INTERUNIVERSITY PH.D. PROGRAM BETWEEN

POLITECNICO DI BARI AND UNIVERSITÀ DEGLI STUDI DI BARI ALDO MORO

IN INDUSTRY 4.0

# Spectroscopic measurement of volatile organic compounds as biomarkers for human breath analysis

## PhD candidate

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## Cycle

XXXVII

## Tutors

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# Description of the research program

The research project aims at realizing an infrared spectrometer for detection of selected VOCs. The BTEX group of VOCs essential for human breath sensing will be selected as first. It consists of four compounds: Benzene, Toluene, Ethylbenzene, and Xylenes. Since the BTEX group absorption in mid-infrared is significantly higher than near-infrared, the mid-infrared range will be considered. BTEX have three main mid-infrared absorption bands centred at $3\ \mu m$, & $\mu m$ **and** $13\ \mu m$. All three bands will be investigated. For 3 μm and 6 μm, commercial laser sources already available at **PolySense Laboratory** located at Physics Department, at University of Bari, will be used. Light sources at $13\ \mu m$ are not commercially available and they will be realized in collaboration with the research group of Alexei Baranov at **Université de Montpellier**, leader in design and realization of quantum cascade lasers at long wavelengths. The spectrometer will be based on TDLAS technique and will consist of a laser source, an absorption cell containing the gas sample and a photodetector. Due to requirement of broadband detection, a custom quartz tuning fork (QTF) will be used as infrared photodetector. The photodetection process is based on light impacting on the QTF that creates a local heat accumulation, and then the increase of local temperature generates nearby a strain field proportional to the thermal expansion coefficient of quartz. This light-induced thermo-elastic effect produces an electrical signal proportional to the absorbed light intensity due to quartz piezoelectricity. As a result, QTF-based photodetector reaches spectrally flat responsivity $> 2\ kV/0$, corresponding to a noise-equivalent power of few $n0/\sqrt{Hz}$, without employing any thermoelectrical cooling systems. The QTF-based photodetector as well as the assembling of the TDLAS-based spectrometer will be realized in collaboration with **Thorlabs GmbH**, a Company leader in design and manufacturing of opto-mechanical components. To accomplish this task, I plan to spend at least one year at Thorlabs GmbH.

Single-gas absorption spectra will be acquired for each VOC as reference spectra, starting from certified concentrations. Then, mixtures with lower concentrations will be generated by using a gas blender, to assess the sensitivity and the ultimate detection limit of the spectrometer for each analysed VOC. In the case of ultimate detection limits lower than expected concentration levels in human breath, Quartz-Enhanced Photoacoustic Spectroscopy (QEPAS) will be also considered as an alternative technique for the spectrometer. QEPAS exploits the photoacoustic effect and uses a quartz tuning fork (QTF) to detect the weak sound waves produced by molecules absorbing modulated light. **PolySense Laboratory** works in collaboration with **Thorlabs GmbH** which is world-leader in design and realization of QEPAS sensors for trace gas detection. The revealed spectra will used to generate new simulated spectra, i.e., linear combinations of the reference ones in order to simulate synthetic mixtures. These simulated spectra will be used as training for an algorithm able to retrieve the sample composition.

For practical purposes, it is crucial to get correct information and reproducible results as well as to establish well-defined protocols for sample collection, preparation, and analytical procedure to encourage the introduction of breath tests and analysis into clinical practice. The second part of the research project will be dedicated to automatizing and standardise the operations of sampling and storing of the breath samples using a manipulator that can perform these tasks quickly, delicately, and repetitively with consistent precision and accuracy. The idea to involve also Additive Manufacturing techniques will be pursued.

For medical human breath sample, there is the necessity to unravel the baseline physiological levels of volatiles present in human breath and understand their relationship with age, gender, ethnicity, stress, diet, and metabolic changes. Machine learning techniques will be employed to analyse breath samples, to elaborate the data and to extrapolate information to both classify VOCs presents in the exhaled breath and identify compounds that can be an indicator of metabolic status, allowing identification of diseases in their early stages. Furthermore, machine learning techniques can be empowered by automatized classification processes enriching the training set, improving accuracy, and reducing the occurrence of false positive and false negative.

# Schedule of the research activities

Insert the research activities that you plan or you have completed for the three years, including any period abroad.

### First academic year

| | Description | Period | Activity abroad |
|---|---|---|---|
| **Insert name of first research activity** | Study of photoacoustic spectroscopy for gas sensing in the infrared range | Nov. 2021 – Nov. 2022 | NO |
| **Insert name of second research activity** | Reconstruction of absorption spectra of selected BTEX | Nov 2021 – Nov. 2022 | NO |

### Second academic year

| | Description | Period | Activity abroad |
|---|---|---|---|
| **Insert name of first research activity** | Infrared spectrometer assembling for detection of selected VOCs | Nov. 2022 – Jun. 2023 | YES at Thorlabs GmbH |
| **Insert name of second research activity** | Study of Machine Learning methods to identify and classify VOCs | Nov 2022 – Nov 2023 | |

### Third academic year

| | Description | Period | Activity abroad |
|---|---|---|---|
| **Insert name of first research activity** | Realization of a ML algorithm for identification and classification of selected VOCs in real samples | Nov. 2023 – Nov. 2024 | NO |
| **Insert name of second research activity** | | | |

# Provisional training and research activities plan

Specify with the related CFU (ECTS) the training activities that you plan to carry out or have completed in the three years (e.g., courses to attend, conferences, seminars, etc.). Please refer to the *Educational regulations of the Doctoral School of Politecnico di Bari*: http://www.poliba.it/sites/default/files/dottorati/regscudopoliba.pdf

Specify with the related CFU (ECTS) the research activities that you plan to carry out in the three years (e.g., individual research activity, supervision of students, integrative seminars to be given by the PhD student, activity of manuscript preparation for conferences or journals, activity of patents preparation, etc.).

