Dry Mass Volume Recovery Using Neural Network Enhanced Bright Field Microscopy

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Abstract

A cell's volume and dry mass density are important biomarkers to track during certain biological processes such as apoptosis. Label-free measurement of these quantities allows for the non-invasive study of these processes in live cells. Under fairly general assumptions, dry mass density may be computed directly from a cell's refractive index (RI), a measure of the delay of light at each point within the cell's volume. Traditional label-free quantitative phase imaging (QPI) is a technique that allows for reconstructions of a cell's optical thickness, which is proportional to the product of the cell's relative RI and thickness. Disentangling the product of thickness and RI traditionally requires making assumptions about one of the two quantities, which may not always be applicable. A separate, more powerful extension of these traditional QPI techniques is optical diffraction tomography (ODT). ODT allows for reconstructions of RI, and thus dry mass volume, through the three-dimensional profile of a sample. Much like x-ray computed tomography (CT), ODT works by imaging a sample at many different angles. At each angle, the traditional QPI techniques can be modified and applied to reconstruct a portion of the total information needed to produce the three-dimensional RI profile of the sample. Currently, commercially available ODT systems require specialized, standalone optical instruments. Transport of intensity equation (TIE) QPI enables ODT with only minor modifications to a conventional bright-field microscope, but suffers from significant artifacts due to limitations in the computational reconstruction algorithms. In this work, we present a modification of TIE to enable ODT for thin samples such as individual cells by using fast-training of a physics-based neural network to mitigate artifacts. We demonstrate this by producing 3D reconstructions of biological samples. The proposed framework shows strong potential for an accurate and reliable 3D RI/dry mass density reconstruction using bright-field microscopes while maintaining reasonable reconstruction times.