1 Hazard

Hemoglobin (Hb) is the protein in blood responsible for transporting oxygen throughout the body. Four hemoglobin subunits bind with and carry up to four oxygen molecules to form oxyhemoglobin (O_2Hb). Carbon monoxide also binds to hemoglobin at the same sites as oxygen, but approximately 218 times more tightly[1], to form carboxyhemoglobin (COHb). Thus, exposure to relatively low levels of carbon monoxide can substantially inhibit the ability of hemoglobin to transport oxygen to the body. Symptoms of exposure to carbon monoxide include but are not limited to headache, nausea, vomiting, dizziness, fatigue, and a feeling of weakness.

2 Model

When an individual is exposed to elevated carbon monoxide concentrations, COHb values will increase until that individual is removed from the hazardous environment. Once removed from the hazard, the COHb is cleared from the body. Consequently two distinct phases (namely uptake during exposure, followed by elimination) exist (Figure 1).

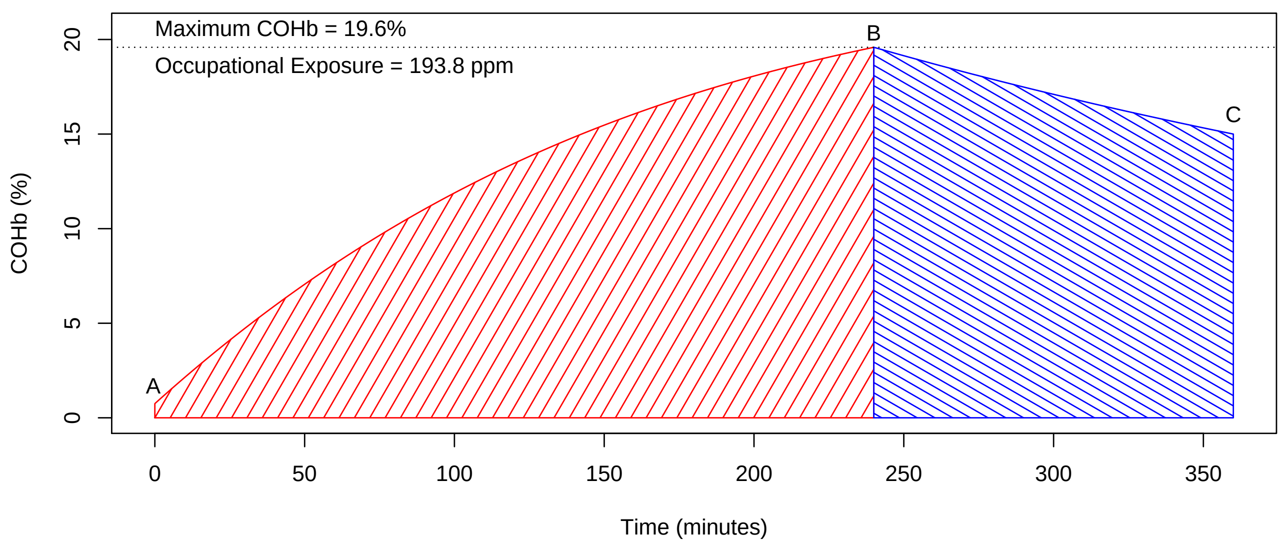

Figure 1. The concentration of carboxyhemoglobin increases while the employee is exposed to carbon monoxide (red) and decreases when no longer exposed (blue). This figure is generated from the sample calculation in Appendix C.

Both phases are modeled by the following first order differential equation known as the Coburn-Forster-Kane (CFK) Equation.[2,3,4]

[1] Haldane J, Smith JL. The Absorption of Oxygen by the Lungs. J Physiol. 1897 Nov 20;22(3):231-58. doi: 10.1113/jphysiol.1897.sp000689. PMID: 16992404; PMCID: PMC1512632. https://physoc.onlinelibrary.wiley.com/doi/pdf/10.1113/jphysiol.1897.sp000689

[2] Coburn RF, Forster RE, Kane PB. Considerations of the physiological variables that determine the blood carboxyhemoglobin concentration in man. J Clin Invest. 1965 Nov;44(11):1899-910. doi: 10.1172/JCI105296. PMID: 5845666; PMCID: PMC289689. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC289689/pdf/jcinvest00297-0185.pdf

[3] Johnson T, Capel J, Paul R, Wijnberg L. Estimation Of Carbon Monoxide Exposures And Associated Carboxyhemoglobin Levels In Denver Residents Using A Probabilistic Version Of NEM. EPA Contract No. 68-D0-0062, Work Assignment No.1-4, JTN 830013-013-02 https://hero.epa.gov/hero/index.cfm/reference/download/reference_id/1712

[4] Johnson T, Mihlan G, LaPointe J, Fletcher K. Estimation of Carbon Monoxide Exposures and Associated Carboxyhemoglobin Levels in Denver Residents Using pNEM/CO (Version 2.0). EPA Contract No. 68-D6-0064, Work Assignment No. 1-19 and 2-24. https://www3.epa.gov/ttn/naaqs/standards/co/previous/codenver1999.pdf

$$\frac{d[\text{COHb}]}{dt} = \frac{V_{\text{CO}}}{V_b} + \frac{P_{I_{\text{CO}}}}{V_b\beta} - \frac{P_{C_{O_2}}}{V_b\beta}\left(\frac{[\text{COHb}]}{M[\text{O}_2\text{Hb}]}\right) \tag{1}$$

This equation shows how the concentration of carboxyhemoglobin in blood, [COHb], responds to three driving forces. The first term is the ratio of two constants, namely the endogenous carbon monoxide production rate (V_{CO}) within the body (equal to 0.007 mL/min)[5] divided by the volume of blood in the body (V_b). The second term is driven by partial pressure of inspired carbon monoxide in air saturated with water vapor at body temperature ($P_{I_{CO}}$). This is the unknown parameter of interest during the uptake phase that is to be determined, and will be treated as the average value throughout the event duration (Δt). This pressure is divided by the term

$$\beta = \frac{1}{D_L} + \left(\frac{P_B - P_{\text{H}_2\text{O}}}{V_A}\right) \tag{2}$$

that consists of the pulmonary diffusion rate of carbon monoxide (D_L), the barometric pressure (P_B), the vapor pressure of water at body temperature ($P_{H_2O} = 47\ torr$), and the alveolar ventilation rate (V_A). The third and final term of the CFK Equation is driven by the mean pulmonary capillary oxygen pressure ($P_{C_{O2}}$). This term includes a ratio of concentration of carboxyhemoglobin ([COHb]) to oxyhemoglobin ([O_2Hb]). The parameter M in this term, known as the Haldane constant,[1] represents hemoglobin's preferential affinity to carbon monoxide over oxygen and is equal to 218.

