Sensitivity Analysis of Whole-Room Indirect Calorimeters at the Steady-state Condition

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***Abstract*—Whole-Room Indirect Calorimeters (WRIC) are accurate tools to precisely measure energy metabolism in humans via calculation of oxygen consumption and carbon dioxide production. Yet, overall accuracy of metabolic measurements relies on the validity of the dynamic model for gas exchange inside the calorimeter volume in addition to experimental and environmental conditions that contribute to the uncertainty of WRIC outcome variables. The aim of this work is to formally study the sensitivity of a WRIC system operated in a push configuration at the steady-state condition to identify the optimal experimental conditions to obtain the best degree of accuracy for outcome metabolic measurements. The results of our sensitivity analysis are then validated with measurements obtained during propane combustion tests performed at the WRIC located at the University Hospital of Pisa. Our results demonstrate that achieving a fractional concentration of carbon dioxide inside the calorimeter >0.2% leads to relative uncertainty <5% for the outcome metabolic measurements when assuming an accuracy class of 1% for gas analyzer instruments.**

***Index Terms*—Sensitivity analysis, Static sensitivity, Energy metabolism, Indirect calorimetry, Metabolic chamber**

I. Introduction

Measuring human Metabolic Rate (MR) represents an important step in determining nutritional needs. Estimation of MR through wearable devices, often relying on heart rate measurements, has been widely discussed in the scientific literature and results are often inaccurate, with authors' stated errors in MR estimation ranging from 25% to 50% [1], [2]. Recently, Levikari *et al.* [3] proposed an integrative approach to increase the accuracy of MR estimation by combining a thermoelectric heat flux sensor with heart rate measurement, in conjunction with a humidity sensor to take into account evaporative heat transfer, resulting in an accuracy improvement at low MR levels (e.g., resting conditions), while still achieving error $\geq$30% for higher MR levels.

On the other hand, Whole-Room Indirect Calorimeters (WRICs) represent the gold standard method to precisely measure the rate of metabolic rate in humans via calculation of oxygen (O_2) consumption and carbon dioxide (CO_2) production based on indirect calorimetry principles [4], [5]. The accurate assessment of human energy metabolism by WRIC systems allows the characterization of each person's metabolic phenotype informative for the individual susceptibility to weight gain and obesity [6], [7]. On the basis of an established dynamic WRIC model for gas exchange [8]–[10] and known WRIC air volume, the rates of O_2 consumed ($\dot{V}O_2$) and CO_2 produced ($\dot{V}CO_2$) by an individual inside a WRIC operated in a push (or pull) configuration can be calculated upon measurements of air inflow (or outflow) rate and fractional concentrations of O_2 and CO_2 both in inflow air and in WRIC air. Accordingly, the overall uncertainty of $\dot{V}O_2$ and $\dot{V}CO_2$ outcome estimate relies on the uncertainty of measurements of air flow rate by mass flow meter/controller and O_2 and CO_2 concentrations by gas analyzers, which ultimately impact also the uncertainty of metabolic rate calculated by applying indirect calorimetry equations to $\dot{V}O_2$ and $\dot{V}CO_2$ estimates.

For instance, unpredictable variations in O_2 and CO_2 concentrations in fresh air due to environmental influences [11] or changes in WRIC air during the course of experiments may propagate through the WRIC model equations and constitute a source of error for $\dot{V}O_2$ and $\dot{V}CO_2$ estimates. Quantifying the impact of each WRIC variable on outcome measurements may provide insight into the best experimental conditions that can minimize the effects of measurements errors and model uncertainties to ensure more accurate estimates of outcome metabolic quantities [12].

In fact, air inflow rate can be precisely adjusted by a mass flow controller (or by a voltage-controlled blower) in a push-calorimeter to ultimately achieve a pre-determined steady-state value for the fractional concentration of CO_2 inside the WRIC [10], [13]. Yet, the quantification of uncertainty in outcome WRIC measurements arising from the uncertainty in inflow rate and CO_2 measurements is warranted to identify the optimal experimental conditions for these two WRIC system variables.

The aim of the present study is to conduct a formal sensitivity analysis of WRIC model for gas exchange in steady-state conditions to quantify the impact of each WRIC system variable on the uncertainty of $\dot{V}O_2$ and $\dot{V}CO_2$ outcome measurements. This work is an extended version of a previously published conference paper, originally presented at the IEEE International Symposium on Medical Measurements and Applications (MeMeA 2022) [14]. By validating our sensitivity analysis results with measurements obtained during propane combustion experiments, herein we get the following new main results:

- The CO_2 concentration inside the calorimeter represents the most important WRIC system variable that has the greater impact on the uncertainty of WRIC outcome measurements.

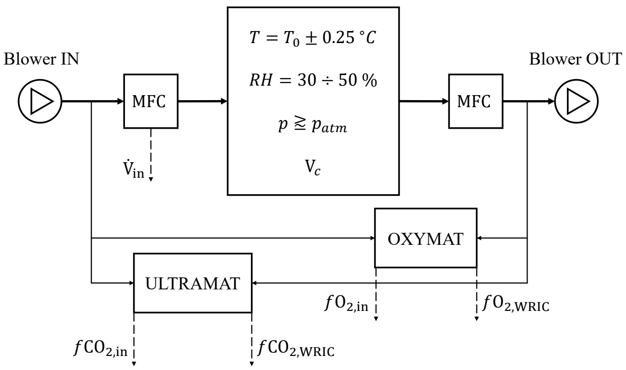


Fig. 1. Schematic representation of a whole-room indirect calorimeter (push-pull configuration) showing measured quantities.

