TO THE EDITOR: Nguyen and Kurtz (3) presented an equation expressing the concentration of sodium in plasma water, $[\text{Na}^+]_{\text{pw}}$ (Eq. 11). They claim that “the new physiological insights provided by this model can for the first time provide a basis for understanding quantitatively how changes in the plasma protein concentration modulate the $[\text{Na}^+]_{\text{pw}}$.” An associated editorial heralds the equation as a major advance in the field (1). Unfortunately, the authors’ claim is founded on a misunderstanding.

Nguyen and Kurtz’s equation was derived by expressing plasma osmolality as some factor ($g$) times total body osmolality, where $g$ is seen as close to unity and quantifying the effect of the presence of nonpermeant proteins in the plasma. This relationship was then expanded to express the plasma and total body osmolalities as simple functions of the quantities of sodium, potassium, and all other osmotically active species in the plasma and total body water, and the volumes of these compartments. The derivation is correct but inelegant in two respects: first, because both “total exchangeable” and “osmotically inactive” sodium and potassium are introduced into the equation and then the latter are subtracted from the former to obtain surrogates for “osmotically active” concentrations; second, because the derivation involves several unwieldy unnecessary repetitions. The lack of elegance is arguably important because it obscures the essence of the manipulations being presented. Significantly, the final Eq. 11 contains the unelaborated factor $g$.

The derivation of Nguyen and Kurtz’s equation for $[\text{Na}^+]_{\text{pw}}$ is notable for the absence of two principles that are essential in a solution of the Gibbs-Donnan equilibrium that their paper claims to model. First, no account is made of the electrical potential across the interface between body compartments. Second, their analysis does not consider the requirement for electroneutrality within body compartments. For example, they take no account of the mean number of negative charges on plasma proteins. What this means is that the phenomenon that they claim to be modeling is actually not addressed in their paper; it is left expressed in the unelaborated factor $g$.

The nature of their equation becomes apparent when we consider how it is used in their paper. Taking data from a major textbook for the total osmotic concentrations and the separate osmotic concentrations of sodium and potassium in plasma, interstitium, and the intracellular compartment, and choosing unsourced but standard compartment volumes, the authors calculate $g$ (1.0023) and their equation returns a value for $[\text{Na}^+]_{\text{pw}}$ of 142 mosmol/lH$_2$O on the left hand side after inserting this textbook value of 142 mosmol/lH$_2$O on the right hand side of the equation. The equation is self-fulfilling because it is merely an interrelationship of compartmental osmotic concentrations; it cannot provide a value for $[\text{Na}^+]_{\text{pw}}$ unless one is entered. This can be demonstrated in a straightforward manner by substituting for the terms on the right hand side of Nguyen and Kurtz’s Eq. 11 according to the definitions of these terms listed in unnumbered equations on page 1295 to obtain the result: $[\text{Na}^+]_{\text{pw}} = [\text{Na}^+]_{\text{pw}}$.

There is internal evidence from the paper that there may have been unease with obtaining a result that is entered into the calculation. In a footnote on page 1295 of their paper, referring to the point in the calculation in which $[\text{Na}^+]_{\text{pw}} = 142$ mosmol/lH$_2$O is entered into the right hand side of their equation, Nguyen and Kurtz write: “The osmolar quantity of plasma osmotically active Na can also be determined by calculating the product of $V_{\text{pw}}$ (plasma volume) and the difference between the plasma osmolality and the sum of the osmolality of all the non-Na osmoles, i.e. (plasma osmolality – non-Na osmolality) $\times V_{\text{pw}}$. This calculation does not require the value of the $[\text{Na}^+]_{\text{pw}}$.” The two sentences in this footnote are clearly inconsistent.

An inkling that all is not well with the analysis of Nguyen and Kurtz was earlier provided by Ring (4), who let the interstitial fluid volume in their equation vary between 1 and 40 liters and obtained the same value for $[\text{Na}^+]_{\text{pw}}$ in all cases. In a reply to Ring’s letter, Nguyen and Kurtz (2) regarded it as a strength of their model that it “will accurately predict the correct $[\text{Na}^+]_{\text{pw}}$ regardless of what estimate of plasma, ISF, and intracellular fluid volumes one use (sic) to validate the model.”

REFERENCES