

# Formalization of Siggaard-Andersen nomogram and derivation of the base excess for the physicochemical domain

*A supplementary material to Modern and traditional approaches combined into an effective gray-box mathematical model of full-blood acid-base by Filip Ježek and Jiří Kofránek, 2018*

## Formalization of the Siggaard-Andersen nomogram

The Siggaard-Andersen nomogram [1] used to be solved graphically with a pH-pCO<sub>2</sub> semi-logarithmic graph by finding appropriate values on the base excess (BE) and buffer base (BB) curves and connecting the two points by a line on which we read the pCO<sub>2</sub> and pH values relationship. With the emergence of computers, the author of this nomogram then approximated it by the well-known Van Slyke equation ([2], further updated in [3]). To minimize both the approximation and extrapolation errors (especially for haemoglobin), we employ our own methodology to give an exact formalization of the original Siggaard-Andersen nomogram. Our approach is based on the graphical method of reading from the semi-logarithmic nomogram.

Because the haemoglobin (Hb) buffer strength depends also on oxygen saturation (sO<sub>2</sub>), we assume full oxygen saturation (sO<sub>2</sub> = 1). Otherwise, the BE could be corrected to BE<sub>ox</sub> (base excess of a full oxygenated blood), as described in [4]:

$$(1) \quad \underline{BE_{ox} = BE - 0.2 \cdot (1 - sO_2) \cdot Hb}; \quad [\text{mEq/l; mEq/l; -; g/100ml}]$$

For further reference, we assume full saturation and thus BE<sub>ox</sub> = BE. Then, the buffer base (BB) can be computed from BE as follows [1]:

$$(2) \quad BB = BE + 0.42 \cdot Hb + 41.7; \quad [\text{mEq/l; mEq/l; g /100ml}]$$

These values are then used as an input to the BE and BB curves to provide pCO<sub>2</sub> and pH values. We formulate the functions of BB and BE curves and fit them to the original data of [5], as reproduced by [6], using one fourth and three sixth-order polynomials with the Matlab Curve Fitting Toolbox:

$$(3) \quad f_{pCO_2BB}(BB) = \sum_{i=0}^6 C_{pCO_2BB_i} \cdot BB^i$$

$$(4) \quad f_{pHBB}(BB) = \sum_{i=0}^6 C_{pHBB_i} \cdot BB^i$$

$$(5) \quad f_{pCO_2BE}(BE) = \sum_{i=0}^6 C_{pCO_2BE_i} \cdot BE^i$$

$$(6) \quad f_{pHBE}(BE) = \sum_{i=0}^4 C_{pHBE_i} \cdot BE^i$$

|                 | i=0      | i=1                   | i=2                    | i=3                     | i=4                    | i=5                     | i=6                   |
|-----------------|----------|-----------------------|------------------------|-------------------------|------------------------|-------------------------|-----------------------|
| $C_{pCO_2BB_i}$ | -97.0551 | 8.2352                | -38.1x10 <sup>-3</sup> | -3.2x10 <sup>-3</sup>   | 72.7x10 <sup>-6</sup>  | -640.9x10 <sup>-9</sup> | 2.1x10 <sup>-9</sup>  |
| $C_{pHBB_i}$    | 39.9871  | 0.3537                | -46.5x10 <sup>-3</sup> | 231.6x10 <sup>-6</sup>  | 3.8x10 <sup>-6</sup>   | -513.9x10 <sup>-9</sup> | 8.3x10 <sup>-9</sup>  |
| $C_{pCO_2BE_i}$ | 7.2888   | -0.0678               | 4.07x10 <sup>-3</sup>  | -111.7x10 <sup>-6</sup> | 1.6x10 <sup>-6</sup>   | -13.0x10 <sup>-9</sup>  | 0.40x10 <sup>-9</sup> |
| $C_{pHBE_i}$    | 7.4001   | 11.9x10 <sup>-3</sup> | 175.6x10 <sup>-6</sup> | 2.5x10 <sup>-6</sup>    | 131.3x10 <sup>-9</sup> |                         |                       |

Table 1: Parameter values for precise formalisation of the SA nomogram (eq. 3 - 6)

Given the equation of the line as

$$(7) \quad y = mx + c$$

where  $m$  can be expressed from two measurement points ( $x_1, y_1$ ) and ( $x_2, y_2$ ) as:

$$(8) \quad m = (y_2 - y_1)/(x_2 - x_1)$$

and the y-intercept  $c$  is given by the point ( $x_1, y_1$ ) for  $x_1 = 0$ , we derive

$$(9) \quad y = \frac{(x - x1)(y2 - y1)}{(x2 - x1)} + y1$$

where the x values are logarithmic readings of pCO<sub>2</sub>, whereas the y values are readings of pH. We then substitute the functions into the line equation, such that:

(10)

$$pH = \frac{(\log_{10} pCO_2 - \log_{10} f_{pCO_2BB})(f_{pHBB} - f_{pHBE})}{(\log_{10} f_{pCO_2BB} - \log_{10} f_{pCO_2BE})} + f_{pHBB}$$

We can use any equation-based modeling language to derive the following function for pH from equations (2) - (10) and find a steady-state solution for the pH:

$$(11) \quad pH_{SA} = f_{SA}(BE, pCO_2, Hb, sO_2)$$

This method of formalization of the SA nomogram provides a perfect fit with the original data, at the cost of more complex computations. Especially it does feature a correct linear asymptotic behavior for extreme values of Hb, which is critical for our approach.

For a graphical comparison to the single Van Slyke equation [2] and the equation provided by Zander [7], which is claimed to be even more precise [6], see Figure S1. The sum of the RMS error of our approach with the original data [8] is below  $10^{-3}$  [unitless]. Thus, this expression of Siggaard-Andersen technique yields superior results as exact as the nomogram itself and does not introduce any additional error. The source code for the Modelica implementation is accessible at [9] in *FullBloodAcidBase.FullBloodEmpirical.SAoriginal*.