- By allowing CO_2 concentration inside the calorimeter to rise from fresh air levels to concentration greater than 0.2% at the WRIC steady-state condition, it is possible to reduce the relative uncertainty of $\dot{V}O_2$ and $\dot{V}CO_2$ outcome measurements below 5%.

II. Methods

Fig. 1 shows a schematic representation of a WRIC system, highlighting the most important components, parameters, and measured quantities. If blowers are installed both on the inlet and outlet air pipes, the WRIC system can be operated either as a push, or pull, or push-pull. Assuming a push operation, the air inflow rate $\dot{V}_{in}$ [L/min] can be controlled and measured using a mass flow controller.

The equations [8], [10] for $\dot{V}O_2$ and $\dot{V}CO_2$ measurements [mL/min] of an individual residing inside the chamber as a function of $\dot{V}_{in}$ and gas concentrations of inflow air and chamber air can be written as

$$\begin{aligned} \dot{V}O_2 &= \Big(-\dot{V}_{in} \times \big(fO_{2,WRIC} \times H - fO_{2,in}\big) + \\ &\quad - V_{WRIC}\frac{dfO_{2,WRIC}}{dt}\Big) \times 10 \\ \dot{V}CO_2 &= \Big(\dot{V}_{in} \times \big(fCO_{2,WRIC} \times H - fCO_{2,in}\big) + \\ &\quad - V_{WRIC}\frac{dfCO_{2,WRIC}}{dt}\Big) \times 10 \end{aligned}, \tag{1}$$

which, neglecting the derivative contributions, can be rewritten in steady-state (static) condition as

$$\begin{aligned} \dot{V}O_2 &= -\dot{V}_{in} \times \big(fO_{2,WRIC} \times H - fO_{2,in}\big) \times 10 \\ \dot{V}CO_2 &= \dot{V}_{in} \times \big(fCO_{2,WRIC} \times H - fCO_{2,in}\big) \times 10 \end{aligned}, \tag{2}$$

where $fO_{2,in}$, $fCO_{2,in}$, $fO_{2,WRIC}$, and $fCO_{2,WRIC}$ are the fractional concentrations of O_2 and CO_2 (expressed as percentage) in inflow air and inside the WRIC, respectively [10]. The quantity H is the Haldane factor based on nitrogen balance in fresh and WRIC air. At the steady-state, the Haldane factor is equal to:

$$H = \frac{100 - fO_{2,in} - fCO_{2,in}}{100 - fO_{2,WRIC} - fCO_{2,WRIC}}. \tag{3}$$

The metabolic rate (MR, kcal/min) can be derived using the Lusk's equation on the basis of $\dot{V}O_2$ and Respiratory Exchange Ratio (RER) defined as:

$$RER = \frac{\dot{V}CO_2}{\dot{V}O_2}, \tag{4}$$

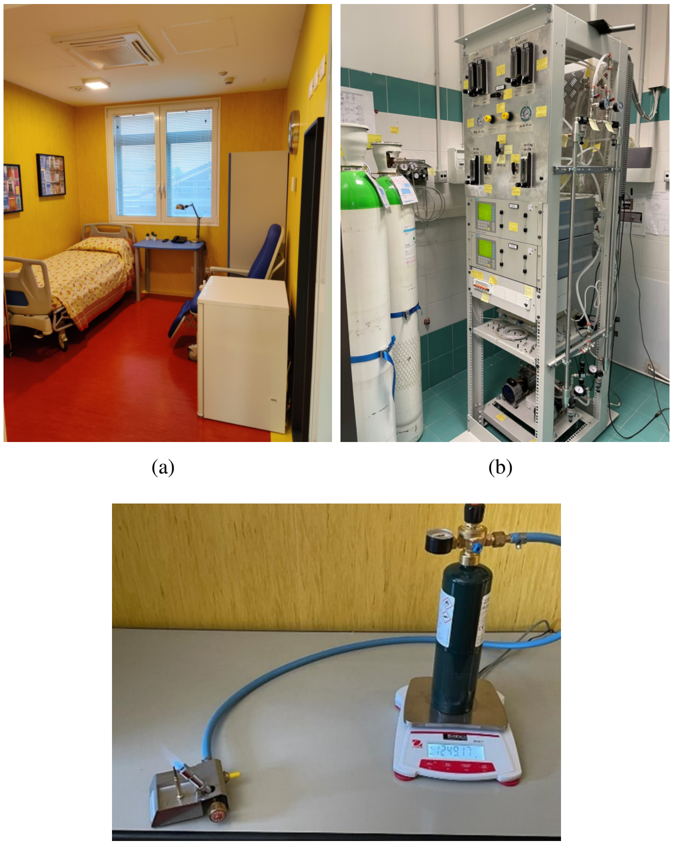
$$MR = \dot{V}O_2 \times (4.686 + (\mathrm{RER} - 0.707) \times 1.2321)\,. \tag{5}$$

In our data simulations for sensitivity analysis of WRIC model, the fractional concentrations of O_2 and CO_2 in inflow air ($fO_{2,in}$ and $fCO_{2,in}$) were assumed to be constant at 20.93% and 0.03%, respectively. Further, the RER was set to 0.6 to model a chemically pure propane gas combustion, commonly used for WRIC validation tests [12] as those performed in the current study for validation of sensitivity analysis results. Since the following analysis considers fixed and known values for O_2 and CO_2 concentrations at the inlet to the metabolic chamber, the model variables are reduced to 3, $\dot{V}_{in}$, $fO_{2,WRIC}$, and $fCO_{2,WRIC}$. Due to the assumptions for constant inflow gas concentrations, $\mathrm{RER} = 0.6$, and nitrogen balance, the concentrations inside the chamber ($fO_{2,WRIC}$, and $fCO_{2,WRIC}$) are related to each other. Accordingly, the independent WRIC model variables considered in our simulations are reduced from 5 to 2, namely, $\dot{V}_{in}$, and $fCO_{2,WRIC}$.