## First academic year

| | Description | Period | Duration | CFU |
|---|---|---|---|---|
| **PhD courses** | Complex Networks: Big Data modelling and learning | June 2022 | 20h | 2 |
| | Flexible and Stretchable Electronics | Feb. 2022 | 20h | 2 |
| | Green photonics for a sustainable economy | TBD | 20h | 2 |
| | | | | |
| **Master's degree courses** | | | | |
| | | | | |
| **Participation to seminars and international congresses or workshops** | International School of Quantum Electronics 2022 | Oct. 2022 | 5 days | 5 |
| | | | | |
| **Presentation of research products at international congresses or workshops** | | | | |
| | | | | |
| | **TOTAL OF CFU FOR TRAINING ACTIVITIES** | | | 11 |
| **Individual research activity** | Assembling of a photoacoustic sensor for BTEX detection. Calibration and assessment of ultimate performance | Nov. 2021 – Nov. 2022 | 975h | 39 |
| **Students' supervision** | Support to master's degree students in the thesis activity | TBD | 100h | 4 |
| **Integrative didactive activities** | | | | |
| **Preparation of manuscripts for conferences or journals** | Writing and reviewing of academic articles for journal and / or conference publications | TBD | 150h | 6 |
| | **TOTAL OF CFU FOR RESEARCH ACTIVITIES** | | | 49 |
| | **TOTAL OF CFU FOR YEAR I** | | | **60** |

## Second academic year

| | Description | Period | Duration | CFU |
|---|---|---|---|---|
| **PhD courses** | | | | |

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| **Master's degree courses** | Physics of Sensors and Laboratory of Spectroscopy | Oct. 2022 – Dic. 2022 | 60h | 6 |
| | Machine Learning for Physics | Sept. 2022 – Jen. 2023 | 60h | 6 |
| **Participation to seminars and international congresses or workshops** | SPIE Photonics West (The International Society for Optics and Photonics) | Mar. 2023 | 5 days | 5 |
| | Participation in one international conference on Machine Learning | TBD | | 1 |
| **Presentation of research products at international congresses or workshops** | Presentation in one international conference | TBD | | 2 |
| | | | | |
| | **TOTAL OF CFU FOR TRAINING ACTIVITIES** | | | 20 |
| **Individual research activity** | Assembling of an infrared spectrometer. Study of ML techniques for analysis of complex mixtures | Nov. 2022 – Nov. 2023 | 850h | 34 |
| **Students' supervision** | Support to master's degree students in the thesis activity | TBD | 50h | 2 |
| **Integrative didactive activities** | | | | |
| **Preparation of manuscripts for conferences or journals** | Writing and reviewing of academic articles for journal and / or conference publications | TBD | 100h | 4 |
| | **TOTAL OF CFU FOR RESEARCH ACTIVITIES** | | | 40 |
| | **TOTAL OF CFU FOR YEAR II** | | | **60** |

## Third academic year

| | **Description** | **Period** | **Duration** | **CFU** |
|---|---|---|---|---|
| **PhD courses** | Hollow Core Waveguide Devices | May 2024 – Jun. 2024 | 16h | 2 |
| | Mixed Reality for data visualization in the Smart Factory | TBD | 20h | 2 |
| | Human-based Smart Manufacturing Systems | TBD | 20h | 2 |
| | | | | |
| **Master's degree courses** | | | | |
| | | | | |
| **Participation to seminars and** | Participation in one international conference on Machine Learning | TBD | | 2 |

| | | | | |
|---|---|---|---|---|
| **international congresses or workshops** | | | | |
| | | | | |
| **Presentation of research products at international congresses or workshops** | Presentation in one international conference | TBD | | 2 |
| | | | | |
| | **TOTAL OF CFU FOR TRAINING ACTIVITIES** | | | 10 |
| **Individual research activity** | Development of a ML-based algorithm to identify and classify VOCs. System's validation. | Nov. 2023 – Nov 2024 | 1000h | 40 |
| **Students' supervision** | Support to master's degree students in the thesis activity | TBD | 100h | 4 |
| **Integrative didactive activities** | | | | |
| **Preparation of manuscripts for conferences or journals** | Writing and reviewing of academic articles for journal and / or conference publications | TBD | 150h | 6 |
| | **TOTAL OF CFU FOR RESEARCH ACTIVITIES** | | | 50 |
| | **TOTAL OF CFU FOR YEAR III** | | | **60** |
| | **TOTAL OF CFU FOR THE WHOLE PHD COURSE** | | | **180** |