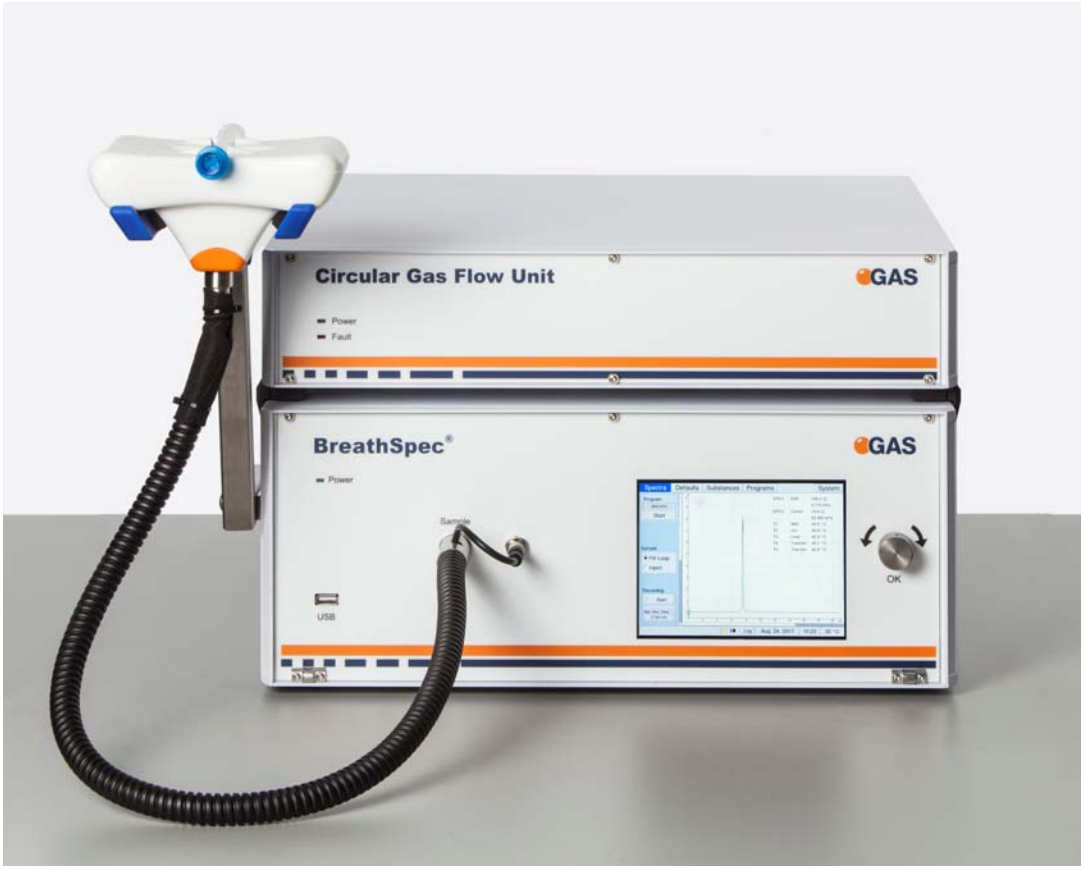
BreathSpec®

Gas Chromatograph-Ion Mobility Spectrometer for VOC Trace Detection



INTRODUCTION

The BreathSpec® is a combination of a classical gas chromatograph coupled to an ion-mobility-spectrometer (GCxIMS). Dual physical separation of volatile compounds together with the outstanding sensitivity of the IMS allows the detection and quantification of compounds in complex matrices down to the low ppb level – allowing direct analysis of volatile compounds in human breath.

Equipped with a gas recycling unit (CGFU) the BreathSpec® only needs a power supply for operation. Hence the equipment setup can be mobile to enable point-of-care testing.

Versatile sampling possibilities offer coverage of various measurement scenarios while respecting non-invasiveness to the breath-donor and hygienic standards.

The flexible sampling possibilities allow a direct sample introduction via a by-pass arrangement on its handheld connected via a heated tube to actively suck-in breath by an integrated pump. Alternatively, remote sampling using disposable syringes assures a cost effective and ultimate hygienic handling of exhaled breath. In this case the breath-donor does not need to be close to the analytical device.

In both sampling setups interrupted sampling acts can be repeated without delay. Compounds of interest can be determined from breath as-sampled, hence undesired alteration of the breath composition as it can be observed e.g. when using gas extraction pre-concentrators, is avoided.

Analysis runtimes depend on gas chromatographic column type and target compounds. A typical multiple compound scan using the GC-IMS takes only 10 minutes.

Non-Invasiveness

One major benefit of breath analysis for medical applications is its non-invasiveness. Consistently the sampling process should be as convenient and as calmative as possible. Moreover a disposable and straight-forward breath sampling set-up same as procedure is essential for hygienic considerations and to reduce stress for the breath donor. Since the sample is analyzed remote to the proband a further reduction of stress can be assured.

