SPECIAL SECTION GUEST EDITORIAL

Infrared and Raman Spectroscopy

Modern vibrational spectroscopy is a powerful tool for biomedical applications. The biochemical information content is high and there is a vast body of literature connecting spectral features to specific molecular structures and environments. Infrared and Raman spectra contain many bands that can be used to identify molecules and, in some cases, to measure the composition of complex, multi-component samples. The positions and relative intensities of various spectral bands can also be used to probe the primary, secondary, tertiary, and quaternary structure of biopolymers. There is now a large body of biophysical/biochemical literature connecting spectral features with molecular structure and environment and a specialized tissue literature that builds on this. Equally importantly, modern instruments are compact, reliable, and easy to use and are supported by powerful software that enables extraction of even subtle features and correlations.

Two important developments of the 1990s have dramatically increased the utility of vibrational spectroscopies in biomedicine. The development of fiber optic probes enabled remote measurements, including handheld probes that can be placed on or near a specimen. The progress here has been greatest in Raman spectroscopy because scientists and engineers can take advantage of materials and devices that have been developed for fiber-based telecommunications, as well as for fiber-based chemical sensors. Although chalcogenide optical fibers for the infrared are available, they are not as widely available as silica fibers and are used by relatively few laboratories. The second major advance has been the extension of microprobe technology to spectroscopic imaging. Microscopes that can acquire spectroscopically resolved Raman or mid-infrared images have enabled visualization of chemical and physical information in formats that are familiar to life scientists. Progress has been greatest in infrared spectroscopic imaging. Many of the major Fourier transform infrared (FTIR) microprobe vendors have introduced microscope-based imagers. Fewer Raman instrument vendors have been active in introducing imaging systems. Most investigators rely on point-point Raman mapping or on imagers that they have built themselves.

Some other noteworthy trends include the continuing development of surface-enhanced Raman spectroscopy (SERS), which provides enhanced detection limits at low laser power, and the revival and rapid development of coherent Raman spectroscopy. SERS extends Raman spectroscopy into the range of immunoassay concentrations and even, in some cases, to single molecules. Coherent anti-Stokes Raman microscopy has been especially successful at the single cell level, although progress at the tissue level has been less rapid. Finally, we should mention the widespread adoption of sophisticated multivariate analysis tools to enhance the value of spectroscopic information. Multivariate statistical approaches have enabled classification of specimens as diseased or healthy based on subtle changes in spectra. Self-modeling curve resolution has been used to extract spectra of otherwise undetectable components from infrared and Raman images. The need for independent validation is widely recognized. However, there is a continued trend in the blind use of statistical tools and we expect the work described in this special section to serve as a field of use model for many analysis techniques.

In this special section we have brought together a group of specialists in tissue vibrational spectroscopy to discuss the latest developments in their own research and to assess progress in their fields. These papers describe applications to or instrumentation for diagnostics, with emphasis on noninvasive or minimally invasive measurements, as well as the use of vibrational spectroscopy to further basic biomedical science. The methods used include infrared, near-infrared (NIR), and Raman spectroscopies. Overall, this special section demonstrates the broad range of utility and value of vibrational spectroscopy in biomedicine.

Despite all of the activity in the field, there has been less progress toward translation of vibrational spectroscopic methods to the clinical setting, especially as compared to other optical methods such as optical coherence tomography, video-rate confocal reflectance microscopy, and fluorescence endoscopy. Several explanations have been proposed. Some suggest that the multiplicity of competing technologies (FTIR, NIR, Raman, and recently coherent Raman) is confusing. The nonspecialist cannot reliably sort out the conflicting claims of the spectroscopists and has neither time nor resources to evaluate them all. Another school of thought holds that there has been no “killer application” that would cause rapid adoption of spectroscopy and pave the way for other applications. Vibrational spectroscopy has been undeniably useful and may even be greatly superior to competing methods in some cases. Yet it has not provided information that clinicians need and can obtain in no other way. Thirdly, both Raman and IR spectroscopies are not routinely compatible with endoscopic applications, because of intrinsic challenges in suppressing unwanted signals from the waveguides themselves. There are also fundamental physical limitations. The weak light levels of spontaneous Raman scattering usually dictate several seconds of acquisition per observation point, precluding the acquisition of images under clinical time constraints. Similarly, water absorption limits noninvasive infrared spectroscopy. As with all optical techniques in the visible and near-IR, diffusive light scattering is a major impediment to noninvasive Raman spectroscopy. No technological advances have allowed recovery of spectra from tissue several centimeters beneath the skin. None of these drawbacks impede examination of excised tissue specimens, however.

An important role of this journal is to assist in the translation of basic optical science and engineering to the clinic. As the papers presented in this special section demonstrate, vibrational spectroscopy is ready for translation in some or all of the areas represented here, and in others as well. By collecting a wide range of papers in one readily accessible place, we hope to aid in that process.

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