THE AUTHOR FILE

Jerome Mertz

Microscopy without fluorescence to peek under the tissue surface

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Books about optics were scattered around his house growing up, says Jerome Mertz, a faculty member in Boston University's biomedical engineering department. Optics is his father's line of work. "There was even a telescope he built in the back yard," Mertz says. "What else could I do but go into optics?"

He completed his PhD in physics at Université Paris VI and the University of California, Santa Barbara. Mertz did two postdoctoral fellowships, one at Universität Konstanz in Germany and the other at Cornell University in Ithaca, New York, after which he was a researcher at the École Supérieure de Physique et de Chimie Industrielles (ESPCI) in Paris. "There is something aesthetically pleasing about optics, and physics in general, that I find fascinating," he says, which is what motivates him to develop and apply new types of optical microscopy techniques for biological research.

Since 2003, when he began at Boston University—where he also holds appointments in the physics department and electrical and computer engineering department—Mertz's focus has been on improving two-photon excitation fluorescence microscopy and developing novel phase-contrast techniques.

With his latest work, he and his colleagues present oblique back-illumination microscopy (OBM): a way to see under the surface of tissue without fluorescence labeling or any other kind of probe. Working on their technology, in which the illumination and detection optics are on the same side of a sample, Mertz and his team scoured the literature for possible overlaps with other groups, but they found that no one had tried it before. In making OBM a reality, he credits his students and luck, along with "a capacity to follow up on that luck," he says. Music is another added ingredient. For Mertz, the grant-writing process calls for a musical score: in his case, it is listening to Tom Waits.

Most microscopists decry the use of light scattering. However, it is suitable for Mertz's technique, because, in his view, here is "one of the few cases that I know of where scattering in tissue is actually useful, as opposed to detrimental." The approach

lets scientists peer into their samples and look at tissue *in vivo* in new ways because OBM is not impaired by thick and opaque tissues. "Actually, the tissue has to be thick for the technique to work at all," Mertz says. His efforts to put OBM into practice draw on high-tech endoscopy design that has become available in recent years. He used a miniature endomicroscopy probe, which is challenging to make.

The OBM technique delivers microscopy-level resolution and offers a look at cells inside the body: for example, in the tissue lining of the colon or the lungs. Techniques with this type of resolution already exist but generally harness fluorescence indicators. "Ours allows you to see under the surface based on nonfluorescence; we don't have to inject any fluorescent dyes," Mertz says.

He believes the technology can advance the work of scientists in the field of *in vivo* imaging. He also hopes it can find its place in the clinic, for brain and lung imaging and any approach to human-tissue examination involving miniature endoscopy probes. Today's colonoscopies generally do not deliver high-resolution images or permit a peek under the tissue surface. Mertz is currently developing an endoscope with high resolution based on OBM for use in colonoscopies.

Chances are, Mertz will put his ideas to work in two countries: he is both French and American and has held research positions in the United States and France. Prior to his current post, he was research director at the Centre National de la Recherche Scientifique (CNRS), where he worked to advance microscopy techniques. "I guess I was very lucky to have gotten in," he says, referring to the selective process with which CNRS decides on staff appointments. He wants to continue to be anchored in both countries, says Mertz.

"I had the tremendous fortune of being raised in two cultures," he says. In the same way that he has split his time between his two home countries over the course of his education and research career, he now plans joint endeavors with scientists in France. "I have worked there; I have a lot of colleagues there, a lot of friends there. There would be no problem starting up collaborations," he says.

Vivien Marx

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Ford, T., Chu, K.-K. & Mertz, J. Phase-gradient microscopy in thick tissue with oblique back-illumination. *Nat. Methods* **9**, 1195–1197 (2012).