Carbon Monoxide Levels in the Extravehicular Mobility Unit by Modeling and Operational Testing

Matthew S. Makowski; Jason R. Norcross; David Alexander; Robert W. Sanders; Johnny Conkin; Millennia Young

INTRODUCTION: Carbon monoxide (CO) is a toxic gas with potential for detriment to spaceflight operations. An analytical model was developed to investigate if a maximum CO contamination of 1 ppm in the oxygen (O_2) supply reached dangerous levels during extravehicular activity (EVA). Occupational monitoring pre- and postsuited exposures provided supplementary data for review.

METHODS: The analytical model estimated O_2 and CO concentrations in the extravehicular mobility unit (EMU) based on O_2 and CO flow rates into and out of the system. The model was based on 3 h of prebreathe at 15.2 psia, 8 h of EVA at 4.3 psia, and 1 h at 15.2 psia for suit doffing. The Coburn-Forster-Kane equation was used to calculate crewmember carboxyhemoglobin saturation (COHb%) as a function of time. Monitoring of hemoglobin CO saturation (S_pCO) with a CO-oximeter was conducted pre- and post-EVA during operations on the International Space Station and in ground-based analog environments.

RESULTS: The model predicted a maximum P_{CO} in the EMU of 0.061 mmHg and a maximum crewmember COHb% of 2.1%. Operational S_pCO measurements in mean $\pm$ SD during ground-based analog testing were 0.7% $\pm$ 1.8% pretest and 0.5% $\pm$ 1.5% posttest. S_pCO values on the ISS were 1.5% $\pm$ 0.7% pre-EVA and 1.1% $\pm$ 0.3% post-EVA.

DISCUSSION: The model predicted that astronauts are not exposed to toxic levels of CO during EVA and operational measurements did not show significant differences between S_pCO levels between pre- and post-EVA.

KEYWORDS: gas exchange, spaceflight, pressure suit, Coburn-Forster-Kane equation, CO-oximeter.

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The concern for carbon monoxide (CO) contamination in the extravehicular mobility unit (EMU) aboard the International Space Station (ISS) originated when one of the high-pressure O_2 tanks was found to have a CO level outside of the specification maximum of 1 ppm by volume. This tank was to supply crewmembers with breathable O_2 for extravehicular activity (EVA), including prebreathe, depressurization, EVA, and repressurization. The major concern with CO contamination in the EMU is the absence of a scrubbing mechanism for CO. As O_2 is consumed by the crewmember, replacement O_2 continuously flows into the EMU from the portable life support system (PLSS). Any contaminants in the O_2 supply, including CO, will accumulate through time. The problem of accumulation is potentially worsened by the endogenous production of CO that occurs during heme (ferroprotoporphyrin IX) catabolism. There is no capability for measurement of CO in space suits or carboxyhemoglobin (COHb) during suited exposures; therefore, the only available tools to evaluate this concern were modeling and pre- and postsuited exposure testing.

The assessment of CO accumulation in the EMU presented here was twofold. First, an analytical model was developed to predict CO dynamics in the EMU to verify that the current CO standard requiring 1 ppm or less of CO in the O_2 supply is adequate to limit crewmember toxicity. Second, hemoglobin CO saturation (S_pCO) pre- and post-EVA was compared during operations on the ISS and in testing in ground-based analog

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environments to verify that CO saturation did not significantly increase during EVA.

METHODS

Model Assumptions

To predict the amount of CO accumulation in the EMU during EVA under worst-case conditions, an analytic model was developed that estimated gas flow into and out of the EMU. The model calculated CO and O_2 concentrations in the EMU at the end of discrete time intervals, and the Coburn-Forster-Kane (CFK) equation was used to calculate crewmember carboxyhemoglobin concentration ([COHb]).[5] The model was based on the following assumptions:

1. Gas components in the EMU mixed thoroughly and instantaneously.
2. EMU gas composition was modeled as two components: O_2 and CO. Partial pressures of CO_2, H_2O, and N_2 were assumed physiologically negligible to the primary question and modeled at 0 mmHg.
3. Energy expenditure rates within each phase (prebreathe, EVA, post-EVA) were constant.
4. Changes in EMU pressure during purge, depressurization, and repressurization took negligible time.
5. Endogenous CO production rate was constant.
6. Total moles of gas in the EMU at a given pressure were constant.
7. Viscosity of gas was independent of pressure based on the ideal gas law.
8. Suit leak had a flow rate proportional to the pressure differential across the suit wall.

Model Parameters

The analytical model to predict CO accumulation in the EMU was developed under worst-case conditions with the duration of prebreathe, EVA, and post-EVA overestimated to account for unexpected delays. The durations of events leading up to and following EVA are shown in **Table I**. Unlike ambient conditions on the ISS where O_2 concentration is 21%, operations within the EMU are conducted at near 100% O_2 concentration. The model accounted for EVA preparation procedures with a 3-h in-suit prebreathe at a near 100% O_2 concentration at 15.2 psia, slightly above the ISS nominal pressure of 14.7 psia, as specified in the NASA in-suit light exercise (ISLE) pressure profile requirements. During prebreathe, the metabolic rate of 600 $BTU \cdot h^{-1}$ was used to represent ISLE performed by the crewmember to more quickly mobilize and exhale N_2. For the EVA, the model accounted for a constant in-suit pressure of 4.3 psia for a duration of 8 h. Finally, 1 h was allotted for post-EVA activities at 15.2 psia, overestimating time needed to doff the EMU. Pressure within the EMU (P_{EMU}) in Table I is substituted for barometric pressure in the CFK equation. The model set the EMU floodable volume at 42 L, which excluded crewmember volume with an in-suit temperature of 25°C. EMU floodable volume typically ranges from about 28 L to about 57 L with 42 L as an intermediate value.

