**Topic0350**

**Calorimetry: Titration Microcalorimetry**

In a common type of calorimeter, aliquots of one liquid (solution or solvent) are injected into a sample cell containing another liquid. The rise in temperature accompanying injection of each aliquot is recorded. The calorimeter is calibrated electrically.

With advances in microelectronics and calorimeter design the volume of liquids required in titration calorimetry has dropped so that only micro-litres of aliquots are injected into a sample cell having a volume of the order 1 cm$^3$. Operation of the calorimeter is under the control of a mini-computer. The sensitivity of these calorimeters is such that recorded heats are of the order of $10^{-6}$ J. In a typical experiment sample and reference cells, held in an evacuated enclosure, are heated such that the temperatures of both cells increase at the rate of a few micro-kelvin per second. The electronic heaters and thermistors are coupled so that these temperatures (plus that of the adiabatic shield) stay in step. Under computer control, aliquots of a given solution from a micro-syringe are injected into the sample cell at predetermined intervals. The operation of the calorimeter is readily understood where the chemical processes in the sample cell following injection of an aliquot are exothermic. In this case the temperature of the solution in the sample cell increases so heating of this cell is stopped. The reference cell continues to be heated until at some stage the temperatures of both sample and reference cells are again equal, when again both cells are heated in preparation for the next injection of an aliquot. The computer records how much heat was produced by the electric heaters in the reference cell to recover the situation of equal temperatures. This amount of heat must have been produced effectively by chemical processes in the sample cell.

Titration microcalorimetry [1] has had a major impact in biochemistry with respect to the study of enzyme - substrate binding [2-5].
The starting point of the thermodynamic analysis is the definition of the extensive variable enthalpy $H$ of a closed system in terms of temperature, pressure and composition; equation (a).

$$H = H[T, p, \xi]$$  \hspace{1cm} (a)

The complete differential of equation (a) takes the following form.

$$dH = \left( \frac{\partial H}{\partial T} \right)_{p, \xi} \cdot dT + \left( \frac{\partial H}{\partial p} \right)_{T, \xi} \cdot dp + \left( \frac{\partial H}{\partial \xi} \right)_{T, p} \cdot d\xi$$  \hspace{1cm} (b)

The key term in the present context is the last term in equation (b) which describes a change in enthalpy at constant $T$ and $p$.

$$dH = \left( \frac{\partial H}{\partial \xi} \right)_{T, p} \cdot d\xi$$  \hspace{1cm} (c)

In the present context the change in composition/organisation $d\xi$ refers to the contents of the sample cell accompanying injection of an aliquot from the syringe. Heat $q$ is recorded following injection of $dn^0_j$ moles of chemical substance $j$ into the sample cell on going from injection number $I$ to injection number $I+1$.

$$\left[ \frac{q}{dn^0_j} \right]_{I}^{I+1} = \left[ \left( \frac{\partial H}{\partial \xi} \right)_{T, p} \cdot \frac{d\xi}{dn^0_j} \right]_{I}^{I+1}$$  \hspace{1cm} (d)

Equation (d) is the key to titration microcalorimetry. The recorded quantity $q$ on the left-hand side of equation (d) is the recorded heat at injection number $I+1$ when further $dn^0_j$ moles of chemical substance $j$ are injected into the sample cell. The right-hand-side shows that the recorded ratio $\left[ \frac{q}{dn^0_j} \right]_{I}$ is related to the dependence of enthalpy $H$ on composition, $\left( \frac{\partial H}{\partial \xi} \right)_{T, p}$, and the dependence of composition/organisation on the amount of substance $j$ injected. Plots of $\left[ \frac{q}{dn^0_j} \right]_{I}$ as a function of injection number are called enthalpograms.
Equation (d) highlights an underlying problem in the analysis of experimental results. The recorded quantity is heat $q$ and no information immediately emerges concerning the chemical processes responsible although we note that the sign of heat $q$ is not predetermined; i.e. processes can be exo- or endo- thermic. The r.h.s. of equation (d) involves the product of two quantities, \( \frac{\partial H}{\partial \xi} \left. \right|_{T,p} \) and \( \frac{d\xi}{dn_j} \).

We have no ‘a priori’ indication concerning how to pull these terms apart. In other words we require a model for the chemical processes in the sample cell.

**Footnotes**


