

## The Accuracy of Calculated Base Excess in Blood

Werner Lang\* and Rolf Zander

Institut für Physiologie und Pathophysiologie, Fachbereich  
Medizin der Johannes Gutenberg-Universität, Mainz,  
Germany

Most equations used for calculation of the base excess (*BE*, mmol/l) in human blood are based on the fundamental equation derived by Siggaard-Andersen and called the Van Slyke equation:  $BE = Z \cdot [c\text{HCO}_3(\text{P}) - c_{7.4}\text{HCO}_3(\text{P})] + \beta \cdot (\text{pH} - 7.4)$ . In simple approximation, where *Z* is a constant which depends only on total hemoglobin concentration (*cHb*, g/dl) in blood, three equations were tested: the ones proposed by Siggaard-Andersen (SA), the National Committee for Clinical Laboratory Standards (NCCLS) or Zander (ZA). They differ only slightly in the solubility factor for carbon dioxide ( $\alpha\text{CO}_2$ , mmol/l·mmHg) and in the apparent *pK* (*pK'*), but more significantly in the plasma bicarbonate concentration at reference pH ( $c_{7.4}\text{HCO}_3(\text{P})$ , mmol/l) and in  $\beta$ , the slope of the  $\text{CO}_2$ -buffer line (mmol/l) for whole blood. Furthermore, the approximation was improved either by variation in *Z* ( $r_c$ ), or in the apparent *pK* (*pK'*) with changing pH. Thus, from a total of seven equations and from a reference set for pH,  $p\text{CO}_2$  and *BE* taken from the literature (*n*=148), the base excess was calculated. Over the whole range of base excess (–30 to +30 mmol/l) and  $p\text{CO}_2$  (12 to 96 mmHg), mean accuracy ( $\Delta BE$ , mmol/l) was greatest in the simple equation according to Zander and decreased in the following order:  $\pm 0.86$  (ZA);  $\pm 0.94$  (ZA,  $r_c$ );  $\pm 0.96$  (SA,  $r_c$ );  $\pm 1.03$  (NCCLS,  $r_c$ );  $\pm 1.40$  (NCCLS);  $\pm 1.48$  (SA); and  $\pm 1.50$  (*pK'*).

For all clinical purposes, the Van Slyke equation according to Zander is the best choice and can be recommended in the following form:

$$BE = (1 - 0.0143 \cdot c\text{Hb}) \cdot [0.0304 \cdot p\text{CO}_2 \cdot 10^{\text{pH} - 6.1} - 24.26] + (9.5 + 1.63 \cdot c\text{Hb}) \cdot (\text{pH} - 7.4) - 0.2 \cdot c\text{Hb} \cdot (1 - s\text{O}_2),$$

where the last term is a correction for oxygen saturation ( $s\text{O}_2$ ). Hence, base excess can be obtained with high accuracy (<1 mmol/l) from the measured quantities of pH,  $p\text{CO}_2$ , *cHb*, and  $s\text{O}_2$  in any sample, irrespective of whether venous or arterial blood is used. Clin Chem Lab Med 2002; 40(4):404–410

**Key words:** Base excess; Van Slyke equation.

**Abbreviations:** Base excess (mmol/l), calculated from the Van Slyke equation, as recommended by:  $BE_{\text{calc}}$ (NCCLS), the National Committee of Clinical Laboratory Standards;  $BE_{\text{calc}}$ (NCCLS,  $r_c$ ), NCCLS and variation of the distribution factor for bicarbonate  $r_c$ ;

$BE_{\text{calc}}$ (SA), Siggaard-Andersen;  $BE_{\text{calc}}$ (*pK*), Siggaard-Andersen and variation of apparent *pK*;  $BE_{\text{calc}}$ ( $r_c$ ) or  $BE_{\text{calc}}$ (SA,  $r_c$ ), Siggaard-Andersen and variation of the distribution factor for bicarbonate  $r_c$ ;  $BE_{\text{calc}}$ (ZA), Zander;  $BE_{\text{calc}}$ (ZA,  $r_c$ ), Zander and variation of the distribution factor for bicarbonate  $r_c$ .

### Introduction

Since the introduction of modern measuring techniques for pH, carbon dioxide and oxygen partial pressures,  $p\text{CO}_2$  and  $p\text{O}_2$ , and the combination with subsequent data processing into blood gas analysis, all standard acid-base parameters can be calculated without nomograms. Most of the algorithms for calculation of the base excess (*BE*, mmol/l) in oxygenated whole blood ( $s\text{O}_2=1.0$ ) *in vitro* are based on the fundamental base excess (*BE*)-equation from Siggaard-Andersen, also called the Van Slyke equation (1, 2). In a general form, this equation can be written as:

$$BE = Z \cdot [c\text{HCO}_3(\text{P}) - c_{7.4}\text{HCO}_3(\text{P})] + \beta \cdot (\text{pH} - 7.4) \quad [1]$$