A solution to the CFK Equation is equation is sought for the specific boundaries of each phase (uptake and elimination) but first a generic solution is developed through integration for the change in carboxyhemoglobin over a time interval Δt.

$$\Delta t = \int_{[\text{COHb}]_i}^{[\text{COHb}]_f} \frac{1}{\frac{V_{CO}}{V_b} + \frac{P_{I_{CO}}}{V_b\beta} - \frac{P_{C_{O_2}}}{V_b\beta}\left(\frac{[\text{COHb}]}{M[\text{O}_2\text{Hb}]}\right)} d[\text{COHb}] \tag{3}$$

As explained above, all of the terms within the integral are constant with the exception of the concentrations of oxyhemoglobin ([O_2Hb]) and carboxyhemoglobin ([COHb]). These two terms are related through the limited and constant binding capacity of hemoglobin (Hf). From the molecular weight of oxygen, one can calculate that a gram of hemoglobin can combine with 1.39 ml of oxygen but the empirically determined value is lower than this and varies with each individual. A value of 1.38 mL of gas at standard temperature (0℃) and pressure (760 mm Hg), dry (no water vapor) per gram of human hemoglobin is used in this application to remain historically consistent with the previous version of this application. Assuming that COHb is the only relevant dyshemoglobin present allows for the concentration of O_2Hb to be expressed in terms of the concentration of COHb.[6]

$$Hf\ Hb = [\text{O}_2\text{Hb}] + [\text{COHb}] \tag{4}$$

$$\Delta t = \int_{[\text{COHb}]_i}^{[\text{COHb}]_f} \frac{1}{\frac{V_{CO}}{V_b} + \frac{P_{I_{CO}}}{V_b\beta} - \frac{P_{C_{O_2}}}{V_b\beta}\left(\frac{[\text{COHb}]}{M(Hf\ Hb - [\text{COHb}])}\right)} d[\text{COHb}] \tag{5}$$

[5] Coburn, RF, Blakemore WS, and Forster RE. Endogenous carbon monoxide production in man. J Clin Invest. 1963 Jul;42(7):1172-8. doi: 10.1172/JCI104802. PMID: 14021853; PMCID: PMC289385. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC289385/pdf/jcinvest00283-0188.pdf

[6] Tikuisis P, Madill HD, Gill BJ, Lewis WF, Cox KM, Kane DM. A critical analysis of the use of the CFK Equation in predicting COHb formation. Am Ind Hyg Assoc J. 1987 Mar;48(3):208-13. doi: 10.1080/15298668791384643. PMID: 3578032. https://pubmed.ncbi.nlm.nih.gov/3578032/

Integration of Equation 5 (see Appendix B for details) results in the following closed form solution requiring iteration.

$$\ln\left(\frac{[\text{COHb}]_i Q - S}{[\text{COHb}]_f Q - S}\right) = \frac{Q}{R}\left(\frac{\Delta t\, Q}{V_b\, \beta\, M} + [\text{COHb}]_i - [\text{COHb}]_f\right) \tag{6}$$

$$Q = \beta\, M\, V_{CO} + M\, P_{I_{CO}} + P_{C_{O_2}} \tag{7}$$

$$R = Hf\; Hb\, P_{C_{O_2}} \tag{8}$$

$$S = Hf\; Hb\, M(V_{CO}\, \beta + P_{I_{CO}}) \tag{9}$$

3 Approach

If the uptake phase extends from time A to time B and the elimination phase extends from time B to time C Equation 6 can first be applied to the elimination phase as shown in Equation 10. This equation can be solved, through iteration, to determine the concentration of COHb in the blood at time B as $[\text{COHb}]_B$.

$$\ln\left(\frac{[\text{COHb}]_B Q_e - S_e}{[\text{COHb}]_C Q_e - S_e}\right) = \frac{Q_e}{R_e}\left(\frac{\Delta t_e\, Q_e}{V_b\, \beta_e\, M} + [\text{COHb}]_B - [\text{COHb}]_C\right) \tag{10}$$

$$Q_e = \beta_e\, M\, V_{CO} + M\, P_{I_{CO_e}} + P_{C_{O_{2e}}} \tag{11}$$

$$R_e = Hf\; Hb\, P_{C_{O_{2e}}} \tag{12}$$

$$S_e = Hf\; Hb\, M(V_{CO}\, \beta_e + P_{I_{CO_e}}) \tag{13}$$

Equation 6 can be applied to the uptake phase as shown in Equation 14. Solving this equation for the uptake phase is more complicated compared to the elimination phase because the parameter to be determined (exposure to carbon monoxide) drives the parameters $P_{I_{CO_u}}$, $P_{C_{O2_u}}$, and β_u. The constitutive relationships for these parameters, as well as other parameters such as blood volume, V_b, will be discussed in the next section.

$$\ln\left(\frac{[\text{COHb}]_A Q_u - S_u}{[\text{COHb}]_B Q_u - S_u}\right) = \frac{Q_u}{R_u}\left(\frac{\Delta t_u\, Q_u}{V_b\, \beta_u\, M} + [\text{COHb}]_A - [\text{COHb}]_B\right) \tag{14}$$

$$Q_u = \beta_u\, M\, V_{CO} + M\, P_{I_{CO_u}} + P_{C_{O_{2u}}} \tag{15}$$

$$R_u = Hf\; Hb\, P_{C_{O_{2u}}} \tag{16}$$

$$S_u = Hf\; Hb\, M(V_{CO}\, \beta_u + P_{I_{CO_u}}) \tag{17}$$

4 Constitutive Relations

The constitutive relations presented in this section provide closure to the model.

4.1 Partial Pressure of Inspired Carbon Monoxide

The partial pressure of carbon monoxide in the inspired air ($P_{I_{CO}}$) is the carbon monoxide mole fraction of the air (x_{CO}) multiplied by the barometric air pressure that is not due to the saturated vapor pressure at the body temperature ($P_B - P_{H2O}$).

$$P_{I_{CO}} = x_{CO}\,(P_B - P_{H_2O}) \tag{18}$$

4.2 Mean Pulmonary Capillary Oxygen Pressure

Similarly the mean pulmonary capillary oxygen pressure is predicted by

$$P_{C_{O_2}} = x_{O_2}\left(P_B - P_{H_2O} - P_{I_{CO}}\right) - \Delta P_a \tag{19}$$

where ΔP_a is the oxygen pressure differential between the saturated alveoli and the pulmonary capillaries.[7]

4.3 Pulmonary Diffusion Rate and Alveolar Ventilation Rate

Literature values for pulmonary diffusion rates of carbon monoxide, D'_L, and alveolar ventilation rates, V'_A, are correlated to activity level as shown in Table 1.[8,9,10]

Table 1. Activity Levels.

