# Development of a sensor system for analysis of human breath exhale

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## Introduction

For upcoming topics like environmental monitoring, breath gas analysis, energy consuming processes or exhaust emission tests, trace gas analysis gets progressively more important. [1]

Being a young and highly promising research field, **breath analysis** is still facing severe obstacles regarding daily application in clinics and doctor's offices. One of them is a missing technical approach allowing cost efficient and small reliable sensor systems, which furthermore enable real time analysis of one or multiple breath constitutents of interest, so called biomarkers.

In comparison to established investigation methods like absorption spectroscopy, the concept of photoacoustic spectroscopy holds advantages when it comes to the development of a highly sensitive sensing device for multiple compounds with eliminating the need of very complex measurement conditions.

This poster is meant to provide information about human breath analysis and the task of developing a photoacoustic sensor system for the analysis of human breath exhale.

## State of the art

A generic overview of exhaled breath analysis is given by Figure 1. It visualizes the different steps from comprehensive analysis towards the development of small and cheap Point of Care (POC) devices, which measure a single or few target analytes only. A study can usually be summarized in three steps:

1. The breath is sampled and if necessary pre-concentrated
2. The analysis itself by means of GC-MS, SIFT-MS or PTR-MS
3. Processing of the measured data

Such analytical devices convince with high reproducibility, robustness and the provided comprehensive spectrum. However, these techniques are rather expensive, immobile, require frequent maintenance and lack of easy handling mandatory for daily use in clinics or doctor's offices.

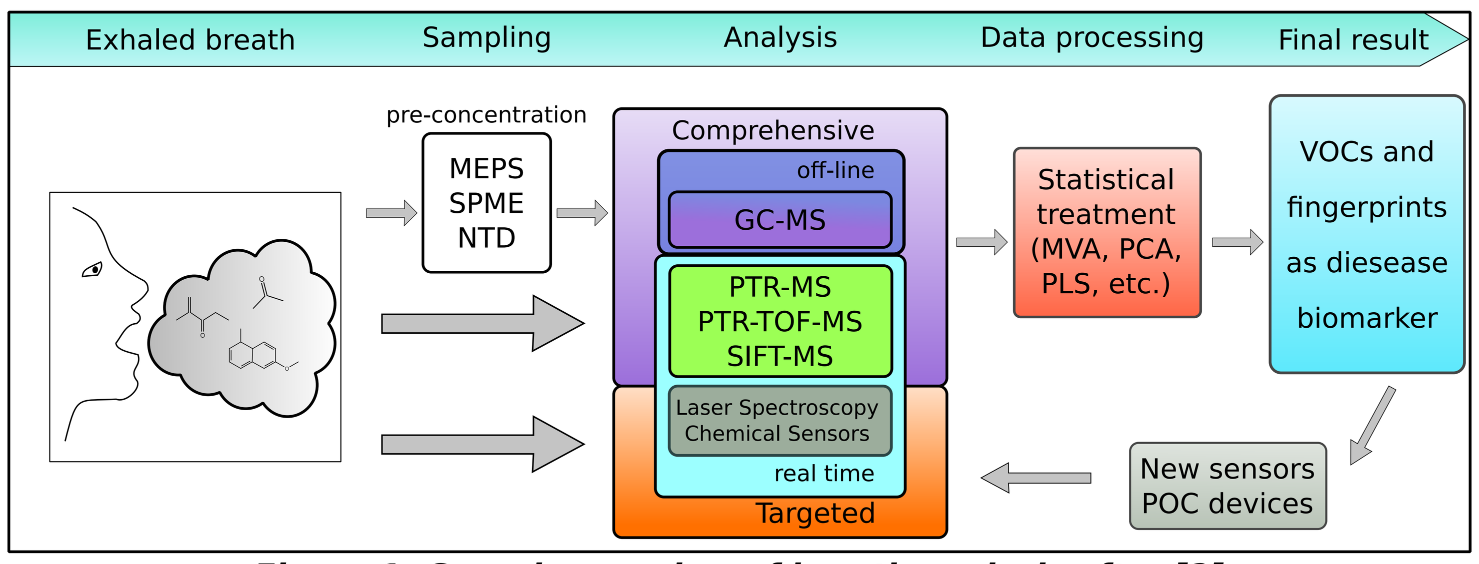


***Figure 1: Generic overview of breath analysis after [2]***

*MEPS - microextraction by packed sorbent, SPME - Solid phase microextraction, NTD - needle trap device, GC - gas chromatography, MS - mass spectrometry, PTR - proton transfer reaction, TOF - time of flight, SIFT - selected ion flow tube, MVA - multivariate analysis, PCA - principal component analysis, PLS - partial least-square, VOC - volatile organic compound*

