High-Performance Miniaturized Raman System for Challenging Applications

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Abstract

We present a high-performance miniaturized Raman spectrometer engineered to deliver laboratory-grade analytical capabilities in a compact, robust, and application-ready platform. The system features a dual-channel optical architecture that enables simultaneous acquisition of sample and internal reference spectra on a CMOS detector, ensuring real-time Raman shift and intensity calibration. This design compensates for laser drift and environmental fluctuations, providing long-term spectral stability under both 785 nm and 660 nm excitation. Advanced preprocessing algorithms - including Raman shift and intensity correction, anti-mode-hop deconvolution and spectral deblurring - further enhance spectral accuracy and reproducibility.

Quantitative performance is demonstrated across multiple challenging scenarios. Surface-enhanced Raman spectroscopy (SERS) measurements of BPE and methotrexate (MTX) on nanostructured substrates highlight high sensitivity and strong signal-to-noise ratios enabled by optimized optical throughput and pixel-averaging strategies. Highly confocal illumination supports through-container measurements, effectively reducing fluorescence contributions from glass and enabling non-invasive analysis of liquids. Chemometric modelling using partial least squares (PLS) regression allows accurate quantification of methanol in water-ethanol mixtures across both fingerprint (400-2300 cm^{-1}) and high-wavenumber (2750-3900 cm^{-1}) regions.

For biomedical applications, a high numerical aperture (NA = 0.95) Raman probe was developed for in-vivo skin measurements. The probe enables depth-resolved spectral acquisition at 10–20 μm beneath the skin surface with sharp vertical focusing on the CMOS sensor. Measurements collected from finger, hand, and cheek demonstrate reproducible detection of key biochemical signatures, including CH and OH vibrational bands. The system

provides stable performance across multiple anatomical sites, supporting future applications in non-invasive diagnostics and skin biochemistry monitoring.

The platform also supports confocal Raman microscopy and bacterial analysis. Diffraction-limited spatial resolution was demonstrated through 1 μm polystyrene bead imaging and axial depth profiling. Raman mapping of bacterial samples deposited on CaF_2 substrates enabled collection of species-specific spectral fingerprints. Machine learning–based analysis of Raman maps produced a robust confusion matrix for bacterial classification, demonstrating high identification accuracy.

Together, the compact optomechanical design, integrated calibration strategy, and advanced spectral processing establish a scalable pathway toward portable, high-end Raman systems capable of reliable chemical, biomedical, and industrial analysis outside traditional laboratory environments.