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# Optimization of E-nose Technology for Detecting Nonanal: a COVID-19 Biomarker in Exhaled Breath

Christelle GHAZALY<sup>a\*</sup>, Krystyna BILETSKA<sup>a</sup>, Etienne A. THEVENOT<sup>b</sup>, Philippe DEVILLIER<sup>c,d</sup>, Emmanuel NALINE<sup>c,d</sup>, Stanislas GRASSIN-DELYLE<sup>c,e</sup>, Emmanuel SCORSONE<sup>a</sup>

<sup>a</sup> Université Paris-Saclay, CEA, LIST, F-91120 Palaiseau, France

<sup>b</sup> Département Médicaments et Technologies pour la Santé (DMTS), Université Paris-Saclay, CEA, INRAE, MetaboHUB, 91191 Gif-sur-Yvette, France

<sup>c</sup> Hôpital Foch, Exhalomics, Département des maladies des voies respiratoires, Suresnes, France

<sup>d</sup> VIM Suresnes, UMR-0892, Université Paris-Saclay, UVSQ Suresnes, France.

<sup>e</sup> Infection et inflammation, Département de Biotechnologie de la Santé, Université Paris-Saclay, UVSQ, INSERM, Montigny le Bretonneux, France

Email: christelle.ghazaly@cea.fr

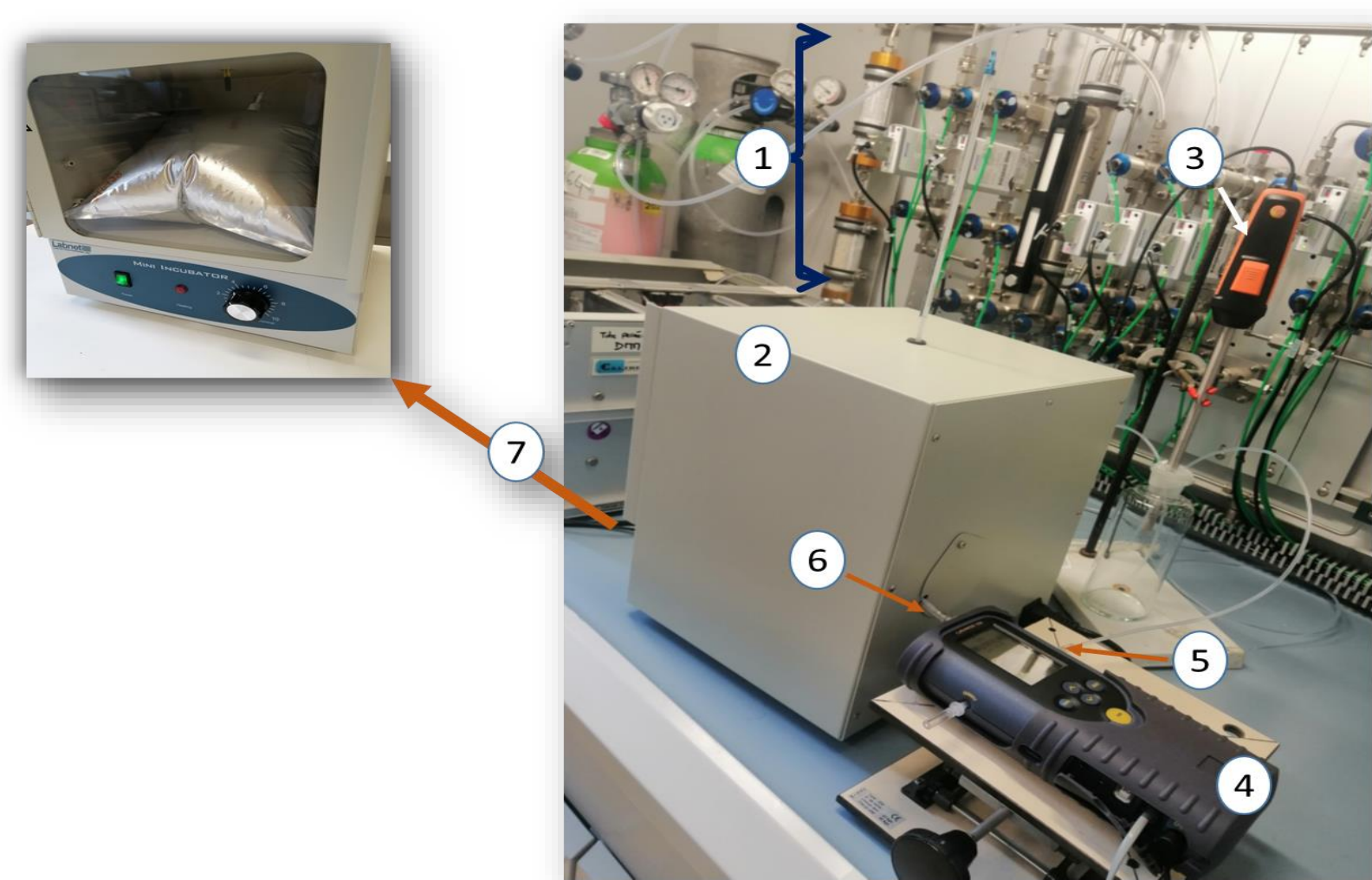


## Abstract

A low-cost, rapid and non-invasive diagnosis of Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) infection is needed for the prevention and control of the pandemic. Coronavirus disease 2019 (COVID-19) mainly affects the respiratory tract and lungs. Therefore, analysis of exhaled breath could be an alternative scalable method for reliable SARS-CoV-2 screening. In this work, an experimental protocol