A Novel Modeling and Inversion Method to Image Weakly Scattering Sub-cellular Structure

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Non-invasive assessment of the health of an embryo or a single cell is an open issue of critical importance for the success of certain procedures like in vitro fertilization. To achieve this goal, we need a three dimensional understanding of the investigated structure, such as how mitochondria are distributed within the cell, or how many cells reside in the embryo. Advanced microscopy can provide both amplitude and phase information from multiple views, but obtaining detailed volumetric information is challenging. In particular, imaging mitochondria is usually quite difficult since there may be 100,000 of these tiny low-contrast scatterers overlapping each other within the cell.

Although the electromagnetic properties of cellular structures exhibit slight variations relative to the background, methods based on the Born approximation are not suitable to image these objects since their overall electrical sizes are quite large when they are probed in or near the visible spectrum, and the observed scattered light is in the farfield of the cell.

In this work, we present a novel method to image these objects in two dimensions, which is based on the expansion of the target object function in terms of Fourier-Bessel coefficients, and an alternative approximation for the total fields within the scatterer. This approximation satisfies the continuity of the total tangential fields at the object-background boundary for each circular mode using the known incident and observed scattered fields, and takes into account the fact that the refractive index distribution along structures being investigated varies slightly around a known mean value. The resulting linear system of equations is solved via Tikhonov regularization for the unknown expansion coefficients. This approach can be readily extended to more realistic 3D cases.

To illustrate the method, a number of Finite-Difference Time-Domain (FDTD) simulations involving cells models with miscellaneous organelle distributions, such as aggregated, perinuclear, cortical mitochondria distributions, have been performed. Basic ideas of the FDTD method, such as total-field scattered-field formulation, near to far field transform, PML absorbing boundary condition have been employed to obtain the far zone scattered fields due to the cell models under plane wave illumination. These far zone scattered fields have been utilized to form the image of the probed objects. Remarkably accurate reconstructions of the general density distribution of the subcellular structure have been obtained.