SARS CoV-2 infection screening via the exhaled breath fingerprint obtained by FTIR spectroscopic gas phase analysis: A proof of concept

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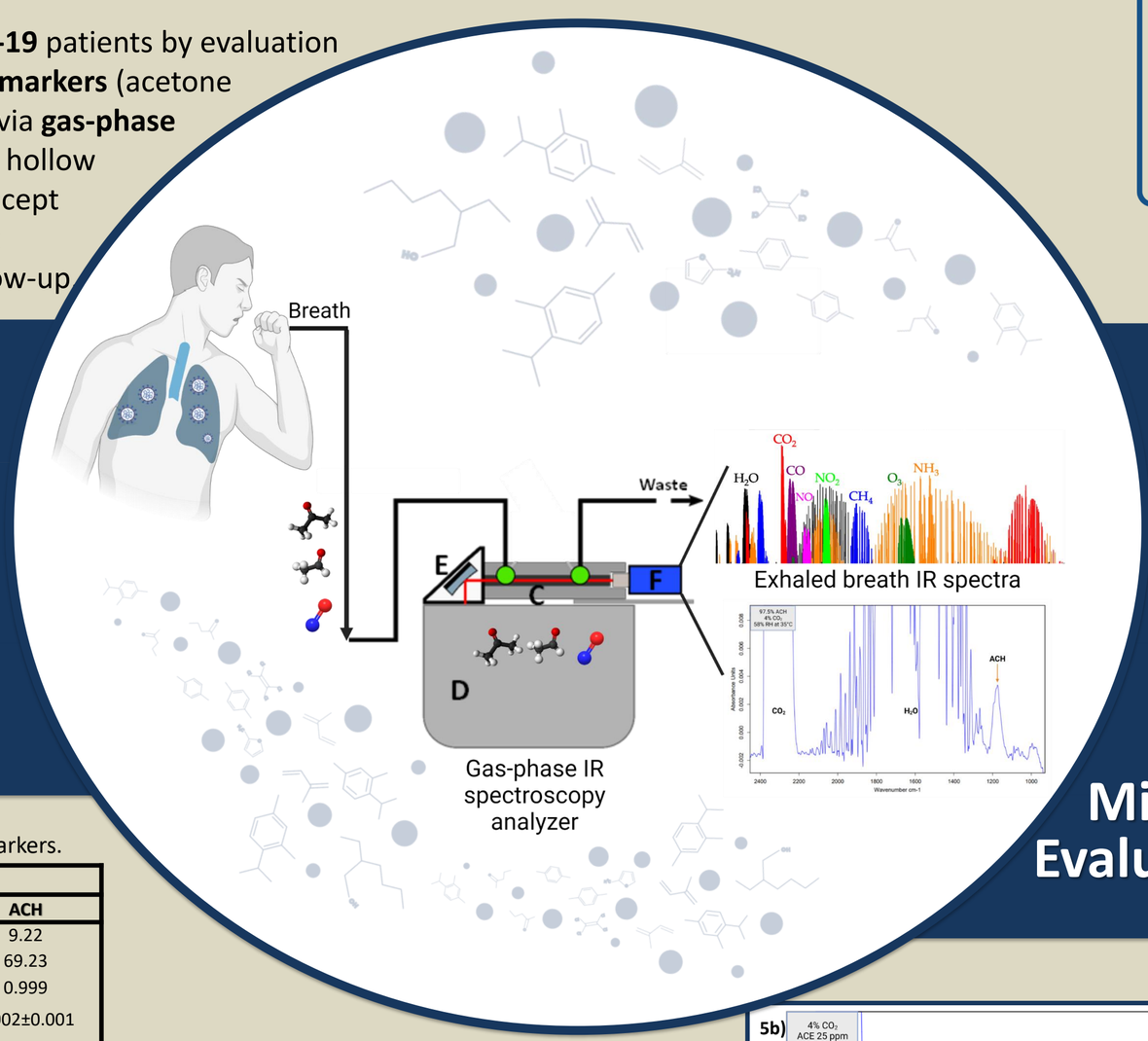
Introduction

The COVID-19 pandemic remains a global challenge now with the **long-COVID arising**. Mitigation measures focused on case counting, assessment and determination of variants and their likely targets of infection and transmission, the pursuit of drug treatments, use and enhancement of masks, social distancing, vaccination, post-infection rehabilitation, and **large population screening**. The latter is of utmost importance given the current scenario of infections, reinfections, and long-term health effects.

