Reply to Kang and Brooks: Comment on the calculations in protein thermodynamics

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This is a response to a letter by Kang and Brooks (1).

In their comments, Kang and Brooks (1) purport to have identified several errors in the isothermal calorimetry (ITC) data used to calculate the thermodynamic cycle described in Table 2 of our paper (2). However, we disagree with this assertion because it does not consider the standard deviations that are inherent in the experimental data and which are reported in the table. The values for ΔG^0, ΔH^0, and ΔS^0 possess uncertainty. Thus, calculations of ΔG^0 from ΔH^0 and $-T\Delta S^0$ values, as suggested by Kang and Brooks, would be prone to additional and unnecessary error since the $-T\Delta S^0$ values were calculated from ΔG^0 and ΔH^0, which originate from experimentally derived parameters. For example, calculation of the ΔG^0 from its enthalpic and entropic components for the interaction between maltose-binding protein (MBP) and sAB-11M with 1 mM maltose is $(-14 \pm 2) + (2 \pm 2) = \mathbf{-12 \pm 3}$ kcal/mol, which has larger error, as expected, but remains equivalent to the experimentally derived ΔG^0 value ($\mathbf{-11.4 \pm 0.1}$ kcal/mol).

We agree that equivalent energetic paths of a thermodynamic cycle must remain true regardless of path. When calculations were necessary, such as the determination of ΔS^0, appropriate uncertainty was accounted for and suitably indicated at the end of the calculation (3). The thermodynamic parameters have been rounded to present the final values with appropriate significant figures. Consequently, the thermodynamic values cannot be subjected to additional calculations without including the associated error in the calculations. For example, the energetic relationship for two equivalent paths along the cycle can be calculated, such as path A: $T\Delta S^0_{\text{Maltose: MBP}} + T\Delta S^0_{\text{MBP: sAB-11M in 1 mM maltose}}$, and path B: $T\Delta S^0_{\text{MBP: sAB11M}} + T\Delta S^0_{\text{Maltose: MBP in 5-fold molar excess sAB-11M}}$. Using the data presented in Table 2, path A $= (10.4 \pm 0.1) + (-2 \pm 2) = \mathbf{8 \pm 2}$ kcal/mol and path B $= (6 \pm 2) + (2 \pm 1) = \mathbf{8 \pm 2}$ kcal/mol, which observes the expected equality within the limits of the accuracy of the measurements.

With regard to the other comment by Kang and Brooks, we thank them for pointing out a typographical error in Fig. 5 and Table 2. We had made the correction in the final version that has been published (2).

The authors declare that they have no conflicts of interest with the contents of this article.

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