## Biomarker

Until today more than 3.500 different VOCs have been detected in human breath. Every human commonly exhales between 200 to 300 VOCs. The most abundant species are nitrogen, oxygen, water and carbon dioxide. The rest are trace constituents with volume concentrations of a few parts per million (ppm) down to the parts per billion (ppb) region and some even lower.

Why choosing **acetone** as biomarker of interest?

1. Relatively easy to measure
2. Metabolism pathway is known and well understood
3. Manageable spectrum of correlated diseases (e.g. heart failure, epilepsy)
4. Provides clinical relevant information

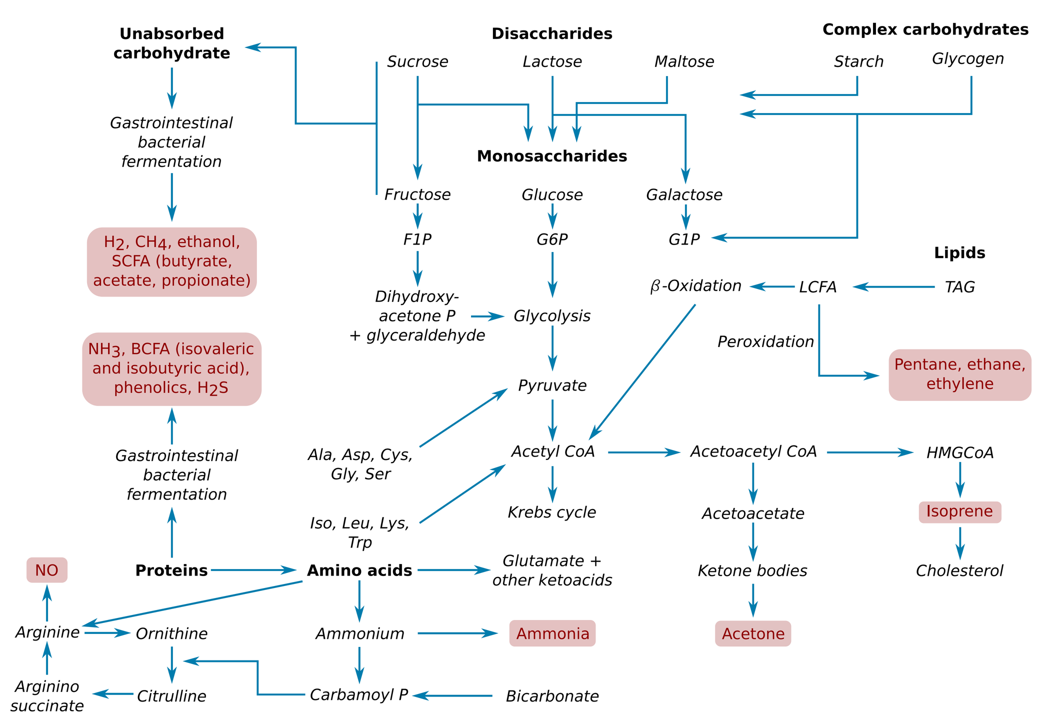


***Figure 2: Pathways of potential biomarkers (marked in red) after [3]***

*SCFA – Short-Chain Fatty Acids; BFCA – Branched-Chain Fatty Acids; LCFA – Long-Chain Fatty Acids; TAG – Triacylglyceride; F1P – Fructose-1-Phosphate; G1P – Glucose-1-Phosphate; G6P – Glucose-6-Phosphate; Carbamoyl P – Carbamoyl-Phosphate; HMG - Hydroxy-Methyl-Glutaryl; CoA – Coenzym A*

## Photoacoustic Spectroscopy (PAS)

First observed by Alexander Graham Bell in 1880, the photoacoustic principle is based on molecular oscillations, stimulated by light of specific wavelengths for each different molecule. [4]

As shown in Figure 3, gas molecules are excited by an amplitude modulated lightsource with at a certain wavelength. The gas molecules absorb the irradiated light, which leads to a thermal expansion. Caused by the modulation of the excitation light, each thermal expansion is followed by a contraction of the gas. Due to this periodic sequence of expansion and contraction of the gas, pressure oscillations are created, which may also be described as acoustic waves.