For a full characterization of outcome WRIC measurements at the steady-state, the measurement uncertainty in inflow rate and gas concentrations must be taken into account and propagated through the measurement model obtained from the equations (2), (3), (4) and (5). The sensitivity analysis of WRIC model is important in order to possibly minimize uncertainty for $\dot{V}O_2$ and $\dot{V}CO_2$ enhancing the accuracy of outcome metabolic measurements (RER and MR). Based on the Haldane factor and Lusk's equation, the partial derivatives can be analytically derived with respect to the measured quantities. We assume the input variables of WRIC model (inflow rate and gas concentrations) to be uncorrelated in the normal operation of the WRIC. Then, it is possible to propagate the measurement uncertainty of the measured quantities with a first-order Taylor series approximation of the WRIC model, as recommended by the GUM [15]. In the following, the metabolic chamber at the University Hospital of Pisa is taken as example to analyze the overall uncertainty budget with real-case values for input quantities based on specific instrumentation.

III. Measurement Setup

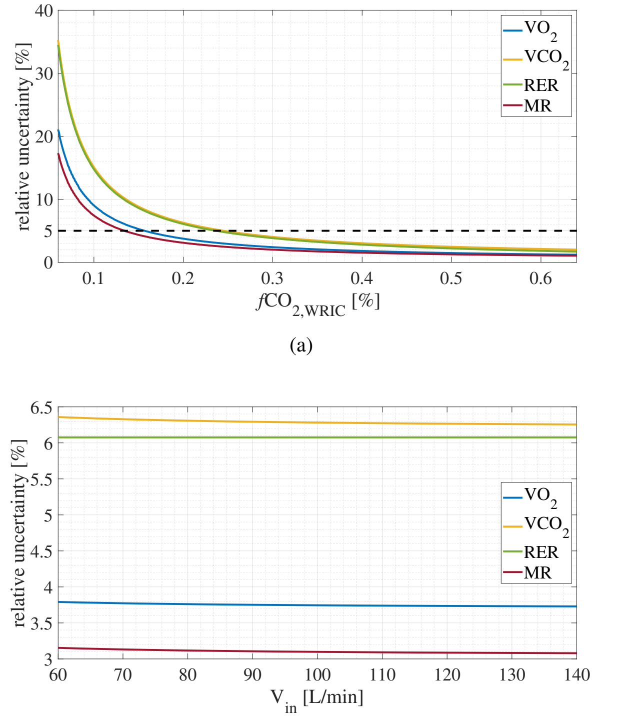
The metabolic chamber at the University Hospital of Pisa, Italy [16] is 3.60 m long, 3.00 m wide, and 2.70 m high (total volume of 29.16 m3). The chamber, shown in Fig. 2 (a), has climate control, with an air conditioning (HVAC) system utilizing chilled water pipelines and electric heating coils to maintain temperature within 0.5 °C and relative humidity within 30% $\div$ 50%. Sample of WRIC air is drawn by membrane pumps, dried to a humidity level <1,000 ppm using a gas sample dryer (Perma Pure LLC) driven by counterflowing dry medical air, and then sent to absolute gas



(a) (b)

(c)

Fig. 2. Whole-room indirect calorimeter located at the University Hospital of Pisa, Italy (a), instrumentation rack hosting the gas analyzers (b), instrumentation for propane combustion (c).



(a)

(b)

Fig. 3. Trends of relative uncertainty for $\dot{V}O_2$, $\dot{V}CO_2$, RER, and MR as a function of $fCO_{2,\mathrm{WRIC}}$ with $\dot{V}_{\mathrm{in}} = 100$ L/min (a) and air inflow rate at $fCO_{2,\mathrm{WRIC}} = 0.2\%$ (b).

analyzers (Siemens Ultramat/ Oxymat 6). A voltage-controlled blower (Ametek, Windjammer) draws fresh air from outside the building and the inflow rate to the WRIC is finely tuned by a mass flow controller (Teledyne Hastings Instruments, Digital 300 series, range: 300 L/min). The overall declared accuracy of mass flow controller can be expressed as:

$$\pm\,(0.2\%\ \text{fullscale} + 0.5\%\ \text{reading}) \tag{6}$$

Fig. 2 (b) shows the instrumentation rack hosting the two gas analyzers (Siemens Ultramat/Oxymat 6) used to measure the O_2 and CO_2 concentrations both in fresh air and WRIC air. The Ultramat gas analyzer operates according to the infrared two-beam alternating light principle, measuring the gases whose absorption bands lie within the infrared wavelength range from 2 µm to 9 µm. In our laboratory, this analyzer cell is used to measure CO_2 concentration. Concerning the O_2 concentration, this is measured with the Oxymat cell, whose principle of operation is based on the paramagnetic alternating pressure principle. Before each WRIC experiment, both cells of gas analyzers are calibrated with two-point linear equation using tanks containing gases with known concentrations. Specifically, the Oxymat cell is calibrated between 20% and 21% while the Ultramat cell is calibrated in the CO_2 range 0 $\div$ 10,000 ppm (0% $\div$ 1%). The maximum declared error both for O_2 and CO_2 concentrations is reported by the manufactuRER to be:

