Calorimetry Inside and Outside the Box

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The late Gary Ackers used to rant about "the cult of calorimetry". His grievance was his belief that a "*long-standing tradition of equating thermodynamics with only a single technique (i.e., calorimetry) had contributed to the narrow and insular perception of the field and its potential*."[1] I joined the calorimetry cult somewhat late in my career, after my graduate and postdoctoral training and a few years into my first faculty position. Reliable calorimeters had become commercially available, so investigators no longer had to build their own instruments and might become cult members, albeit by sneaking in the back door by buying, rather than building, their instrument. This raised some concerns: "*To some extent, these new groups of calorimeter users introduced a scientific culture which was different from that honoured by the classical thermochemist. Many of the new calorimetrists, particularly those within the applied sector, used their calorimeters mainly as 'process monitors' and as other kinds of analytical tools, rather than as thermodynamic instruments. Thermodynamic studies in biochemistry, for example, were conducted on samples which were poorly defined by traditional standards in thermochemistry. Properties like 'precision', 'baseline stability' and 'detection limit' often took preference over 'accuracy'*."[2] This talk will offer old and new examples of my use of calorimetry in my studies of nucleic acid stability and in the characterization of nucleic acid binding interactions. Most of my time was spent trying to not make stupid mistakes and to try to adhere to at least some of the standards passed on to me by older and wiser practitioners of calorimetry. Eventually, probably because of my poor thermochemical training, I broke many rules to attempt to use calorimetry as a clinical diagnostic tool. My colleague Nichola Garbett and I found that human plasma (a complex fluid with >2000 proteins!) from "healthy" individuals showed a consistent, well-defined DSC thermogram. Remarkably, the DSC thermograms from diseased individuals differ from healthy control samples in reproducible ways, and each disease studied so far seems to have its own characteristic thermogram. It remains to be seen if these thermograms will actually be useful as diagnostics, but their potential is promising. *I have been supported throughout my career by grants CA35635 (NCI) and GM077422 (NIGMS).*

1 G. K. Ackers & D. W. Bolen. The Gibbs conference on biothermodynamics: Origins and evolution. *Biophysical Chemistry* **64** (1997) 3-5

2 I. Wadso. Neither calorimeters nor calorimetrists are what they used to be. *Thermochimica Acta* **300** (1997) 1-5