During EVA, there is no specific mechanism to remove CO. Throughout all activities within the EMU, the only route of CO escape is through inherent suit leak and venting during suit depressurization. Without a CO scrubbing mechanism, CO accumulates in the EMU from two sources. The first source is exogenous supply from a contaminated O_2 supply. The second source is low-level endogenous production by the crewmember. During each phase of EVA activities, the O_2 tank regulator maintains a set pressure within the EMU rather than a set O_2 level. The model made use of this control mechanism by holding constant the total moles of gas in the EMU at each given pressure.

Maximum CO contamination of the O_2 supply for the model was determined based on NASA safety requirements (NASA document SSP-30573) stating that the combined CO and CO_2 levels must remain below 1 ppm by volume with total O_2 purity at least 99.990%. Adhering to this requirement, the model used the worst-case value of 1 ppm CO for O_2 tank contamination. The model assumed an initial CO concentration within the EMU as equal to the CO contamination concentration in the supply O_2 tank since the EMU is flushed by the supply tank during the initial pressurization of the EMU to 15.2 psia.

The EMU O_2 purge and pressurization to 15.2 psia, depressurization to 4.3 psia, and repressurization to 15.2 psia following EVA were defined as a step function, with the assumption of negligible time between pressure changes. During these brief pressure changes, [COHb] and oxyhemoglobin concentration ([O_2Hb]) were held constant. While these processes take several minutes, they are much shorter than the 3 h, 8 h, and 1 h allotted for prebreathe, EVA, and post-EVA, respectively.

The leak rate of the suit is bound by the NASA specification of a maximum leak rate of $0.035\ L \cdot min^{-1}$ defined at a standard of 760 mmHg at 21.1°C [NASA Extravehicular Mobility Unit (EMU) LSS/SSA Data Book, Rev P]. The model used an intermediate value of $0.01\ L \cdot min^{-1}$ at the defined temperature and pressure. Modeling of the leak was based on two assumptions: 1) viscosity is independent of pressure (ideal gas law); and 2) flow rate is proportional to pressure differential from inside to outside the EMU (Poiseuille's law). An additional assumption was that of laminar gas flow through the leak.

An endogenous CO production rate of $0.015\ mL \cdot min^{-1}$ at standard temperature and pressure

Table I. Simulation Run Parameters.

PHASE	DURATION (h)	P_{EMU} (psia)	ACTIVITY LEVEL (BTU/h)	CALCULATED O_2 CONSUMPTION (mole $O_2 \cdot min^{-1}$)
Prebreathe	3	15.2	600	0.024
EVA	8	4.3	1000	0.040
Post-EVA	1	15.2	600	0.024

P_{EMU}: pressure in the extravehicular mobility unit; EVA: extravehicular activity.

was chosen from a study in which CO production was determined in subjects breathing 100% O_2 at ambient atmospheric pressure.[5] This value was chosen as a worst case since the majority of the modeled scenario used a lower partial pressure of O_2, 4.3 psia, during the EVA phase. In comparison, a lower endogenous CO production of 0.007 mL · min^{-1} was reported when subjects were breathing lower O_2 partial pressures (20–30% O_2 at ambient atmospheric pressure).[4] Gas carrying capacity of hemoglobin was calculated as 0.19 mL gas at standard temperature and pressure dry (STPD) per mL blood using a hemoglobin concentration of 14 g · dL^{-1} and the value of 1.38 mL O_2 at STPD per g Hb.[15]

Energy expenditure was set to 600 BTU · h^{-1} during prebreathe with the astronaut performing ISLE and 1000 BTU · h^{-1} during EVA. O_2 consumption rate at these activity levels was calculated based on a respiratory exchange ratio (RER) of 0.8. Specifically, a conversion factor of 415 BTU per mol O_2 consumed (438 kJ/mol O_2) was extrapolated from 478 kJ/mol O_2 at a RER of 1.0 and 418 kJ/mol O_2 at a RER of 0.7.[11]

