Biological Design Doctoral Defense

Near-infrared Contrast Agents for Cell Type Identification and Detection Utilizing Photoacoustics

School for Engineering of Matter, Transport and Energy

Joel Lusk

Advisor: Dr. Barbara Smith

Abstract

The imaging and detection of specific cell types deep in biological tissue is critical for the diagnosis of cancer and the study of biological phenomena. Current high-resolution optical imaging techniques are depth limited due to the high degree of optical scattering that occurs in tissues. To address these limitations, photoacoustic (PA) techniques have emerged as noninvasive methods for the imaging and detection of specific biological structures at extended depths in vivo. In addition, near-infrared (NIR) contrast agents have further increased the depth at which PA imaging can be achieved in biological tissues. The goal of this research is to combine novel PA imaging and NIR labeling strategies for the diagnosis of disease and for the detection of neuronal subtypes. Central Hypothesis: Utilizing custom-designed PA systems and NIR labeling techniques will enable the detection of specific cell types in vitro and in mammalian brain slices. Work presented in this dissertation addresses the following: (Chapter 2): The custom photoacoustic flow cytometry system combined with NIR absorbing copper sulfide nanoparticles for the detection of ovarian circulating tumor cells (CTCs) at physiologically relevant concentrations. Results obtained from this Chapter provide a unique tool for the future detection of ovarian CTCs in patient samples at the point of care. (Chapter 3): The custom photoacoustic microscopy (PAM) system can detect genetically encoded nearinfrared fluorescent proteins (iRFPs) in cells in vitro. Results obtained from this Chapter can significantly increase the depth at which neurons and cellular processes can be targeted and imaged in vitro. (Chapter 4): Utilizing the Cre/lox recombination system with AAV vectors will enable selective tagging of dopaminergic neurons with iRFP for detection in brain slices using PAM. Thus, providing a new means of increasing the depth at which neuronal subtypes can be imaged and detected in the mammalian brain. Significance: Knowledge gained from this research could have significant impacts on the PA detection of ovarian cancer and extend the depth at which neuronal subtypes are imaged in the mammalian brain.