Development and characterization of electronic noses for the rapid detection of COVID-19 in exhaled breath

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DEVELOPMENT AND CHARACTERIZATION OF ELECTRONIC NOSES FOR THE RAPID DETECTION OF COVID-19 IN EXHALED BREATH

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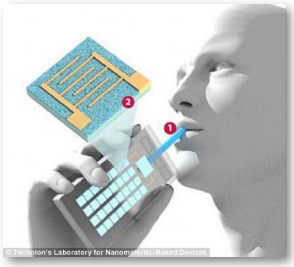
INTRODUCTION

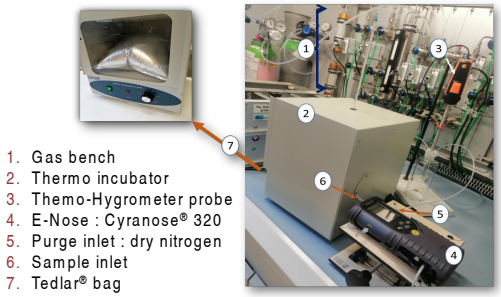
Non-invasive and rapid approach is needed for diagnosis of COVID-19. In this work, exhaled breath analysis using e-Nose is presented as an innovative technique to identify the COVID-19 specific VOCs. The analytical performances of Cyranose®, a commercial e-Nose device, were investigated under controlled conditions towards this goal. Sensitivity, limit of detection and reproducibility of standardized VOCs existing in the breath was assessed. In addition, the effect of various experimental conditions on sensor response was evaluated, including temperature, relative humidity, flow and sampling time, aiming to select the optimal parameters and to validate it in clinical trials to detect the COVID-19 biomarkers. Cyranose® exhibits high sensitivity and reproducible response towards acetone and nonanal, with a limit of detection of 63 ppb and 20 ppb respectively. Furthermore, results show that the variability of relative humidity, temperature and flow sampling, induced a significant sensors response variation, whereas, varying the sampling time does not affect significantly the sensor response.



Breath analysis using Cyranose®:
an array of 32 gas sensors
1- Sampling of an exhaled breath by Cyranose®
2- A nanocomposite chemiresistive gas sensors

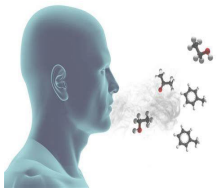
MATERIALS & METHODS

Experimental Setup



1. Gas bench
2. Thermo incubator
3. Themo-Hygrometer probe
4. E-Nose : Cyranose® 320
5. Purge inlet : dry nitrogen
6. Sample inlet
7. Tedlar® bag

1- Tedlar® Bag containing:
- ✓ Exhaled breath of a control patient
- ✓ Generated classical VOCs (acetone, ethanol…)
- ✓ Specific vapor identified as a biomarker for COVID-19 (nonanal)



https://www.researchsea.com/asia_research_news_2018.php

Evaluation of analytical performances of Cyranose®

2- Sampling & Analysis

Assessment under controlled conditions
- ✓ Sensitivity
- ✓ Limit of detection
- ✓ Reproducibility
- ✓ Repeatability
- ✓ Stability
- ✓ Limitations
- ✓ Impact of various experimental conditions on the response:
  - Relative humidity
  - Flow rate
  - Sampling time
  - Temperature

3- Data processing & Statistical treatment

- ✓ ***Pcnose:*** provided with Cyranose®
- ✓ ***E-NaiR:*** software tool for e-Nose devices developed by CEA-JOLIOT and used for data processing of clinical trials at Foch Hospital

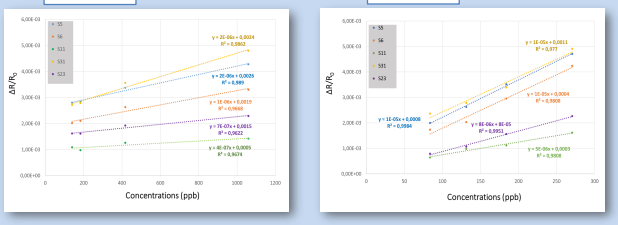
Selection of the most appropriate conditions to detect the biomarkers of COVID-19 in a complex mixture of VOCs from the breath