Alveolar ventilation, $\dot{V}_A$, in mL · min^{-1} at body temperature and pressure saturated (BTPS), was calculated from minute ventilation, $\dot{V}_E$, in mL · min^{-1} at BTPS, and respiratory rate, *f*, in min^{-1}, using $\dot{V}_A = 0.993\,\dot{V}_E - 132\,f$ as described by Peterson and Stewart.[15] $\dot{V}_A$ was subsequently converted from BTPS to STPD to comply with CFK equation requirements. Formulas for both $\dot{V}_E$ and *f* as functions of O_2 consumption rate ($\dot{V}o_2$) were estimated from data reported in the Operation Everest II study, in which healthy young male subjects were studied under various ambient pressures.[17] The data set from the Operation Everest II study at a barometric pressure of 760 mmHg with partial pressure inspired O_2 (P_Io_2) at 150 mmHg was used as the EMU maintains at least 150 mmHg O_2 through all phases of operation. By regressing $\dot{V}_E$ on $\dot{V}o_2$ using data from the Operation Everest II study, the following model was estimated: $\dot{V}_E = 0.0049\,\dot{V}^2o_2 + 13.04\,\dot{V}o_2 + 6799$ with an R^2 value of 0.998. Regressing *f* on $\dot{V}o_2$, the following model was estimated: $f = 0.0089\,\dot{V}o_2 + 8.22$ with an R^2 value of 0.978. Of note, this approach resulted in an overestimation of $\dot{V}_E$. Actual P_Io_2 in the suit was greater than 150 mmHg given that 15.2 psia prebreathe equates to 786 mmHg and 4.3 psia EVA equates to 222 mmHg. The validity of this method is further addressed below in limitations. $\dot{V}o_2$, in mL · min^{-1} at STPD at each activity level, was calculated from moles of O_2 consumed and the conversion factor of 22.4 L O_2 per mole O_2 at STPD. **Table II** summarizes all physiological parameters and the assumed values used in the development of the EMU CO model.

Table II. Physiological Parameters.

TERM	VALUE	SYMBOL	UNITS	REFERENCE
Respiratory Exchange Ratio	0.8	R	-	
Hemoglobin concentration	14	Hb	g · dL^{-1}	
Hemoglobin O_2 carrying capacity*	1.38		mL · g^{-1}	Peterson & Stewart[15]
Hemoglobin gas carrying capacity*	0.19	$[XHb]$	mL · (mL blood)$^{-1}$	
Carboxyhemoglobin Initial*	0.0024	$[COHb]_o$	mL · (mL blood)$^{-1}$	Peterson & Stewart[15]
Endogenous CO production in hyperoxic environment*	0.015	$\dot{V}_{CO_{prod}}$	mL · min^{-1}	Coburn et al.[5]
Relative affinity of hemoglobin for CO	218	M	-	Peterson & Stewart [15]
Lung diffusing capacity for CO	30	$D_{L_{CO}}$	mL · (min · mmHg) $^{-1}$	Coburn et al.[5]
Water vapor pressure at 37°C	47.1	P_{H_2O}	mmHg	
Blood volume	5000	V_b	mL	Coburn et al.[5]
Alveolar ventilation (Prebreathe)*	10.3	$\dot{V}_A$	L · min^{-1}	
Alveolar ventilation (EVA)*	15.6	$\dot{V}_A$	L · min^{-1}	
Mean pulmonary capillary O_2 tension	variable	P_{CO_2}	mmHg	
Inspired CO tension	variable	$P_{I_{CO}}$	mmHg	

* At STPD.
EVA: extravehicular activity.

Analytical Model

The model calculated amounts of O_2 and CO in the EMU at the end of 1-min intervals based on O_2 and CO flow rates into and out of the system as described by **Fig. 1**.

$$\dot{V}_{tank} = \dot{V}o_2 + \dot{V}co_{uptake} + \dot{V}_{leak} - \dot{V}co_{prod} \qquad \text{Eq. 1}$$

Eq. 1 models the O_2 supply tank regulator maintaining a constant pressure within the EMU through repletion of volume as it is lost through O_2 consumption, human CO uptake, and EMU leakage. The gas repletion rate is offset by the slow rate of endogenous CO produced and exhaled into the EMU. The terms are $\dot{V}_{tank}$ as the rate of O_2 along with CO contaminant gas flow into the EMU from the O_2 supply tank, $\dot{V}o_2$ as the rate of O_2 consumption by the astronaut, $\dot{V}co_{uptake}$ as CO inhalation and uptake rate by the astronaut, $\dot{V}_{leak}$ as the EMU gas leak rate, and $\dot{V}co_{prod}$ as endogenous CO production rate by the astronaut.

Estimation of O_2 and CO

In the model, total moles of O_2 and CO were calculated at the end of each 1-min interval based on gas flow rates. Moles were used for simplicity of calculations at the pressure discontinuities when transitioning between the different phases of prebreathe, EVA, and post-EVA. Total moles of gas in the EMU were constant within each phase. The CFK equation was then used to calculate crewmember [COHb] at the end of each 1-min interval.[5]

Moles of CO present in the EMU were calculated at the end of each unit time by determining the amount of CO accumulated in the EMU within the unit time followed by subtracting off the moles of CO lost in the EMU leak during the unit time. The method is shown below in Eqs. 2–5. For simplicity, moles of CO lost in the leak were accounted for as an instantaneous event occurring at the end of the unit time. The term $t\_$ represents the end of unit time just prior to accounting for

