MODELING OF PHYSIOLOGICAL ACID–BASE EQUILIBRIA IN SINGLE AND MULTIPLE COMPARTMENTS

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Acid–base physiology is of interest in clinical medicine because of the substantial morbidity and mortality associated with acid–base disorders. In order to classify and treat these disorders, it is desirable to understand and quantify them, and therefore the ability to calculate physiological concentrations relevant to acid–base homeostasis is also of interest. Equilibrium thermodynamics has been able to provide an accurate model for acid–base equilibria for over fifty years, but until relatively recently, the necessary input data and computing power to apply such calculations to physiological systems were not available for routine application.

Using a simple conceptual model, it is shown how complete expressions for total titratable base (CB) and strong ion difference (SID) can be obtained to describe physiological acid–base equilibria in single physiological compartments (1). In the presence of a steady state across compartments, the relevant multicompartment equilibria can also be computed (2).

Using theoretical and experimental input data (1,2), explicit equations can be derived for the plasma compartment and the erythrocyte compartment to yield a modelforhumanwholebloodin vitrogivenbythelinear approximations

$$\begin{aligned}\mathrm{C_B(B)} = &\{1 - 0.49\phi_B(\mathrm{E})\}[\mathrm{HCO_3^-}]_P \\ &+ \{1 - \phi_B(\mathrm{E})\}\{\mathrm{C}_{Alb}(\mathrm{P})(8.0\,\mathrm{pH(P)} \\ &+ 53) + \mathrm{C}_{Phos}(\mathrm{P})(0.30\,\mathrm{pH(P)} - 0.4)\} \\ &+ \mathrm{C}_{Hgb}(\mathrm{B})\{10.2\,\mathrm{pH(P)} + 12.4\} + \phi_B(\mathrm{E}) \\ &\{0.07\,\mathrm{pH(P)} - 0.5\} \qquad (1)\end{aligned}$$

and

$$\begin{aligned}\mathrm{SID(B)} = &\{1 - 0.49\phi_B(\mathrm{E})\}[\mathrm{HCO_3^-}]_P \\ &+ \{1 - \phi_B(\mathrm{E})\}\{\mathrm{C}_{Alb}(\mathrm{P})(8.0\,\mathrm{pH(P)} - 41) \\ &+ \mathrm{C}_{Phos}(\mathrm{P})(0.30\,\mathrm{pH(P)} - 0.4)\} \\ &+ \mathrm{C}_{Hgb}(\mathrm{B})\{10.2\,\mathrm{pH(P)} - 73.6\} \\ &+ \phi_B(\mathrm{E})\mathrm{C}_{DPG}(\mathrm{E})\{0.70\,\mathrm{pH(P)} - 0.5\} \qquad (2)\end{aligned}$$

where CB(B) and SID(B) indicate the total titratable base and strong ion difference of human whole blood, respectively,andCAlb(P)andCPhos(P)are the albumin and phosphate concentrations of plasma,respectively.//ΦB(E) is the whole blood hematocrit, CHgb(B) is the hemoglobin concentration of whole blood, CDPG(E) is the 2,3-diphosphogycerate concentration in the erythrocyte, pH(P) is- the plasma pH, and [HCO3]P is the plasma bicarbonate concentration. All concentrations are in millimoles per liter.

This model accurately reproduces the experimental base excess titration curveforhuman whole blood(2,3). Protons are also buffered in the acute phase by the interstitial compartment (3,4). The complexity and heterogeneity of the interstitium makes a precise model difficult to obtain; however, by applying the Siggaard-Andersen approximation for the interstitium (3,4), expressions for CB and SID of the combined interstitial, plasma, and erythrocyte multiple compartment system gives the linear approximations

$$\begin{aligned}\mathrm{C_B}(IPE) = &\left\{1 - \frac{0.49\lambda\phi_B(E)\,V_B}{V_{IPE}}\right\}[\mathrm{HCO_3^-}] \\ &+ \left(1 - \frac{\lambda\phi_B(E)\,V_B}{V_{IPE}}\right)\{\mathrm{C}_{Alb}(\mathrm{P})(8.0\,\mathrm{pH(P)} + 53) \\ &+ \mathrm{C}_{Phos}(\mathrm{P})(0.30\,\mathrm{pH(P)} + 0.4)\} \\ &+ \frac{\lambda V_B}{V_{IPE}}\mathrm{C}_{Hgb}(\mathrm{B})\{10.2\,\mathrm{pH(P)} + 12.4\} \\ &+ \frac{\lambda\phi_B(E)\,V_B}{V_{IPE}}\mathrm{C}_{DPG}(\mathrm{E})\{0.70\,\mathrm{pH(P)} - 0.5\} \\ &\qquad (3)\end{aligned}$$

and

$$\mathrm{SID}(IPE) = \left\{1 - \frac{0.49\lambda\phi_B(E)V_B}{V_{IPE}}\right\}[\mathrm{HCO_3^-}]$$
$$+ \left(1 - \frac{\lambda\phi_B(\mathrm{E})V_B}{V_{IPE}}\right)\{\mathrm{C}_{Alb}(\mathrm{P})(8.0\,\mathrm{pH(P)} - 41)$$
$$+ \mathrm{C}_{Phos}(\mathrm{P})(0.30\,\mathrm{pH(P)} + 0.4)\}$$
$$+ \frac{\lambda V_B}{V_{IPE}} C_{Hgb}(B)\{10.2\,\mathrm{pH(P)} - 73.6\}$$
$$+ \frac{\lambda\phi_B(\mathrm{E})V_B}{V_{IPE}}\mathrm{C}_{DPG}(\mathrm{E})\{0.70\,\mathrm{pH(P)} - 0.5\} \qquad (4)$$

with CB(IPE) and SID(IPE) indicating the total titratable base and strong ion difference of the interstitial, plasma, and erythrocyte system. VIPE is the total volume of that system. VB is the blood volume, and k is the total hematocrit factor, which is typically near unity. The other symbols and variables are as given above.The Henderson- Hasselbalch equation for plasma may be utilized to obtain PCO2 interms of bicarbonate.Together these relationships reproduce the experimental acute human in vivo carbon dioxide titration curve for otherwise normal individuals, as well as the experimental human strong ion difference value for the interstitial, plasma, and erythrocyte system, equal to 40 mM (5).

For constant noncarbonate buffer concentration, DCB And DSID are equal,and DCB(P) and DCB(B) equal the base excess of plasma and whole blood,respectively.DCB(IPE)is the base excess of the interstitial, plasma, and erythrocyte system, which is Siggaard-Andersen's base excess of the Extracellular fluid, also referred to as the standard base excess

(4). Calculations such as these may further the understanding and quantification of acid–basedisorders.

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