Activity Level	Description	Examples	D'_L (mL/min/mmHg)	V'_A (L/min)
0	Resting	reading, computer	20	6
1	Light	walking, cycling	25	12
2	Moderate	cooking, driving	30	18
3	Heavy	loading, shoveling	40	24
4	Very Heavy	jogging, climbing	50	30

Pulmonary diffusion rates, D_L, deviate from literature values due to variation in oxygen partial pressure, x_{O2}, according to Equation 20.

$$D_L = \frac{D'_L}{1 + 0.0031\left(x_{O_2}\left(\frac{P_B - P_{H_2O}}{\text{mmHg}}\right) - 150\right)} \tag{20}$$

Alveolar ventilation rates, V_A, used in the CFK Equation deviate from literature values due to the use of different reference standards, according to Equation 21.

$$V_A = V'_A\left(\frac{P_B - P_{H_2O}}{760\,\text{mmHg}}\right)\left(\frac{273.15\,\text{K}}{310.15\,\text{K}}\right) \tag{21}$$

5 Application

For pedagogical purposes a minimalistic SMath[11] model is included as Appendix C. Figure 1 is a graph of the results from this sample calculation. Note that an initial approximations must be provided to initiate the iterative solution to both

[7] Peterson JE, Stewart RD. Predicting the carboxyhemoglobin levels resulting from carbon monoxide exposures. J Appl Physiol. 1975 Oct;39(4):633-8. doi: 10.1152/jappl.1975.39.4.633. PMID: 1194155. https://journals.physiology.org/doi/abs/10.1152/jappl.1975.39.4.633

[8] Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr. Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc. 1993 Jan;25(1):71-80. doi: 10.1249/00005768-199301000-00011. PMID: 8292105. https://journals.lww.com/acsm-msse/Abstract/1993/01000/Compendium_of_Physical_Activities__classification.11.aspx

[9] Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR Jr, Schmitz KH, Emplaincourt PO, Jacobs DR Jr, Leon AS. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc. 2000 Sep;32(9 Suppl):S498-504. doi: 10.1097/00005768-200009001-00009. PMID: 10993420. https://journals.lww.com/acsm-msse/Fulltext/2011/08000/2011_Compendium_of_Physical_Activities__A_Second.25.aspx

[10] Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett Jr DR, Tudor-Locke C, Greer JL, Vezina J, Whitt-Glover MC, Leon AS. The Compendium of Physical Activities Tracking Guide. Healthy Lifestyles Research Center, College of Nursing Health Innovation, Arizona State University. https://sites.google.com/site/compendiumofphysicalactivities/

[11] Andrey Ivashov, SMath Version 0.99 (build 7691) https://en.smath.com/view/SMathStudio/

the uptake and elimination phases. Because hemoglobin has such a strong preferential affinity to carbon monoxide, relative to oxygen, the rate of change in carboxyhemoglobin is slow and the measure value, $[\mathrm{COHb}]_C$, can be used as a good initial approximations for $[\mathrm{COHb}]_B$. For the uptake phase a reasonable initial approximations for the average carbon monoxide concentration, x_{CO2}, is found by setting the denominator of the logarithm of Equation 14 to zero to drive the equation to steady state ($t \to \infty$).

$$x_{CO} \approx \frac{(\beta_u\, M\, V_{CO} + (P_B - P_{\mathrm{H_2O}})\, x_{\mathrm{O_2}u} - \Delta P_a)\, [\mathrm{COHb}]_B - V_{CO}\, \beta_u\, Hf\, Hb\, M}{(Hf\, Hb\, M - [\mathrm{COHb}]_B\, (M - x_{\mathrm{O_2}u}))(P_B - P_{\mathrm{H_2O}})} \tag{22}$$

Oxygen therapy can be administered by first responders prior to measuring carboxyhemoglobin levels. This can also be modeled using Equation 23 as an additional elimination phases from time C to time D with its own set of parameters.

$$\ln\left(\frac{[\mathrm{COHb}]_C Q_t - S_t}{[\mathrm{COHb}]_D Q_t - S_t}\right) = \frac{Q_t}{R_t}\left(\frac{\Delta t_t\, Q_t}{V_b\, \beta_t\, M} + [\mathrm{COHb}]_C - [\mathrm{COHb}]_D\right) \tag{23}$$

$$Q_t = \beta_t\, M\, V_{CO} + M\, P_{I_{CO_t}} + P_{C_{O_{2t}}} \tag{24}$$

$$R_t = Hf\, Hb\, P_{C_{O_{2t}}} \tag{25}$$

$$S_t = Hf\, Hb\, M (V_{CO}\, \beta_t + P_{I_{CO_t}}) \tag{26}$$

The model is now extended to the R programming language[12] (Appendix D) with functions that can be used universally across multiple phases. For example the function used to solve for the concentration of carboxyhemoglobin in the blood at the beginning of the oxygen therapy phase, $[\mathrm{COHb}]_C$, is consequently also used to solve for the concentration of carboxyhemoglobin in the blood at the beginning of the elimination phase, $[\mathrm{COHb}]_B$. Another sample calculation is provided as Appendix E that makes use of the COHb.R library for units, constants, lookup tables, functions, and a non-linear equations solver.[13] Figure 2 shows the results of this sample calculation.

6 Correlations

The following correlations are used to enhance the usability of this model.

6.1 Blood Volume

Blood volume (V_b) can estimated[14] based upon the individuals height (H) and weight (W) for both males

$$\left(\frac{V_b}{\mathrm{mL}}\right) = 366.9\left(\frac{H}{\mathrm{m}}\right)^3 + 32.19\left(\frac{W}{\mathrm{kg}}\right) + 604.1 \tag{27}$$

and females.

$$\left(\frac{V_b}{\mathrm{mL}}\right) = 356.1\left(\frac{H}{\mathrm{m}}\right)^3 + 33.08\left(\frac{W}{\mathrm{kg}}\right) + 183.3 \tag{28}$$

[12] R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. Version 3.6.3 (2020-02-29) https://www.R-project.org/.

[13] Berend Hasselman (2018). nleqslv: Solve Systems of Nonlinear Equations. R package version 3.3.2. https://CRAN.R-project.org/package=nleqslv

[14] Sharma R, Sharma S. Physiology, Blood Volume. 2020 Apr 25. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–. PMID: 30252333. https://www.ncbi.nlm.nih.gov/books/NBK526077/