In eq. [1], the concentration of plasma bicarbonate ( $c\text{HCO}_3$ , mmol/l) at measured pH, and at reference pH (7.4) can be calculated from the known Henderson-Hasselbalch equation for the carbon dioxide/carbonic acid system in the form:

$$c\text{HCO}_3 = \alpha\text{CO}_2 \cdot p\text{CO}_2 \cdot 10^{\text{pH} - \text{pK}'} \quad [2]$$

where  $\alpha\text{CO}_2$  (mmol/l·mmHg) and *pK'* indicate the concentrational solubility of carbon dioxide, and the apparent *pK* of the first dissociation step of carbonic acid in human plasma, respectively. Thus, in calculating whole blood base excess according to eqs. [1] and [2], only the following measured quantities in arterial blood must be known: plasma pH,  $p\text{CO}_2$  (mmHg) and total hemoglobin concentration in blood (*cHb*, g/dl). In the past, several *BE*-equations were developed for use in blood gas calculators which differed only slightly in the solubility factor,  $\alpha\text{CO}_2$ , and in the apparent *pK*, but more significantly in the plasma bicarbonate concentration at reference pH,  $c_{7.4}\text{HCO}_3(\text{P})$ , and in the factor  $\beta$  (mmol/l), the slope of the  $\text{CO}_2$ -equilibration line for whole blood if plotted in a Davenport diagram (plasma bicarbonate concentration vs. pH). At normal plasma protein concentration (72 g/l),  $\beta$  is approximated as a linear function of the total hemoglobin concentration. For  $\beta$ , however, two equations exist:  $9.5 + 1.63 \cdot c\text{Hb}$ , and  $7.7 + 1.43 \cdot c\text{Hb}$ , both originating from Siggaard-Andersen. The first was derived from the original set of experimental data (3, 4) for the base excess curve, and the buffer base curve at normal temperature, formerly at 38 °C, and the second from the revised data set (2) at normal temperature, then at 37 °C. On the other hand, the factor *Z*, which de-

\*E-mail of the corresponding author:  
wlang@mail.uni-mainz.de

scribes the distribution of bicarbonate between red blood cells and plasma depends only on hemoglobin concentration, and is the same in most applied BE-equations:  $Z=1-0.0143 \cdot \text{cHb}$ .

Although only the second equation for  $\beta$  (5) is recommended by the National Committee for Clinical Laboratory Standards (NCCLS), both equations are still in use for calculation of the base excess (6–8). The aim of this work was therefore to test the accuracy of the different BE-equations with respect to a set of recommended values for pH,  $p\text{CO}_2$ , and base excess ( $BE_{\text{ref}}$ ) in normal oxygenated human blood. Since in recent literature no other comprehensive data are available, the revised data of Siggaard-Andersen (2) for the base excess curve, the buffer base curve and the titration curves at constant  $p\text{CO}_2$  at different BE-values were taken as a reference set. How the calculated BE was affected by either variation of Z, or of apparent  $pK$  with changing pH was also tested. However, in most equations for calculation of the base excess, the effect of oxygen saturation of hemoglobin ( $s\text{O}_2$ ) on base excess has not been considered, even in the NCCLS document (5), since measurement of the acid-base status is performed in arterial blood. Only, when base excess is determined in venous blood, which is routinely available by venipuncture, must oxygen saturation be taken into account, e.g. by the use of the practical Van Slyke equation, proposed according to Zander (8).

## Materials and Methods

### Reference values for pH, $p\text{CO}_2$ and BE in oxygenated human blood

The most comprehensive acid-base data for the oxygenated human blood at 37 °C, with a normal concentration of hemoglobin (15 g/dl) and total plasma protein (72 g/l) are those published by Siggaard-Andersen in 1974 (2), and these were used as reference values: the triple set of pH,  $p\text{CO}_2$  and BE for the base excess curve (BE-range: -22 to +22 mmol/l;  $p\text{CO}_2$  in the low or normal range: 12 to 41 mmHg, taken from a table: n=45), the buffer base curve (BE-range: -32 to +32 mmol/l;  $p\text{CO}_2$  mostly in the high range: 49 to 96 mmHg, also from a table: n=65) and the titration curves (from a figure: n=38) at constant  $p\text{CO}_2$  of 28.7, 40 and 66 mmHg at different BE-values: 0, +3, +8, +13, +18, +23, +28, and -2, -7, -12, -17, -22, -27 mmol/l. BE

from the buffer base curve was calculated as the difference between the actual and normal (48 mmol/l) buffer base concentrations. To obtain the corresponding pH values from the original figure representing the titration curves, given as a plot of BE on the ordinate vs. pH at constant  $p\text{CO}_2$ , the figure was scanned into a PC and evaluated at the intersections of a perpendicular through each experimental point of base excess and the pH-axis. Thus, a whole set of reference values (n=148) for pH,  $p\text{CO}_2$  and BE over a wide range of base excess and of carbon dioxide partial pressure in normal oxygenated human blood was available. Under normal buffering conditions, the accuracy of the reference values at given BE, expressed as standard deviation according to Siggaard-Andersen (2, 3), was approximately  $\pm 0.002$  for pH, and  $\pm 0.01$  for  $\Delta \log p\text{CO}_2$ , corresponding to  $\pm 2.3\%$  in  $p\text{CO}_2$ .

