MS03-01 | Protein Thermodynamic Parameters to Understand and Guide Crystallisation

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Stability of protein molecules is recognised as a crucial parameter for their crystallisation. Melting (denaturation) temperature T_m, or thermostability, is an easily obtainable and widely used measure of stability, and choice of source organisms, ligands and co-factors of the protein to be crystallised is often guided by an increase in T_m. Thermodynamic stability (ΔG of unfolding), consisting of enthalpic and entropic components due to intramolecular interactions, internal degrees of freedom and hydration effects, is a more complex and less well-studied parameter. We have shown using Differential Scanning Calorimetry, that common crystallisation salts can drastically influence the thermodynamic stability of proteins and these changes are not always reflected in the corresponding T_m shifts.

The Hofmeister series has for decades been associated with protein crystallisation. However, apart from the well-known effects of the various ions with respect to protein solubility (which have low predictive power for crystallisation), no specific “Hofmeister effects” have been discovered that could rationalise the preference of different proteins for specific salts with respect to crystallisation. Relating various components of thermodynamic stability to the presence of ions found at different points on the Hofmeister series, one such potential correlation is proposed.

Obtaining reliable thermodynamic data from a sufficiently large and varied set of proteins, needed for establishing meaningful, general conclusions and strategies, is a difficult task, especially when we do not know in advance what to look for. This talk will therefore mostly aim to give some general directions and ideas for future research.