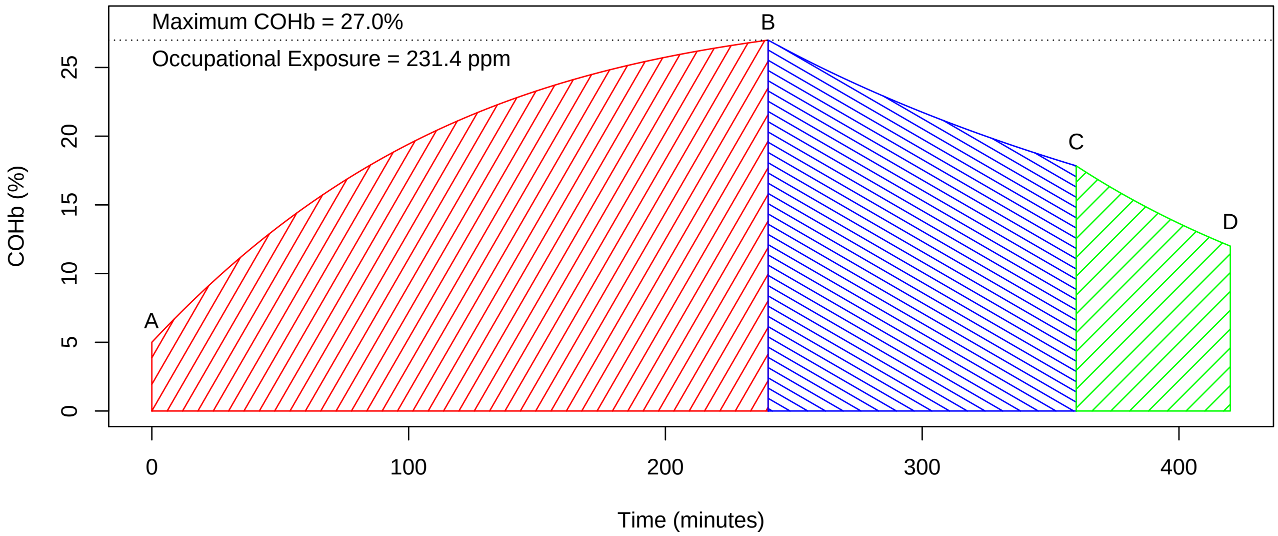

Figure 2. Similar to Figure 1 the red and blue portions of the graph show the uptake and elimination phases respectively. The green portion shows how the concentration of carboxyhemoglobin continues to decrease through oxygen therapy. This figure is generated from the sample calculation procedure found in Appendix E.

6.2 Barometric Pressure

Barometric pressure can be estimated from elevation, z, with the barometric formula where g is the standard acceleration due to gravity ($9.806\,65\,\mathrm{m/s^2}$), R_g is the universal gas constant ($8.314\,459\,8\,\mathrm{J/mole/K}$), M is the molar mass of air (29.9644 gram), T_b is standard temperature (288.15 K) and L_B the temperature lapse rate of Earth's atmosphere ($-0.0065\,\mathrm{K/m}$).[15]

$$P_b = P' \left(\frac{T_b}{T_b + L_B\, z} \right)^{\frac{g\,M}{R_g\,L_B}} \tag{29}$$

6.3 Hemoglobin in Blood by Gender

When the concentration of hemoglobin in the blood is unknown the average for each gender can be applied for a male, 15.8 gm/dL, or for a female, 14.2 gm/dL.[16,17]

6.4 Tobacco Smoke

The initial concentration of carboxyhemoglobin in the blood before exposure, $[\mathrm{COHb}]_0$, is higher for a tobacco smoker than a non-smoker. This value has been correlated to five different levels based upon the average number of cigarettes smoked per day, as shown in Table 2. Additionally, a steady-state equivalent exposure to carbon monoxide has been

[15] U.S. Standard Atmosphere, 1976, Equation 33a, page 12. https://apps.dtic.mil/dtic/tr/fulltext/u2/a035728.pdf

[16] Johnson, C. L., Abraham, S. Hemoglobin and Selected Iron-Related Findings of Persons 1-74 Years of Age: United States. Advance Data From Vital and Health Statistics; No. 46, January 26,1979. https://www.cdc.gov/nchs/data/ad/ad046acc.pdf

[17] Murphy WG, The sex difference in haemoglobin levels in adults — Mechanisms, causes, and consequences, Blood Rev (2014). http://dx.doi.org/10.1016/j.blre.2013.12.003

correlated to each of these levels. This value can be used as the known exposure for the elimination phase or subtracted from the value found for the uptake phase to determine the exposure.

Table 2. Smoker Status.

Smoker Status (SS)	Description	Cigarettes Per Day	$[COHb]_0$ (%)	Steady-state (ppm)
0	Non-smoker	0	0.75	3.9
1	Passive	6	2	12.0
2	Smoker	20	5	32.5
3	Chain	40	10	69.8
4	Cigar	67	20	158.1

7 Uncertainty

OSHA quantifies uncertainty with a parameter known as the sampling and analytical error (SAE) which is proportional to the ratio of the mean to the standard deviation of a measurable population characteristic, Equation 30. If standard deviations are assigned to each input parameter used in this calculation the Monte Carlo method can be applied to generate a population of results that can be used to calculate an error SAE value for that population.

$$SAE = 1.64485\,\frac{\sigma}{\mu} \tag{30}$$

8 User Interface

A user interface for this model was created with the R package Shiny[18]

[18] Winston Chang, Joe Cheng, JJ Allaire, Yihui Xie and Jonathan McPherson (2020). shiny: Web Application Framework for R. R package version 1.5.0. https://CRAN.R-project.org/package=shiny

Appendices

A Variables

Table 3. Values for R sample calculation that persist the duration of the simulation.

Symbol	Description	Value	Units
Hb	hemoglobin (measured in blood)	16^i	gram/dL
z	elevation	4000^i	feet
P_b	atmospheric pressure	656.3847^c	mmHg
W	weight of employee	150^i	pounds
H	height of employee	72^i	inches
V_b	blood volume	5.038392^c	liters
M	Haldane constant	218^x	
Hf	binding capacity of hemoglobin	1.38^x	mL/g
P_{H2O}	vapor pressure at the body temperature	47^x	mmHg
V_{CO}	endrogenous carbon monoxide production rate	0.007^x	mL/min
ΔP_a	oxygen pressure differential	49^x	mmHg
SS	smoker status	2^i	

^{i} Input value. ^{c} Calculated value. ^{x} Constant.

Table 4. Duration values for R sample calculation for each phase.

Symbol	Description	Uptake	Elimination	Therapy	Units
t	duration	240^i	120^i	60^i	minutes
AL	activity Level	3^i	1^i	0^i	
x_{O_2}	oxygen Level	21^i	21^i	80^i	%
x_{CO}	carbon monoxide level	246.2797^c	14.92857^c	256.9266^c	ppm
V_A	alveolar ventilation rates	16.94801^c	8.474003^c	4.237002^c	L/min
D_L	pulmonary diffusion rate	42.93184^c	26.8324^c	5.714191^c	mL/min/mmHg
β	beta	3.554932^c	6.550838^c	19.12965^c	(mmHg sec)/mLL
$P_{I_{CO}}$	partial Pressure of Inspired Carbon Monoxide	0.1500791^c	0.009097243^c	0^c	mmHg
$P_{C_{O_2}}$	mean Pulmonary Capillary Oxygen Pressure	78.93927^c	78.96888^c	438.5078^c	mmHg
	cigarettes smoked	2^i	1^i	0^i	
	exposure from first hand smoke	14.92857^c	14.92857^c	0^c	ppm

^{i} Input value. ^{c} Calculated value. ^{x} Constant.

Table 5. Values for R sample calculation between phases.