Hence, research toward **screening platforms** has been emphasized to provide more **sensitive, specific, and reliable** tests that are **accessible** to the entire population. Thereby, the **prognosis** of the disease can be assessed along with a subsequent **health follow-up** of patients with **sequelae of COVID-19**.

AIM: The simulation of **exhaled breath of COVID-19** patients by evaluation of three identified COVID-19 indicator **breath biomarkers** (acetone (ACE), acetaldehyde (ACH) and nitric oxide (NO)) via **gas-phase infrared spectroscopy using** substrate-integrated hollow wave-guide (iHWG) technology as a proof-of-concept principle for the detection of the infected patient **exhaled breath fingerprints** and subsequent follow-up.



Methodology

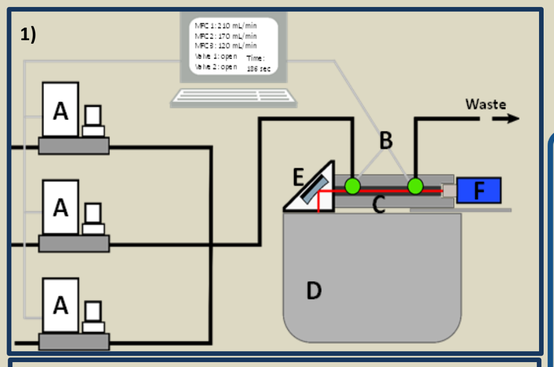


Figure 1. Measurement setup with MFCs (A), valves (B), iHWG (C), infrared spectrometer (D), OAPM (E), and infrared detector (F).

1 Calibration and validation

1.1) Biomarkers: ACE, ACH, NO
1.2) 4% of CO_2
1.3) 58% r.h. @ 36°C
1.4) LOD, LOQ, linearity (r), sensitivity (m), precision (repeatability and reproducibility)

2 Measurements

2.1) Experimental setup (**Figure 1**)
2.2) Automatic operation
2.3) Total gas flow: 500 mL/min
2.4) Stopped-flow mode
2.5) Set-up purge (synthetic air)
2.6) Background measurement
2.7) Gas mixture measurement

3 Data acquisition

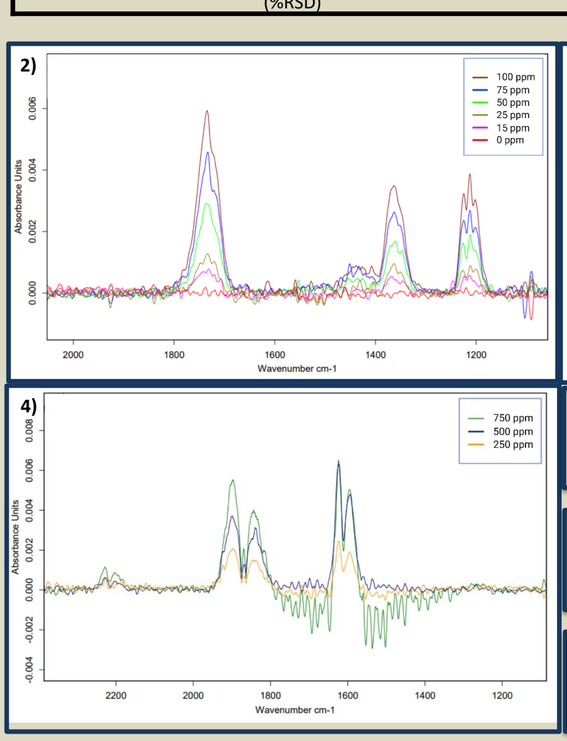
3.1) Range: 4000 to 700 cm^{-1}
3.2) Resolution: 2 cm^{-1}
3.3) Averaging 64 scans

Results

Calibration and validation

Table 1. Validation parameters for each of the investigated biomarkers.