using an electronic nose (“e-nose”) for identifying a specific respiratory imprint in COVID-19 patients was optimized. The analytical performances of the Cyranose<sup>®</sup>, a commercial e-nose device, were characterized by using a gas rig. In addition, the effect of various experimental conditions on its sensor array response was assessed, including relative humidity, sampling time and flow rate, aiming to select the optimal parameters. We also evaluated whether the Cyranose<sup>®</sup> could distinguish between expired air from five healthy patients spiked or not with nonanal, identified as one putative COVID-19 biomarker. Electrical resistance variation of 32 sensors was recorded in real-time by using the PC-nose software during all tests. A statistical data analysis was applied to e-nose sensor response using a software called “Enair” developed on purpose and using a built-in optimized algorithm. Cyranose<sup>®</sup> reveals a possible detection of low concentrations of nonanal (5 ppb) in breath and a significant discrimination from others Volatile Organic Compounds (VOCs) of healthy patients.

## Materials & Methods

### A. Experimental setup



1. Gas bench
2. Thermo incubator
3. Thermo-hygrometer probe
4. E-nose : Cyranose<sup>®</sup> 320
5. Purge inlet : N<sub>2</sub>-94%RH
6. Sample inlet
7. Tedlar<sup>®</sup> bag

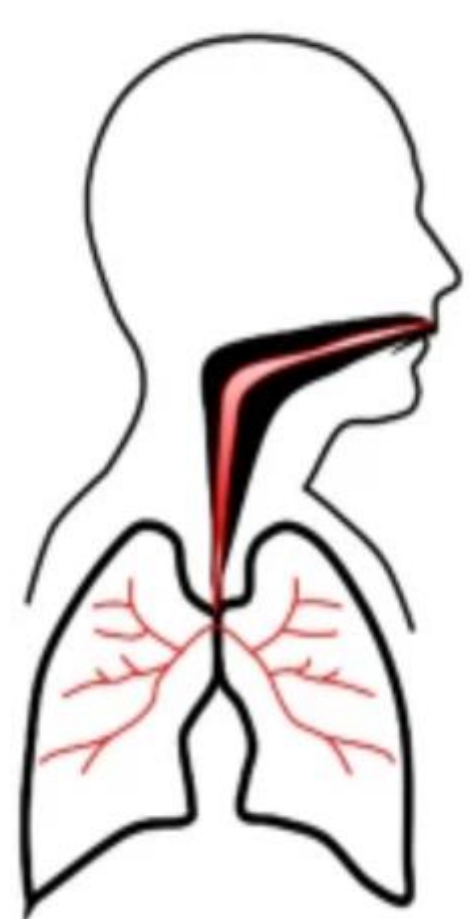
### B. Procedure of exhaled breath analysis by Cyranose<sup>®</sup>

