Breath analysis as a diagnostic tool for early disease detection

EURAMET
European Association of National Metrology Institutes

The need for the project

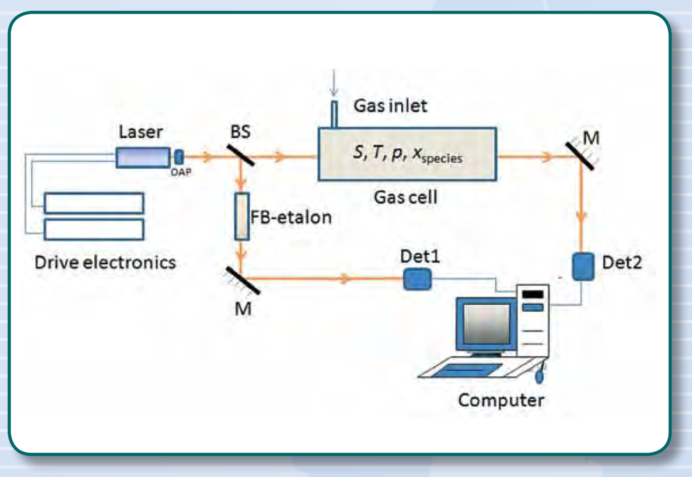
Early disease detection can literally mean the difference between life and death for diseases such as cancer, where the prospects of curing patients are significantly higher following early diagnosis. Breath analysis is a non-invasive method for monitoring the volatile organic compounds present in an individual's exhaled breath and is one of the clinical tests that can be used for early disease detection.

Recent advancements in laser absorption spectroscopy techniques have led to the development of small, calibration-free devices for performing breath analysis tests, with time-resolved measurements. However, despite these advancements, the accuracy and reliability of breath analysis measurements needs to be considerably improved.

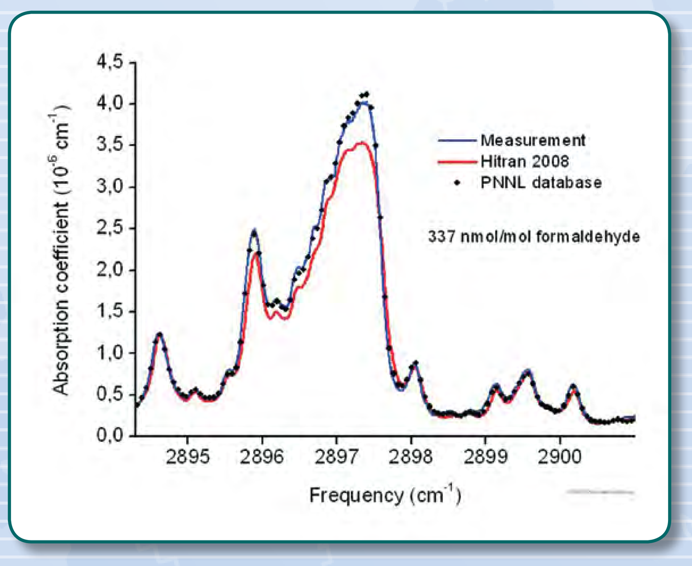
This project addresses these measurement issues with the aim of producing reliable identification and quantification of selected compounds present in exhaled breath.

Technical achievements

The project has demonstrated that measurements of methane, carbon monoxide and carbon dioxide can be performed with an expanded uncertainty of 1-2% with detection limits down to amount–of–substance fractions of 1 nmol mol^{-1} or better. This level of uncertainty is negligible in comparison with the natural variations in amount of these components in human breath. For other targeted molecules, such as methanol, ethanol, acetone, formaldehyde and ammonia, the uncertainty ranges between 3-5%, because of adsorption effects in gas sampling systems.



Tunable diode laser-based setup for breath analysis.

