Extracting information from ultrabroadband mid-infrared spectra of breath

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Recent developments in ultrabroadband laser sources enable acquisition of high signal-to-noise mid-infrared (MIR) spectra spanning 2–11.5 µm [1]. The ability to extract concentrations of multiple molecular species simultaneously with ppb detection limits opens up applications in breathomics: the field of mapping compounds in breath as a helpful, non-invasive medical diagnostic. While this field has traditionally been dominated by mass spectrometric methods, optical techniques can complement the investigated chemical space with other and smaller molecules than those detectable by mass spectrometry. On the other hand, spectroscopy has the potential to be miniaturized and to have its cost reduced massively.

Recently [2], we have developed a breath analysis platform based on an ultra-broadband (2.9–11.5 µm) MIR laser, dedicated online breath sampling system, and Fourier transform spectrometer. While providing unprecedented spectral bandwidth and sensitivity, translating measurements into robust physiological information remains a major challenge. The traditional approach of fitting compounds using classical least-square fitting (CLS) from a reference database is being challenged by untargeted analysis techniques such as principal component analysis (PCA), partial least-square fitting (PLS), and other machine learning techniques. In figure 1a/b, a representative measurement of human breath is fitted using both molecular references (1a) and PCA loadings (1b). PC2 seems to pick up on the signature of methane. In figure 1c, it is demonstrated how untargeted analysis (PCA) of different interventions can be distinguished well merely using the measured absorbance spectrum as input. The high-resolution MIR spectra, moreover, also enable targeted fitting to quantify the concentration and observe trends in specific molecular compounds that can be linked to specific physiological conditions. Relating the results from both targeted and untargeted analysis gives us insight into which physiological variations are captured by identified molecular species and which remain encoded only in the full spectra.

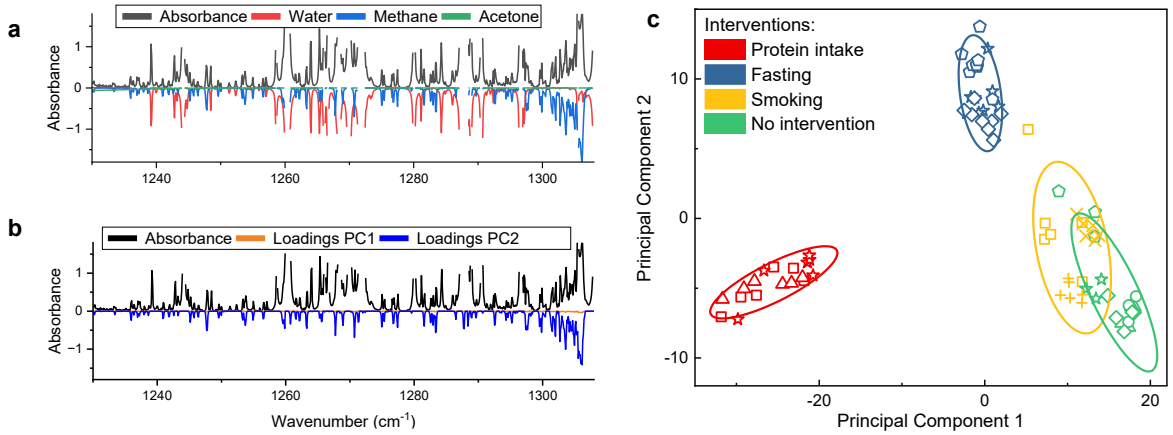

Figure 1: (**a/b**) The absorbance of a representative breath sample is displayed. Regions of saturation are removed before fitting references (mirrored in the horizontal axis). (**a**) Molecular species are fitted using references from HITRAN (water, methane) and PNNL (acetone). (**b**) Loadings corresponding to PC1 and PC2 are shown. In this spectral region, PC1 has little contribution while PC2 resembles methane reliably. The PCA is performed on the whole spectrum from 2.9–11.5 µm. (**c**) Clustering based on PCA is shown to differentiate between interventions. The ellipses indicate the 95% confidence intervals of each cluster.

References:

[1] R. Krebbers, K. van Kempen, F. J. M. Harren, S. Vasilyev, I. F. Peterse, S. Lücker, A. Khodabakhsh, and S. M. Cristescu, *Ultra-broadband spectroscopy using a 2–11.5 µm IDFG-based supercontinuum source*, Opt. Express, **32**(8), 14506, 2024.
[2] R. Krebbers, M. Huisman, K. van Kempen, J. Meurs, A. Khodabakhsh, S. M. Cristescu, *Multi-species breath biomarker profiling with an ultra-broadband (2.9–11.5 µm) spectroscopic platform*, arXiv:2605.20139 [physics.optics], 2026.