### Base excess calculated from the Van Slyke equation as proposed by different authors

The base excess (BE, mmol/l) in human blood was calculated using eqs. [1] and [2] from the Van Slyke equation, originally derived by Siggaard-Andersen (1) and modified by different authors, as shown in Table 1. In this Table, the first five equations have the same Z-factor and differ only in the following parameters:  $\alpha\text{CO}_2$ , the solubility of  $\text{CO}_2$ ,  $pK'$ , the apparent  $pK$  for carbonic acid,  $c_{7,4}\text{HCO}_3^-$ , the concentration of bicarbonate at reference pH=7.400, all in human plasma, and  $\beta$ , the slope of the carbon dioxide equilibration line for whole blood in the Davenport plot. Since, in Table 1, the first equation from Siggaard-Andersen (1966) is obsolete and similar to that proposed by Müller-Plathe, only the following equations were used: the second equation, revised by Siggaard-Andersen (2), abbreviated  $BE_{\text{calc}}$  (SA), the fourth equation, proposed by the National Committee for Clinical Laboratory Standards,  $BE_{\text{calc}}$  (NCCLS), and the fifth equation, proposed by Zander,  $BE_{\text{calc}}$  (ZA) (Table 1).

### The Van Slyke equation modified by variation in Z and in apparent $pK$

According to Siggaard-Andersen (2), the factor Z can be described by the following equation:

$$Z = 1 - (1 - r_c) \cdot \text{Hct} \quad [4]$$

where Hct is the hematocrit and  $r_c$  is defined as the concentrational distribution ratio of bicarbonate between erythrocytes (E), and plasma (P):  $r_c = \text{cHCO}_3^-(\text{E})/\text{cHCO}_3^-(\text{P})$ .

For  $r_c$ , which depends on pH, an empirical relationship was used (2):

$$r_c = 0.57 - 0.28 \cdot \Delta \text{pH} - 0.082 \cdot (\Delta \text{pH})^2 \quad [5]$$

where  $\Delta \text{pH} = \text{pH} - 7.400$ .

**Table 1** The Van Slyke equation (eq. [1]), modified by different authors for calculation of the base excess (BE, mmol/l) in oxy-

genated human blood with normal concentrations of hemoglobin (15 g/dl) and normal total plasma proteins (72 g/l) at 37 °C.

Z	Value	$\beta$ (mmol/l)	Value (mmol/l)	$c_{7,4}\text{HCO}_3^-$ (mmol/l)	$pK'$	$\alpha\text{CO}_2$ (mmol/l·mmHg)	Reference
$1-0.0143 \cdot \text{cHb}$	0.7855	$9.5+1.63 \cdot \text{cHb}$	33.95	24.0	6.10	0.0300	Siggaard-Andersen (3)
$1-0.0143 \cdot \text{cHb}$	0.7855	$7.7+1.43 \cdot \text{cHb}$	29.11	24.1	6.104	0.0306	Siggaard-Andersen (2)
$1-0.0143 \cdot \text{cHb}$	0.7855	$9.5+1.63 \cdot \text{cHb}$	33.95	24.21	6.105	0.0307	Müller-Plathe (6)
$1-0.0143 \cdot \text{cHb}$	0.7855	$7.7+1.43 \cdot \text{cHb}$	29.11	24.8	6.095	0.0307	NCCLS (5)
$1-0.0143 \cdot \text{cHb}$	0.7855	$9.5+1.63 \cdot \text{cHb}$	33.95	24.26	6.10	0.0304	Zander (8)
$1-(1-r_c) \cdot \text{Hct}$	1	$7.7+1.43 \cdot \text{cHb}$	29.11	24.1	6.104	0.0306	this work
$1-0.0143 \cdot \text{cHb}$	0.7855	$7.7+1.43 \cdot \text{cHb}$	29.11	24.1	2	0.0306	this work

<sup>1</sup> Z value variable with pH:  $Z=1 - \text{Hct} \cdot [0.43 + 0.28 \cdot (\text{pH} - 7.4) + 0.082 \cdot (\text{pH} - 7.4)^2]$ , derived from eqs. [4] and [5]

<sup>2</sup>  $pK'$  value variable with pH (eq. [6]):  $pK'=6.125 - \log_{10}(1 + 10^{\text{pH}-8.7})$

Similarly, to take into account the dependency of the apparent pK on the pH in human plasma, the following empirical equation, also derived by Siggaard-Andersen (2), was used:

$$pK' = 6.125 - \log_{10} (1 + 10^{pH-8.7}) \quad [6]$$

The effect on calculated base excess of variation of Z,  $BE_{calc}$  ( $r_c$ ), due to eqs. [4] and [5], and of apparent pK,  $BE_{calc}$  (pK'), due to eq. [6], in the Van Slyke equation was examined first for the revised Siggaard-Andersen equation (see the last two equations in Table 1).

*The Van Slyke equation and the effect of oxygen saturation on base excess*

The effect of oxygen saturation of hemoglobin ( $sO_2$ ) on the base excess was quantitatively described by Siggaard-Andersen (2) and can be written as follows:

$$BE = BE(sO_2) - 0.2 \cdot cHb \cdot (1 - sO_2) \quad [7]$$

BE is the base excess, as originally defined by Siggaard-Andersen, at full oxygen saturation ( $sO_2=1$ ), whereas  $BE(sO_2)$  is the base excess calculated by the Van Slyke equation from measured pH,  $pCO_2$ , cHb and  $sO_2$  in the blood sample. In par-

ticular, for completely deoxygenated blood ( $sO_2=0$ ) with normal hemoglobin concentration (cHb=15 g/dl), the correction term is 3 mmol/l which must be subtracted from the calculated base excess at zero oxygen saturation,  $BE(sO_2=0)$ , and in mixed venous blood ( $sO_2=0.75$ ) it is 0.75 mmol/l. Therefore, this was not taken into account in most equations used in blood gas calculators, which are programmed to accept only arterial blood samples. For routine diagnosis in the blood, however, most samples are obtained by venipuncture from the cubital vein with varying oxygen saturation ( $sO_2 \approx 0.5$ ), and for calculation of the base excess from venous blood the correction term for oxygen saturation ( $\approx 1.5$  mmol/l) was included in the Van Slyke equation proposed by Zander (8). It is evident that the base excess (BE) obtained from the measurement in venous blood must be the same as that measured in arterial blood.