Validation of optimized analytical protocol in clinical trials

RESULTS

Calibration of Cyranose® in the presence of VOCs

1. Acetone | **2. Nonanal**



Cyranose® shows high sensitivity towards:
- ✓ Acetone: VOC normally found in the breath of a healthy patient. Limit of Detection: 63 ppb
- ✓ Nonanal: VOC presents in the exhaled breath of COVID-19 patients*. Limit of detection: 20 ppb

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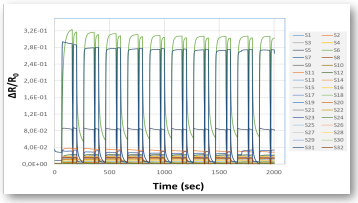
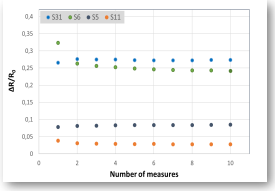
Test of an exhaled breath of a control patient

➢ ***Real-time response of 32 sensors of Cyranose®:***
- *Sample:* exhaled breath of a control patient
- *Baseline:* ultra-pure dry nitrogen
- *Flow rate:* 120 mL/min
- *Baseline & Sampling time:* 60 secondes & 90 secondes



Calculation of resistance variation

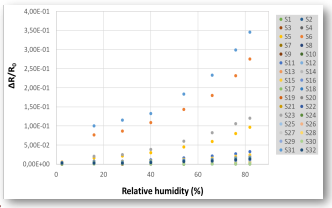
*for sensors: **S5**; **S6**; **S11** and **S31***



- ✓ Four sensors exhibit meaningful responses for VOCs in the exhaled breath of a control patient
- ✓ High repeatability and reproducibility of resistance variations for ten successive measurements

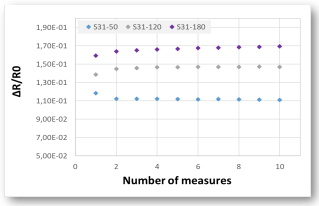
Effect of various experimental conditions on sensor response

A- *Relative humidity rate*



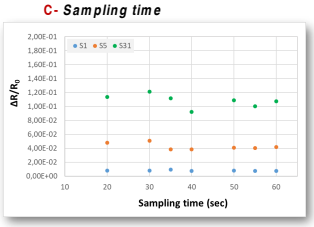
Increasing relative humidity from 2% to 84% affected positively sensors variations.

B- *Sampling flow rate*



- ✓ *The highest resistance variations are obtained by applying a high flow rate of 180 mL/min.*
- ✓ *Repeatable variations are obtained under 92% RH for ten successive measurements.*

C- *Sampling time*



Varying sampling time from 20 s to 60 s does not affect significantly sensor's response.

CONCLUSIONS & PERSPECTIVES

Identification of the COVID-19 specific VOCs by breath analysis technique using a commercial e-Nose device is the challenge of this project.

- ✓ Characterization and evaluation of the analytical performances of Cyranose® under controlled experimental conditions show:
  - High sensitivity to acetone vapors, normally existing in the exhaled breath, with a limit of detection of 63 ppb.
  - Meaningful response to nonanal vapors, presents in the breath of COVID-19 patients, with a limit of detection of 20 ppb.
  - Repeatable and reproducible responses to VOCs existing in the exhaled breath of a control patient.
  - The Sensor response variations depends potentially on relative humidity changes and sampling flow rate used.
- ✓ Selection of the most appropriate protocol and data processing algorithm for COVID-19 diagnosis.
- ✓ Validation of the optimized analytical strategy in clinical trials.