$$\pm\,(1\%\ \text{measuring range}) \tag{7}$$

where the measuring range for O_2 and CO_2 concentrations was 1% for both cells. Consequently, assuming a uniform distribution for errors, the resulting uncertainty for O_2 and CO_2 concentrations can be evaluated as 1% divided by $\sqrt{3}$. Fig. 2 (c) shows the instrumentation used for propane combustion tests. Five different experiments were performed in the WRIC located at the University Hospital of Pisa: these tests consisted in a complete propane combustion followed by a wash-out period. A bottle of instrument grade (99.2% purity) propane (Air Liquide) was placed on a calibrated balance (Ohaus SKX2202) (Fig. 2 (c)) on the desk inside the WRIC. The balance was connected to the WRIC computer via serial connection for continuous measurements of weight of the lecture bottle every minute to calculate the propane combustion rate and expected $\dot{V}CO_2$ and $\dot{V}O_2$ based on stoichiometry. The balance measures the weight of the bottle with a resolution of 0.01 g and a standard deviation due to repeatability of 0.02 g. Each propane combustion test was conducted by lighting up the propane bottle, manually adjusting the flame to $\sim$2 cm in height, and then closing the WRIC door. Before each test, gas analyzer were calibrated using two gas tanks (zero and span) containing a known mixture of O_2 and CO_2 (Air Liquide).

IV. Sensitivity Analysis

A. Uncertainty analysis

The propagation of uncertainty values reported in (6) and (7) through the equations of WRIC model described by (2), (3), (4) and (5) leads to the relative uncertainty values as function of $f\mathrm{CO}_{2,\mathrm{WRIC}}$ and $\dot{\mathrm{V}}_{\mathrm{in}}$ shown in Fig. 3. In our simulations, the values for $\dot{\mathrm{V}}_{\mathrm{in}}$ ranged from 60 to 140 L/min, while CO_2 concentration inside the WRIC, $f\mathrm{CO}_{2,\mathrm{WRIC}}$, ranged from 0.06% to 0.64%. Considering the general parameter K with its uncertainty $u(K)$, the relative uncertainty is derived as $u(K)/K$ for each operating point of the model, i.e., for each combination of $\dot{\mathrm{V}}_{\mathrm{in}}$ and $f\mathrm{CO}_{2,\mathrm{WRIC}}$, given the value of other variables in the model. For each of the four outcome quantities ($\dot{\mathrm{V}}\mathrm{O}_2$, $\dot{\mathrm{V}}\mathrm{CO}_2$, RER, and MR), the trend of the relative uncertainty as a function of $f\mathrm{CO}_{2,\mathrm{WRIC}}$ was similar. The relative uncertainty of all three outcome estimates was practically unaffected by differences in air inflow rate $\dot{\mathrm{V}}_{\mathrm{in}}$, as shown in Fig. 3 (b) at $f\mathrm{CO}_{2,\mathrm{WRIC}} = 0.2\%$. Conversely, there was a substantial, nonlinear influence of $f\mathrm{CO}_{2,\mathrm{WRIC}}$ on the relative uncertainty of each of the four outcome estimates, such that relatively higher values of outcome relative uncertainty (>10%) were observed at relatively lower values (<0.1%) of $f\mathrm{CO}_{2,\mathrm{WRIC}}$. Since during WRIC experiments (e.g., propane combustion) $f\mathrm{CO}_{2,\mathrm{WRIC}}$ typically increases from fresh air levels (∼0.03%) to values >0.2% as a result of an ongoing combustion inside the WRIC, the relative uncertainty of outcome measurements decreases to values below 5% with increasing $f\mathrm{CO}_{2,\mathrm{WRIC}}$ as shown in Fig. 3 (a). Taken together, these results indicate that the main WRIC system variable to be controlled in order to minimize the effect of measurement uncertainty on outcome quantities is the fractional concentration of CO_2 inside the WRIC rather than air flow rate.

To quantify and summarize this main result of our sensitivity analyses, Table I shows the absolute and relative uncertainty estimates calculated for specific values of $\dot{\mathrm{V}}_{\mathrm{in}}$ and $f\mathrm{CO}_{2,\mathrm{WRIC}}$ in our data simulation for steady-state values for RER equal to 0.60, 0.87 and 1.00. In particular, three arbitrary values (low, intermediate, high) were chosen across the experimental range for $\dot{\mathrm{V}}_{\mathrm{in}}$ (60 L/min, 100 L/min, and 140 L/min), while two values were selected for $f\mathrm{CO}_{2,\mathrm{WRIC}}$ (0.06% and 0.2%). Overall, the relative uncertainty of $\dot{\mathrm{V}}\mathrm{CO}_2$ was higher than that of $\dot{\mathrm{V}}\mathrm{O}_2$ or MR, even though the highest relative uncertainty was on RER. As also observed above, differences in inflow rate $\dot{\mathrm{V}}_{\mathrm{in}}$ had an almost negligible impact on relative uncertainty of all four outcome quantities. Conversely, there was a strong effect of CO_2 concentration inside the WRIC on all uncertainties, such that all relative uncertainty values substantially decreased below 5% at a value of about 0.2% for $f\mathrm{CO}_{2,\mathrm{WRIC}}$ and further below 2% (∼1% for MR) at a value of 0.5% for $f\mathrm{CO}_{2,\mathrm{WRIC}}$ (Fig. 3 (a)). Similar results were obtained for higher RER values (0.87 and 1.00, Table I) as observed in more physiological conditions.