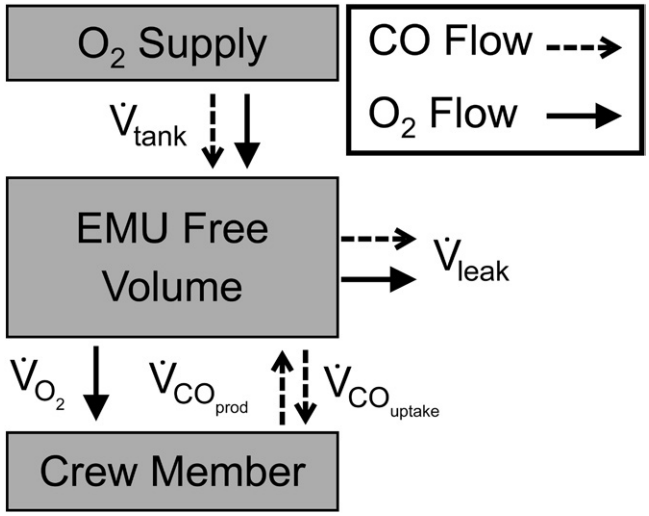

Fig. 1. Graphical representation of gas flow in the model.

the leak, t_+ represents the end of unit time just after accounting for the leak, and $t_+ - 1$ represents the end of the prior unit time after accounting for the leak. Eq. 2 defines CO moles in the EMU before accounting for the leak $[n_{CO}(t_-)]$ as the summation of CO moles in the EMU at the end of the prior unit of time $[n_{CO}(t_+ - 1)]$, CO moles introduced from the supply tank ($n_{CO_{supply}}$), and CO moles from human production ($n_{CO_{prod}}$) minus CO moles removed from the EMU by human uptake ($n_{CO_{uptake}}$). Specifically,

$$n_{CO}(t_-) = n_{CO}(t_+ - 1) + n_{CO_{supply}} + n_{CO_{prod}} - n_{CO_{uptake}} \quad \text{Eq. 2}$$

where the term $n_{CO_{uptake}}$ was determined using the CFK equation and is described below.

To determine CO moles lost due to the EMU leak, $n_{CO_{leak}}$ was defined as

$$n_{CO_{leak}} = n_{CO}(t_-) \times \frac{n_{leak}}{n_{EMU}} \quad \text{Eq. 3}$$

where $n_{CO}(t_-)$ is CO moles in the EMU at end of unit time prior to accounting for the leak, n_{leak} is moles of gas leaked during unit time, and n_{EMU} is total moles of gas in the EMU. Gas leaks were assumed to occur at the end of each unit time. By making this assumption, the model approximates the continuous change of CO within each unit time in the EMU.

The total CO moles in the EMU after accounting for the leak is set equal to CO moles in the EMU before accounting for the leak minus CO moles lost in the leak,

$$n_{CO}(t_+) = n_{CO}(t_-) - n_{CO_{leak}} \quad \text{Eq. 4}$$

Using Eq. 5, the total O_2 moles in the EMU after accounting for the leak is estimated by the total moles of gas in the EMU minus the total CO moles in the EMU after accounting for the leak. Specifically,

$$n_{O_2}(t_+) = n_{EMU} - n_{CO}(t_+) \quad \text{Eq. 5}$$

Estimation of CO Uptake and Production

The CFK equation was used to model CO uptake and production by the crewmember in the EMU.[5] Moles of CO $[n_{CO}(t_+)]$ and O_2 $[n_{O_2}(t_+)]$, obtained from Eqs. 4 and 5, respectively, were converted to mmHg for use in the CFK equation. A modified version of the original CFK equation is presented in Eq. 6, after solving for $[COHb]_t$ and substituting P_{EMU} for barometric pressure. Additionally, multiple substitutions were used for clarity. Note that A through E in Eq. 6 were calculated at the end of each time interval to calculate $[COHb]_{t_+}$. Specifically,

$$[COHb]_{t_+} = A \times [(B - C - D) \times e^{-E} + C + D] \quad \text{Eq. 6}$$

where

$$A = [O_2Hb]_{t_+ - 1} \times M \times P_{c_{O_2}}^{-1}$$

$$B = [COHb]_{t_+ - 1} \times P_{c_{O_2}} \times ([O_2Hb]_{t_+ - 1} \times M)^{-1}$$

$$C = \dot{V}_{CO_{prod}} \times [D_{L_{CO}}^{-1} + (P_{EMU} - P_{H_2O}) \times \dot{V}_A^{-1}]$$

$$D = P_{I_{CO}}$$

$$E = P_{c_{O_2}} \times t \times (M \times V_b \times [O_2Hb]_{t_+ - 1} \times \left[D_{L_{CO}}^{-1} + \left(P_{EMU} - P_{H_2O}\right) \times \dot{V}_A^{-1}\right])^{-1}$$

Note that $[O_2Hb]$ and [COHb] were based on values at the end of the present unit time or at the end of the previous unit time as designed by the notation t_+ and $t_+ - 1$, respectively. The terms in Eq. 6 are defined in Table I and Table II. For each discrete time interval, t was set to 1 min. Values for all parameters in Eq. 6 were calculated at the end of the current time interval except for $[O_2Hb]_{t_+ - 1}$ and $[COHb]_{t_+ - 1}$, which used the value from the end of the previous time interval. Mean pulmonary capillary O_2 tension ($P_{c_{O_2}}$) in mmHg was calculated by subtracting 49 mmHg from P_IO_2 to account for CO_2 in alveoli and average values across all pulmonary capillaries.[15] P_IO_2 in mmHg was calculated by using, $P_IO_2 = F_IO_2 \times (P_{EMU} - P_{H2O})$. Here the fraction of inspired O_2 (F_IO_2) is equal to the proportion of O_2 in the EMU. P_{EMU} is equal to 15.2 psia for the prebreathe and post-EVA phases and 4.3 psia during the EVA. P_{H2O} accounts for water vapor in the crewmember's airway. $[O_2Hb]$ was calculated using $[O_2Hb]_{t_+} = [XHb] - [COHb]_{t_+}$, where $[XHb]$ is hemoglobin gas carrying capacity.

