RO Thesis Topics: Did the patient get better? Determine the health condition of patients in intensive care by using data-driven modelling.

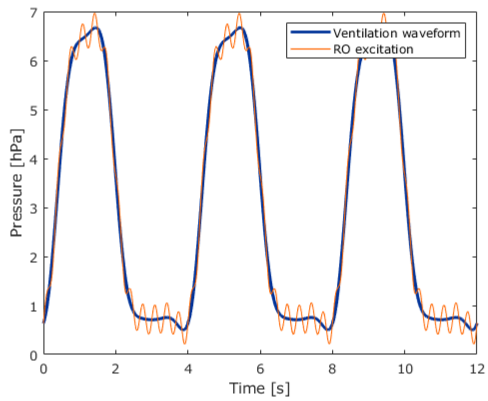
Motivation

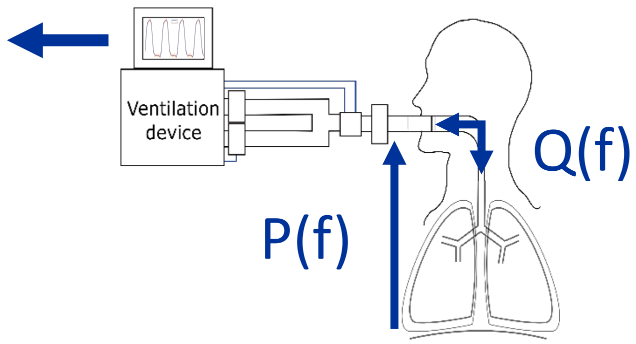
In this thesis, you will use measurement and modelling techniques to help doctors determine the health status of a patient in intensive care.

When patients end up in an intensive care unit (ICU), they are often subjected to artificial mechanical ventilation to be able to breathe. Although this ventilation is essential for the patient's survival, every hour that the patient does not breathe independently, there is an increase in complications and mortality. For that reason, the status of the lungs must be continuously monitored, to determine when the patients are ready to 'wean' (i.e. get used to breathing spontaneously and independently again).

Context

These thesis proposals are framed in an ongoing research project in collaboration with the ICU of the UZBrussel, where we use Respiratory Oscillometry (RO) to track the evolution of the state of the lungs. Our RO technique improves upon the state-of-the-art by being non-invasive, robust and easy to apply across different ventilation modes, a highly needed innovation. RO uses data-driven modelling techniques to identify the lung impedance by applying small pressure oscillations (i.e. excitation using a multisine) onto the breathing or ventilation. Information about the respiratory mechanics can be extracted from this impedance, including the resistance (R) and the elastance (E) of the lung. This RO protocol has been implemented in a professional mechanical ventilator device and received regulatory approval. A clinical trial is currently (and probably until September 2024) being executed. This will give us a lot of data with a lot of potentially interesting information to discover.





RO Thesis Topic 1: Advancing Respiratory Monitoring: Refining Data-Driven Modelling for Longitudinal Assessment in Clinical Practice.

Promotor: Prof. John Lataire; Co-promotor: ICU director Prof. Joop Jonckheer, Andy Keymolen.

In this master's thesis project, you will delve into the realm of respiratory monitoring to unearth valuable insights that could improve patient care. The objective of this thesis is to discern statistically significant parameter variations across multiple measurements obtained from individual patients. The proposed approach is as follows:

<u>Getting up to topic:</u>

- **Exploration of Respiratory Oscillometry (RO):** Unravel the potential of RO in assessing lung impedance. Through a comprehensive survey of literature and state-of-the-art techniques, you will gain a deep understanding of how RO measurements can illuminate the health status of patients.
- **Hands-on Simulation and Mc Invent Trial Setup**: Gain practical experience by simulating RO techniques in various realistic scenarios. Familiarize yourself with the intricacies of the clinical trial setup and the experiments conducted that gathered the data.
- **Data Processing Mastery:** Learn the art of data cleaning and preprocessing to ensure the accuracy and reliability of measurements. Through meticulous removal of transients and breathing artefacts, you will prepare the data for in-depth analysis.