*Accuracy of calculated base excess*

The base excess calculated from the different Van Slyke equations,  $BE_{calc}$ , was compared with the reference base excess,  $BE_{ref}$ . With respect to the latter, accuracy was defined as the difference between calculated base excess and reference base

**Table 2** Comparison of base excess calculated ( $BE_{calc}$ ) using equations proposed by Siggaard-Andersen (SA), the National Committee for Clinical Laboratory Standards (NCCLS), Zander (ZA), and modified by variation of the distribution ratio of bicarbonate between red blood cells and plasma ( $r_c$ ), and of apparent pK (pK') with reference values for BE ( $BE_{ref}$ ).

pH	$pCO_2$ (mmHg)	$BE_{ref}$ (mmol/l)	$BE_{calc}$ (SA) (mmol/l)	$BE_{calc}$ (NCCLS) (mmol/l)	$BE_{calc}$ (ZA) (mmol/l)	$BE_{calc}$ ( $r_c$ ) (mmol/l)	$BE_{calc}$ (pK') (mmol/l)
Base excess curve <sup>1</sup>							
7.226	11.6	-22	-19.23	-19.69	-20.01	-20.30	-19.29
7.229	13.5	-21	-18.52	-18.97	-19.29	-19.55	-18.59
7.233	15.3	-20	-17.81	-18.25	-18.56	-18.79	-17.89
7.237	17.1	-19	-17.08	-17.50	-17.82	-18.01	-17.17
7.242	18.9	-18	-16.31	-16.71	-17.02	-17.19	-16.40
7.247	20.6	-17	-15.56	-15.94	-16.25	-16.38	-15.65
7.253	22.3	-16	-14.75	-15.12	-15.41	-15.52	-14.85
7.259	24.0	-15	-13.92	-14.27	-14.56	-14.63	-14.03
7.266	25.7	-14	-13.03	-13.37	-13.64	-13.69	-13.14
7.273	27.3	-13	-12.16	-12.48	-12.74	-12.76	-12.27
7.281	28.9	-12	-11.22	-11.52	-11.77	-11.76	-11.33
7.289	30.4	-11	-10.29	-10.57	-10.81	-10.77	-10.40
7.297	31.7	-10	-9.41	-9.67	-9.89	-9.84	-9.52
7.306	33.0	-9	-8.46	-8.70	-8.91	-8.83	-8.57
7.315	34.1	-8	-7.55	-7.78	-7.97	-7.88	-7.66
7.324	35.2	-7	-6.63	-6.84	-7.01	-6.91	-6.73
7.334	36.1	-6	-5.71	-5.90	-6.04	-5.94	-5.80
7.344	37.0	-5	-4.76	-4.94	-5.06	-4.94	-4.84
7.354	37.8	-4	-3.83	-3.99	-4.09	-3.97	-3.90
7.365	38.5	-3	-2.85	-3.00	-3.07	-2.96	-2.91
7.377	39.1	-2	-1.84	-1.96	-2.00	-1.90	-1.87
7.388	39.6	-1	-0.90	-0.01	-1.02	-0.93	-0.91
7.400	40.0	+0	+0.08	-0.01	0.00	+0.08	+0.09
7.412	40.3	+1	+1.03	+0.96	+1.00	+1.06	+1.07
7.425	40.5	+2	+2.03	+1.97	+2.05	+2.08	+2.10
7.438	40.6	+3	+3.00	+2.96	+3.07	+3.07	+3.10
7.451	40.6	+4	+3.93	+3.91	+4.06	+4.02	+4.08
7.465	40.6	+5	+4.97	+4.96	+5.15	+5.06	+5.15
7.479	40.5	+6	+5.96	+5.98	+6.20	+6.07	+6.20
7.494	40.3	+7	+7.00	+7.03	+7.30	+7.10	+7.29
7.509	40.0	+8	+8.00	+8.04	+8.35	+8.09	+8.35
7.525	39.6	+9	+9.03	+9.09	+9.44	+9.11	+9.44
7.541	39.1	+10	+10.01	+10.08	+10.48	+10.07	+10.50
7.558	38.5	+11	+11.01	+11.11	+11.56	+11.05	+11.58
7.576	37.9	+12	+12.11	+12.22	+12.73	+12.12	+12.77

Table 2 Continued.