1. Sampling of exhaled breath from healthy donors in 3 Liter Tedlar<sup>®</sup> bag

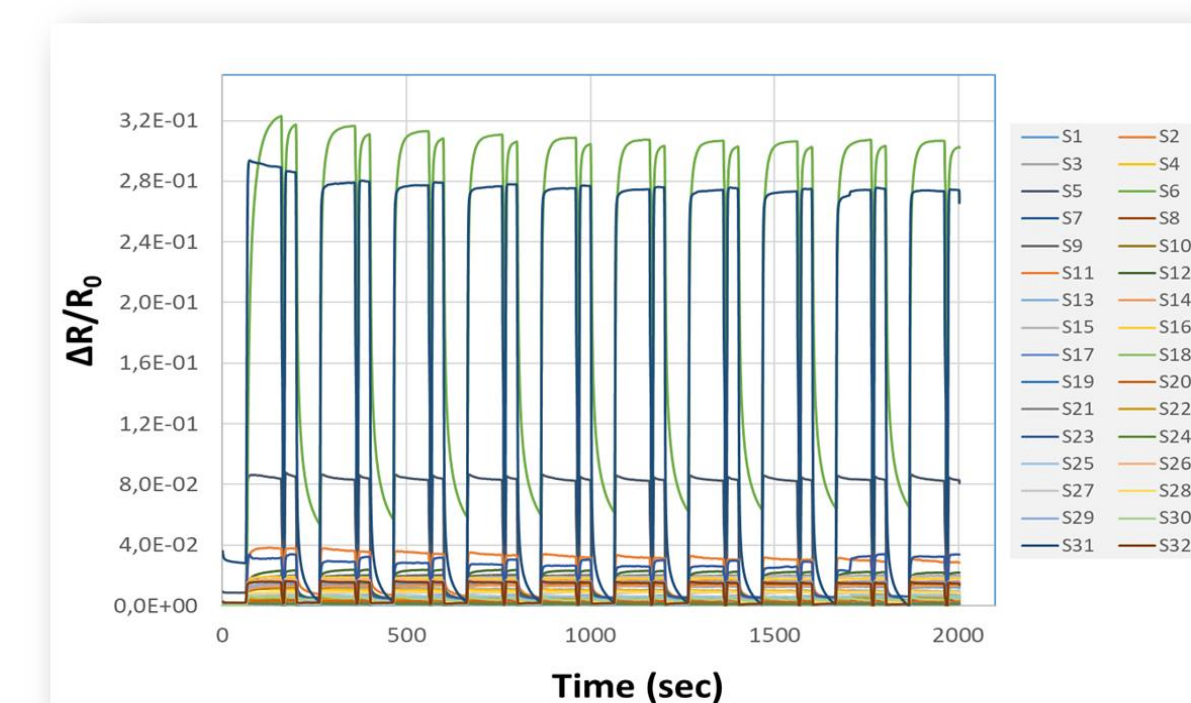
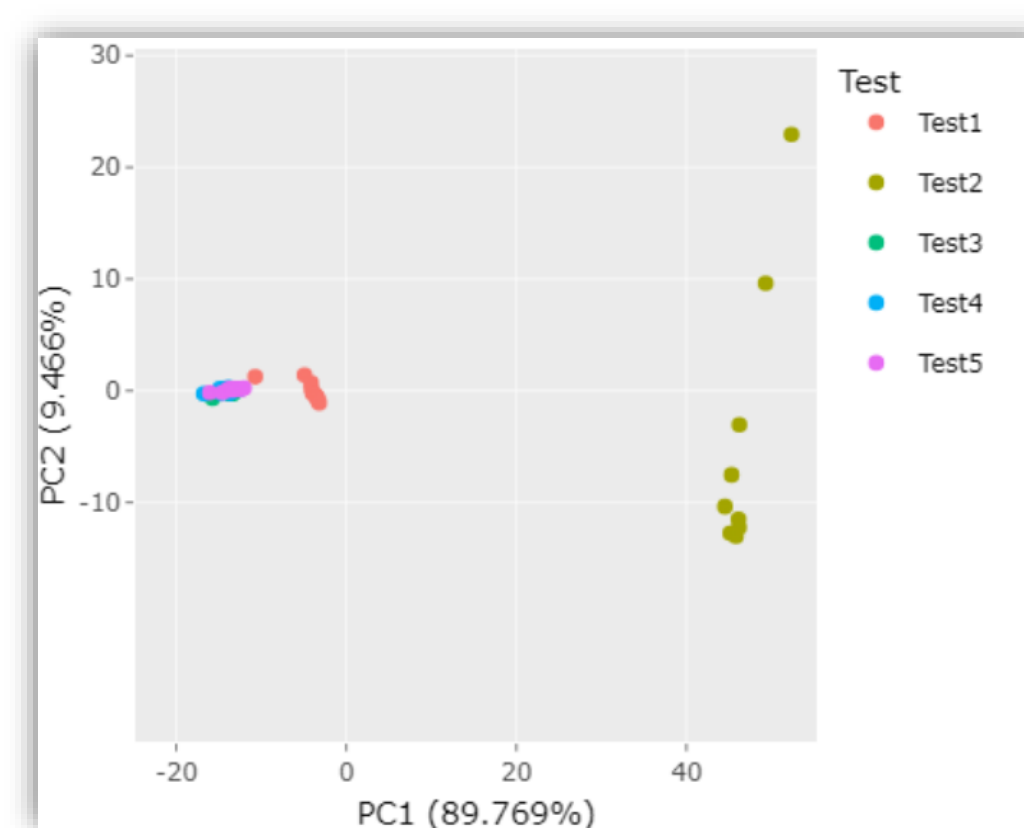
2. Exhaled breath analysis under optimized experimental conditions

