and features such as speed, displacement, directionality, and branching. We also introduce novel hyperspectral imaging methods combined with multicolor organelle-specific staining for simultaneous multi-parametric physiological profiling of multiple organelles in live cells, applicable to both non-tumorigenic and cancerous cell lines.

Bio: Michelle Digman is the William J. Link Chair and Professor in the Department of Biomedical Engineering at the University of California Irvine. She is currently the Director of the Laboratory for Fluorescence Dynamics and Director of W.M. Keck Nanoimaging Lab. She served as Co-equity advisor for the Henry Samueli School of Engineering for 5 years and BME Associate Chair for Graduate Affairs for 3 years. She received her MS and PhD in Chemistry from University of Illinois at Chicago and did her postdoctoral work at the University of Illinois, Urbana-Champaign in the Department of Physics.