<u>Design and development of novel techniques.</u>

- **Innovative Parameter Estimation Techniques:** Elevate your skills by improving estimation techniques to enable longitudinal assessment of model parameters. Begin with a first-order model and progress towards more sophisticated models tailored to capture diagnostic-rich low-frequency regions [1].
- **Efficient Automation:** Streamline the analysis process by automating data processing, allowing for efficient examination of multiple patient datasets.
- **Development of User-Friendly Application:** Translate your findings into actionable insights with the development of a user-friendly application. This application will provide clinicians with longitudinal assessments of identified parameters, from the MC Invent patients as an example but applicable in future trials, facilitating informed decision-making in patient care.
- **Collaboration with Physicians:** Engage in discussions with physicians to validate the clinical relevance of identified parameters and ensure the ergonomic design of the application. Your collaboration will bridge the gap between technological innovation and clinical practice.
- **Predictive Modelling for Liberation from Mechanical Ventilation:** Utilize the longitudinal assessments to develop a predictive model for determining a patient's readiness for weaning from mechanical ventilation. This predictive tool will empower clinicians to make informed decisions, ultimately leading to improved patient outcomes.

<u>Work approach:</u>

We encourage you to take ownership of the project, unleash your creativity, and push the boundaries of oscillometry. With access to dedicated workspace and state-of-the-art equipment, you will have the support and resources needed to excel in your research endeavors.

[1] Bates, Jason HT. Lung mechanics: an inverse modelling approach. Cambridge University Press, 2009.

RO Thesis Topic 2: Advancing Respiratory Mechanics Analysis: A time-varying modelling approach.

Promotor: Prof. John Lataire; Co-promotor: ICU director Prof. Joop Jonckheer, Andy Keymolen.

In the intricate dance of breathing, the inspiratory phase sees respiratory muscles contract, while during exhalation, they relax. This physiological ballet holds critical clues for clinicians, as contracted muscles typically exhibit increased stiffness. Leveraging this insight, we anticipate periodic fluctuations in the elastance estimate of a patient's respiratory system throughout each breath. For ICU physicians, this dynamic provides invaluable insights, with heightened inspiratory stiffness signalling strengthening respiratory muscles and potentially heralding readiness for liberation from mechanical ventilation.

Yet, elastance is just the tip of the iceberg. As we delve deeper into within-breath analysis, we uncover a realm ripe for exploration within respiratory oscillometry. While non-parametric estimations have proven highly beneficial [1], parametric modelling has thus far shown promise primarily in simulation [2]. With this thesis, we endeavour to push the boundaries of innovation by crafting a robust parametric identification strategy for within-breath analysis in mechanically ventilated patients.

Our overarching goal is clear: to discern statistically significant within-breath parameter changes across multiple measurements from individual patients. To achieve this, we propose a multifaceted approach:

<u>Getting up to topic: </u>Similar as in RO thesis topic 1

<u>Design and development of novel techniques.</u>

- Implement estimation techniques to detect a time-varying behaviour of the model parameters. Starting from [2] and improving towards more complex models
- Design an excitation signal that allows an improved identification of the time-varying parameters
- Design an experiment to prove that the excitation signal improves upon the state-of-the-art
- Develop a longitudinal assessment strategy for the time-varying parameters

<u>Work approach:</u>

We encourage you to take ownership of the project, unleash your creativity, and push the boundaries of oscillometry. With access to a dedicated workspace and state-of-the-art equipment, you will have the support and resources needed to excel in your research endeavours.

[1] Veneroni, Chiara, et al. "Oscillatory respiratory mechanics on the first day of life improves prediction of respiratory outcomes in extremely preterm newborns." Pediatric Research 85.3 (2019): 312-317.

[2] Alamdari, Hamed Hanafi, Kamal El-Sankary, and Geoffrey N. Maksym. "Time-varying respiratory mechanics as a novel mechanism behind frequency dependence of impedance: a modeling approach." IEEE transactions on biomedical engineering 66.9 (2018): 2433-2446.

RO thesis topic 3: Investigating the Impact of Oscillometry on Ventilation Asynchrony: A Novel Approach.

Promotor: Prof. John Lataire; Co-promotor: ICU director Prof. Joop Jonckheer, Andy Keymolen.

Ventilation asynchrony, a critical concern in patient care, occurs when ventilators fail to detect a patient's inspiratory effort in a timely manner. Traditionally, this effort is identified through peak flow signals generated during inspiration. However, the introduction of oscillometry into ventilation monitoring has introduced new challenges, as it overlays excitation signals onto the ventilation waveform, leading to subtle flow fluctuations during expiration.