The actual breath sampling requires one exhalation only. The proband exhales into the breath sampler. During the second half of the exhalation 5ml of breath are sampled into a common syringe. Drawing the syringe‘s plunger can be done by the proband or by an assistant/nurse (e.g. as shown in figure 1). If the sampling fails it can be repeated instantly. Only successful breath samples are analyzed and hence device‘s void times are minimized.

In case of inability of probands to exhale actively (e.g. unconsciousness) breath sampling can be taken from cavities or be otherwise adapted.

Figure 1: Manual sampling option: Exhaled breath is sampled into a reservoir (syringe) and afterwards manually injected into the device (figure 2).

Sample feed to Analyzer

The sampled breath is fed for analysis by manually injecting it into the GC-IMS’s Luer-port adaptor (figure 2) or automatically introduced into the device by using the handheld sampling option (figure 3).

Figure 2: Sample injection into the Luer-port of the device.

Stability of stored Breath

Storage of breath in capped syringes is limited. At room temperature humidity condenses on the walls leading to a sink for hydrophilic compounds. Conditioning of the syringes to body temperature prevents the condensation.

Common disposable syringes are produced from polypropylene PP. When the plunger is pulled out shortly before sampling, outgasing of volatiles from the syringe is low due to the ‘fresh‘ surface. During storage of breath in capped syringes a series of volatiles will gas out of the syringe‘s material. These specific compounds can be identified and respected in the analysis result.

When stored at room temperature a storage time of approx. 10 minutes should not be exceeded.

Figure 3: Handheld sampling option. Direct sampling of exhaled breath via by-pass on handheld, heated hose and sample introduction through pump .

Beyond breath Sampling

Next to the dynamic breath the sampling of static volatiles is accessible using syringes: The analysis of volatile compounds in e.g. mouth or nose cavities may supply additional information.

Gas Chromatographic (GC) Separation

The BreathSpec® by G.A.S. mbH can be equipped with commercially available GC columns. The GC mode is isothermal. Chromatographic focussing is achieved by electronic pressure controller guided carrier gas flow ramping. Figure 4 indicates the GC resolution by compiling selected compounds' signals from human breath and the headspace of an aqueous mixture of 2-ketones.

1 methanol
2 ethanol
3 2-propanol
4 1-propanol
5 acetone
6 acetonitril
7 2-butanone
8 2-pentanone
9 2-hexanone
10 2-heptanone

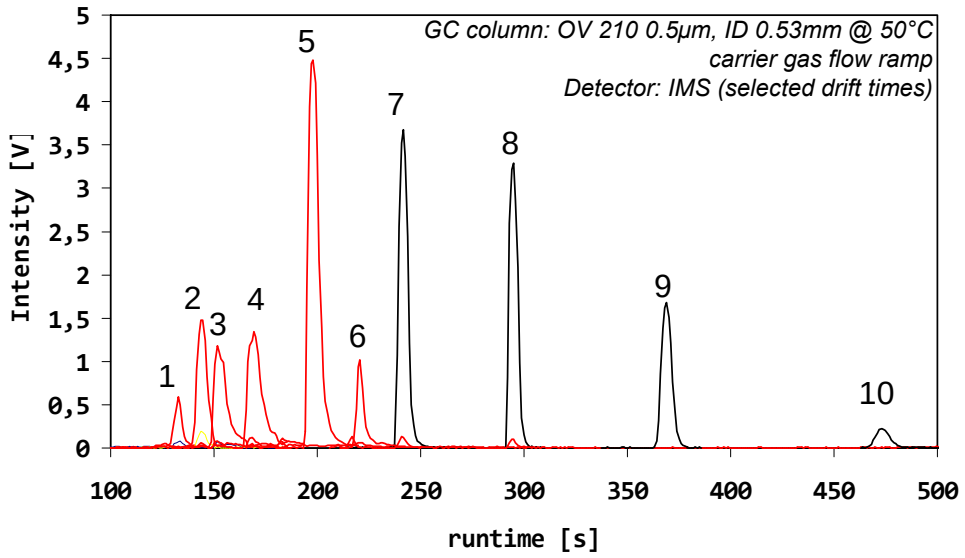


Figure 4: *Compiled single peak GC chromatograms of a breath and a 2-ketone mixture's measurement: RED signal peaks are taken from a measurement of human breath, black peaks result from headspace analysis of a ketone mixture*