When exciting the gas in an acoustic resonator, a maximum of the pressure change could be located at a known position in the resonator. Creating a small hole at this special location in the resonator offers the possibility to measure the acoustic wave by detectors like microphones.

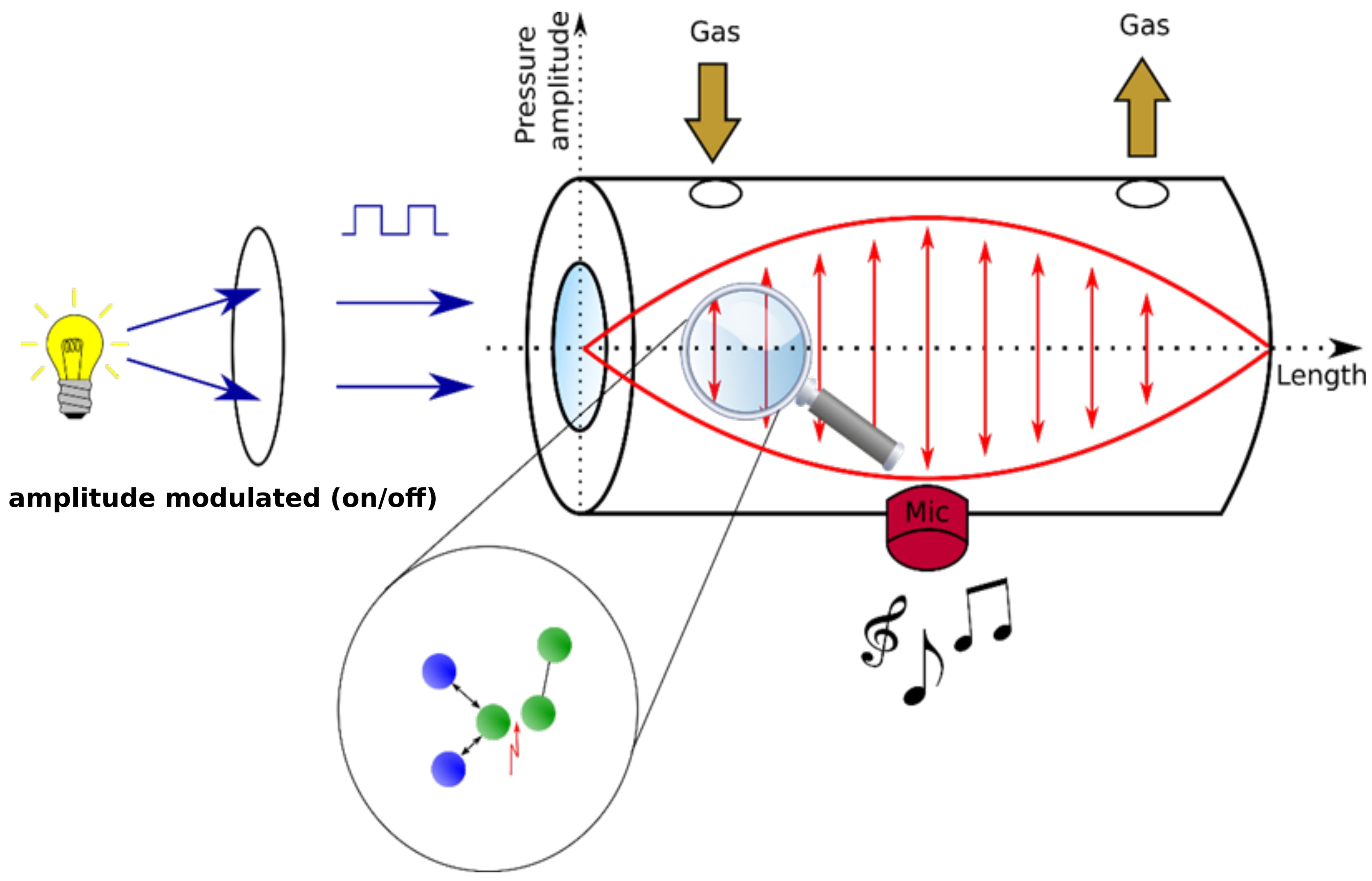


***Figure 3: Photoacoustic principle***

*The length of the acoustic resonator as well as the frequency of the acoustic wave depend on the modulation frequency of the light source. The acoustic wave, generated by the oscillations of the gas molecules, can be measured by the microphone device. The measured sound pressure stands in direct proportion to the concentration of the analyzed gas molecules inside the acoustic resonator.*