3. Data processing & Statistical analysis

- a. Blank exhaled breath
- b. Exhaled breath (1 donor) + acetone / nonanal
- c. Exhaled breath (5 donors) + 5 ppb nonanal



- ✓ Baseline purge time : 60 seconds
- ✓ Sample purge time : 90 seconds
- ✓ Sampling flow rate : 120 mL/min
- ✓ Training repeat : 10 measurements
- ✓ Measurement mode: automatic
- ✓ Sample temperature : 37°C



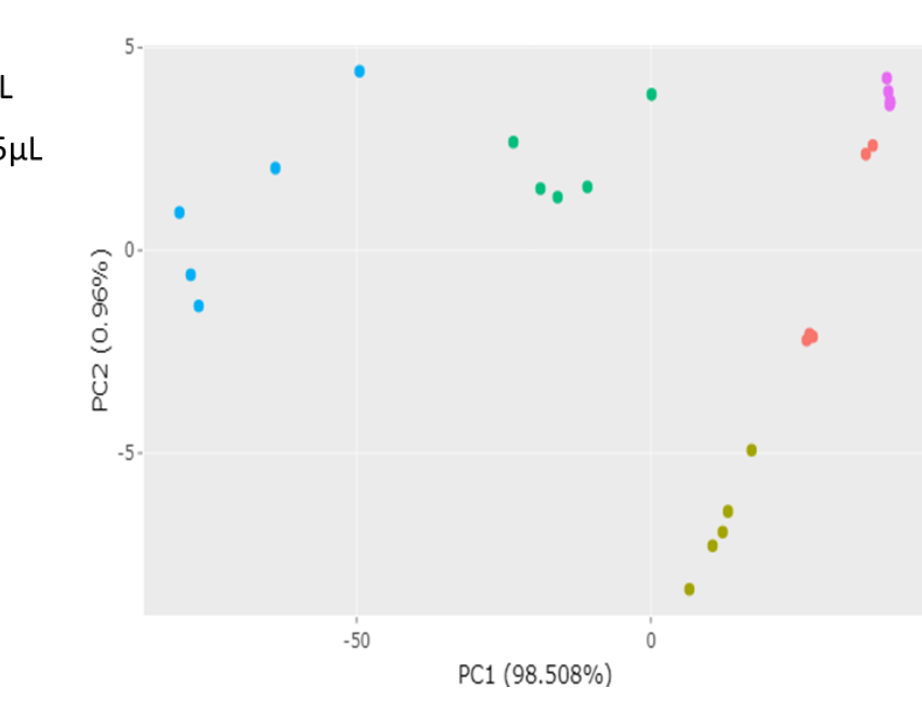
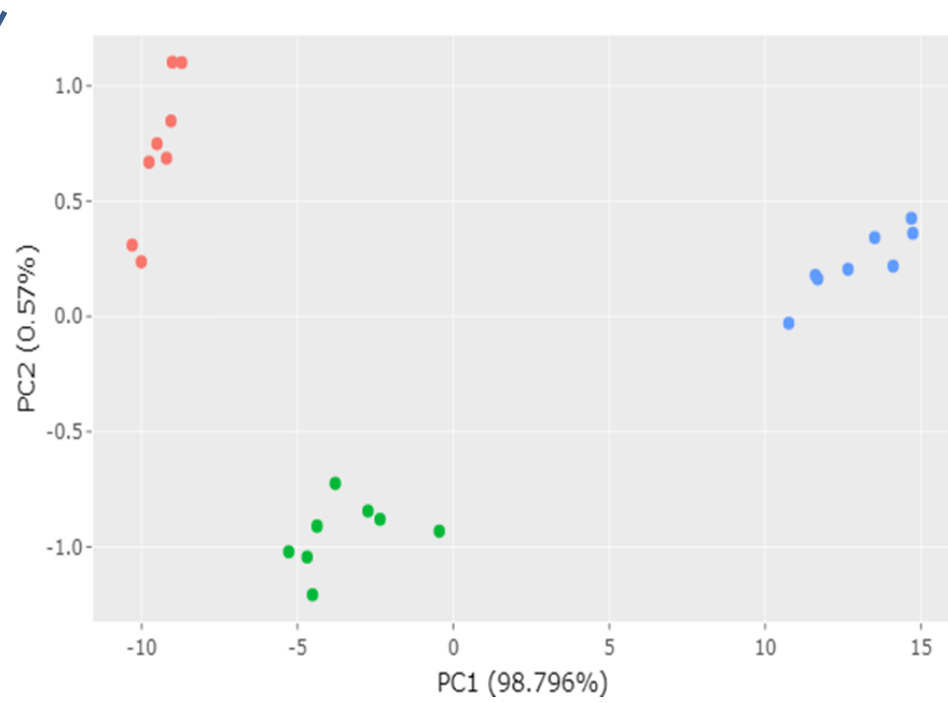
- **PC-Nose :**
- Sensigent software
- Real-time sensor response  $\Delta R/R_0 = (R - R_0)$