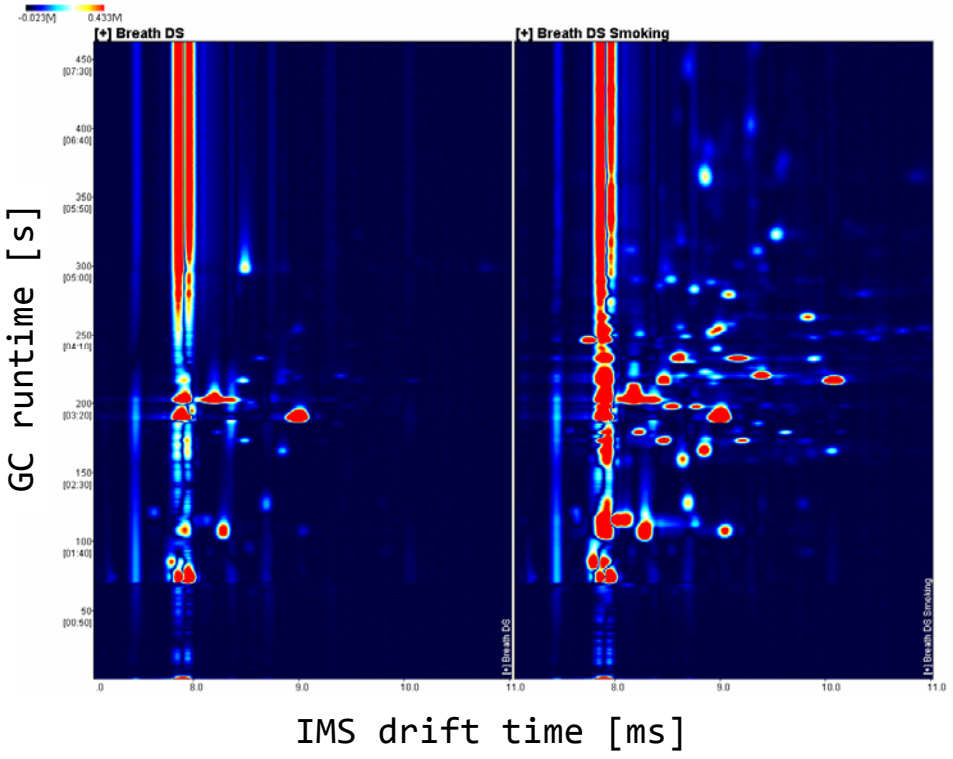
Ion Mobility Spectrometer Separation and Detection

Analytes elute from the GC column directly into the IMS, where soft atmospheric-pressure chemical ionization generates respective analyte ions. The ions diffuse, guided by an electric field gradient, through a tube of defined length. The ion current reveals the ions concentration as intensity of signal peaks, while the specific drift times reveal information on the ion species.

The two separations result in a 2-dimensional (orthogonal) separation of compounds. The signals intensity correlates to the analyte concentration. Figure 5 shows the contour plot representation of two breath measurements.

Figure 5: *Contour Plot of two GC-IMS measurements of human breath of one proband.*
LEFT: Normal Breath
RIGHT: After smoking one cigarette
The GC separation is represented on the y-axis. The x-axis corresponds to the IMS drift times. Signal intensities are given in a color gradient.

GC column: OV 210 0.5µm, ID 0.53mm @ 50°C; carrier gas flow ramp
IMS @ 50°C



Detectable Compounds

The IMS's working principle is based on compounds ionizability. Typically all carbohydrates that carry a heteroatom (S, N, O, P, halogenides) can be ionized. Both negatively and positively ion species can be detected by selection of the respective IMS mode.

Exemplary compounds that are detected in ‚regular' human breath are:

- IMS in **positive** polarization:

  volatile aldehydes / ketones / acids / alcohols / mercaptanes / nitrils / acrylates, terpenes / dimethylsulfide

- IMS in **negative** polarization:

  NO, H_2S, halogenated compounds

Applications

- Monitoring regular breath compounds
- Research for anomalous compounds or compounds' ratios
- Detection of intoxication
- Mapping of pharmacocinetics by monitoring volatile species or metabolites

Features

Analytical
Working Principal: Gas Chromatograph coupled to Ion Mobility Spectrometer (GC-IMS)
IMS Ionization: ^{3}H-Tritium (<380MBq, below EURATOM exemption limit of 1GBq, no licence necessary)
IMS Model: Time-of-Flight / 10cm tube; Potential ± 5.000V
GC columns: General capillary columns, up to 60m@ID0.32mm / 30m@ID0.53mm
Flow control: Electronic pressure controller
Sampling: Heated 6-port-valve incl. sample pump

Technical
Dimension [mm]: 450 x 500 x 295 (WxDxH)
Weight [kg]: approx. 20kg
Operation: Stand-alone through build-in computer, input by touch screen (6.4") or rotary pulse button
Data interfaces: USB, Ethernet, Current loop interface [optional]

Maintenance intervals
Device: 2 years
Filter exchange: approx. 3 months (by customer)
Device cleaning: Built-in bake out function

TOXI TRIAGE

BREATHSPEC®

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