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## High-performance miniaturized Raman systems for challenging applications

We present a novel miniaturization strategy that allows us to create versatile compact Raman spectrometers and microscopes based on cheap non-stabilized laser diodes, densely-packed optics, and non-cooled small pixel size sensors. We demonstrate that the achieved performance is comparable with expensive and bulky research-grade Raman systems. Our miniaturization concept is based on real-time calibration of Raman shift and Raman intensity using a built-in reference channel that is independent of the main optical path1. We have demonstrated the miniaturization of the whole device dimensions down to several centimeters and achieved excellent sensitivity, low power consumption, perfect wavenumber and intensity calibration combined with high spectral resolution of around 7 cm<sup>-1</sup> within the spectral range of 400-4000 cm<sup>-1</sup> [1]. We demonstrate possible solutions to the most critical Raman miniaturization challenges: need for laser temperature and power stabilization, reduction of sensor dark noise, compensation on pixel-to-pixel quantum efficiency variation, laser optical isolation and achieving high spectral resolution. Moreover, the proposed miniaturization strategy provides shifted-excitation Raman difference spectroscopy and spatially offset Raman spectroscopy functions as a derivative of the working principle [2-3].

The high performance and vast versatility offered by our strategy facilitate simple integration into various applications. As examples, we show the quantification of methanol in alcoholic beverages through a glass bottle, in-vivo Raman measurements of human skin, quantification of p-coumaric acid and serine during fermentation by E. coli bacteria, high resolution Raman mapping, quantitative SERS mapping of the anti-cancer drug methotrexate and in-vitro bacteria identification by Raman mapping. We foresee that the proposed miniaturization strategy will allow realization of super-compact Raman spectrometers for integration in e.g. smartphones and medical devices.

## References

[1] llchenko, 0. et al. An apparatus for carrying out Raman spectroscopy. https://patentscope.wipo.int/search/en/detail.isf?docId=WO2019145005 (2019). [2] Gebrekidan MT, Knipfer C, Stelzle F, Popp J, Will S, Braeuer A. SERDS evaluation strategy for the efficient isolation of Raman spectra from extreme fluorescence interference. J Raman Spectroscopy (2016) 47: 198-209. [3] Mosca S, Conti C, Stone N, Matousek P. Spatially offset Raman spectroscopy. Nat Rev Methods Prim (2021) 1: 21.

**Figures** 



Figure 1: Figure 1. (a) Photo of miniaturized Raman system with in-built reference channel, (b) CMOS sensor image that demonstrates simultaneous acquisition of main and reference Raman signals from laser excitation at 785 nm, (c) laser stability experiment versus time that represents raw Raman spectra variation of polystyrene in the reference channel under laser excitation wavelength 785 nm and (d) variation of raw Raman spectra of polypropylene in the main channel under laser excitation wavelength 785 nm, (e) Raman spectra of polypropylene in the main channel versus time after multiple calibration and pre-processing steps being applied.