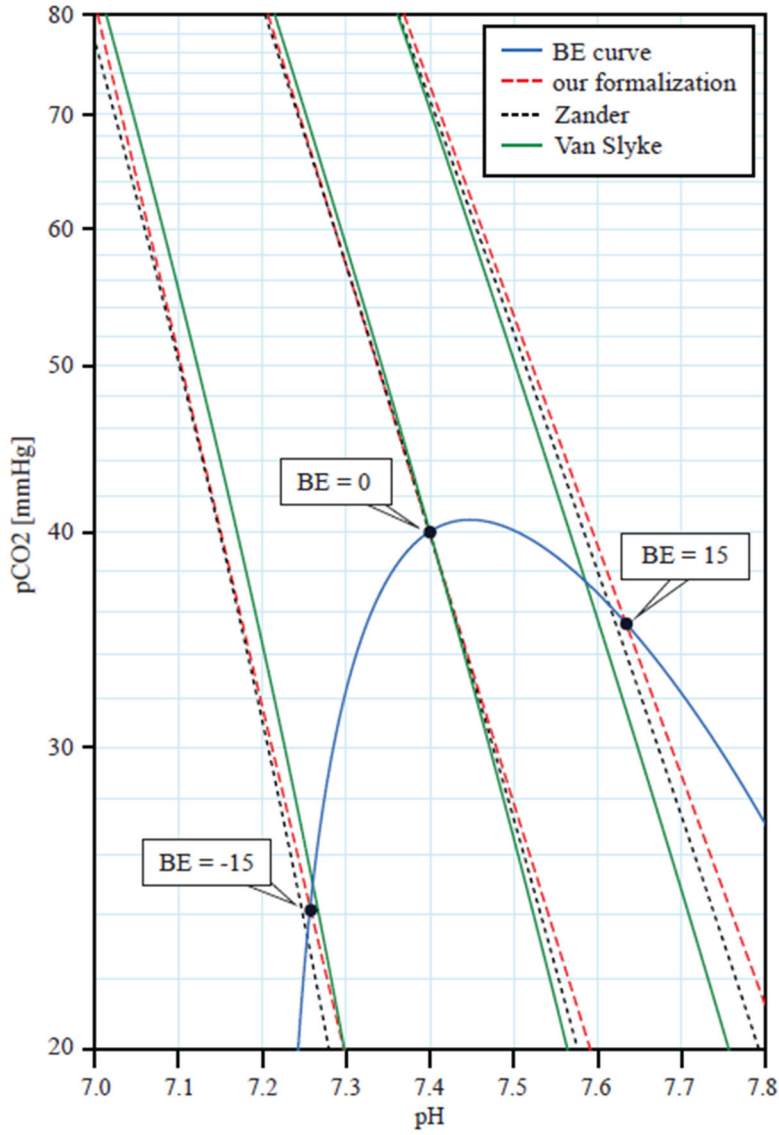


Figure S1: The result of our formalization in comparison to the “Van Slyke equation” formalization by Siggaard-Andersen [4] and to the formalization by Zander [7] for BE -15, 0 and 15.

## Derivation of the Base Excess in the physico-chemical domain

We employ the model described by Fencl et al. [10]:

$$(12) \quad HCO_3 = \frac{24.4 \times 10^{-9} \times pCO_2}{10^{-pH}}$$

$$(13) \quad P = -Pi \times (0.309 pH - 0.469)$$

$$(14) \quad \text{albuminCharge} = -(10\text{Alb}) \times (0.123\text{pH} - 0.631)$$

$$(15) \quad \text{SID} + \text{albuminCharge} + P + (-1 \cdot \text{HCO}_3) = 0$$

*albuminCharge*, *P* and *SID* are the charge concentrations of the respective substances, expressed in [mEq/l], whereas *Alb* is the input albumin concentration in [g/dl] and *Pi* is the input phosphate concentration in [mmol/l]. To be consistent with the Fencel's formulation,  $\text{HCO}_3^-$  is also expressed as the concentration in [mmol/l]. Equations (11) – (14) form a functional expression for the calculation of pH from physico-chemical (further shortened to *PC*) model, which can be numerically solved by the Modelica tool to find a steady-state solution to the equations:

$$(16) \quad \text{pH}_{PC} = f_{\text{pH}_{PC}}(\text{SID}, \text{pCO}_2, \text{Pi}, \text{Alb})$$

For computation of *SID*, the Modelica language provides a straightforward reuse of the physicochemical model. We employ the same equations (11) - (14) and specify the pH as an input and *SID* as an output variable, such that:

$$(17) \quad \text{SID} = f_{\text{SID}_{PC}}(\text{pH}, \text{pCO}_2, \text{Pi}, \text{Alb})$$

For computation of *NSID*, we just specify the normal conditions as the inputs:

$$(18) \quad \text{NSID} = f_{\text{NSID}_{PC}}(\text{pH} = 7.4, \text{pCO}_2 = 40 \text{ mmHg}, \text{Alb}, \text{Pi})$$

, where *Alb* [g/dl] and *Pi* [mmol/l] are the actual values. Then, the base excess for physicochemical model ( $\text{BE}_{PC}$ ) reads:

$$(19) \quad \text{BE}_{PC} = \text{SID} - \text{NSID}$$

For more precise yet computationally more demanding calculation, one might employ more detailed calculations of albumin and phosphate charge (equations 12 - 14), e.g. the Figge-Fencel model [11]. For implementation of both cases, as well as detailed physico-chemical approach by Wolf [12], see the model source code [9].

# References

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