**Advantages** of PAS compared to classic absorpton spectroscopy:

1. It is a direct and offset free measurement method
2. High potential regarding miniatuirzation
3. High dynamic and linear detection range (from ppb to promille)
4. Cost efficent components (e.g. cell phone microphone as detector)

## Challenges ahead

PAS is a sensor principle, which has a high potential to meet all necessary requirements to become a state of the art instrument in everyday use of clinics, though several challenges are still ahead.

1. Cross interference suppression

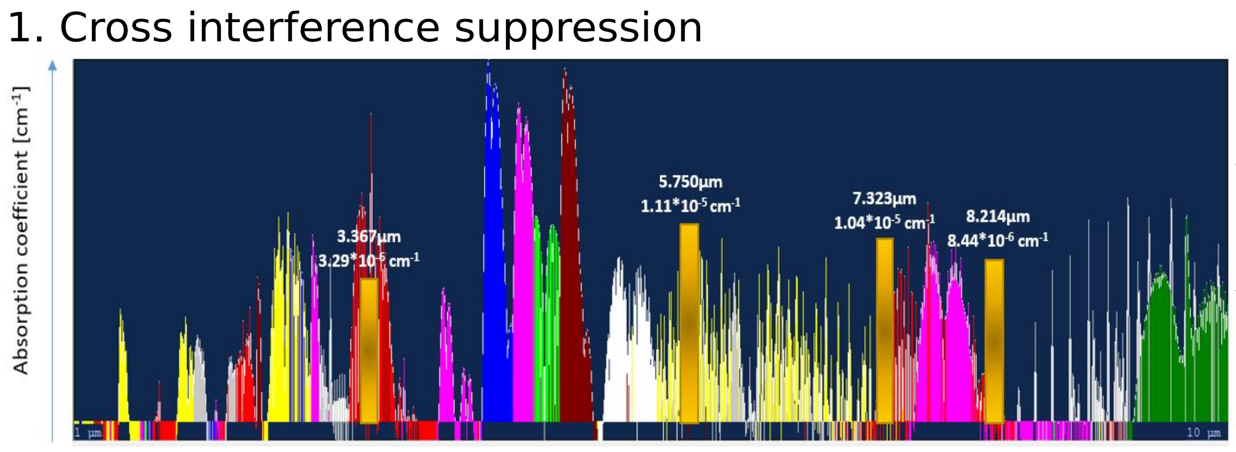


***Figure 4: IR interference species***

*Absorption sepctrum in the infrared region for the higher abundand constitutents of breath (excluding ethanol, methanol and isoprene). Acetone absorption peaks are marked by yellow columns. (Intensity of the columns not related to their actual absorption intensity)*

2. Highly sensitive measurements due to low analyte concentrations
3. Real time measurement in the sub-second region
4. High reliability and reproducibility in a complex sample matrix

Within this work a sensor design will be developed, which has the ability to measure acetone, a highly interesting biomarker, in human breath exhale sufficiently accurate to provide clinical relevant information for the treating doctor.

## References

[1] AMA (Verband für Sensorik und Messtechnik e.V.): *Sensor-Trends 2014*.

[2] J. Pereira et al., "Breath analysis as a potential and non-invasive frontier in disease diagnosis: An overview," Metabolites, vol. 5, no. 1, pp. 3-55, 2015

[3] O. A. Ajiola et. al.: "Effects of dietary nutrients on volatile breath metabolites," J. Nurt. Sci., vol 2, no. October, pp. 1-15, 2013

[4] A. G. Bell: "On the production and reproduction of sound by light". In: *The American Journal of Science* 20.118 (1880), pp. 305-324.

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