B. Weight of uncertainty sources

Assuming a value of 100 L/min for air inflow rate, the weight of each contribution to the variance on $\dot{\mathrm{V}}\mathrm{O}_2$, $\dot{\mathrm{V}}\mathrm{CO}_2$, RER, and MR can be quantified. For instance, the square of the uncertainty on the MR can be written based on a linear approximation of the WRIC model assuming no correlation between quantities as:

$$u\,(\mathrm{MR})^2 = C\left(\dot{\mathrm{V}}_{\mathrm{in}}\right)^2 + C\,(f\mathrm{O}_{2,\mathrm{in}})^2 + C\,(f\mathrm{CO}_{2,\mathrm{in}})^2 + \\ + C\,(f\mathrm{O}_{2,\mathrm{WRIC}})^2 + C\,(f\mathrm{CO}_{2,\mathrm{WRIC}})^2\,, \tag{8}$$

where C is the respective contribution which, taking the air inflow rate as an example, can be derived as

$$C\left(\dot{\mathrm{V}}_{\mathrm{in}}\right)^2 = \left(\frac{\partial\mathrm{MR}}{\partial\dot{\mathrm{V}}_{\mathrm{in}}}\right)^2 u\left(\dot{\mathrm{V}}_{\mathrm{in}}\right)^2. \tag{9}$$

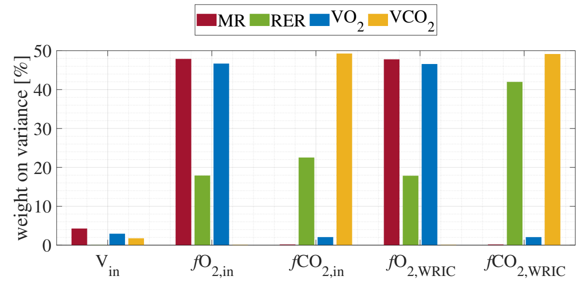


Fig. 4. Weight (%) of each WRIC measured variable on total variance of $\dot{\mathrm{V}}\mathrm{O}_2$, $\dot{\mathrm{V}}\mathrm{CO}_2$, RER, and MR estimates for a CO_2 concentration inside the WRIC equal to 0.2%.

The ratios between each squared contribution and the squared uncertainty calculated for $f\mathrm{CO}_{2,\mathrm{WRIC}} = 0.2\%$ are shown in Fig. 4, where the bars show the contribution of input variables (i.e., inflow rate and O_2 and CO_2 measurements both in fresh air and in WRIC air) on outcome variances of $\dot{\mathrm{V}}\mathrm{O}_2$, $\dot{\mathrm{V}}\mathrm{CO}_2$, RER, and MR. Concordant with the results shown on Fig. 3 (b), the inflow rate $\dot{\mathrm{V}}_{\mathrm{in}}$ has a negligible influence on overall variance for all four outcome quantities. The variance of RER is influenced similarly by all the input variables $\dot{\mathrm{V}}_{\mathrm{in}}$, with the greatest contribution from the fractional concentration of CO_2 within the chamber ($f\mathrm{CO}_{2,\mathrm{WRIC}}$). Conversely, the significant contributions to MR variance are ascribable to the fractional concentrations of O_2 (both in inflow air and in WRIC air equally), but not to the fractional concentrations of CO_2 whose impact was negligible. In summary, not only it is recommended to promptly reach a steady-state value at relatively higher $f\mathrm{CO}_{2,\mathrm{WRIC}}$ compared to that in fresh air (e.g., 0.2%) to minimize the relative uncertainty on the outcome measurements as shown in Fig. 3, but also to accurately measure O_2 concentrations as they collectively constitute the main contributions to the overall uncertainty of MR measurements. To validate these results obtained in our simulations with actual measurements, five propane combustion tests were conducted and their data analyzed with respect to our sensitivity analysis framework.

V. Measurement Results

For each propane combustion experiment, actual measurements of gas concentrations and inflow rate were applied to the steady-state model in (2). Fig. 5 shows the measurements

TABLE I
STEADY-STATE VALUES, ABSOLUTE AND RELATIVE UNCERTAINTY FOR THE STUDIED QUANTITIES.

Data at $RQ = 0.6$			Steady-state values			Absolute uncertainty				Relative uncertainty [%]			
$\dot{V}_{in}$ [L/min]	$fCO_{2,WRIC}$ [%]	$fO_{2,WRIC}$ [%]	$\dot{V}CO_2$ [L/min]	$\dot{V}CO_2$ [L/min]	MR [kcal/min]	$\dot{V}O_2$ [mL/min]	$\dot{V}CO_2$ [mL/min]	RER	MR [kcal/min]	$\dot{V}O_2$	$\dot{V}CO_2$	RER	MR
60	0.06	20.88	0.030	0.018	0.137	6.33	4.90	0.21	23.68	21.0	27.3	34.4	17.3
100	0.06	20.88	0.050	0.030	0.229	10.55	8.17	0.21	39.44	21.0	27.3	34.4	17.3
140	0.06	20.88	0.070	0.042	0.320	14.77	11.44	0.21	55.20	21.0	27.3	34.4	17.3
60	0.20	20.67	0.171	0.102	0.777	6.48	4.99	0.04	24.51	3.8	4.9	6.1	3.2
100	0.20	20.67	0.285	0.170	1.296	10.66	8.25	0.04	40.14	3.7	4.9	6.1	3.1
140	0.20	20.67	0.399	0.238	1.814	14.87	11.52	0.04	55.85	3.7	4.8	6.1	3.1
Data at $RQ = 0.87$			Steady-state values			Absolute uncertainty				Relative uncertainty [%]			
$\dot{V}_{in}$ [L/min]	$fCO_{2,WRIC}$ [%]	$fO_{2,WRIC}$ [%]	$\dot{V}CO_2$ [L/min]	$\dot{V}CO_2$ [L/min]	MR [kcal/min]	$\dot{V}O_2$ [mL/min]	$\dot{V}CO_2$ [mL/min]	RER	MR [kcal/min]	$\dot{V}O_2$	$\dot{V}CO_2$	RER	MR
60	0.06	20.89	0.023	0.020	0.112	6.33	4.91	0.32	23.67	27.7	24.8	37.2	21.2
100	0.06	20.89	0.038	0.033	0.186	10.55	8.17	0.32	39.43	27.7	24.8	37.2	21.2
140	0.06	20.89	0.053	0.046	0.260	14.77	11.44	0.32	55.20	27.7	24.8	37.2	21.2
60	0.20	20.74	0.117	0.102	0.573	6.40	4.99	0.06	24.12	5.5	4.9	7.2	4.2
100	0.20	20.74	0.195	0.170	0.954	10.60	8.26	0.06	39.80	5.4	4.9	7.2	4.2
140	0.20	20.74	0.273	0.238	1.336	14.81	11.53	0.06	55.54	5.4	4.8	7.2	4.2
Data at $RQ = 1$			Steady-state values			Absolute uncertainty				Relative uncertainty [%]			
$\dot{V}_{in}$ [L/min]	$fCO_{2,WRIC}$ [%]	$fO_{2,WRIC}$ [%]	$\dot{V}CO_2$ [L/min]	$\dot{V}CO_2$ [L/min]	MR [kcal/min]	$\dot{V}O_2$ [mL/min]	$\dot{V}CO_2$ [mL/min]	RER	MR [kcal/min]	$\dot{V}O_2$	$\dot{V}CO_2$	RER	MR
60	0.06	20.91	0.013	0.013	0.067	6.33	4.90	0.61	23.66	48.0	37.1	60.7	35.5
100	0.06	20.91	0.022	0.022	0.111	10.55	8.17	0.61	39.43	48.0	37.1	60.7	35.5
140	0.06	20.91	0.031	0.031	0.155	14.77	11.44	0.61	55.20	47.9	37.1	60.7	35.5
60	0.20	20.76	0.102	0.102	0.515	6.38	4.99	0.08	24.03	6.3	4.9	7.9	4.7
100	0.20	20.76	0.170	0.170	0.858	10.59	8.26	0.08	39.73	6.2	4.9	7.9	4.6
140	0.20	20.76	0.238	0.238	1.201	14.80	11.53	0.08	55.47	6.2	4.8	7.9	4.6