pH	pCO <sub>2</sub> (mmHg)	BE <sub>ref</sub> (mmol/l)	BE <sub>calc</sub> (SA) (mmol/l)	BE <sub>calc</sub> (NCCLS) (mmol/l)	BE <sub>calc</sub> (ZA) (mmol/l)	BE <sub>calc</sub> (r <sub>c</sub> ) (mmol/l)	BE <sub>calc</sub> (pK') (mmol/l)
7.594	37.2	+13	+13.14	+13.27	+13.83	+13.11	+13.91
7.613	36.4	+14	+14.19	+14.34	+14.95	+14.11	+15.07
7.633	35.5	+15	+15.25	+15.41	+16.09	+15.11	+16.25
7.654	34.5	+16	+16.31	+16.48	+17.23	+16.10	+17.45
7.676	33.5	+17	+17.45	+17.63	+18.45	+17.15	+18.75
7.699	32.3	+18	+18.47	+18.67	+19.56	+18.08	+19.94
7.724	31.1	+19	+19.65	+19.87	+20.84	+19.14	+21.33
7.750	29.8	+20	+20.79	+21.02	+22.08	+20.14	+22.69
7.777	28.4	+21	+21.85	+22.10	+23.25	+21.06	+24.01
7.806	26.9	+22	+22.92	+23.17	+24.43	+21.96	+25.36
$\Delta BE_{\text{mean}}^2$		$\pm 0.91$	$\pm 0.76$	$\pm 0.96$	$\pm 0.46$	$\pm 1.31$	
Buffer base curve <sup>1</sup>							
6.889	15.6	-32	-28.35	-28.84	-30.41	-31.14	-28.98
6.890	21.0	-31	-27.52	-28.00	-29.58	-30.23	-28.18
6.891	26.2	-30	-26.73	-27.19	-28.78	-29.35	-27.41
6.893	31.1	-29	-25.94	-26.38	-27.98	-28.48	-26.64
6.896	35.8	-28	-25.14	-25.56	-27.17	-27.59	-25.86
6.901	40.3	-27	-24.29	-24.69	-26.29	-26.64	-25.03
6.908	44.6	-26	-23.37	-23.75	-25.35	-25.62	-24.13
6.917	48.7	-25	-22.38	-22.74	-24.32	-24.51	-23.16
6.925	52.6	-24	-21.43	-21.78	-23.34	-23.46	-22.23
6.934	56.3	-23	-20.45	-20.78	-22.32	-22.36	-21.27
6.943	59.8	-22	-19.47	-19.78	-21.31	-21.27	-20.31
6.952	63.1	-21	-18.50	-18.79	-20.30	-20.19	-19.35
6.961	66.2	-20	-17.53	-17.80	-19.30	-19.11	-18.40
6.970	69.1	-19	-16.57	-16.83	-18.30	-18.05	-17.46
6.979	71.8	-18	-15.62	-15.86	-17.32	-17.00	-16.52
6.989	74.3	-17	-14.63	-14.85	-16.29	-15.90	-15.55
6.998	76.7	-16	-13.69	-13.89	-15.30	-14.86	-14.61
7.007	79.0	-15	-12.74	-12.92	-14.32	-13.82	-13.67
7.017	81.1	-14	-11.74	-11.90	-13.28	-12.72	-12.69
7.027	83.0	-13	-10.76	-10.90	-12.26	-11.64	-11.72
7.036	84.7	-12	-9.85	-9.98	-11.32	-10.65	-10.82
7.046	86.3	-11	-8.88	-8.99	-10.30	-9.59	-9.86
7.056	87.7	-10	-7.93	-8.02	-9.31	-8.55	-8.91
7.066	89.0	-9	-6.97	-7.05	-8.32	-7.51	-7.96
7.076	90.2	-8	-6.02	-6.07	-7.32	-6.47	-7.01
7.086	91.3	-7	-5.06	-5.10	-6.32	-5.44	-6.06
7.096	92.3	-6	-4.10	-4.12	-5.33	-4.40	-5.11
7.106	93.1	-5	-3.17	-3.18	-4.36	-3.40	-4.18
7.117	93.8	-4	-2.17	-2.16	-3.31	-2.32	-3.18
7.127	94.4	-3	-1.25	-1.22	-2.35	-1.34	-2.25
7.137	94.9	-2	-0.33	-0.29	-1.39	-0.35	-1.33
7.148	95.3	-1	+0.66	+0.72	-0.36	+0.70	-0.34
7.159	95.6	0	+1.64	+1.72	+0.67	+1.75	+0.65
7.169	95.8	+1	+2.53	+2.63	+1.60	+2.70	+1.55
7.180	95.9	+2	+3.50	+3.62	+2.61	+3.72	+2.52
7.191	96.0	+3	+4.49	+4.62	+3.64	+4.76	+3.52
7.202	96.0	+4	+5.46	+5.61	+4.66	+5.79	+4.51
7.213	95.9	+5	+6.42	+6.59	+5.67	+6.80	+5.48
7.224	95.7	+6	+7.37	+7.56	+6.66	+7.79	+6.45
7.235	95.4	+7	+8.31	+8.51	+7.63	+8.76	+7.40
7.247	95.0	+8	+9.32	+9.54	+8.69	+9.81	+8.43
7.258	94.6	+9	+10.24	+10.48	+9.66	+10.77	+9.38
7.269	94.1	+10	+11.15	+11.41	+10.62	+11.71	+10.31
7.281	93.6	+11	+12.17	+12.44	+11.68	+12.76	+11.36
7.293	93.0	+12	+13.17	+13.46	+12.73	+13.78	+12.39
7.305	92.3	+13	+14.15	+14.45	+13.75	+14.78	+13.40
7.317	91.5	+14	+15.10	+15.42	+14.75	+15.74	+14.38
7.329	90.7	+15	+16.05	+16.39	+15.76	+16.71	+15.38
7.341	89.9	+16	+17.02	+17.38	+16.77	+17.69	+16.39