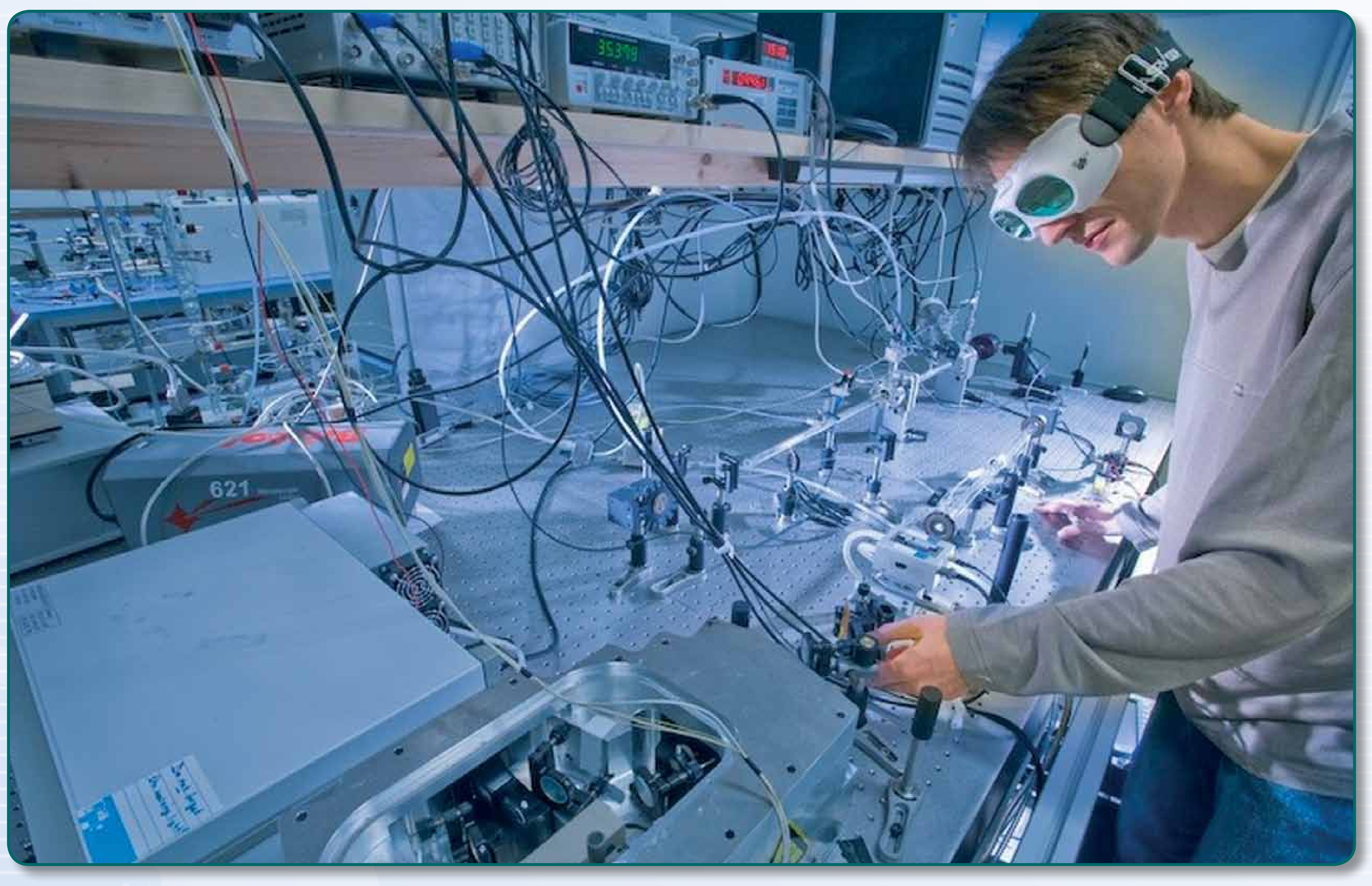


Comparison of the measured formaldehyde spectrum with the HITRAN and PNNL database. Formaldehyde could be of medical interest as some studies found elevated levels in the exhaled breath of patients with primary lung cancer.

For the above listed molecules, reference data has been obtained and compared to spectroscopic databases, which are used as a basis to convert spectroscopic data into gas composition data. For ethane and formaldehyde it was found that the most widely used database HITRAN was incomplete and several tabulated line strengths had an error of more than 10%.

Methods and protocols were also developed for applying various spectroscopic techniques in breath analysis. One protocol linked laser-based spectrometric principles to metrological aspects of breath analysis and explained how equipment should be calibrated to obtain traceable measurements from spectroscopic reference data.

Experiments with moisture removal from gas mixtures have demonstrated the versatility of these techniques and enabled the quantification of errors introduced by sample preparation.



Cavity ring down spectrometer operating in the mid-infrared wavelength region.

