SERS-based detection schemes in biological and biomedical applications

Dana Cialla-May[1,2,3], Karina Weber[1,2,3], Jürgen Popp[1,2,3]

1) Leibniz Institute of Photonic Technology (IPHT), Albert-Einstein-Straße 9, 07745 Jena, Germany
2) Friedrich Schiller University Jena, Institute of Physical Chemistry and Abbe Center of Photonics, Helmholtzweg 4, 07743 Jena, Germany
3) InfectoGnostics Research Campus Jena, Centre for Applied Research, Philosophenweg 7, 07743 Jena, Germany
e-mail: dana.cialla-may@leibniz-ipht.de

Powerful detection schemes in bioanalytics are associated with the requirements for molecular specificity, high sensitivity and fast detection times. Surface enhanced Raman spectroscopy (SERS) is known to meet those requirements and the strong capability of this method in bioanalytical detection schemes is due to the enhancement of the molecular specific Raman fingerprint by 6 to 8 orders of magnitude employing plasmonic active nanostructures. [1] Various SERS detection schemes are available, e.g. label-free or direct SERS, SERS labels or tags for immune assays as well as molecular sensors to detect small molecules or ions. Within this presentation a detailed overview about label-free SERS approaches [2] are given allowing for applications in biology or biomedicine.
Employing label-free SERS (i.e. the molecules of interest are interacting with the metallic surface of the SERS substrate), two different carotenoids (lycopene and β-carotene) are investigated in tomato extract samples. [3] Here, a training model was created from lycopene/β-carotene mixtures to achieve the estimation of the lycopene and β-carotene percentage in real extracts. The obtained results were compared with HPLC measurements and a good agreement was found for most of the samples illustrating the potential of SERS in bioanalytics.
In combination with SERS, microfluidic systems (Lab-on-a-chip, LOC) are developed to allow for high-throughput measurements and reproducible measuring conditions. As an example, the broad spectrum antibiotic levofloxacin is characterized within simulated urine mimicking a complex biological matrix employing LOC-SERS. [4] First, different parameters such as matrix complexity, aggregation time and matrix dilution on the overall SERS signal is investigated. Within the second part of this study, levofloxacin is spiked in human urine and the quantitative analysis is achieved down to a root means square error of prediction (RMSEP) between 0.058 and 0.16 mM for the different investigated urine samples.
To summarize, due to the complex composition of real biological and medical samples (e.g. salts, degradation products, metabolic endproducts, proteins, water, etc.), a number of challenges and limitations occurs: (i) salts can cause aggregation of the SERS active colloidal nanoparticles as well as the degeneration of nanostructure surfaces; (ii) degradation products or metabolic endproducts show a strong affinity toward the metallic surface and/or are highly concentrated; (iii) proteins will form a corona on metallic nanoparticles. Thus, in label-free SERS approaches the analyte molecule needs to show a high affinity toward the metallic surface and clean up processes are required when the background signal is dominating the SERS response.

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References:
[1] D. Cialla-May, X.-S. Zheng, K. Weber, J. Popp, *Chem. Soc. Rev.*, 46, 3945-3961 (2017).
[2] X.-S. Zheng, I. J. Jahn, K. Weber, D. Cialla-May, J. Popp, *Spectrochim Acta A Mol Biomol Spectrosc.*, 197, 56-77 (2018).
[3] A. I. Radu, O. Ryabchykov, T. W. Bocklitz, U. Huebner, K. Weber, D. Cialla-May, J. Popp, *Analyst,* 141, 4447-4455 (2016).
[4] I. J. Hidi, M. Jahn, M. W. Pletz, K. Weber, D. Cialla-May, J. Popp, *J. Phys. Chem. C*, 120, 20613-20623 (2016).