Uptake of CO

The uptake rate of CO by the crewmember was calculated using the rate of change in [COHb], since it represents CO storage within the human part of the suit-human system. At the end of each unit time, the total CO moles bound to hemoglobin, $n_{COHb}(t_+)$, was calculated by converting $[COHb]_{t_+}$ from mL · (mL blood)$^{-1}$ to moles · (mL blood)$^{-1}$ and multiplying it by the total blood volume. The rate of change of n_{COHb} was used to determine $n_{CO_{uptake}}$ in Eq. 2 using $n_{CO_{uptake}} = n_{COHb}(t_+ - 1) - n_{COHb}(t_+ - 2)$. While n_{COHb} is a function of parameters within the present unit time, the rate of

change relied upon values from the two prior unit times as designated by $(t_+ - 1)$ and $(t_+ - 2)$.

Hemoglobin Saturation Studies

Subjects. Ground and orbital measurements of peripheral hemoglobin CO saturation (S_pCO) were collected pre- and post-EVA on ground-based EVA analogs and the ISS. S_pCO measurement was a noninvasive measuring technique acquired as part of an operational investigation initiated by NASA Johnson Space Center Space Medicine Group as a result of concern over the possible contamination of the O_2 supply with 1 ppm CO. No specific study was set up to evaluate S_pCO measurements in the EVA suit, rather existing suited exposures were used to opportunistically collect the data. The ground-based analog tests included space station airlock test article (SSATA), PLSS, and vacuum pressure integrated suit test (VPIST). ISS EVA and SSATA runs were operational exposures and all these subjects were astronauts. PLSS and VPIST tests were hardware evaluations and subjects were recruited for these tests from the pool of suited test subjects representative of the age, anthropometry, and fitness of the astronaut corps. These volunteer test subjects were recruited after approval of test procedures through the NASA Johnson Space Center IRB. Test subject demographics for each testing condition are presented in **Table III**. All participants were nonsmokers.

Equipment. S_pCO measurements were obtained with the Rad-57 CO-oximeter (Masimo Corporation, Irvine, CA) with a reusable sensor. This device has a display resolution of 1% with standard deviation of ±3% per the manufacturer and peer-reviewed literature.[16,18] S_pCO measurements were performed in triplicate and averaged with repeated measurements on upper extremity digits 2, 3, and 4 for ground EVA analog runs. Single S_pCO measurements on digit 2 were acquired for orbital EVAs. CO concentration of the O_2 supply during these exposures were defined by a specification of less than 1 ppm.

Procedures

Ground-based analogs. The SSATA test procedure was designed to train astronauts in EVA operations and assess airlock and EMU equipment. SSATA operational training covered procedures during prebreathe, depressurization, activities in vacuum, and repressurization. S_pCO measurements took place 1 to 2 h before suit donning. The crewmember entered the airlock, donned the EMU, performed a leak check at 4.3 psid, and purged the suit with near 100% O_2 for 12 min. A 4-h resting prebreathe was performed followed by chamber depressurization to 5 psia for suit leak check followed by depressurization to vacuum (0.10 mmHg) with suit pressure at 4.3 psid. The astronaut remained in vacuum for 1 h and performed low metabolic activities. Following a 10-min repressurization, S_pCO measurements were acquired and the EMU was doffed.

The purpose of the VPIST test procedure was to perform human integrated testing while evaluating the CO_2 and humidity control and other Orion hardware. S_pCO measurements took place 1 to 2 h before donning the suit. After suit donning, the suit was leak checked at 4.3 psid then purged with near 100% O_2 at 0.8 psid for a minimum of 10 min to achieve ≥95% O_2. Resting prebreathe with near 100% O_2 took place for 4 h. After prebreathe, suit pressure was regulated to 4.3 psid and the chamber was depressurized to 5 psia for a brief suit leak check followed by depressurization to vacuum (0.30 mmHg). Throughout the test, all subjects were resting in seats on their backs in low metabolic demand conditions. Vacuum operations lasted 1 to 1.5 h and were followed by a 10-min repressurization. Posttest S_pCO measurements were obtained within 5 min of returning to ambient pressure.

The PLSS test procedure was designed to evaluate the PLSS in vacuum with a volunteer test subject under a high metabolic demand for 6 h. S_pCO measurement, EMU suit donning, leak check, O_2 purge, prebreathe, 5 psia leak check, depressurization to vacuum (0.2 mmHg), and repressurization are similar to those described for the SSATA test procedure. However, the PLSS procedure required the test subject to remain at vacuum for 6 h while completing metabolically demanding tasks. The goal metabolic profile consisted of six 1-h increments, each consisting of ~40 min of elevated energy expenditure with intervening ~20-min durations of 400 BTU · h^{-1}. The elevated energy levels were 800 to 1000 BTU · h^{-1} with one peak at 2000 BTU · h^{-1} during the fourth hour. S_pCO was measured within 15 min of suit doffing.

