

# Abstract

This doctoral project was initiated during the COVID-19 pandemic, in response to the urgent need for effective respiratory support. Continuous positive airway pressure (CPAP) therapy became widely used to treat hypoxemic respiratory failure, but traditional devices presented critical issues, including high oxygen consumption, dependence on high-pressure gas lines, excessive noise, and contamination risks. To address these challenges, an innovative closed-circuit ventilation system was proposed. The primary goal of this research was to guide the design, development, and characterization of this novel ventilatory system through a reliable *in silico* and *in vitro* coupled approach. The study was structured into three main parts, focusing on: (1) patient safety, (2) accurate delivery of ventilatory therapy, and (3) therapy effectiveness.

Patient safety was addressed by investigating CO<sub>2</sub> rebreathing with non-invasive ventilation (NIV) interfaces, specifically helmets and total-face masks. Computational fluid dynamics (CFD) simulations were developed to analyze CO<sub>2</sub> accumulation and distribution. These simulations were supported by experimental studies to obtain boundary conditions and validation data. Optimized layouts were identified to minimize rebreathing risk while maintaining flexibility in interface choice.

Ventilatory therapy delivery was ensured through the development of a multidomain 0D model to represent the components of the innovative ventilation system. Comparative *in vitro* studies of commercial devices provided reference performance ranges. The simulations demonstrated how design choices, including interface leak management and resistance distribution, influenced therapeutic pressure and patient comfort. The model enabled the selection of optimal configurations that aligned with commercial standards, highlighting the importance of fine-tuning ventilation system components.

Therapy effectiveness was evaluated using a 0D cardiopulmonary model to simulate the physiological response to positive end-expiratory pressure (PEEP). This model integrated lung recruitment and collapse dynamics as well as pulmonary perfusion, enabling the assessment of blood oxygenation. Statistical validation using synthetic patient data confirmed the model's potential in guiding PEEP titration, a key challenge in critical care.

In conclusion, this research demonstrated the value of a combined *in silico*/*in vitro* approach in optimizing the design and functionality of innovative ventilatory systems. The proposed methods and findings lay the groundwork for further advancements in respiratory support technology.