**Table 2** Continued.

pH	$p\text{CO}_2$ (mmHg)	$BE_{\text{ref}}$ (mmol/l)	$BE_{\text{calc}}(\text{SA})$ (mmol/l)	$BE_{\text{calc}}(\text{NCCLS})$ (mmol/l)	$BE_{\text{calc}}(\text{ZA})$ (mmol/l)	$BE_{\text{calc}}(r_c)$ (mmol/l)	$BE_{\text{calc}}(pK')$ (mmol/l)
7.353	89.0	+17	+17.96	+18.33	+17.76	+18.63	+17.37
7.366	88.0	+18	+18.97	+19.36	+18.82	+19.64	+18.43
7.379	86.9	+19	+19.95	+20.35	+19.84	+20.61	+19.46
7.392	85.8	+20	+20.93	+21.35	+20.88	+21.58	+20.49
7.405	84.6	+21	+21.86	+22.30	+21.86	+22.50	+21.49
7.418	83.4	+22	+22.80	+23.26	+22.85	+23.42	+22.49
7.431	82.2	+23	+23.74	+24.21	+23.85	+24.34	+23.50
7.444	80.9	+24	+24.63	+25.11	+24.79	+25.20	+24.46
7.457	79.6	+25	+25.52	+26.02	+25.72	+26.05	+25.42
7.470	78.2	+26	+26.34	+26.86	+26.60	+26.84	+26.33
7.484	76.7	+27	+27.23	+27.75	+27.54	+27.68	+27.30
7.498	75.2	+28	+28.11	+28.64	+28.47	+28.50	+28.27
7.512	73.6	+29	+28.91	+29.46	+29.33	+29.25	+29.17
7.526	72.0	+30	+29.70	+30.26	+30.17	+29.97	+30.06
7.540	70.4	+31	+30.47	+31.04	+31.00	+30.68	+30.94
7.555	68.7	+32	+31.28	+31.86	+31.87	+31.42	+31.87
$\Delta BE_{\text{mean}}^2$			$\pm 1.86$	$\pm 1.80$	$\pm 0.74$	$\pm 1.34$	$\pm 1.58$
Base excess titration curves at constant $p\text{CO}_2$ : 28.7, 40 and 66 mmHg <sup>1</sup>							
6.949	28.7	-27	-24.43	-24.86	-26.26	-26.67	-24.59
7.076	28.7	-22	-19.88	-20.28	-21.22	-21.40	-20.05
7.181	28.7	-17	-15.71	-16.06	-16.65	-16.69	-15.87
7.281	28.7	-12	-11.29	-11.59	-11.84	-11.83	-11.41
7.375	28.7	-7	-6.63	-6.87	-6.82	-6.86	-6.66
7.459	28.7	-2	-1.96	-2.13	-1.82	-2.00	-1.84
7.490	28.7	0	-0.09	-0.24	+0.17	-0.10	+0.10
7.535	28.7	+3	+2.77	+2.67	+3.21	+2.79	+3.11
7.608	28.7	+8	+7.85	+7.83	+8.57	+7.81	+8.51
7.675	28.7	+13	+13.05	+13.13	+14.04	+12.83	+14.16
7.739	28.7	+18	+18.60	+18.77	+19.84	+18.06	+20.31
7.798	28.7	+23	+24.28	+24.56	+25.76	+23.31	+26.76
6.900	40	-27	-24.37	-24.77	-26.38	-26.74	-24.58
7.016	40	-22	-19.87	-20.23	-21.44	-21.53	-20.87
7.113	40	-17	-15.69	-16.00	-16.88	-16.81	-15.92
7.206	40	-12	-11.21	-11.47	-12.04	-11.87	-11.42
7.291	40	-7	-6.64	-6.83	-7.14	-6.95	-6.79
7.370	40	-2	-1.88	-2.00	-2.07	-1.94	-1.93
7.400	40	0	+0.08	-0.01	0.00	+0.08	+0.09
7.443	40	+3	+3.04	+3.00	+3.13	+3.11	+3.16
7.507	40	+8	+7.84	+7.88	+8.18	+7.94	+8.18
7.570	40	+13	+13.08	+13.21	+13.67	+13.10	+13.74
7.628	40	+18	+18.42	+18.66	+19.25	+18.27	+19.51
7.681	40	+23	+23.81	+24.14	+24.85	+23.38	+25.42
7.731	40	+28	+29.39	+29.83	+30.63	+28.58	+31.64
6.829	66	-27	-23.58	-23.92	-25.85	-26.05	-23.89
6.928	66	-22	-19.16	-19.45	-21.05	-20.96	-19.50
7.011	66	-17	-15.03	-15.27	-16.60	-16.29	-15.40
7.093	66	-12	-10.49	-10.66	-11.74	-11.26	-10.86
7.169	66	-7	-5.79	-5.89	-6.75	-6.16	-6.15
7.234	66	-2	-1.33	-1.36	-2.03	-1.40	-1.65
7.261	66	0	+0.66	+0.67	+0.07	+0.70	+0.37
7.300	66	+3	+3.70	+3.75	+3.26	+3.87	+3.46
7.357	66	+8	+8.50	+8.64	+8.28	+8.81	+8.38
7.410	66	+13	+13.40	+13.63	+13.40	+13.78	+13.45
7.460	66	+18	+18.46	+18.79	+18.66	+18.84	+18.74
7.505	66	+23	+23.42	+23.84	+23.80	+23.73	+23.97
7.549	66	+28	+28.69	+29.22	+29.25	+28.85	+29.59
$\Delta BE_{\text{mean}}^2$			$\pm 1.28$	$\pm 1.19$	$\pm 0.92$	$\pm 0.52$	$\pm 1.55$

