Differential Scanning Calorimetry (DSC) – Microcal VP-DSC

In a nutshell: Precise analysis of thermally-induced structural transitions in proteins, DNA, RNA, micellar complexes, and other biomolecular systems.

Services: Biophysics Facility offers DSC as an open-access instrument. First-time users must complete training before gaining access to the instrument reservation calendar.

Location: Building 50, room 3123

Description: The differential scanning calorimeter measures the constant pressure heat capacity (C_p) by monitoring the difference in the amount of heat absorbed by the sample solution and an equal amount of a matching buffer as the temperature of both solutions is slowly increased. For thermally induced transitions DSC directly identifies the transition temperature (T_m) and the associated excess heat capacity which allows the determination of the enthalpy of the transition (ΔH_{cal}). DSC, unlike optical approaches used to study stability and melting behavior of molecules (CD, fluorescence, UV-Vis), permits characterization of multiple transitions in a single run. Furthermore, it is not constrained to the two-state data analysis model, which is commonly used when calculating van't Hoff enthalpy (ΔH_{vH}) from data obtained by optical methods.

Typical applications:

- Stability and folding studies of protein and nucleic acids
- Assessment of the effects of mutations on protein stability
- Characterization of nucleic acids, lipids, membranes, and micellar systems
- Measurements of the effect of ligand binding on protein stability. This allows the determination of the affinity of a very tight binding, with K_A up to approximately 10^{20} M^{-1}.

Basic instrument specifications:

- Temperature range: from -10°C to 130°C
- Scan rate: 0 to 90 deg/hour.
- Cells: lollipop-shaped tantalum cells, nominal volume 0.5 mL

Sample requirements and recommended buffers: A matching buffer is required to load the reference cell. Dialysis is recommended to equilibrate the composition of the sample and reference buffer. Both sample and buffer should be degassed before the experiment. The recommended buffers for DSC analysis include phosphate, glycine, and acetate. Tris and DTT should not be used for DSC measurements. Substitute DTT with BME or TCEP. Viscous buffer components will complicate degassing and loading.

Please confirm that the sample does not precipitate in the temperature range of the DSC run. This can be check by heating the sample in the test tube, or by using the DLS. Since DSC experiments are time-consuming, for protein samples it is recommended to perform a

preliminary nanoDSF analysis to help planning the DSC scans. Always consider the cleaning strategy – DSC cells are not removable.

Minimum sample amount: The recommended protein sample concentration is in the 0.1 to 2 mg/mL range. Approximately 0.7 to 1 mL sample volume is required for the DSC cell loading.