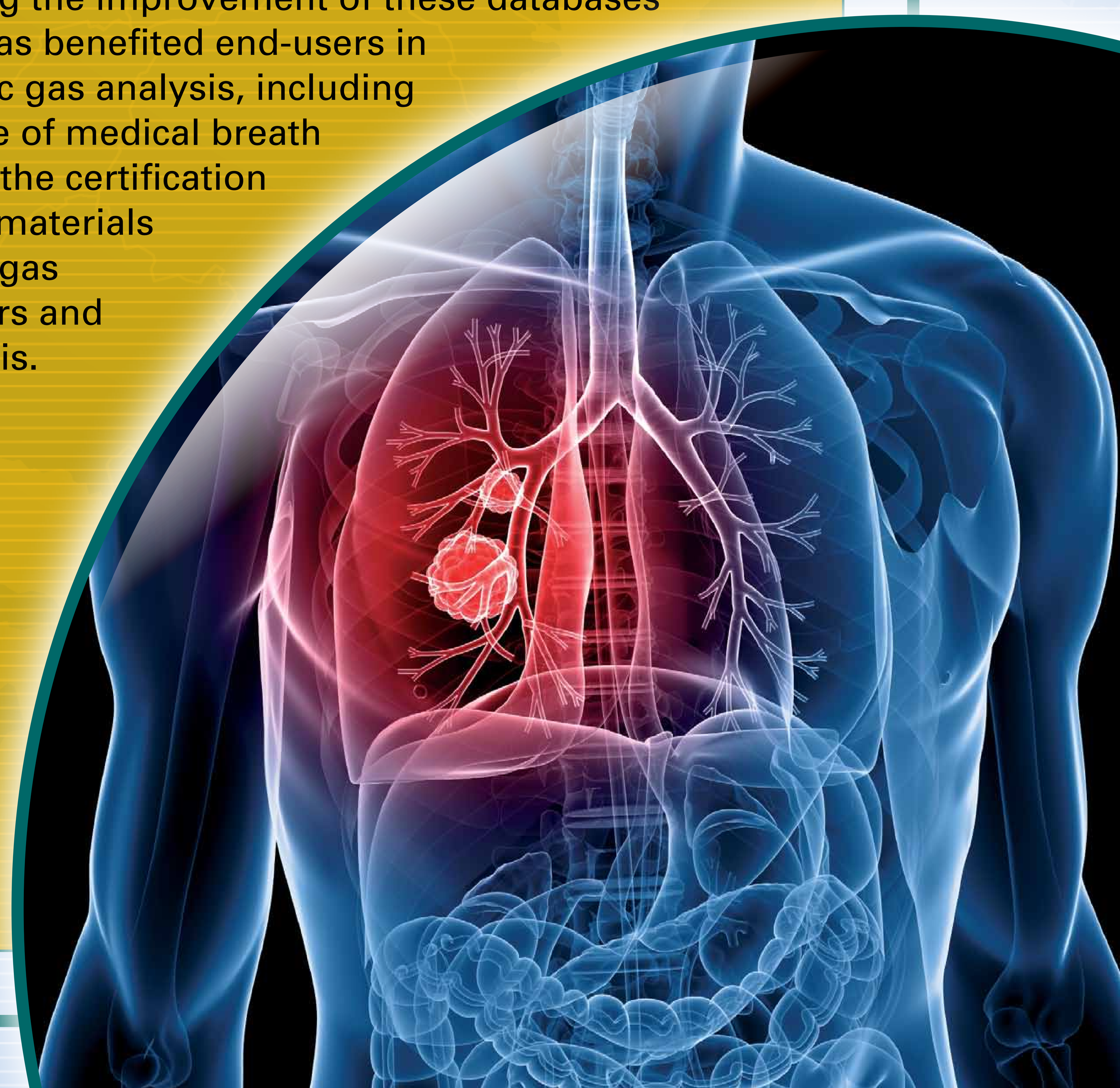
Supporting the medical community

Successfully demonstrated the potential application of spectroscopic techniques in the medical field. The techniques and methods developed have resulted in improved measurement quality for medical trials, leading to reduced repetition of measurements and an improved basis for combining the results from different trials.

Improving spectroscopic reference data

Virtually anyone who uses spectroscopic techniques uses databases such as HITRAN and PNNL in order to convert spectroscopic measurement data into gas compositions. The accuracy of the gas composition derived depends on the accuracy of the gas mixtures used for obtaining these reference data. The project showed that the HITRAN database was incomplete for ethane and formaldehyde and several line strengths had an error of more than 10%.

By supporting the improvement of these databases the project has benefited end-users in spectroscopic gas analysis, including those outside of medical breath analysis e.g. the certification of reference materials for specialty gas manufacturers and purity analysis.



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