<sup>1</sup> reference data from Siggaard-Andersen (2); <sup>2</sup> mean deviation between calculated and reference base excess, defined in eq. [8]

excess,  $d_i = BE_{\text{calc}} - BE_{\text{ref}}$ , and for comparison, the mean deviation of base excess ( $\Delta BE_{\text{mean}}$ ) was taken as the square root of the quadratic sum of all  $d_i$ , divided by the total number (n) of values in the reference set:

$$\Delta BE_{\text{mean}} = \pm \sqrt{(\sum d_i^2 / n)} \quad [8]$$

## Results and Discussion

The calculated base excess from the Van Slyke equation according to Siggaard-Andersen,  $BE_{\text{calc}}$  (SA), according to the National Committee for Clinical Laboratory Standards,  $BE_{\text{calc}}$  (NCCLS), and according to Zander,  $BE_{\text{calc}}$  (ZA), with variations in Z,  $BE_{\text{calc}}$  ( $r_c$ ), and in apparent pK,  $BE_{\text{calc}}$  (pK'), were compared with the corresponding reference values for pH,  $pCO_2$  and BE for the base excess curve, the buffer base curve and the base excess titration curves at constant  $pCO_2$  of 28.7, 40 and 66 mmHg (Table 2). For the base excess curve (n=45), the mean deviation of the calculated base excess ( $\Delta BE_{\text{mean}}$ ) was:  $\pm 0.91$  (SA),  $\pm 0.76$  (NCCLS),  $\pm 0.96$  (ZA),  $\pm 0.46$  ( $r_c$ ) and  $\pm 1.31$  (pK'); for the buffer base curve (n=65):  $\pm 1.86$  (SA),  $\pm 1.80$  (NCCLS),  $\pm 0.74$  (ZA),  $\pm 1.34$  ( $r_c$ ) and  $\pm 1.58$  (pK'); and for the base excess titration curves at constant  $pCO_2$  (n=38):  $\pm 1.28$  (SA),  $\pm 1.19$  (NCCLS),  $\pm 0.92$  (ZA),  $\pm 0.52$  ( $r_c$ ) and  $\pm 1.55$  (pK'). With respect to the base excess curve, all originally proposed equations, (SA), (NCCLS) and (ZA), yielded excellent results (<1 mmol/l), in contrast, however, to those in the other two reference sets (>1 mmol/l). It is also obvious that the different approximations in the Van Slyke equation do not necessarily lead to better results. Whereas the accuracy of the calculated base excess is significantly improved by varying Z,  $BE_{\text{calc}}$  ( $r_c$ ), in all three reference sets, it is decreased by a variation of the apparent pK,  $BE_{\text{calc}}$  (pK'), in the two sets for the base excess curve and for the base excess titration curves, and only slightly increased in the buffer base curve. This is essentially in agreement with Gabel (9), who found that the results were not improved by the correction of apparent pK for pH, using a linear relation from Severinghaus. Therefore, only after the successful variation of Z in the Van Slyke equation, according to Siggaard-Andersen, this variation was

also tested in the other two equations, according to NCCLS and to Zander, abbreviated (SA,  $r_c$ ), (NCCLS,  $r_c$ ), and (ZA,  $r_c$ ). In Table 3, the mean deviation of the calculated base excess,  $\Delta BE_{\text{mean}}$ , from all equations decreases significantly for the base excess curve. It also decreases for the buffer base curve and for the base excess titration curves, but correspondingly increases if it is calculated according to Zander. The variation of Z in the Van Slyke equation can be compared with the Thomas algorithm (10), a rigorous approach which includes the Donnan effect, plasma protein concentration, carbamate formation and the effect of oxygen saturation of hemoglobin, and which was also used for the calculation of the base excess. In comparison to simple equations, the mean accuracy is not superior (Table 3). With respect to the reference values (n=148) as a whole set, the best results (<1 mmol/l) were obtained by calculation from the simple Van Slyke equation, according to Zander ( $\pm 0.86$ ), from the Thomas algorithm ( $\pm 0.88$ ) or from the modified Van Slyke equation by variation of Z, also according to Zander ( $\pm 0.94$ ) and according to Siggaard-Andersen ( $\pm 0.96$ ). This order is caused primarily by the weight of the values (n=65) for the buffer base curve and the mean accuracy of calculated base excess, which is greater in the simple Van Slyke equation according to Zander ( $\pm 0.74$ ) than in all other equations (>1 mmol/l). The most striking difference in the Van Slyke equation according to Zander is the use of the old  $\beta$  value from the literature (6–8), which still continued to be used, even though the revised value was established by Siggaard-Andersen in 1974 (2).