Symbol	Description	A	B	C	D	Units
$\%COHb$	fraction of COHb	5^c	26.99093^c	17.83802^c	12^i	%
[COHb]	concentration of COHb	0.01104000^c	0.05959598^c	0.03938635^c	0.02649600^c	mL/mL

^{i} Input value. ^{c} Calculated value. ^{x} Constant.

B Development of closed form solution to the CFK Equation

The following substitutions

$$x = [\text{COHb}] \tag{31}$$
$$A = [\text{COHb}]_i \tag{32}$$
$$B = [\text{COHb}]_f \tag{33}$$
$$\alpha_1 = \frac{V_{CO}}{V_b} + \frac{P_{I_{CO}}}{V_b \beta} \tag{34}$$
$$\alpha_2 = \frac{P_{C_{O_2}}}{V_b\,\beta\,M} \tag{35}$$
$$\alpha_3 = Hf\ Hb \tag{36}$$

are applied to Equation 5 to yield the following simplified version for integration.

$$\Delta t = \int_A^B \frac{1}{\alpha_1 + \frac{\alpha_2\,x}{x-\alpha_3}}\,dx \tag{37}$$

Multiply both the numerator and the denominator of the fraction by $(x - \alpha_3)$.

$$\Delta t = \int_A^B \frac{(x-\alpha_3)}{\alpha_1\,(x-\alpha_3) + \alpha_2\,x}\,dx \tag{38}$$

The following substitutions

$$u = \alpha_1\,(x-\alpha_3) + \alpha_2\,x \tag{39}$$
$$du = (\alpha_1\ + \alpha_2)\,dx \tag{40}$$
$$\tag{41}$$

yields.

$$\Delta t = \frac{1}{(\alpha_1+\alpha_2)^2} \int \frac{u - \alpha_2\,\alpha_3}{u}\,du \tag{42}$$

Integration of this equation yields.

$$\Delta t = \frac{u - \alpha_2\,\alpha_3\ \ln(u)}{(\alpha_1+\alpha_2)^2} \tag{43}$$

Undo substitution for u to yield.

$$\Delta t = \frac{\alpha_1\,(x-\alpha_3) + \alpha_2\,x - \alpha_2\,\alpha_3\ \ln(\alpha_1\,(x-\alpha_3)+\alpha_2\,x)}{(\alpha_1+\alpha_2)^2} \tag{44}$$

Collecting x terms yields.

$$\Delta t = \left. \frac{(\alpha_1 + \alpha_2)\, x - \alpha_2\, \alpha_3 \ln((\alpha_1 + \alpha_2)\, x - \alpha_1\, \alpha_3)}{(\alpha_1 + \alpha_2)^2} \right|_A^B \tag{45}$$

The following substitutions

$$q = \alpha_1 + \alpha_2 \tag{46}$$
$$r = \alpha_2\, \alpha_3 \tag{47}$$
$$s = \alpha_1\, \alpha_3 \tag{48}$$
$$\tag{49}$$

are applied to the solution to yield the following simplification.

$$\Delta t = \left. \frac{q\, x - r \ln(q\, x - s)}{q^2} \right|_A^B \tag{50}$$

Applying the limits of integration yields

$$\Delta t = \frac{q\, B - r \ln(q\, B - s) - q\, A + r \ln(q\, A - s)}{q^2} \tag{51}$$

Combining the logarithmic terms yields

$$\ln\left(\frac{q\, A - s}{q\, B - s}\right) = \frac{q}{r}(\Delta t\, q + A - B) \tag{52}$$

The following substitutions

$$Q = q\, V_b\, \beta\, M = \beta\, M\, V_{CO} + M\, P_{I_{CO}} + P_{C_{O_2}} \tag{53}$$
$$R = r\, V_b\, \beta\, M = Hf\, Hb\, P_{C_{O_2}} \tag{54}$$
$$S = s\, V_b\, \beta\, M = Hf\, Hb\, M(V_{CO}\, \beta + P_{I_{CO}}) \tag{55}$$

yield the solution in its final form.

$$\ln\left(\frac{Q\, A - S}{Q\, B - S}\right) = \frac{Q}{R}\left(\frac{\Delta t\, Q}{V_b\, \beta\, M} + A - B\right) \tag{56}$$

C SMath Sample Calculation

Define the Haldane constant, the binding capacity of hemoglobin, the vapor pressure of water at body temperature, and endogenous carbon monoxide production rate, and the oxygen pressure differential between the saturated alveoli and the pulmonary capillaries as constants.

$M := 218 \qquad Hf := 1.38\,\frac{mL}{g} \qquad P_{H2O} := 47\,mmHg \qquad V_{CO} := 0.007\,\frac{mL}{min} \qquad \Delta P_a := 49\,mmHg$

Calculate the partial pressure of inspired carbon monoxide during the elimination phase with Equation 18 from the ambient pressure and the fraction of carbon monoxide in the air

$P_B := 700\,mmHg \qquad x_{CO} := 4\,ppm \qquad P_{I.CO.e} := x_{CO} \cdot \left(P_B - P_{H2O}\right) \qquad P_{I.CO.e} = 0.002612\,mmHg$

Calculate the mean pulmonary capillary oxygen pressure during the elimination phase with Equation 19 from the fraction of oxygen in the air.

$x_{O2} := 21\,\% \qquad P_{C.O2.e} := x_{O2} \cdot \left(P_B - P_{H2O} - P_{I.CO.e}\right) - \Delta P_a \qquad P_{C.O2.e} = 88.12945\,mmHg$

Calculate the diffusion rate for an employee who is resting during the elimination phase with Equation 20 and the appropriate value from Table 1.

$$D`_{L.e} := 20\,\frac{mL}{min\,mmHg} \qquad D_{L.e} := \frac{D`_{L.e}}{1 + 0.0031 \cdot \left(x_{O2} \cdot \left(\frac{P_B - P_{H2O}}{mmHg}\right) - 150\right)} \qquad D_{L.e} = 20.8311\,\frac{mL}{min\,mmHg}$$

Calculate the alveolar ventilation for an employee who is resting during the elimination phase with Equation 21 and the appropriate value from Table 1.

$$V`_{A.e} := 6\,\frac{L}{min} \qquad V_{A.e} := V`_{A.e} \cdot \left(\frac{P_B - P_{H2O}}{760\,mmHg}\right) \cdot \left(\frac{273.15\,K}{310.15\,K}\right) \qquad V_{A.e} = 4.540255\,\frac{L}{min}$$

Calculate β for the elimination phase with Equation 2.

$$\beta_e := \frac{1}{D_{L.e}} + \left(\frac{P_B - P_{H2O}}{V_{A.e}}\right) \qquad \beta_e = 11.509780\,\frac{mmHg\,sec}{mL}$$

Calculate Q, R, and S for the elimination phase with Equations 11, 12, and 13 from amount of hemoglobin in the blood.

$$Hb := 15.8\,\frac{gram}{100\,mL} \qquad Q_e := \beta_e \cdot M \cdot V_{CO} + M \cdot P_{I.CO.e} + P_{C.O2.e} \qquad Q_e = 88.99160\,mmHg$$

$$R_e := Hf \cdot Hb \cdot P_{C.O2.e} \qquad R_e = 19.21575\,mmHg$$

$$S_e := Hf \cdot Hb \cdot M \cdot \left(V_{CO} \cdot \beta_e + P_{I.CO.e}\right) \qquad S_e = 0.187983\,mmHg$$

Calculate the concentration of COHb in the blood from the measured fraction of COHb in the blood when it was measured.