- **Enair software:**
- Developed by CEA-JOLIOT and applied for data processing of clinical trials at Foch Hospital
- Statistical data analysis using a built-in algorithm
- Extraction step of « Area Under the Curve » (AUC) feature from different measurements
- Visualization of extracted data by **Principal component analysis (PCA)**

## Results

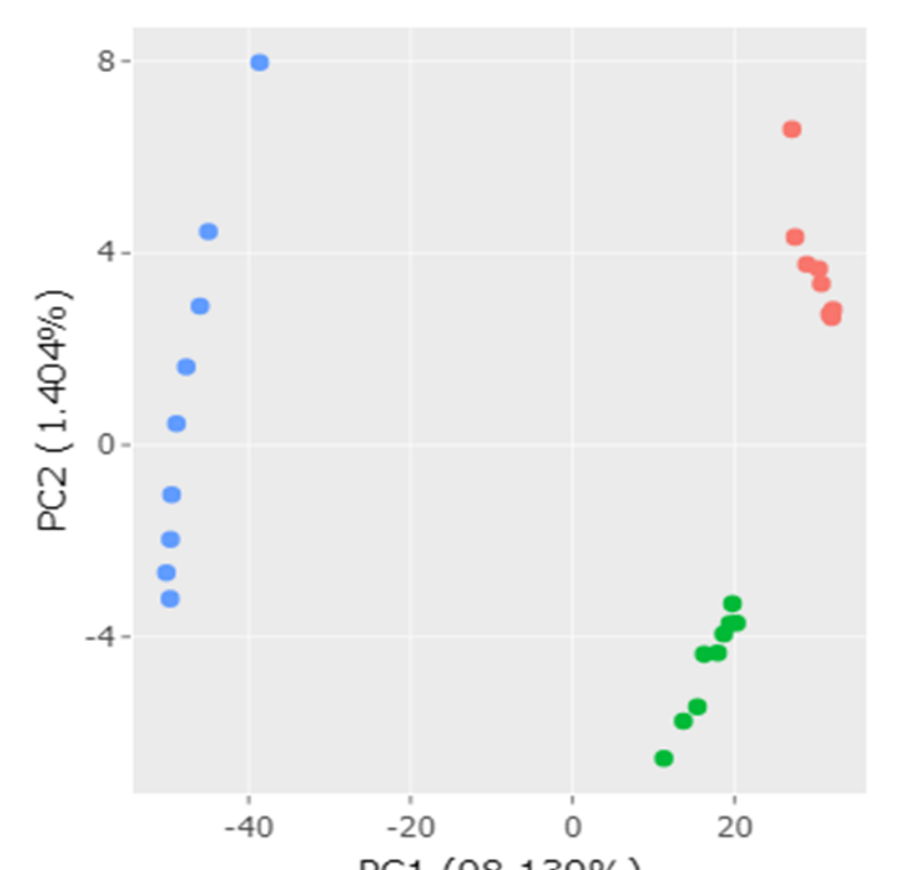
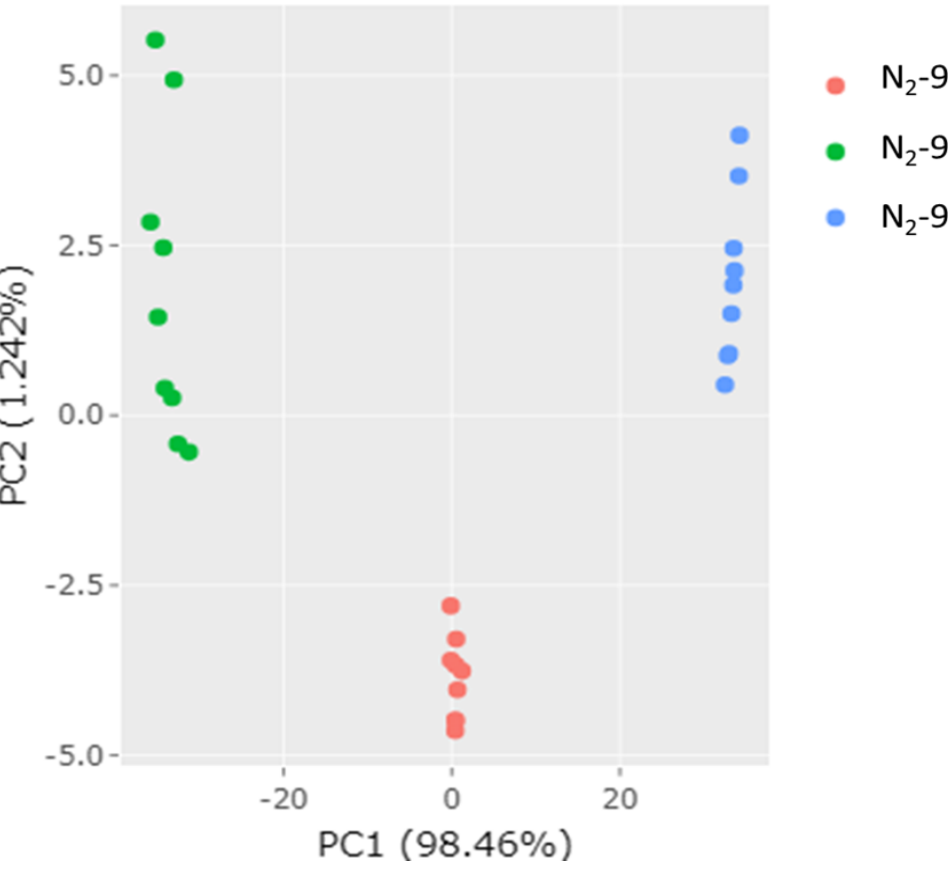
### □ Detection of traces of Acetone & Nonanal using the Cyranose<sup>®</sup>

#### Acetone



Measures	Samples	Acetone volume (μL)	Acetone concentration (ppm)
1	N <sub>2</sub> -94%RH	0	0
2		1	57
3		2.5	127
4	Exhaled breath (ExB)	0	0.208
5		0.5	25.3
6		1	60.5
7		2	122
8		2.5	157