## Conclusions

### Recommended Van Slyke equation

From several equations used for calculation of the base excess and checked for accuracy by comparison with recommended reference values in oxygenated normal human blood taken from Siggaard-Andersen (2), the Van Slyke equation according to Zander yields the best results ( $\pm 0.86$ ). Even though approximation in the particular Van Slyke equation is improved by either varia-

**Table 3** Mean deviation of calculated base excess ( $\Delta BE_{\text{mean}}$ ) from the Van Slyke equation according to Siggaard-Andersen (SA), according to the National Committee for Clinical Laboratory Standards (NCCLS) and according to Zander (ZA), in comparison to subsequent variation of Z: (SA,  $r_c$ ), (NCCLS,  $r_c$ )

BE-reference data	n <sup>1</sup>	Mean deviation of calculated base excess, $\Delta BE_{\text{mean}}$ , due to:						
		(SA) (mmol/l)	(SA, $r_c$ ) (mmol/l)	(NCCLS) (mmol/l)	(NCCLS, $r_c$ ) (mmol/l)	(ZA) (mmol/l)	(ZA, $r_c$ ) (mmol/l)	Thomas-algorithm (mmol/l)
BE-curve	45	$\pm 0.91$	$\pm 0.46$	$\pm 0.76$	$\pm 0.32$	$\pm 0.96$	$\pm 0.64$	$\pm 0.68$
BB-curve	65	$\pm 1.86$	$\pm 1.34$	$\pm 1.80$	$\pm 1.47$	$\pm 0.74$	$\pm 1.10$	$\pm 1.15$
BE-titration curves	38	$\pm 1.28$	$\pm 0.52$	$\pm 1.19$	$\pm 0.58$	$\pm 0.92$	$\pm 0.96$	$\pm 0.46$
Total	148	$\pm 1.48$	$\pm 0.96$	$\pm 1.40$	$\pm 1.03$	$\pm 0.86$	$\pm 0.94$	$\pm 0.88$

<sup>1</sup> number of values in the reference set

and (ZA,  $r_c$ ), and to the Thomas-algorithm (10) for the different sets of reference values for the base excess ( $BE_{\text{ref}}$ ) from Table 2: base excess curve, buffer base curve, and base excess titration curves.

tion of Z in the distribution ratio ( $r_c$ ) of bicarbonate between cells and plasma, or of apparent pK with pH, its accuracy is greatest, and 83.8% of all values (n=148) do not deviate by more than  $\pm 1$  mmol/l from reference BE.

Therefore, the equation according to Zander should be preferred to that originally proposed by Siggaard-Andersen (SA), or by the National Committee for Clinical Laboratory Standards (NCCLS), and can be recommended for calculation of the whole blood base excess (BE) in the following form:

$$BE = (1 - 0.0143 \cdot cHb) \cdot \{ [0.0304 \cdot pCO_2 \cdot 10^{pH-6.1} - 24.26] + (9.5 + 1.63 \cdot cHb) \cdot (pH - 7.4) \} - 0.2 \cdot cHb \cdot (1 - sO_2),$$

where the additional last term takes into account the oxygen saturation ( $sO_2$ ), so that base excess is obtainable with high accuracy from measured quantities of pH,  $pCO_2$ , cHb and  $sO_2$  in any sample, irrespective of whether venous or arterial blood is used (8).

## References

1. Siggaard-Andersen O. The Van Slyke equation. *Scand J Clin Lab Invest* 1977; 37:Suppl 146:15–20.
2. Siggaard-Andersen O. The acid-base status of the blood, 4th ed. Copenhagen: Munksgaard, 1974:44–60.
3. Siggaard-Andersen O, Engel K. A new acid-base nomogram: an improved method for the calculation of the relevant blood acid-base data. *Scand J Clin Invest* 1960; 12:177–86.
4. Siggaard-Andersen O. Titratable acid or base of body fluids. *Ann NY Acad Sci* 1966; 133:41–58.
5. National Committee for Clinical Laboratory Standards (NCCLS) Document C12-T2. Definitions of quantities and conventions related to blood pH and gas analysis, 2nd ed. NCCLS 1991; 11(18):1–7.
6. Müller-Plathe O. Säure-Basen-Haushalt und Blutgase, 2nd ed. Stuttgart, New York: Thieme, 1982:180.
7. Müller-Plathe O. Die Basenabweichung: Definitionen und Konventionen. *Anästhesiol Intensivmed Notfallmed Schmerzther* 1995; 30:Suppl 1:34–5.
8. Zander R. Die korrekte Bestimmung des Base-Excess (BE, mmol/l) im Blut. *Anästhesiol Intensivmed Notfallmed Schmerzther* 1995; 30:Suppl 1:36–8.
9. Gabel RA. Algorithms for calculating and correcting blood-gas and acid-base variables. *Resp Physiol* 1980; 42:211–32.
10. Thomas LJ. Algorithms for selected blood acid-base and blood gas calculations. *J Appl Physiol* 1972; 33:154–8.

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Corresponding author: Dr. Werner Lang, Institut für Physiologie und Pathophysiologie, Fachbereich Medizin der Johannes Gutenberg-Universität, Saarstrasse 21, 55099 Mainz, Germany  
Phone: 49-6131-3925778, Fax: 49-6131-3924079  
E-mail: wlang@mail.uni-mainz.de