$\%COHb_C := 15\,\% \qquad COHb_C := \%COHb_C \cdot Hf \cdot Hb \qquad COHb_C = 0.032706$

Use a nonlinear equation solver with Equation 10 to find the COHb concentration at the begining of the elimination phase from the duration of the elimination phase and the volume of blood in the body.

$\Delta t_c := 120\,min \qquad V_b := 5\,L$

$$COHb_B := solve\left(\ln\left(\frac{COHb_B \cdot Q_e - S_e}{COHb_C \cdot Q_e - S_e}\right) = \frac{Q_e}{R_e} \cdot \left(\frac{\Delta t_c \cdot Q_e}{V_b \cdot \beta_e \cdot M} + COHb_B - COHb_C\right), COHb_B, COHb_C, 3 \cdot COHb_C\right)$$

$COHb_B = 0.04270695$

Calculate the percent COHb in the blood at the beginning of the elimination phase.

$$\%COHb_B := \frac{COHb_B}{Hf \cdot Hb} \qquad \%COHb_B = 19.58675\,\%$$

Calculate the concentration of carboxyhemoglobin at the beginning of the uptake phase using the fraction of carboxyhemoglobin in the blood of a non-smoker listed in Table 2.

$\%COHb_A := 0.75\ \%$ $\qquad COHb_A := \%COHb_A \cdot Hf \cdot Hb$ $\qquad COHb_A = 0.001635$

Calculate the diffusion rate for an employee who is performing moderate work during the uptake phase with Equation 20 and the appropriate value from Table 1.

$$D`_{L.u} := 30\ \frac{mL}{min\ mmHg} \qquad D_{L.u} := \frac{D`_{L.u}}{1 + 0.0031 \cdot \left(x_{O2} \cdot \left(\frac{P_B - P_{H2O}}{mmHg} \right) - 150 \right)} \qquad D_{L.u} = 31.24665\ \frac{mL}{min\ mmHg}$$

Calculate the alveolar ventilation for an employee who is performing moderate work during the uptake phase with Equation 21 and the appropriate value from Table 1.

$$V`_{A.u} := 18\ \frac{L}{min} \qquad V_{A.u} := V`_{A.u} \cdot \left(\frac{P_B - P_{H2O}}{760\ mmHg} \right) \cdot \left(\frac{273.15\ K}{310.15\ K} \right) \qquad V_{A.u} = 13.62077\ \frac{L}{min}$$

Calculate β for the uptake phase with Equation 2.

$$\beta_u := \frac{1}{D_{L.u}} + \left(\frac{P_B - P_{H2O}}{V_{A.u}} \right) \qquad \beta_u = 4.796696\ \frac{mmHg\ sec}{mL}$$

Since the partial pressure of inspired carbon monoxide and the mean pulmonary capillary oxygen pressure are both dependent upon the concentration of CO and this is what we seek as a solution these parameters must be defined as function of CO concentration.

$$P_{I.CO.u}\left(x_{CO}\right) := x_{CO} \cdot \left(P_B - P_{H2O}\right) \qquad P_{C.O2.u}\left(x_{CO}\right) := x_{O2} \cdot \left(P_B - P_{H2O} - P_{I.CO.u}\left(x_{CO}\right)\right) - \Delta P_a$$

Similarly Q, R, and S for the uptake phase are dependent upon the concentration of CO.

$$Q_u\left(x_{CO}\right) := \beta_u \cdot M \cdot V_{CO} + M \cdot P_{I.CO.u}\left(x_{CO}\right) + P_{C.O2.u}\left(x_{CO}\right)$$

$$R_u\left(x_{CO}\right) := Hf \cdot Hb \cdot P_{C.O2.u}\left(x_{CO}\right)$$

$$S_u\left(x_{CO}\right) := Hf \cdot Hb \cdot M \cdot \left(V_{CO} \cdot \beta_u + P_{I.CO.u}\left(x_{CO}\right)\right)$$

Use a nonlinear equation solver with Equation 14 to find the concentration of carbon monoxide during the uptake phase. But first we bound the solve function with Equation 22.

$$\Delta t_u := 240\ min$$

$$x_{CO.L} := \frac{\left(\beta_u \cdot M \cdot V_{CO} + \left(P_B - P_{H2O}\right) \cdot x_{O2} - \Delta P_a\right) \cdot COHb_B - V_{CO} \cdot \beta_u \cdot Hf \cdot Hb \cdot M}{\left(Hf \cdot Hb \cdot M - COHb_B \cdot \left(M - x_{O2}\right)\right) \cdot \left(P_B - P_{H2O}\right)} \qquad x_{CO.L} = 149.9035\ ppm$$

$$x_{CO.H} := 1.3 \cdot x_{CO.L} \qquad x_{CO.H} = 194.8745\ ppm$$

$$x_{CO.e} := solve\left(\ln\left(\frac{COHb_A \cdot Q_u\left(x_{CO}\right) - S_u\left(x_{CO}\right)}{COHb_B \cdot Q_u\left(x_{CO}\right) - S_u\left(x_{CO}\right)} \right) = \frac{Q_u\left(x_{CO}\right)}{R_u\left(x_{CO}\right)} \cdot \left(\frac{\Delta t_u \cdot Q_u\left(x_{CO}\right)}{V_b \cdot \beta_u \cdot M} + COHb_A - COHb_B \right), x_{CO}, x_{CO.L}, x_{CO.H} \right)$$