#### Nonanal

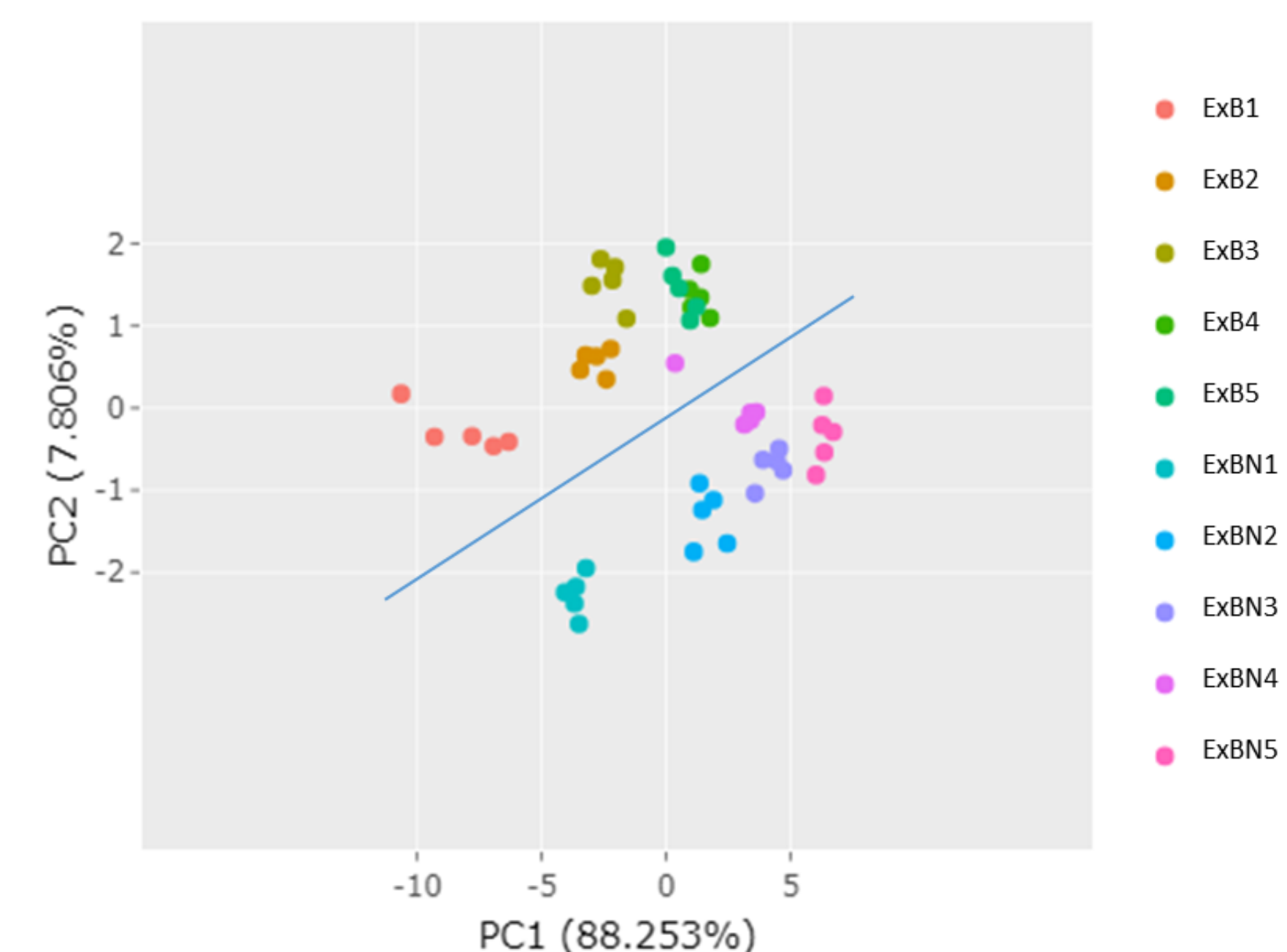


Measures	Samples	Nonanal volume (μL)	TVOC concentration (ppm)
1	N <sub>2</sub> -94%RH	0	0
2		0.5	25
3		1.5	53
4	Exhaled breath	0	0.817
5		0.5	6.6
6		1.5	33

- ✓ Possible detection of various concentrations of acetone or nonanal in the presence of a complexe mixture of VOCs.
- ✓ Clear differentiation between the absence of acetone or nonanal in humidified nitrogen at 94%RH (reference test).
- ✓ Discrimination between exhaled breath from one healthy donor spiked or not with acetone or nonanal.

### □ Evaluation of exhaled breath of five healthy donors

- ✓ Satisfactory discrimination before (ExB1 to ExB5) and after adding 5 ppb of nonanal (ExBN1 to ExBN5), a COVID-19 biomarker.
- ✓ Cyranose<sup>®</sup> sensor's detect low concentrations of nonanal in the presence of others VOCs of healthy patients.
- ✓ Application of “Enair” software for a rapid statistical data processing and PCA plots visualization.



## Conclusions & Perspectives

### Conclusions

- Development of a strategy for analyzing exhaled breath via Cyranose<sup>®</sup>.
- Detection of 5 ppb of nonanal and discrimination among other VOCs in the breath of 5 healthy donors.
- Application of “Enair” software for statistical data processing.

### Perspectives

- Evaluation of the Cyranose<sup>®</sup> in the presence of other Covid-19 biomarkers (e.g. 2,4-octadiene).
- Evaluation of measurement repeatability.
- Validation of the optimized analytical strategy in clinical trials.