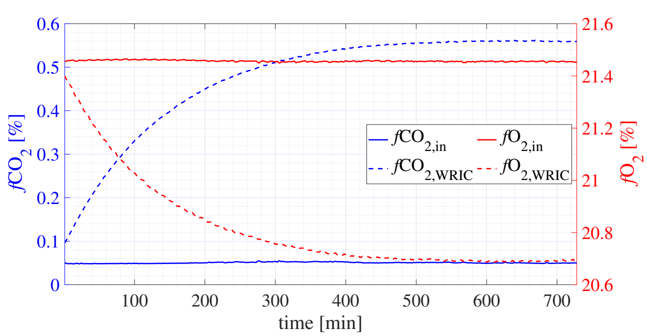
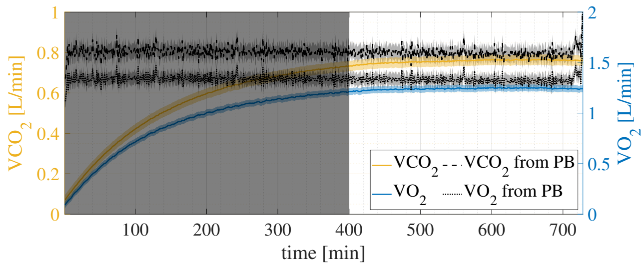
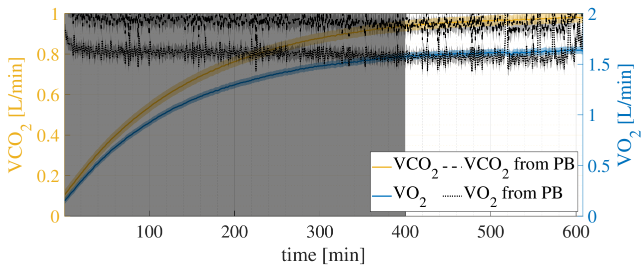


Fig. 5. Inflow and outflow concentration of O_2 and CO_2 measured during the EXP1 propane combustion test.

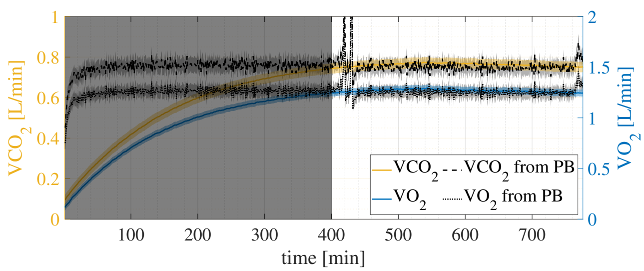
of $fO_{2,in}$, $fCO_{2,in}$, $fO_{2,WRIC}$, and $fCO_{2,WRIC}$ obtained during one propane combustion experiment (EXP1). The time course of CO_2 concentrations within the chamber (left axis, blue dotted curve) starts from fresh air levels of ~0.04% and increases exponentially up to 0.56% at the end of propane combustion. Conversely, the time course of O_2 concentration within the chamber (right axis, red dotted curve) decays from fresh air levels of ~21.4% to about 20.7% at the end of propane combustion. For the static model equations to be correctly applied to propane combustion data, the hypothesis of steady-state condition must hold true. Specifically, steady-state conditions can be considered valid if the results of the dynamic model in (1) are compatible with those of the static model in (2), namely, the contribution of time derivative terms of gas concentration multiplied by chamber volume in (1) must be negligible (e.g., 10-fold smaller) compared to the other terms in (1). Fig. 6 shows the measured values of $\dot{V}O_2$ and $\dot{V}CO_2$ calculated using the steady-state model equations in (2) applied to the data of five propane combustion experiments arbitrarily named EXP1, EXP2, EXP3, EXP4, and EXP5. The shaded part of the figure corresponds approximately to the time interval in which the time derivatives of the concentrations in the metabolic chamber of O_2 and CO_2 cannot be neglected for the purpose of calculating the metabolic rate. For such reason, we observed the data starting from $t = 400$ min. As in the following, the uncertainty on the measured quantities was evaluated by propagation through the steady-state model equations with a first-order Taylor series approximation, as recommended by the GUM [15]. The 95% coverage interval was obtained by extending the absolute uncertainty of the measured quantities with a coverage factor $k = 2$. Both the expected values and the width of the confidence intervals for the measures of $\dot{V}O_2$ and $\dot{V}CO_2$ are in agreement with what was expected from the analysis in Section IV. In Fig. 6, estimates of $\dot{V}O_2$ and $\dot{V}CO_2$ obtained from gas concentration