$$x_{CO.e} = 193.7957\ ppm$$

D R Model

```
library(nleqslv)
library(deSolve)

# units
inch = 0.0254#meter
pound  = 0.45359237#kg
mmHg = 133.322#Pa
mL  = 1e-6#m^3
minute = 60#second
ppm = 1e-6
percent = 1/100
gram = 1e-3#kg
liter = 1e-3#m^3
hour = 60*minute#second
ft = 0.3048#m

# constants
M = 218
Hf = 1.38*mL/gram
PH2O = 47*mmHg
PA = 49*mmHg
VCO = 0.007*mL/minute
g = 9.80665#m/s^2
Rg = 8.3144598#J/mol/K
Mb = 28.9644*gram#/mole
Pb = 760*mmHg
Tb = 288.15#K
Lb = -0.0065#K/m
hb = 0#m

# lookup tables
AL.des <- c("resting","light work","moderate work","heavy work")
AL <- function(x) AL.des[round(x+1)]
AL.dat = c(0, 1, 2, 3, 4)
DL.dat = c(20, 25, 30, 40, 50)*mL/minute/mmHg
DL.tab <- function(AL) approx(AL.dat,DL.dat,AL)$y
DL.tab <- function(AL) {
  AL = ifelse(AL<0, 0, AL)
  AL = ifelse(AL>4, 4, AL)
  approx(AL.dat,DL.dat,AL)$y
}

DL.1 <- function(AL,PB,x.O2) DL.tab(AL) / (1 + 0.0031/mmHg * (x.O2 * (PB - PH2O) - 150*mmHg))
DL.2 <- function(AL,PB,x.O2) DL.tab(AL) / (1 + (0.0031/mmHg + (1.27624E-05/mmHg^2) *
                          (x.O2 * (PB - PH2O) - 150*mmHg)) * (x.O2 * (PB - PH2O) - 150*mmHg))
DL <- function(AL,PB,x.O2) {
  if (x.O2 > 0.21) DL.2(AL,PB,x.O2)
```

```
  else DL.1(AL,PB,x.O2)}
DL <- function(AL,PB,x.O2) ifelse(x.O2 > 0.21, DL.2(AL,PB,x.O2), DL.1(AL,PB,x.O2))
VA.dat = c(6, 12, 18, 24, 30)*liter/minute
VA <- function(AL,PB) approx(AL.dat,VA.dat,AL)$y*(PB-PH2O)/(760*mmHg)*(273.15/310.15)
VA <- function(AL,PB) {
  AL = ifelse(AL<0, 0, AL)
  AL = ifelse(AL>4, 4, AL)
  approx(AL.dat,VA.dat,AL)$y*(PB-PH2O)/(760*mmHg)*(273.15/310.15)
}
SS.dat = c(0, 1, 2, 3, 4)
XCOHb.dat = c(0.0075, 0.02, 0.05, 0.1, 0.2)
cigs.dat = c(0, 6, 20, 40, 67)
steadyState.dat = c(3.9, 12.0, 32.5, 69.8, 158.1)*ppm
XCOHb.0_s <- function(SS) {
  SS = ifelse(SS<0, 0, SS)
  SS = ifelse(SS>4, 4, SS)
  approx(SS.dat,XCOHb.dat,SS)$y
}
steadyState_s <- function(SS) {
  SS = ifelse(SS<0, 0, SS)
  SS = ifelse(SS>4, 4, SS)
  approx(SS.dat,steadyState.dat,SS)$y
}
XCOHb.0_c <- function(cigs) {
  cigs = ifelse(cigs<0, 0, cigs)
  cigs = ifelse(cigs>67, 67, cigs)
  approx(cigs.dat,XCOHb.dat,cigs)$y
}
steadyState_c <- function(cigs) {
  cigs = ifelse(cigs<0, 0, cigs)
  cigs = ifelse(cigs>67, 67, cigs)
  approx(cigs.dat,steadyState.dat,cigs)$y
}

# constitutive relations
Vb.m <- function(H,W) (366.9*H^3 + 32.19*W + 604.1)*mL
Vb.f <- function(H,W) (356.1*H^3 + 33.08*W + 183.3)*mL
PICO <- function(PB,x.CO) x.CO*(PB-PH2O)
PCO2 <- function(PB,x.CO,x.O2) x.O2*(PB-PH2O-PICO(PB=PB,x.CO=x.CO))-PA
beta <- function(PB,DL,VA) 1/DL + (PB-PH2O)/VA
COHb <- function(XCOHb,Hb) XCOHb*Hf*Hb
x.CO.g <- function(beta,Hb,PB,x.O2,COHb.f) (VCO*beta*Hf*Hb*M+(PA+(PH2O-PB)*x.O2-beta*M*VCO)*
                                              COHb.f)/((PH2O-PB)*(Hf*Hb*M-(M-x.O2)*COHb.f))
P <- function(z) Pb*(Tb/(Tb+Lb*(z-hb)))^(g*Mb/(Rg*Lb))

#functions
CFK <- function (t,COHb,parms,Vb,beta,PICO,PCO2,Hb) {list(VCO/Vb + PICO/(Vb*beta) -
                                                         COHb*PCO2/(M*Vb*beta)/(Hf*Hb-COHb))}
```

```
solnCFK <- function(t,COHb.i,COHb.f,Vb,beta,PICO,PCO2,Hb) {
  Q = beta*M*VCO + M*PICO + PCO2
  R = Hf*Hb*PCO2
  S = Hf*Hb*M*(VCO*beta + PICO)
  Q/R*(t*Q/Vb/beta/M+COHb.i-COHb.f) - log((COHb.i*Q-S)/(COHb.f*Q-S))
}

findInitCOHb <- function(t,COHb.f,Vb,beta,PICO,PCO2,Hb) {
  eqn1 <- function(COHb.i) solnCFK(t=t,COHb.i=COHb.i,COHb.f=COHb.f,Vb=Vb,beta=beta,PICO=PICO,
                                                                              PCO2=PCO2,Hb=Hb)
  nleqslv(f = eqn1, x = COHb.f)$x
}

getInitCOHb <- function(t,COHb.f,Vb,PB,AL,x.O2,x.CO,Hb) {
  DL = DL(AL=AL,PB=PB,x.O2=x.O2)
  VA = VA(AL=AL)
  beta = beta(PB=PB,DL=DL,VA=VA)
  PICO = PICO(PB=PB,x.CO=x.CO)
  PCO2 = PCO2(PB=PB,x.CO=x.CO,x.O2=x.O2)
  findInitCOHb(t=t,COHb.f=COHb.f,Vb=Vb,beta=beta,PICO=PICO,PCO2=PCO2,Hb=Hb)
}

findMeanCO <- function(t,COHb.i,COHb.f,Vb,beta,Hb,PB,x.O2) {
  eqn2 <- function(x.CO) solnCFK(t=t,COHb.i=COHb.i,COHb.f=COHb.f,Vb=Vb,beta=beta,
                        PICO=PICO(x.CO=x.CO,PB=PB),PCO2=PCO2(x.CO=x.CO,PB=PB,x.O2=x.O2),Hb=Hb)
  nleqslv(f = eqn2, x = 1.001*x.CO.g(beta,Hb,PB,x.O2,COHb.f))$x
}

getMeanCO <- function(t,COHb.f,Vb,AL,Hb,PB,x.O2,SS) {
  COHb.i = f.COHb.0(SS=SS,Hb=Hb)
  DL = DL(AL=AL,PB=PB,x.O2=x.O2)
  VA = VA(AL=AL)
  beta = beta(PB=PB,DL=DL,VA=VA)
  findMeanCO(t,COHb.i,COHb.f,Vb,beta,Hb,PB,x.O2)
}

SAE <- function(x) 1.64485*sd(x)/mean(x)
```

