

Translational Efforts for Digital Chemical Pathology with Infrared Laser Scanning Microscopy

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Abstract

Chemical imaging (CI) techniques based on infrared (IR) spectroscopic imaging have seen tremendous interest in recent years, leading to an abundance of on-going research designing new instrumentation. However, the widespread adoption of vibrational CI methods for medical diagnostics in a manner that is commercially viable for clinical translation has been limited. Predominantly, there is lack of capability for recording high-throughput, high-fidelity, and high-reliability measurements that have practical utility. Academic research toward these goals is often confined within the bounds of commercially available off-the-shelf equipment. Nearly all label-free methods are built upon optical systems originally designed for light microscopy and are at best compatible from ultraviolet to near-infrared wavelengths. Alternatively, marginal development of all-reflective optical systems for vibrational CI instruments necessitated compromising performance for compatibility with longer-wavelength light over a broader spectral range at much lower intensities. The lack of component compatibility in the commercial sector for IR optics has hindered rapid development in the field. We have aimed to address these needs by building new rather than building from what is already available. Our newest microscope builds on our recently reported laser scanning confocal microscope (LSM) design. While such technology is commonplace in other spectral ranges, the construction of such an instrument for the mid- to longwave IR spectral bands has long been impractical and incompatible with all commercially available solutions. In this newest generation of our microscopy platform, IR-LSM is capable of in-the-field imaging of whole slides with consistently high-throughput, low-noise, and high resolution. We have demonstrated the ability to in-source the design of critical

optics, software, and mechanics, realizing a new microscope enabling end-users access to chemical imaging of biological samples and more with AI analytics, while providing developers with a new mid-IR compatible platform to expand upon. We discuss current efforts to realize this technology for clinical and research interests.