In-flight EVAs. Orbital EVA S_pCO measurements were coordinated with previously scheduled EVAs. Pre-EVA S_pCO was measured prior to prebreathe. Astronauts entered the airlock and began breathing near 100% O_2 through a mask for at least 60 min. The EMU was then donned and leak checked. The EMU was purged for 15 min to >99% O_2. A 2-h and 5-min in-suit prebreathe that included 50 min of ISLE was completed with near 100% O_2 with the airlock at 14.7 psia and the EMU at 0.5–1.0 psid. In the next 30 min, the EMU was regulated to 4.3 psid, the airlock was depressurized to 5 psia for suit leak check, and the airlock was depressurized to vacuum. EVA was then conducted for variable amounts of time (typically >5 h) followed by a 10 to 20-min pressurization. Post-EVA S_pCO measurements were obtained within 5 min of opening helmet and gloves to airlock pressure.

Table III. Demographics for Each Testing Condition.

TEST CONDITIONS	*N*	MEN	WOMEN
SSATA	2	2	0
PLSS	1	1	0
VPIST	7*	5	2
Orbital EVA	3	3	0

Astronaut ages were excluded for privacy.
* One test subject participated twice.
SSATA: space station airlock test article; PLSS: portable life support system; VPIST: vacuum pressure integrated suit test; EVA: extravehicular activity.

Statistical Analysis

Pre- to Post-EVA S_pCO measures were compared under a permutation testing approach. Under the null hypothesis of no

difference, the pre- and post-EVA measures came from the same distribution; within individuals the values were equally likely to be observed either pre- or post-EVA. Using this fact, an empirical distribution of a test statistic was calculated by analyzing all possible permutations of these labels. The difference between the means of pre- and post-EVA measures was used for this study. An empirical *P*-value was determined by comparing the observed mean difference to the distribution of mean differences calculated from all possible permutations of pre- and post-EVA measures within individuals. The *P*-value was calculated as the total number of permutations at least as extreme as that observed (the absolute value of the permuted mean difference is greater than the absolute value of the observed mean difference) divided by the total number of possible permutations. The CO-oximeter measured to the whole percentage while the statistical model prediction used mean and SD to one decimal place.

RESULTS

The output of the model is shown in **Fig. 2**. The maximum simulated EMU pCO was 0.061 mmHg and the maximum simulated crewmember carboxyhemoglobin saturation (COHb%) was 2.1%. To determine the effect of suit leak rate on the model outputs, simulations were repeated with the leak rate set to no leak and doubled to 0.02 $L \cdot min^{-1}$. With no leak, maximum EMU pCO raised slightly to 0.063 mmHg and maximum COHb% remained at 2.1%. With leak rate doubled, maximum EMU pCO and maximum COHb% both dropped slightly to 0.059 mmHg and 2.0%, respectively.

Carboxyhemoglobin levels in astronauts and volunteer test subjects in orbital EVAs on the ISS and ground-based EVA analogs were collected to ensure safe CO levels during operations. S_pCO values in mean ± SD during ground-based spacesuit exposures were 0.7% ± 1.8% pretest and 0.5% ± 1.5% posttest ($P = 0.57$). S_pCO values during EVA on the ISS were 1.5% ± 0.7% pretest and 1.1% ± 0.3% posttest ($P = 0.31$). S_pCO values in pooled ground and orbital EVA from index finger measures only were 1.1% ± 0.9% pretest and 0.8% ± 0.7% posttest ($P = 0.94$). There was no statistically significant difference in any of these comparisons at the alpha = 0.05 level. With 10 data points, the study is powered (beta > 0.8) to detect a change in S_pCO of 1.0%. Even this level of change is quite low and within measurement error of the CO-oximeter. The experimental change in mean S_pCO was only 0.4%, which is not clinically significant.

DISCUSSION

Fig. 2 shows a maximum pCO of 0.061 mmHg, a maximum COHb% of 2.1%, and a final COHb% of 1.9%. The U.S. Code of Federal Regulations sets a CO exposure limit at an 8-h time-weighted average of 50 ppm by volume at 25°C and 760 torr.[12] This regulation is equivalent to a pCO of 0.038 mmHg at 25°C,

