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Response

Comment on the response by Jan P. Amend and Harold C. Helgeson (with editor's note)

Amend and Helgeson have drawn attention to the large differences between the heat capacities of random coil proteins calculated using our current group additivity parameters [1] and the heat capacities of the unfolded state determined experimentally by Privalov and Makhatadze [2]. This is consistent with the results we reported [1] for the two proteins, ribonuclease A and human calpastatin domain I, in pure water at near neutral pH. As outlined previously [1], a significant fraction of the difference between the calculated and experimental heat capacities is due to the values used for the group contributions of the side-chains of the amino acids arginine and lysine. The method used to derive these quantities [1] yields the quantity $\{C_p^o(R^+) - C_{p,2}^o(H^+)\}$ where $C_p^o(R^+)$ is the partial molar heat capacity of the protonated side-chain and $C_{p,2}^o(H^+)$ is the partial molar heat capacity of the proton. As the absolute heat capacity of the proton as a function of temperature is not known, we are currently unable to make the appropriate corrections, which, as we stressed previously [1], are significant. Similarly, the group heat capacities we reported for the side-chains of aspartic and glutamic acids are valid for the unionized side-chain. Consequently, corrections also have to be applied to these group values when used in additivity calculations for unfolded proteins in aqueous solution at pH values close to neutral.

Editor's Note: In view of the importance of this topic to our understanding of the thermodynamics of polypeptides in solution, we have taken the unusual step of publishing this exchange of views in the hope that it will allow readers the opportunity to judge for themselves the subtleties of the arguments involved. The matter is now, however, closed until further experimental data become available. AC 8 November 2000.

References

[1] M. Häckel, H.-J. Hinz, G.R. Hedwig, A new set of peptide-based group heat capacities for use in protein stability calculations, J. Mol. Biol. 291 (1999) 197–213.

[2] P.L. Privalov, G.I. Makhatadze, Heat capacity of proteins II. Partial molar heat capacity of the unfolded polypeptide chain of proteins: Protein unfolding effects, J. Mol. Biol. 213 (1990) 385–391.

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