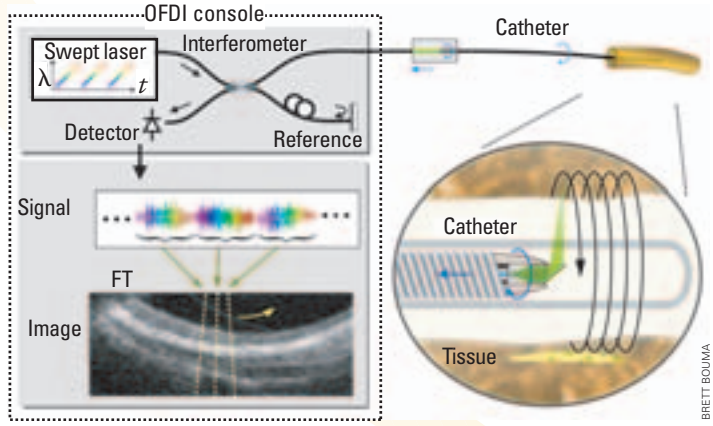
ANALYTICAL CURRENTS

In vivo volumetric optical microscopy for diagnostic imaging

Conditions such as atherosclerotic plaques and epithelial cancers are characterized by microscopic features that are distributed irregularly over a wide area; this makes sampling and detection by excisional or optical biopsy challenging. Now, Brett Bouma and colleagues at Harvard University and Massachusetts General Hospital have developed optical frequency-domain imaging (OFDI), which combines the resolution needed to diagnose pathologies with the speed required for wide-area tissue surveys.



Catheter-based system for volumetric optical microscopy. Imaging is based on spectrally resolved interference between the tissue sample and a reference as a laser source is rapidly tuned from 1264 to 1376 nm.

OFDI has inherited the vertical cross-sectional imaging capabilities and high resolution of optical coherence tomography (OCT), an interferometry-based imaging technique that is already widely used in clinical and research applications. However, OFDI greatly enhances detection sensitivity by substituting frequency-domain ranging techniques for the delay-scanning interferometry of OCT.

This high sensitivity translates into greater speed. With a prototype OFDI system, Bouma and co-workers achieved a 90-fold improvement in sampling speed versus conventional OCT systems. To demonstrate the technique's potential, the researchers imaged a 4.5-cm-long section of swine esophagus in <6 min, and they looked at normal swine coronary arteries and at arteries with stents.

The image resolution and contrast of the OFDI system are the same as those for OCT systems. Because of the improved sampling speed, the authors suggest that OFDI neatly bridges the diagnostic imaging gap between wide-field radiology techniques and point-sampling biopsies. (*Nat. Med.* **2006**, *12*, 1429–1433)

A hybrid microfluidic system for screening and optimization

Screening and optimization experiments play important roles for applications such as biological assays and protein crystallization. Sequential processing is the norm but is slow, and the time delay may lead to false negatives. On the other hand, simultaneous screening and optimization consume more sample.

Rustem Ismagilov and a team of colleagues, led by graduate student Liang Li, at the University of Chicago have a solution that's somewhere in between. They developed a hybrid microfluidic device capable of rapid, simultaneous screening and optimization on nanoliter samples, and they used it to conduct crystallization experiments with model membrane proteins.

In this approach, large (~120–140-nL) plugs—droplets surrounded by carrier fluid—of various reagents are flowed into a microfluidic channel and separated by spacer plugs. Each reagent plug then can be mixed with buffer and substrate streams to split it into smaller plugs. The researchers chose 20 reagents and subdivided them into ~1000 small plugs, each of which represented a distinct experiment. Careful control of pump speeds allowed the experimenters to vary reagent concentration 16-fold across the smaller plugs.

When Ismagilov and co-workers applied the method to membrane protein crystallization, a single researcher conducted a hybrid screen for 48 different reagents on 17 μL of substrate solution (~1900 experimental conditions) in <1 h. The method was compatible with subsequent X-ray diffraction studies. (*Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 19,243–19,248)