## Interferometric Synthetic Aperture Microscopy: Inverse Scattering for Optical Coherence Tomography

Tyler S. Ralston, Daniel L. Marks, P. Scott Carney and Stephen A. Boppart

ow coherence interferometry has a long history for accurately probing depths in biological media. In an effort to better visualize the resulting scattering maps, we used optical coherence tomography (OCT), which provided cross-sectional images and three-dimensional volumes using only one- or two-dimensional scanning, respectively.

Over the past 15 years, OCT has been shown to be useful in many biomedical applications, including ophthalmology, cardiology, developmental biology and microscopy.<sup>2</sup> With the use of near-infrared light, OCT facilitates the noninvasive monitoring of cellular and nuclear organization, proliferation and functionality. A strength of OCT is its ability to recreate object structure based on first-order object scattering, provided that only the data in the confocal region of the lens was used.

OCT has vastly improved the visualization of biological processes. However, it remains unable to resolve features imaged outside of the confocal region. OCT signals are akin to echo pulses from strip-map radar or sonar, where raw data are plotted in adjacent columns. OCT

images do not resolve the single scattering signal acquired between multiple scans, such as those scattering signals that exist outside of the confocal region.

Just as a better description of the field quantities in radar has led to synthetic aperture radar (SAR),<sup>3</sup> modeling the physical parameters in OCT has stimulated the development of a new method called Interferometric Synthetic Aperture Microscopy (ISAM). Specifically, inverse scattering theory for OCT has been used to resolve 3D object structure, taking into account the finite beam width, diffraction, dispersion and defocusing effects.<sup>4</sup>

ISAM has increased the resolution achievable from an OCT signal outside of the confocal parameter of the focusing lens by exploiting the previously undecipherable out-of-focus data within the conventional OCT imaging scheme. Thus, ISAM reconstructions exhibit spatially invariant resolution. Furthermore, the reconstruction algorithm may be implemented for either cross-sectional images or full 3D volumes, and, because of the modest computational complexity of this technique, ISAM is amenable to real-time imaging.

To demonstrate this technique, we present a collection of scatterers having a mean diameter of 2  $\mu$ m suspended in silicone and imaged with cross-sectional ISAM. Our ISAM system is similar to that for spectral-domain OCT,<sup>5</sup> except with additional instrumentation for phase stability and tighter focusing. The multiplexed raw OCT data set must maintain phase stability to ensure proper reconstruction.

The figure displays (a) the original and (b) the reconstruction of an imaging area of 500  $\mu$ m (transverse) by 1,000  $\mu$ m (axial), where the bandwidth is 100 nm, and the spot size is 6  $\mu$ m. The image resolution of point scatterers outside of the confocal region for the original experimental image data is not constant. However, for the reconstruction, the resolution is constant along the entire image with only amplitude variations.

The interference between the light scattered from a group of adjacent particles (boxed) is evident in the original image (top magnified). Our method properly rephases the signal from scatterers to produce a well-resolved image (bottom magnified). This method will be extended to imaging biological samples to achieve high, spatially invariant resolution in 3D.  $\triangle$ 

[ The authors are with the Beckman Institute for Advanced Science and Technology, department of electrical and computer engineering, University of Illinois at Urbana-Champaign, Ill. ]

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