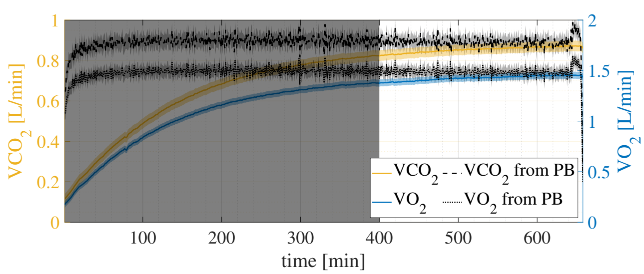
(a) EXP1



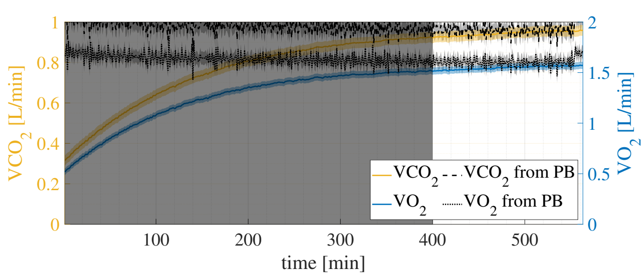
(b) EXP2



(c) EXP3



(d) EXP4



(e) EXP5

Fig. 6. Measurements of $\dot{V}O_2$ and $\dot{V}CO_2$ with 95% coverage interval (C.I.). The time period prior to the steady-state condition is shadowed. Dotted and dashed black curves (with 95% C.I.) represent the expected values of $\dot{V}O_2$ and $\dot{V}CO_2$ from pure propane combustion test (Propane Burn, PB), respectively.

measurements are compared with their expected values (in L/min) on the basis of propane burn stoichiometry as:

$$\begin{aligned} \dot{V}O_{2,\mathrm{PB}} &= \Delta m_P \times 2.540 \\ \dot{V}CO_{2,\mathrm{PB}} &= \Delta m_P \times 1.524, \end{aligned} \tag{10}$$

where the subscript PB refers to the expected value based on propane burn, and

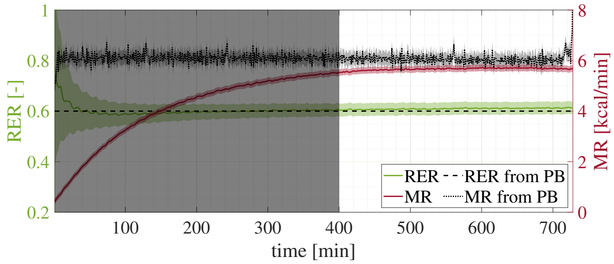
$$\Delta m_P = m_{P,t} - m_{P,t-1} \tag{11}$$

is the change in propane cylinder mass over a minute measured with the Ohaus SKX2202 scale. The uncertainty of mass change over a minute is evaluated by applying the uncertainty propagation to (11) considering the accuracy and resolution of scale and assuming a linear correlation coefficient $\rho = 0.8$ between the consecutive measurements. This value for linear correlation coefficient is justified by the use of the same scale to obtain two measurements, each separated by a minute. Based on the uncertainty of propane mass changes, uncertainty for $\dot{V}O_2$ and $\dot{V}CO_2$ can be calculated using (10). Fig. 6 shows that, at the steady-state, the predicted values for $\dot{V}O_2$ and $\dot{V}CO_2$ using the WRIC static model are compatible with the respective measured values as shown by the overlapping 95% coverage interval.

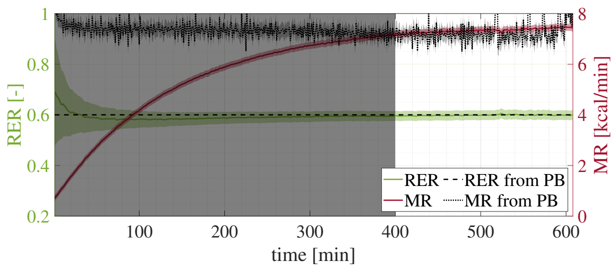
Values for RER and MR were also derived using the model equations (4) and (5) applied to the data of the five propane combustion experiments. The results for each experiment are shown in Fig. 7. During the experiments, the measured RER was approximately constant and equal to 0.6 as expected from a pure propane combustion. Based on the expected values for $\dot{V}O_2$ and $\dot{V}CO_2$ derived from propane weight measurements applied to (10), it is possible to calculate the expected RER and the MR values through (4) and (5). The expected value for RER is constantly equal to 0.6 with null uncertainty, as it comes from the ratio between formulas in (10). As shown in Fig. 7, the expected value for $\mathrm{RER} = 0.6$ is compatible with the results from the WRIC static model based on gas concentration measurements. Similarly, steady-state MR values obtained from gas concentration measurements are in agreement with those expected by the propane combustion as shown by the overlapping 95% coverage interval.