E R Sample Calculation

```
source("COHb.R")
#=========================================== Sample ==========================================#
XCOHb = 12*percent # COHb in blood sample (%)
Hb = 16*gram/(100*mL) # Hemoglobin in blood sample (grams/100mL)
COHb.D = COHb(XCOHb=XCOHb,Hb=Hb) # Fraction of COHb in blood sample (%)
#========================================== Employee ==========================================#
w = 150*pound # Weight (pounds)
h = 72*inch # Height (inches)
Vb = Vb.m(W=w,H=h) # Estimated blood volume of employee (liters)
SS = 2 # Smoker Status
XCOHb.A = XCOHb.0_s(SS=SS) # Fraction of COHb in blood prior to uptake (%)
COHb.A = Hf*Hb*XCOHb.A # COHb in blood prior to uptake
#========================================= Enviroment =========================================#
z = 4000*ft # Elevation
PB = P(z=z) # Atmospheric Pressure (mmHg)
#======================================= Oxygen Therapy =======================================#
t_t = 60*minute # Oxygen Therapy duration (minutes)
AL_t = 0 # Oxygen Therapy activity Level
x.O2_t = 80*percent # Oxygen Therapy oxygen level (% oxygen)
x.CO_t = 0*ppm # Oxygen Therapy carbon monoxide level (ppm)
VA_t = VA(AL=AL_t,PB=PB)
DL_t = DL(AL=AL_t,PB=PB,x.O2=x.O2_t)
beta_t = beta(PB=PB,DL=DL_t,VA=VA_t)
PICO_t = PICO(PB=PB,x.CO=x.CO_t)
PCO2_t = PCO2(PB=PB,x.CO=x.CO_t,x.O2=x.O2_t)
COHb.C = findInitCOHb(t=t_t,COHb.f=COHb.D,Vb=Vb,beta=beta_t,PICO=PICO_t,PCO2=PCO2_t,Hb=Hb)
XCOHb.C = COHb.C/Hf/Hb
#========================================== Elimination ==========================================#
t_e = 120*minute # Elimination duration (minutes)
AL_e = 1 # Elimination activity Level:
x.O2_e = 21*percent # Elimination oxygen level (% oxygen)
fhs_e.cigarettes = 1 # Cigarettes smoked during elimination
x.CO_e.fhs = steadyState_c(cigs=fhs_e.cigarettes*960*minute/t_e) # CO elimination from first hand smoke (pp
x.CO_e.shs = 0*ppm # CO elimination from second hand smoke (ppm)
x.CO_e = x.CO_e.fhs+x.CO_e.shs # Carbon Monoxide Level (ppm)
VA_e = VA(AL=AL_e,PB=PB)
DL_e = DL(AL=AL_e,PB=PB,x.O2=x.O2_e)
beta_e = beta(PB=PB,DL=DL_e,VA=VA_e)
PICO_e = PICO(PB=PB,x.CO=x.CO_e)
PCO2_e = PCO2(PB=PB,x.CO=x.CO_e,x.O2=x.O2_e)
COHb.B = findInitCOHb(t=t_e,COHb.f=COHb.C,Vb=Vb,beta=beta_e,PICO=PICO_e,PCO2=PCO2_e,Hb=Hb)
XCOHb.B = COHb.B/Hf/Hb
#========================================== Uptake ==========================================#
t_u = 240*minute # Uptake duration (minutes)
AL_u = 3 # Uptake activity Level
x.O2_u = 21*percent # Oxygen level (% oxygen)
VA_u = VA(AL=AL_u,PB=PB)
```

```
DL_u = DL(AL=AL_u,PB=PB,x.O2=x.O2_u)
beta_u = beta(PB=PB,DL=DL_u,VA=VA_u)
x.CO_u = findMeanCO(t=t_u,COHb.i=COHb.A,COHb.f=COHb.B,Vb=Vb,beta=beta_u,Hb=Hb,PB=PB,x.O2=x.O2_u)
fhs_u.cigarettes = 2 # Cigarettes smoked during uptake
x.CO_u.fhs = steadyState_c(cigs=fhs_u.cigarettes*960*minute/t_u) # CO uptake from first hand smoke (ppm)
x.CO_u.shs = 0*ppm  # CO uptake from second hand smoke (ppm)
x.CO_u.o = x.CO_u-x.CO_u.fhs-x.CO_u.shs
PICO_u = PICO(PB=PB,x.CO=x.CO_u)
PCO2_u = PCO2(PB=PB,x.CO=x.CO_u,x.O2=x.O2_u)
#============================================ Plot ===========================================#
t.e = 0:t_u
t.e = seq(0,t_u,1)
e = rk4(y=COHb.A,t=t.e,parms=NULL,func=CFK,Vb=Vb,beta=beta_u,PICO=PICO_u,PCO2=PCO2_u,Hb=Hb)
t.c = seq(t_u,(t_e+t_u),1)
c = rk4(y=COHb.B,times=t.c,parms=NULL,func=CFK,Vb=Vb,beta=beta_e,PICO=PICO_e,PCO2=PCO2_e,Hb=Hb)
t.o = seq((t_e+t_u),(t_e+t_u+t_t),1)
o = rk4(y=COHb.C,times=t.o,parms=NULL,func=CFK,Vb=Vb,beta=beta_t,PICO=PICO_t,PCO2=PCO2_t,Hb=Hb)
par(mar=c(4,4,1.5,1.5),mex=0.8,cex=0.8,mgp=c(2,0.5,0),tcl=0.3)
pdf("R_ExamplePlot.pdf", width=10, height=5)
plot(c(0,(t_u+t_e+t_t)/60),c(0,XCOHb.B/percent)*1.05,type='n',xlab="Time (minutes)",ylab="COHb (%)")
polygon(c(0,e[,1]/60,t_u/60), c(0,e[,2],0)/Hf/Hb/percent, col='red', density=10, angle=60)
polygon(c(t_u/60,c[,1]/60,(t_u+t_e)/60), c(0,c[,2],0)/Hf/Hb/percent, col='blue', density=15, angle=-30)
polygon(c((t_u+t_e)/60,o[,1]/60,(t_u+t_e+t_t)/60), c(0,o[,2],0)/Hf/Hb/percent,
                                                                    col='green', density=10, angle=45)
abline(h=XCOHb.B/percent,lty=3)
text(0,1.03*XCOHb.B/percent,sprintf("Maximum COHb = %.1f%%", XCOHb.B/percent),adj = c(0,0))
text(0,0.93*XCOHb.B/percent,sprintf("Occupational Exposure = %.1f ppm", x.CO_u.o/ppm),adj = c(0,0))
text(-3,1.2*XCOHb.A/percent,sprintf("A", x.CO_u.o/ppm),adj = c(0,0))
text(t_u/60,1.05*XCOHb.B/percent,sprintf("B", XCOHb.B/percent))
text((t_u+t_e)/60,1.1*XCOHb.C/percent,sprintf("C", XCOHb.B/percent))
text((t_u+t_e+t_t)/60,1.15*XCOHb/percent,sprintf("D", XCOHb.B/percent))
dev.off()
```