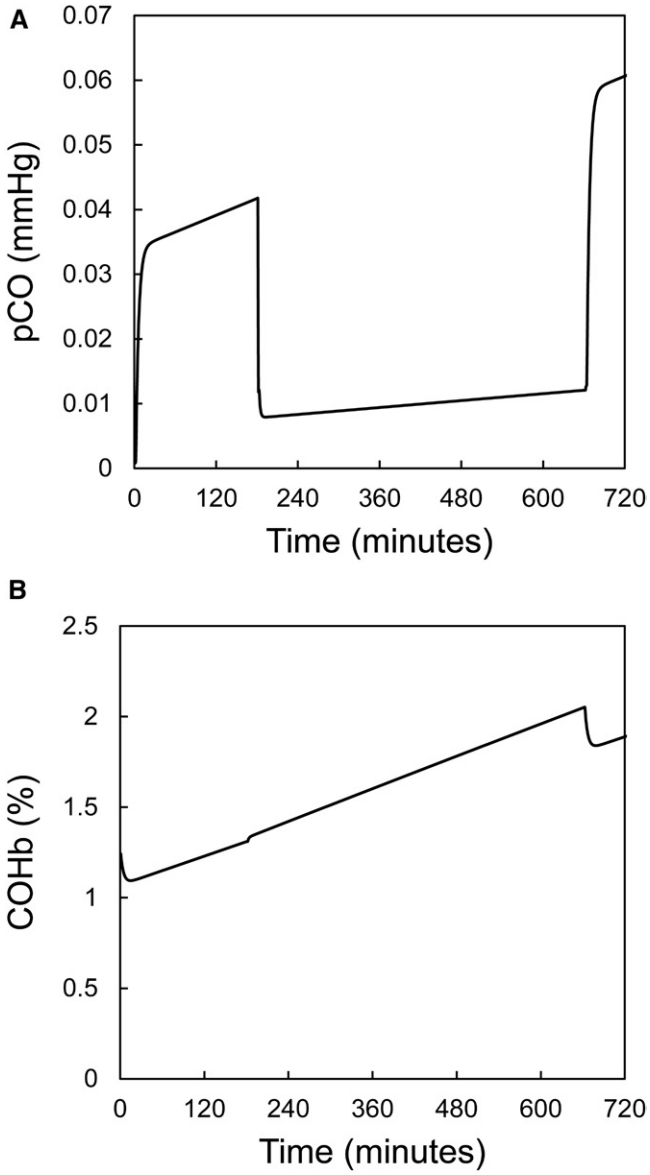

Fig. 2. Output of the analytical model. A) Simulated EMU CO partial pressure. B) Simulated crewmember carboxyhemoglobin percentage saturation.

which is the EMU temperature used in the model. The model generated a maximum 8-h time-weighted average pCO of 0.020 mmHg, well below the 0.038 mmHg threshold. The U.S. Environmental Protection Agency (EPA) stated the lowest level of COHb% that may begin to cause adverse effects is 2.0–2.9%.[1] This range borders a normal COHb% range of 0–2% in nonsmokers.[18] The EPA range is a conservative estimate that accounts for measurement error and a susceptible population with chronic illnesses. The analytical model results gave a maximum COHb% slightly above normal and within the lower end of the range predicted by the EPA to potentially cause toxicity. However, the model used worst-case parameters for durations, endogenous CO production rate, and O_2 supply CO contamination. Prebreathe, EVA, and post-EVA activities of 3 h, 8 h, and 1 h, respectively, were used in the model. Typical orbital EVA durations are prebreathe for 2 h and 5 min, EVA for 6.5 h,

and post-EVA activities for less than 20 min. The rate of CO production was overestimated at 0.015 mL · min^{-1} at standard temperature and pressure based on the literature for breathing 100% O_2 at terrestrial atmospheric pressure rather than a lower value such as 0.007 mL · min^{-1} with breathing 20–30% O_2 at about 1 atm.[4,5] CO production of 0.015 mL · min^{-1} is likely a good estimate during prebreathe and post-EVA, as the partial pressure of O_2 is near 100% O_2 at slightly greater than 1 atm. However, CO production rate during EVA is more likely closer to 0.007 mL · min^{-1} given the astronaut breathes a partial pressure of O_2 slightly above terrestrial ambient conditions during EVA (222 mmHg vs. 150 mmHg). The results of the model with a maximum COHb% of 2.1% are consistent with a previous analysis of CO in the EMU conducted by Bruce and Bruce.[3] Their model predicted a COHb% approaching 2% after an 8-h EVA, with endogenous CO production rate modeled as high as 0.020 mL · min^{-1} and a CO contamination of O_2 supply as high as 2 ppm.[3]

Despite the EMU having no mechanism to remove CO other than inherent suit leak, the model predicted that leak rate has little influence on CO accumulation. COHb% reached 2.1% without a leak and was 2.0% with a leak twice the specification limit. Likewise, maximum EMU pCO was estimated at 0.063 mmHg without a leak and dropped to only 0.059 mmHg with a doubled leak rate. These results are consistent with the Bruce study, where leak rate had negligible effect on COHb%.[3]

Notably, all predicted mean S_pCO values fell well below 2% and the differences between measurements collected before and after simulated or actual EVA were statistically nonsignificant. The operational S_pCO mean values were less than the model COHb% output of about 2%, likely due to the worst-case parameters used in the model.

Operational S_pCO levels were within safe ranges, and the model COHb% was slightly above normal with worst-case parameters. These results suggest that the risk to astronauts will remain low as long as the supply gas meets the requirements of less than 1 ppm CO.

The slopes at different times in the simulation shown in Fig. 2A and B are also important model outputs for extrapolating pCO and COHb% in scenarios with longer durations of prebreathe, EVA, and post-EVA activities. The initial pCO concentration of 7.9×10^{-4} mmHg in Fig. 2A was due to the 1 ppm CO contamination from the O_2 supply tank with the initial flush of the EMU. The rapid increase to ~20 min represented equilibration of CO accumulation from the contaminated supply tank and endogenous CO generation. After the initial rapid rate of accumulation, the rate reached a steady state of 4.3×10^{-5} mmHg pCO · min^{-1} for the remainder of the 180 min prebreathe. The rapid drop in pCO after minute 180 occurred at depressurization of the EMU to 4.3 psia with a subsequent steady state accumulation rate of 8.9×10^{-6} mmHg pCO · min^{-1}. After EVA, the pCO increased rapidly at repressurization and during the next ~20 min with a subsequent return to steady state of 4.3×10^{-5} mmHg pCO · min^{-1}. In Fig. 2B, the initial COHb% of 1.2% was derived from the literature as an average range for a nonsmoker under ambient conditions.[15] After an initial decrease in COHb% as steady state conditions were met, the COHb% increased at a rate of 0.0013% · min^{-1}. The rate of COHb% change during EVA was slightly higher at 0.0015% · min^{-1} and returned to 0.0013% · min^{-1} after EVA.

