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DOCTOR OF ENGINEERING SCIENCES

of **Sebastiaan Priem**

The public defense will take place on **Friday 30th October 2026 at 4pm** in room **K.2.56** (Building K, VUB Main Campus)

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BREATH-BY-BREATH INDIRECT CALORIMETRY BASED ON A DYNAMIC HALDANE TRANSFORMATION: FROM THEORETICAL FRAMEWORK TO CLINICALLY EVALUATED PROTOTYPE

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Abstract of the PhD research

Indirect calorimetry is considered the gold standard for measuring resting energy expenditure and respiratory quotient and relies on the measurement of a patient's rate of oxygen consumption and carbon dioxide production. Despite its established value, its use is constrained by several limitations. First, the use of the Haldane transformation to infer inspired flow, amplifies measurement errors as the inspired oxygen fraction increases, which prevents measurements in patients receiving more than 60-70 % oxygen. Secondly, a single short-term measurement is typically extrapolated to represent the energy expenditure of the patient over a period of 24 hours, which doesn't capture intra- and inter-day variability. Finally, the cost, form factor, maintenance burden and requirement of trained personnel of available devices confine their use to specialised clinical or research environments.

This dissertation establishes a theoretical framework for breath-by-breath indirect calorimetry that determines the oxygen consumption rate without measuring the expired oxygen fraction and without assuming a value for the respiratory quotient. When both the inspired and expired flow rates are measured, the expired inert gas fraction follows from the mass balance of inert gases, and the expired oxygen fraction from the composition of the expired gas. By applying this method, the inspired oxygen fraction no longer appears in a denominator, which analytically avoids the error amplification at high inspired oxygen fractions. Additionally, a dynamic Haldane transformation is introduced, which distributes the volume correction over the exhalation according to the expired CO₂ waveform, and thereby accounts for the dead-space gas at the start of each exhalation.

The requirements for breath-by-breath gas exchange measurements in the clinic and at home are derived from a criterion on the error of REE, and the sensing principles for each quantity are evaluated against them. This analysis shows that flow and CO₂ can be measured directly, whereas the expired oxygen fraction cannot, and leads to a compact prototype that measures flow and CO₂ at the airway opening.

In a pilot comparison with a clinical reference calorimeter (Q-NRG, COSMED) in 12 healthy volunteers, the agreement for REE and gas exchange rates showed no statistically significant mean differences between devices, with limits of agreements comparable to those reported in similar comparison studies, nevertheless individual-level variability remained substantial. Conversely to the parameters mentioned before, RQ did differ significantly between devices. A stability analysis of the reference device showed that this discrepancy was most likely attributed to the sensor drift in the galvanic fuel cell oxygen sensor of the reference. An operating envelope analysis indicates that the prototype covers the ranges encountered in spontaneously breathing, mechanically ventilated and ECMO patients, and identifies the conditions that remain to be met in these configurations.

Together, these findings provide a foundation for breath-by-breath indirect calorimetry in clinical settings where it is currently restricted, and for more frequent metabolic measurements, including outside specialised clinical environments.