Most of the properties of optical fields, such as wavelength, polarization, wavefront curvature or angular spectrum, have been commonly manipulated in a variety of sensing procedures. However, controlling the degree of coherence of light did not find many applications until recently, with the emergence of optical coherence tomography. Since then, a growing number of scattering techniques have relied on temporal coherence gating, which provides efficient target selectivity in a way achieved only by cumbersome short pulse measurements.

The spatial counterpart of temporal coherence, however, has barely been exploited. Recently, we have introduced a tomographic procedure, where the spatial coherence gating is used to probe structural properties of a scattering object over an extended volume and with a very simple detection system.

In many scattering media, similar subwavelength features are reproduced at few wavelengths apart, and determining the structural morphology of such an object requires imaging over a large field of view. While many near-field microscopic techniques offer spatial resolution beyond the classical diffraction limit, scanning a sample over a large area is time-consuming, or, sometimes, practically impossible. Taking advantage of the large field of view accessible when using the spatial coherence gating, we have introduced the principle of variable coherence scattering microscopy (VCSM).

In this novel stochastic sensing approach, the structure being tested is probed by an evanescent field while the scattered intensity is recorded at one single position in the far-field, as illustrated in (a). As shown in (b), spatial coherence gating is achieved by adjusting the degree of coherence of the evanescent field. The second-order statistical properties of the complex susceptibility are then recovered by inducing coherent scattering from regions in the medium, which are separated by a controllable distance $\Delta r_0$. Our variable coherence microscope allows detecting the high spatial frequencies of the scattered field, which are not accessible in regular microscopic techniques (c).

Remarkably, in this novel approach for solving the inverse problem, the subwavelength resolution is achieved from simple far-zone measurements. Furthermore, the technique does not require any moving parts, therefore making VCSM a good candidate for high throughput sensing and screening for various applications in biology and medicine.

The idea of using the spatial coherence properties of radiation in a tomographic procedure is applicable to any type of electromagnetic radiation. Operating on principles of statistical optics, such a sensing technique can become an alternative for various cutting-edge microscopies that rely on isolating small volumes of analyte or that require high-resolution scanning over minute dimensions of a sample.

References
Optically Pinpointing Magnetic Nanoparticles within Biological Tissue

Amy L. Oldenburg and Stephen A. Boppart

An emerging imaging technology known as optical coherence tomography (OCT) provides microscopic in vivo imaging by using interferometry to detect light reflected from deep tissue structures. OCT imaging has been adopted by medical practitioners in many areas, including ophthalmology, cardiology and gastroenterology. Currently, there is an intense search for stains or contrast agents to use with OCT because conventional markers, such as fluorescent dyes, emit incoherent light for which there is no OCT interference signal.¹

Magnetic iron oxides, such as carbohydrate-coated magnetite (Fe₃O₄) nanoparticles, have recently been FDA-approved as human injectable contrast agents for MRI.² This class of particles is highly responsive to a magnetic field gradient, and at lower frequencies than those used in MRI (10 to 100 Hz), they can be mechanically modulated or “wiggled” within the tissue microenvironment. The magnetomotive “wiggling” exhibits a unique optical light scattering signature when probed using OCT. Our group developed a technique in which a modulated magnetic field is applied during OCT imaging, dubbed magnetomotive OCT (MMOCT).³ Using MMOCT, magnetic iron oxide nanoparticles are pinpointed within a standard OCT image, requiring only the addition of a small electromagnetic field to the imaging system.

The basic MMOCT technique involves querying the tissue both before and after application of the magnetic field gradient. By comparing the OCT data before and after, differences are attributed to a magnetic field-specific reaction, thus pinpointing the locations of the magnetic nanoparticles. This concept was first demonstrated in tissue scaffolds containing macrophage cells labeled with magnetic nanoparticles, allowing one to distinguish labeled and unlabeled cells within a thick (1.5 mm deep) sample.³ However, the original MMOCT technique was plagued with motion artifacts during the study of larger living organisms, which are subject to respiration and cardiac-based motions.

The motion artifact problem was resolved in recent work,⁴ where the imaging sample is queried three times: twice with no magnetic field, and once with the magnetic field, analogous to pulse sequences used in MRI. Thus, non-specific background motion is estimated from the first two measurements, which is then subtracted from the magnetic particle-specific signal. This results in the ability to track magnetic nanoparticles within living animals such as the Xenopus laevis African frog tadpole. (See figure.) These tadpoles internalize nanoparticles through their suction feeders, which are subsequently observed inside their gastrointestinal tract.

The nature of particle magnetomotion experimentally agrees with a basic physical model.⁴ Each magnetic particle is displaced a distance that is proportional to the magnetic gradient force. This displacement also disturbs adjacent non-magnetic particles (such as cells and organelles), further enhancing the local MMOCT signal. Because of the high sensitivity of a typical OCT imaging system, nanometer-scale displacements of these particles can be detected.

Another interesting consequence of this technique is that the magnetomotive displacement depends on the elasticity and binding of the nanoparticle within the tissue microenvironment. This has exciting potential applications for tissue elastography, and also measurement of particles binding to cell surface receptors. Ultimately, MMOCT provides a unique platform for studying nanoparticle movement in vivo, with better depth penetration than in conventional microscopy.

References:

Combined OCT/MMOCT imaging in live African frog tadpoles (Xenopus laevis) without (a,b) or with (c,d) exposure to 25 nm iron oxide nanoparticles. Red displays tissue structure and green displays magnetic nanoparticles (top scale bar 500 µm). Region 1: The beating heart. Region 2: Intestine with surface features that are highly modulated by internal magnetic nanoparticles. Internalization of particles is verified by histology (g) compared to control (f); the lower scale bar is 200 µm. Region 3 is a mounting surface intentionally embedded with excreted magnetic particles. (e) Photograph of tadpole.
Interferometric Synthetic Aperture Microscopy: Inverse Scattering for Optical Coherence Tomography

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

Low 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. 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), 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.

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 μm suspended in silicone and imaged with cross-sectional ISAM. Our ISAM system is similar to that for spectral-domain OCT, 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 μm (transverse) by 1,000 μm (axial), where the bandwidth is 100 nm, and the spot size is 6 μm. 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.

References