All Change Please: The Direct Measurement of Change in Complex Systems

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The *direct* measurement of change is the ideal objective of any experimental procedure, since this minimizes the number of assumptions necessary to draw conclusions. However, the increasing desire to study complex, heterogeneous systems (a selection; the interactions of drugs in formulated matrices, assessment of photostability, the swelling and erosion of polymers, the turnover of enzymes in foods and the behavior of micro-organisms in soils) is not matched by an increasing number of analytical tools capable of meeting such a challenge. Calorimetric methods, by virtue of the fact that heat is a universal accompaniment to chemical and physical change, offer a unique opportunity to ameliorate many of these concerns; indeed, virtually any system is amenable to investigation, the only considerations being sample representation and experimental design. This paper reviews some of the approaches that can be adopted to enable the measurement of change directly within complex systems.
In its simplest form, a calorimetric assay should provide a qualitative output for a complex system (for instance, stable/unstable, photostable/photolabile, amorphous/crystalline, interacting/non-interacting, binding/not-binding). Such assays are relatively easy to construct and interpret and are often sufficient for the analyst. The ease with which such measurements are facilitated by the inherent design characteristics of most calorimeters should not be underestimated and is a major factor in the popularity of the technique. The analytical challenge, however, is to move towards quantitative outputs (extent of instability, photostability as a function of wavelength, percent amorphous/crystalline content, mechanism of interaction, quantification of a binding constant) whilst making in-situ measurements. The end-user is then free to decide whether a qualitative analysis is sufficient or whether a quantitative determination is of more value.

Here, the development and use of calorimetric (isothermal and ampoule-breaking) techniques to quantitate change in complex (usually heterogeneous) systems will be discussed, starting with methods to analyze reactions progressing within various media, to methodologies designed to monitor complex systems, to the development of apparatus that allow quantification of specific properties (photostability for example). The range of topics thus encompasses those mentioned above and will serve to demonstrate novel current applications of calorimetry as well as highlight potential areas for future investigation.