

Spectroscopic Characterization of Infections: Identification, Localization and Antibiotic Susceptibility of the Pathogen

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Successful treatment of infection relies on timely identification of the focus, the pathogen and its antibiotic resistance pattern in order to select the appropriate antibiotic treatment as early as possible. Raman spectroscopy as a label-free and non-destructive technique is highly suitable to speed up the time-consuming characterization of infection. Cultivation-independent Raman-based identification methods directly from body fluids require capturing of the bacteria from the dilute suspensions. Two approaches are demonstrated: one using dielectrophoretic forces, the second utilizing centrifugal forces on lab-on-disc microfluidic platforms. With both approaches pathogens can be identified directly from patient's urine samples within a few minutes (35 min with the dielectrophoresis approach [1] and 70 min using the CD microfluidics [2]).

In times of rising antibiotic resistances, rapid and at the same time highly accurate antibiotic susceptibility testing is also of utmost interest. Exemplarily the spectroscopic analysis of the drug-target interactions of vancomycin, a glycopeptide antibiotic, with enterococci is presented. Changes in the bacterial Raman spectra due to antibiotic treatment can be identified already after 30 minutes of treatment. [3] Results from this study have been implemented in an algorithm for the detection of vancomycin resistant enterococci (VRE) within less than 3.5 hours [4].

Not always bacteria are residing in body fluids, but they can hide within cells. Those intracellular infections are difficult to diagnose and to treat. An advanced Raman-based approach is presented to localize and characterize intracellular *Staphylococcus aureus* in three dimensions without the need of any external label. [5]

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References

- [1] Schröder et al., *Anal. Chem.* 85, 10717–10724 (2013).
- [2] Schröder et al., *Biomicrofluidics* 9, 044118 (2015).
- [3] Assmann et al., *Anal. Bioanal. Chem.* DOI 10.1007/s00216-015-8912-y (2015).
- [4] Schröder et al., *Scientific Reports* 5, 8271 (2015).
- [5] Große et al., *Anal. Chem.* 87, 2137-2142 (2015).