

Applications of Thermodynamics for Protein Solutions

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Three examples illustrate how thermodynamic analysis contributes toward establishing improved procedures to control protein behavior in biotechnology and medicine. Perturbed hard-sphere theory, one for liquids and one for solids, is used to calculate a phase diagram (temperature versus density) for an aqueous protein with added electrolytes. In this calculation, the potential of mean force plays an essential role. A new potential of force incorporates not only the usual interactions of colloid theory but, in addition, takes into account dispersion forces between dissolved ions and between such ions and the protein particles; thus, the calculations represent the observed Hofmeister series: some salts are more effective than others in precipitating proteins. The phase diagram serves as a guide for designing a separation process. Thermodynamic studies help to tell us how best to produce a protein pharmaceutical in crystalline form as desired, for example, in insulin, interferon and human growth hormone, or how to prevent crystal formation as desired, for example, in prevention of cataracts and sickle-cell anemia. Finally, thermodynamic analysis of calorimetric titration data provides enthalpic and entropic contributions to the binding of a drug to the AIDS virus. These contributions assist in the design of a drug that is likely to be effective not only for blocking the reproduction of a particular virus but also many of its mutations.