Animal models and human studies have demonstrated that COHb% increases with altitude.[8–10] The effect of high altitude on COHb% is clear when examining the Haldane relationship,[8] $[COHb]/[O_2Hb] = M(P_{CO})/P_{O_2}$. Observe that as P_{O_2} decreases, the ratio between [COHb] and $[O_2Hb]$ increases, resulting in an increased CO uptake and retention at altitude. However, high altitude studies are not representative of the EVA environment. O_2 partial pressure is elevated in the EMU compared to nominal terrestrial conditions. Hyperoxic conditions in the EMU increase P_{O_2} and cause a decrease in the ratio of [COHb] to $[O_2Hb]$. At a given level of exogenous CO (e.g., O_2 supply contamination), less CO binds to hemoglobin in the hyperoxia of EVA than in normoxic terrestrial conditions. This situation parallels the use of hyperbaric O_2 treatment for CO toxicity where high O_2 partial pressure antagonizes CO binding to hemoglobin.[2,8,19]

Despite the clinical concern of CO toxicity, CO is also an important endogenous signaling molecule that is formed at low levels during heme catabolism. Heme oxygenase-1 (HO-1) is the enzyme primarily responsible for CO production.[19] HO-1 catalyzes the reaction that breaks down heme (ferroprotoporphyrin IX) to biliverdin (a bilirubin precursor), Fe^{+2}, and CO by consuming O_2 and NADPH.[19] This HO-1 catalyzed reaction takes place primarily in the liver and spleen.[14] HO-1 activity is increased in inflammatory, infectious, and oxidative states.[14] Of these three, oxidative stress is the most relevant to the spaceflight environment.

Regardless of the increased resiliency to exogenous CO exposure in hyperoxic conditions as demonstrated by the Haldane relationship, in vitro and animal models have shown that high O_2 partial pressure increases oxidative stress and increases endogenous CO production by HO-1.[6,7] In this case, HO-1 protects against oxidative damage in hyperoxic environments.[7,13] The protective role was demonstrated by transfection of HO-1 into human pulmonary epithelial cells with resultant increased HO-1 activity and increased cellular survival in hyperoxic conditions that was reversible with an HO-1 inhibitor.[7] Another study showed that hyperoxic exposure of laboratory rats caused lower airway epithelium and lung interstitium to increase HO-1 levels.[6] An additional experiment transfected rats with HO-1 via an endotracheal route, causing decreased pulmonary injury and mortality in hyperoxic conditions compared to control rats exposed to the same environment.[13] A possible mechanism of the oxidative protection by HO-1 is the antioxidant properties of bilirubin that forms downstream of the HO-1 catalyzed reaction.[13]

The previously mentioned cell and animal model results explain the elevated CO production rate in human subjects breathing higher partial pressures of O_2. This places the crewmember in a situation of producing CO at a more rapid rate during the near 100% O_2 prebreathe and post-EVA due to the higher O_2 partial pressure. The increased endogenous CO

production is offset by the decreased affinity of hemoglobin for CO under hyperoxic conditions with exhalation as the primary route of CO removal from the body. The result is increased accumulation of CO within the EMU due to hyperoxia. However, the COHb% output of the analytical model and the S_pCO operational results demonstrated that for the durations tested, the level of CO accumulation is within acceptable levels.

Several limitations of this study are important to address. The assumptions listed for the model allowed for simplicity of calculation at the cost of potential inaccuracies. Also, deriving $\dot{V}_A$ based on data extrapolated from the Operation Everest II study at a P_IO_2 of 150 mmHg resulted in an overestimate of $\dot{V}_A$. Importantly, the overestimated $\dot{V}_A$ values resulted in slightly increased values of CO accumulation in the suit compared to lower $\dot{V}_A$ inputs. This is consistent with choosing worst case parameters. COHb% was relatively insensitive to changes in $\dot{V}_A$ as a tenfold decrease in $\dot{V}_A$ resulted in negligible COHb% change. Additionally, limits of the operational study include a small sample size, a CO-oximeter with known variability in measurements up to 3% S_pCO, and using low S_pCO values as a surrogate for a safe environment.

The analytical model presented here, which calculated COHb% under worst-case conditions for EVA duration, endogenous CO production, and O_2 supply contamination, predicted a maximum pCO of 0.061 mmHg, a maximum COHb% of 2.1%, and a final COHb% of 1.9%. Operational S_pCO measurements under conditions of ground-based analogs and orbital EVA demonstrated mean S_pCO levels remained less than 2%. The results of the analytical model and operational testing both confirmed that the current standard requiring 1 ppm or less of CO in the O_2 supply limits CO accumulation in the EMU to levels that are not clinically concerning.

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