This master's thesis project aims to explore whether oscillometry exacerbates ventilation asynchrony. Leveraging patient data from the MC Invent trial, in this thesis you will analyze both oscillometry and ventilation measurements to discern any differences in ventilation asynchrony prevalence. Utilizing state-of-the-art identification techniques [1], the project will adapt methodologies to suit the specific context, enabling precise analysis.

In scenarios where ventilation asynchrony is induced, the project will propose and validate an excitation signal design strategy aimed at mitigating its prevalence. This strategy will be tested on simulators to ensure efficacy and patient safety. Furthermore, in cases where ventilation asynchrony is not observed, the project will enhance the design of excitation signals. Current approaches often utilize exponential amplitude decay with a fixed peak-to-peak limit, which may not account for individual patient characteristics. By employing a model-based design strategy, the project seeks to optimize signal amplitudes and minimize flow perturbations that disturb the patient, thus improving patient comfort and outcomes.

Getting up to topic: Similar as in RO thesis topic 1

Design and development of novel techniques.

- Implement a ventilation asynchrony detection mechanism starting from [1]
- Comparative analysis of ventilation asynchrony prevalence between ventilation and oscillometry measurements.
- Development of an innovative excitation signal design strategy tailored to address ventilation asynchrony concerns or improve the amplitude design strategy.
- Experimental validation of the proposed excitation signal's efficacy, surpassing existing benchmarks.

Work approach:

To facilitate efficient collaboration and feedback, the project offers a dedicated workspace within the department. Access to a professional ventilator with oscillometry functionality enables real-world testing on lung emulators, ensuring the practicality and relevance of developed techniques.

[1] L. van de Kamp, J. Reinders, B. Hunnekens et al., Automatic patient-ventilator asynchrony detection framework using objective asynchrony definitions. IFAC Journal of Systems and Control (2024), doi: https://doi.org/10.1016/j.ifacsc.2023.100236.

RO thesis topic 4: Advancing Respiratory Monitoring: Extending Low-Frequency Oscillometry to Non-Invasive Mask Ventilation

Promotor: Prof. John Lataire; Co-promotor: ICU director Prof. Joop Jonckheer, Andy Keymolen.

In the Mc-Invent trial, low-frequency RO provided invaluable insights into respiratory mechanics of patients undergoing ventilation via an endotracheal tube (a tube inserted in the trachea). However, as patients transition to mask ventilation post-tube removal, the current monitoring techniques become ineffective, leaving clinicians without vital information crucial for patient care.

Your mission: enhance low-frequency RO techniques to enable accurate estimations during mask ventilation. To achieve this, you will delve into the complexities posed by higher flow leakage and dead volume inherent in mask ventilation setups. Your approach will involve:

In this thesis, you will improve the low-frequency RO technique such that viable estimations can be obtained during mask ventilation. You will adapt the RO techniques, the excitation signals and modelling processes, such that it can deal with the higher flow leakage (air that leaks via the mask boundaries) and the higher dead volume (air that is in between the sensor and the patient's mouth, encapsulated by the mask). Both elements influence respiratory mechanics estimations negatively. To achieve this, we suggest the following approach:

<u>Getting up to topic:</u> Similar as in RO thesis topic 1

<u>Design and development of novel techniques.</u>

- **Understanding the Impact of Dead Volume and Leakage Flow**: Through rigorous simulation studies, you will investigate the influence of dead volume and leakage flow on respiratory mechanics estimation. This foundational research will inform subsequent technique development.
- **Refinement of Modelling Strategies:** Armed with insights from simulation studies, you will refine modelling strategies to mitigate the negative impact of dead volume and leakage flow. Incorporating prior knowledge, you will develop robust models capable of accurately capturing respiratory dynamics.
- **Innovative Excitation Signal Design:** Central to your endeavor is the design of an excitation signal strategy that is resilient to the challenges posed by dead volume and leakage flow. Through novel design approaches, you will ensure the reliability and accuracy of respiratory mechanics estimations.
- **Experimental Validation:** Rigorous experimentation is paramount to validate the efficacy of your developed techniques. You will design and conduct experiments to demonstrate the working principle and real-world applicability of your innovations, cementing their status as game-changing advancements in respiratory monitoring.

<u>Work approach:</u>

We encourage you to take ownership of the project, unleash your creativity, and push the boundaries of oscillometry. With access to dedicated workspace and state-of-the-art equipment, you will have the support and resources needed to excel in your research endeavors.