ERRATUM: Clarification of and correction to "Mathematical models of oxygen and carbon dioxide storage and transport: the acid-base chemistry of blood", *Critical Reviews™ in Biomedical Engineering*, Issue 3, Volume 33, pp 209–264, 2005

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The paper of Rees and Andreassen[1] describes a mathematical model of the acid-base chemistry of the blood using a mass-balance and mass-action approach and modeling both plasma and red blood cells. Reaction equations are included for both plasma and red blood cell bicarbonate and non-bicarbonate buffers, including the amino end and side chain binding sites of hemoglobin buffers. Oxygen (O_2) binding to hemoglobin is also included in the model allowing representation of the competitive binding of O_2 and hydrogen ions (H^+) on hemoglobin, known as the Bohr-Haldane effect.

In reproducing the results included in this paper it is, we believe, necessary to clarify an issue relating to the application of the mass-action equations included in the model, which if not understood may prevent the reader from reproducing the simulations illustrated in the paper. The paper also includes one error. This short text describes these points in turn.

Equations M23 and M24 of the paper are mass-action equations describing the binding of carbon dioxide (CO_2) on the amino end of hemoglobin in its deoxygenated ($HbNH_2$) and oxygenated (HbO_2NH_2) forms giving carbamino in its deoxygenated ($HbNHCOO^-$) and oxygenated (HbO_2NHCOO^-) forms. The equations are:

$$pH_e = pKcd + \log_{10}(HbNHCOO^- / (HbNH_2\ CO_{2,e})) \quad (M23)$$

$$pH_e = pKco + \log_{10}(HbO_2NHCOO^- / (HbO_2NH_2\ CO_{2,e})) \quad (M24)$$

where terms representing hemoglobin and carbon dioxide are concentrations, and the subscript 'e' is used to denote the erythrocyte fraction.

As for all the mass-action equations included in the paper (M18–M26), values of pH and pK are defined as the negative logarithmic forms of H^+ concentration and equilibrium constants

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respectively, with reference to molal concentrations. This means that application of the mass-action equations requires that values of these variables are specified in moles. For example, values of HbO_2NHCOO^-, HbO_2NH_2, and $CO_{2,e}$ in normal fully oxygenated blood are $HbO_2NHCOO^- = 0.6$ mmol/L, $HbO_2NH_2 = 10.8$ mmol/L, and $CO_{2,e} = 1.04$ mmol/L (Table III, see Rees and Andreassen[1]). Using the value of pKco = 5.46, equation M24 can be solved to give:

$$pH_e = 5.46 + \log_{10}(0.6 \times 10^{-3} / (10.8 \times 10^{-3}\ 1.04 \times 10^{-3})) = 7.19$$

For equations M23 and M24, the logarithmic term is not unitless and as such the same answer is not obtained if values are inserted in millimoles. For other mass action equations (M18–M22 and M25–M26), the logarithmic term is unitless and the unit with which concentrations are specified is therefore unimportant.

In addition to this clarification, it is necessary to highlight an error that exists in Table II, where the percentages associated with the two forms of the amino acid side chains of hemoglobin (RH and R^-) have been interchanged. The corrected table is given below.

TABLE II. Deoxygenated Forms of Hemoglobin*

	Form 1b	**Form 2b**		
	p*K*zd$_R$= 7.32 ⟷		**Amino Forms of Hb**	
Form 1a	$Hb(RH)_bNH_3^+$ (30.2%)	$Hb(R^-)_bNH_3^+$ (22.2%)	$HbNH_3^+$ (52.4%)	↕ p*K*zd = 7.32
Form 2a	$Hb(RH)_bNH_2$ (21.4%)	$Hb(R^-)_bNH_2$ (15.7%)	$HbNH_2$ (37.1%)	↕ p*K*cd = 4.80
Form 3a	$Hb(RH)_bNHCOO^-$ (6.1%)	$Hb(R^-)_bNHCOO^-$ (4.4%)	$HbNHCOO^-$ (10.5%)	
Side chain forms of Hb	$Hb(RH)_b$ (57.7%)	$Hb(R^-)_b$ (42.3%)	Total deoxygenated Hb 5.25 mmol/L (100%) in 75% oxygenated venous blood	

*Six different forms of hemoglobin are represented plus the sum of hemoglobin in the amino end and side chain forms. The p*K*s are given linking rows and columns, that is, describing the various chemical reactions and estimated later in the text (section IV.D). The percentage of total hemoglobin in each form is given for normal mixed venous blood, $pH_p = 7.36$, $PCO_2 = 6.1$ kPa.

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REFERENCES

1. Rees SE, Andreassen S. Mathematical models of oxygen and carbon dioxide storage and transport: the acid–base chemistry of blood. Crit Rev Biomed Eng. 2005;33(3):209–64.