Parameter		Breath Biomarkers		
		NO	ACE	ACH
LOD (ppm)		6.42	13.81	9.22
LOQ (ppm)		42.26	52.57	69.23
Linearity (r)		0.998	0.999	0.999
Sensitivity (CI 95%)		0.0001±0.01	0.001±0.001	0.002±0.001
Precision	Repeatability	3.9-10.4	2.1-17-6	3.4-13.4
	Reproducibility (%RSD)	8.6-10.6	3.1-11.8	3.1-12.4



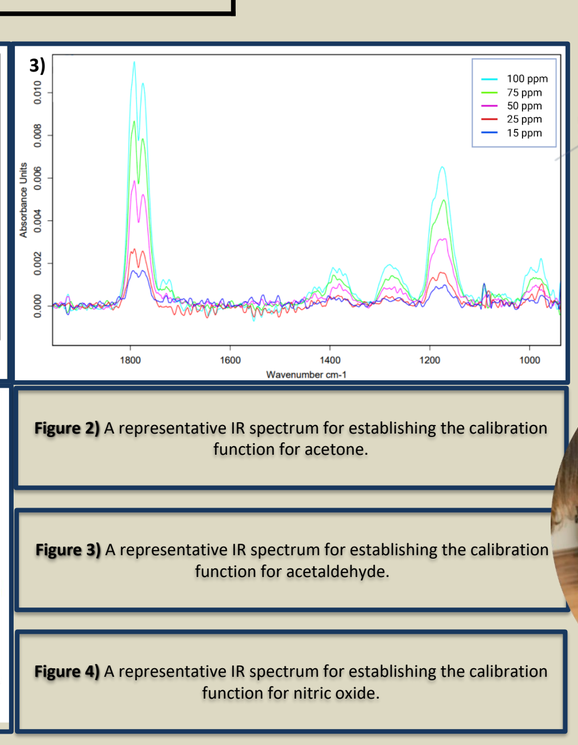
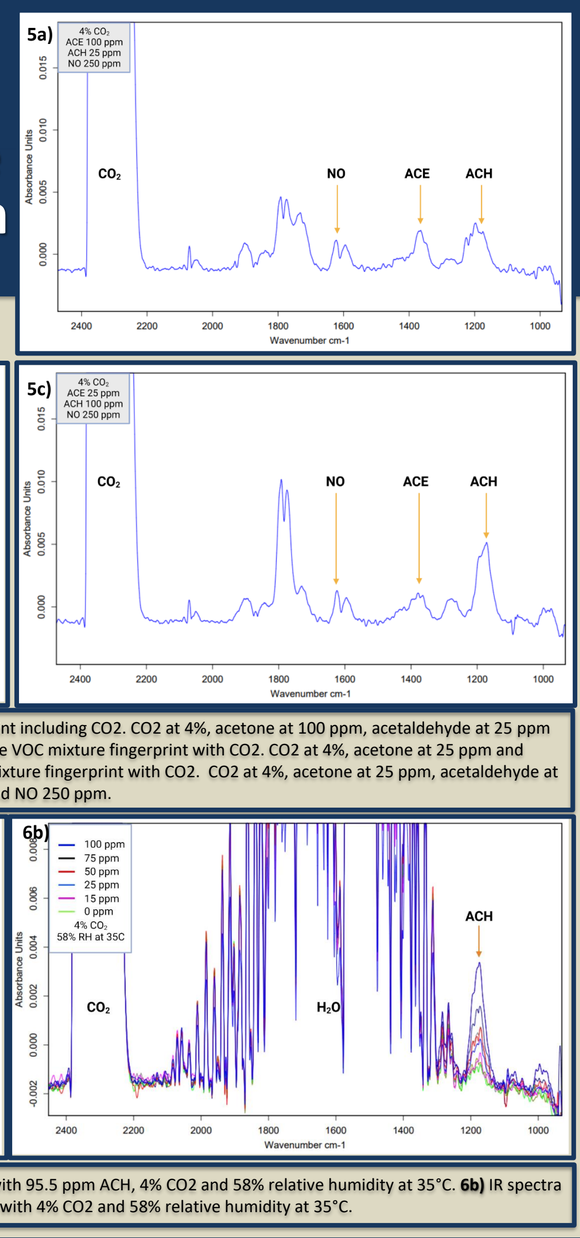


