Raman-Spectroscopic Detection of Induced Drug Resistance Using a Three-Level Chemometric Model

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Antibiotic treatment of bacterial infections is only possible if the strain in question is sensitive to the proposed treatment. The resistance does not need to be expressed permanently in the resistant bacteria, but can also be induced by the presence of the antimicrobial drug. That means, bacteria with such induced resistance will initially respond to the antibiotic treatment, but after a while continue to grow.
We present a study of two *E. faecalis* strains, a vancomycin-sensitive (S) and a strain with VanB resistance (R) induced within ca. 2 h. The two strains have been grown in the presence (V) and absence (C) of 10 µg/ml vancomycin and Raman spectra have been recorded after various time points. A three-level chemometric model is build that can describe the induced resistance. First, the Raman spectra undergo a partial least squares (PLS) projection set up to distinguish vancomycin-treated sensitive bacteria from untreated controls of the same strain. In a second step, linear discriminant analysis (LDA) yields the actual distinction to the degree of vancomycin-sensitivity. Already after 30 min the treated bacteria show full response to the treatment (fig. 1). After 1 h, the resistant strain begins to recover. To detect the induced resistance, the third level model uses the response to vancomycin after 1 and 2 h. Figure 2 shows results of the 2nd level model for independent data (different batches measured at different days). Note that the controls of both strains are projected on top of each other, although only the sensitive strain was used to set up the projection.
Thus, Raman spectroscopic measurement of antibiotic sensitivity promises rapid detection not only of sensitive strains but also of induced resistance.

For experimental details, please see the poster „A novel combination of dielectrophoresis and Raman spectroscopy for the characterization and identification of bacteria directly in body fluids“.

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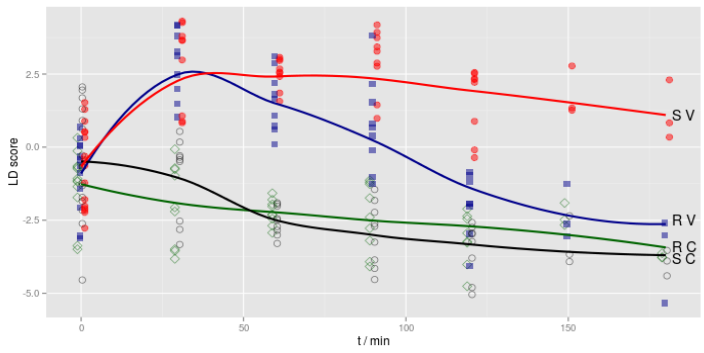

Figure 1: vancomycin sensitivity scores (model level 2) as a function of the time of vancomycin exposure. After 30 min, both strains show full reaction to vancomycin, but already after 60 min, the resistant strain begins to recover. (Abbreviations: see text)

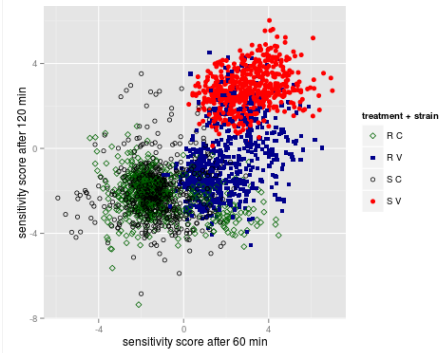

Figure 2: vancomycin sensitivity scores after 1 and 2 h of exposure allow differentiation between sensitive strain and induced resistance as well as negative controls (independent batches and days).