Considering the values of RER estimated from gas concentration measurements (Fig. 7, green), the uncertainty of estimated RER, as quantified by the width of coverage interval, was higher at the beginning of experiments when the CO_2 concentration inside the chamber was lower, but it decreased over time as the CO_2 concentration increased above 0.2%. In each combustion test, the estimated MR (Fig. 7, red) remained constant at the steady-state condition although with different steady-state value among the five combustion tests. Similarly, the uncertainty of MR was also approximately constant throughout the course of the experiment.

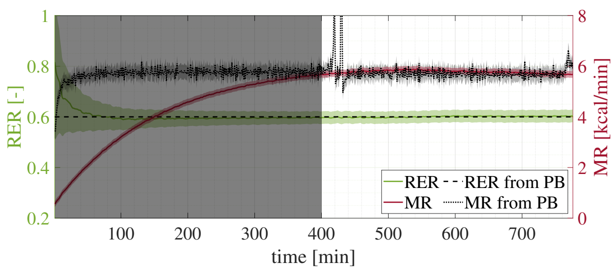
To further validate the main results of our sensitivity analysis reported in Section IV, the relationship between $fCO_{2,\mathrm{WRIC}}$ and the relative uncertainty on the measured quantities $\dot{V}O_2$, $\dot{V}CO_2$, RER, and MR was investigated. Fig. 8 shows steady-state data from EXP1 as representative



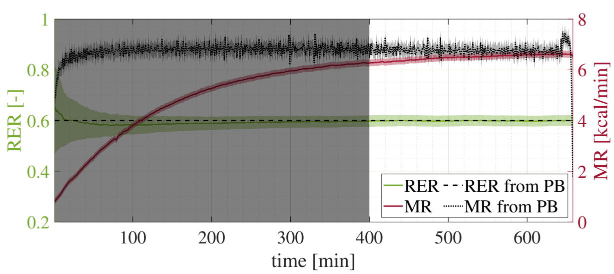
(a) EXP1



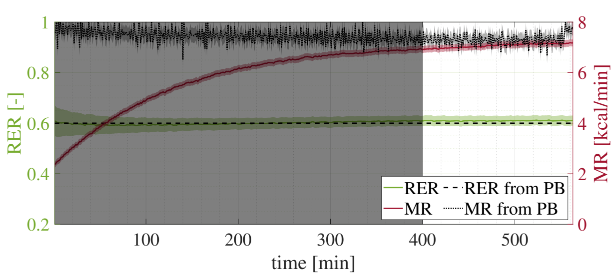
(b) EXP2



(c) EXP3



(d) EXP4



(e) EXP5

Fig. 7. Measurements of RER and MR with 95% coverage interval (C.I.). The time period prior to the steady-state condition is shadowed. Dotted and dashed black curves (with 95% C.I.) represent the expected values of RER and MR from pure propane combustion test (Propane Burn, PB), respectively.

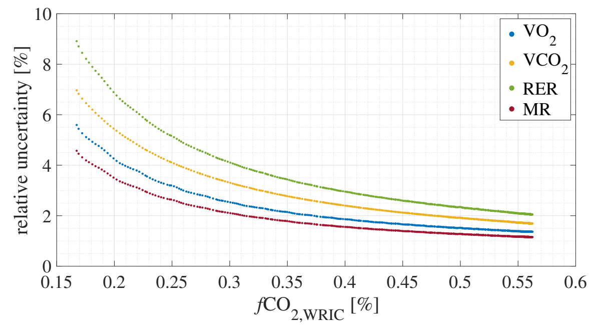


Fig. 8. Relationships between CO_2 concentration inside the chamber and relative uncertainty of outcome WRIC variables at the steady-state in EXP1.

experiment. Likewise to what we obtained in our data simulations whose results are shown in Fig. 3 (a), all the relative uncertainties calculated during propane combustion tests decay below 5% as $f\mathrm{CO}_{2,\mathrm{WRIC}}$ increases from fresh air values to values around 0.2%, and further below 2% reaching steady-state values >0.5% at the end of propane combustion tests. This confirms the validity of our sensitivity analysis and confirms that CO_2 concentration inside the calorimeter is pivotal to minimize the relative uncertainty of outcome metabolic variables. For the best of our knowledge, our current study represents the first attempt to conduct a formal sensitivity analysis of WRIC dynamic model to objectively identify the WRIC variables that have the greatest impact on uncertainty of outcome measurements. As such, our current results provide a guidance for the best environmental conditions in a WRIC system that allow to minimize uncertainty of metabolic measurements, thereby improving accuracy of RER and MR estimates. Yet, a limitation of our current study is that the sensitivity analyses were limited to the steady-state condition, thus they did not consider the impact of time derivative terms that are negligible at the WRIC steady-state. Future studies are warranted to evaluate the impact of uncertainty both of WRIC volume and time derivative terms for O_2 and CO_2 concentration on WRIC outcome measurements during dynamic conditions.

VI. Conclusion

In this paper, we analytically studied the static sensitivity of whole-room indirect calorimeters operating in a push configuration to quantify the contributions of air flow rate and measurements of gas concentration on outcome WRIC measurements ($\dot{\mathrm{V}}\mathrm{O}_2$, $\dot{\mathrm{V}}\mathrm{CO}_2$ and MR). After propagating the measurement uncertainty through the equations of WRIC model at the steady-state condition, results of sensitivity analysis were validated using measurement data acquired during propane combustion experiments. Collectively, we demonstrated that the fresh air inflow set point does not affect the relative uncertainty of WRIC outcome measurements, while achieving a CO2 concentration inside the calorimeter greater than 0.2% at the steady-state condition allows to reduce the relative uncertainty of all the outcome metabolic measurements to values smaller than 5% when assuming an accuracy class of 1% for gas analyzer measurements.

VII. Acknowledgements

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