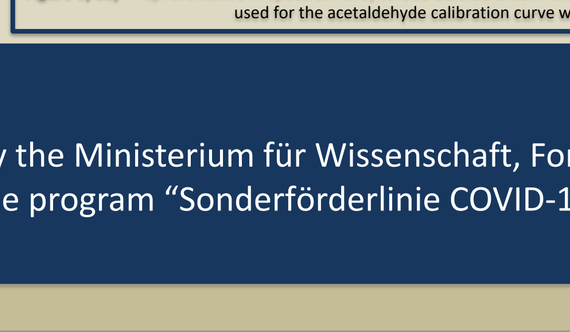
Figure 2) A representative IR spectrum for establishing the calibration function for acetone.

Figure 3) A representative IR spectrum for establishing the calibration function for acetaldehyde.

Figure 4) A representative IR spectrum for establishing the calibration function for nitric oxide.

Gas Mixture Evaluation





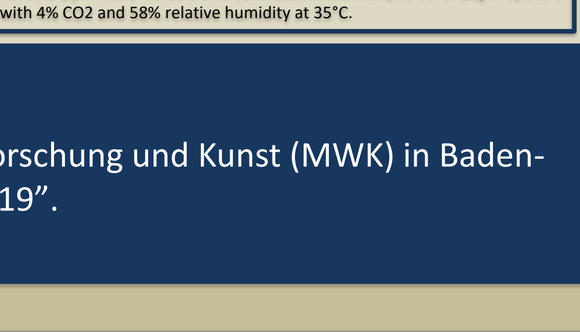


Figure 5) 5a) A representative IR spectrum of the VOC mixture fingerprint including CO2. CO2 at 4%, acetone at 100 ppm, acetaldehyde at 25 ppm and nitric oxide at 250 ppm. **5b)** A representative IR spectrum of the VOC mixture fingerprint with CO2. CO2 at 4%, acetone at 25 ppm and acetaldehyde at 75 ppm. **5c)** A representative IR spectrum of the VOC mixture fingerprint with CO2. CO2 at 4%, acetone at 25 ppm, acetaldehyde at 100 ppm and NO 250 ppm.

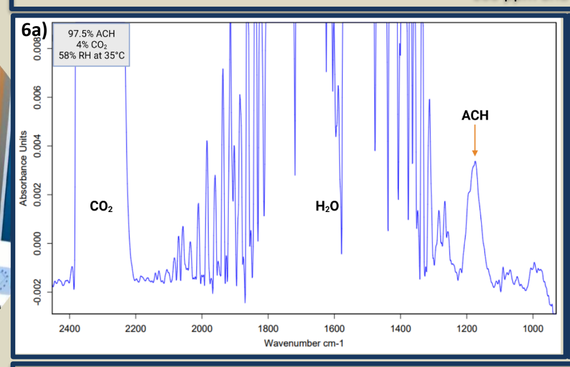


Figure 6) 6a) A representative IR spectrum of synthetic exhaled breath with 95.5 ppm ACH, 4% CO2 and 58% relative humidity at 35°C. **6b)** IR spectra used for the acetaldehyde calibration curve with 4% CO2 and 58% relative humidity at 35°C.

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