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Thermochimica Acta 355 (2000) 89–94
thermochimica acta
www.elsevier.com/locate/tca

Future projections from some past developments in calorimetric instruments and techniques at Brigham Young University, 1960–2000

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Received 6 September 1999; accepted 8 September 1999

Abstract

The reasons for the rapid and widespread successes of continuous titration solution calorimetry, isothermal power-compensation flow calorimetry, high-precision heat-conduction calorimetry, and temperature-scanning heat-conduction calorimetry are examined. The characteristics of these successes are used to make general predictions about the future of calorimetry. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Brigham Young University; Calorimetry; Titration; Flow; Kinetics; Metabolism

1. Introduction

“The past is our only guide to the future.”

The previous four decades have seen calorimetry progress from ‘do-it-yourself’ instrumentation to the present when commercially available calorimeters can meet most measurement needs. Although reaction vessels are frequently modified to suit the requirements for a particular measurement, it is rare that an existing commercial calorimeter cannot be found to accommodate the required reaction vessel.

Several calorimeter designs that were first conceived or modified at BYU were eventually produced commercially by Tronac, Hart Scientific, or Calorimetry Sciences Corporation. The purpose of this paper is to survey the development of some of those calorimeters and some of the more significant applications. The survey is limited to those developments in which I was personally involved. The reason for reviewing these past events is to try to derive some sense of direction as to where the field of calorimetry might go in the early years of the next century.

2. Continuous titration calorimetry

The advent of small, bead-in-glass thermistors in the late 1950s made possible relative temperature measurements with a noise level of only a few microdegrees and a time constant of a fraction of a second. As such measurements required only a simple wheatstone bridge, a constant voltage supply such as a battery, and a millivolt strip chart recorder, this arrangement was quickly adapted for thermometric titrations for analyses of solutes [1]. In 1962, as a

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PII: S0040-6031(00)00439-1

graduate student under the direction of James J. Christensen and Reed M. Izatt, I began construction of a precision, continuous titration, isoperibol, temperature-rise calorimeter based on a thermistor bridge for temperature measurement and a specially designed glass Dewar as a reaction vessel. Both the motor-driven buret and the reaction vessel were immersed in a constant temperature water bath. Besides incorporating a constant rate buret with titrant external to the reaction vessel and a low-noise thermistor-bridge for temperature measurement, other novel features of the calorimeter were the glass Dewars with thermal equilibration times of less than 0.5 s and a double water bath system that controlled temperature to about 0.1 millidegree. A description of this calorimeter was published in 1965 [2] by which time Tronac was marketing a similar instrument.

These calorimeters and the continuous titration method proved to be particularly useful in four applications. (a) Determination of enthalpy changes for solution reactions of a series of many similar compounds. For example, proton ionization reactions of carboxylic acids or of amines. During a 2-year period (1963–1965) with the one prototype instrument operating in an assembly line fashion, values of enthalpy changes were obtained for all of the proton ionization reactions of all of the carboxylic acids, amines, amino acids, pyrimidines, purines, nucleosides, and nucleotides that were then available in reasonable purity from Aldrich [3–6]. Several more years were required to analyze and publish the data from those experiments. (b) Determination of enthalpy changes for metal-ligand binding where several simultaneous reactions occur [7]. (c) Identification of reducing agents and acids and bases in samples of airborne particulate matter [8,9], and determination of microconstants [10], all cases where the enthalpy change is used as the identifier of the reaction. (d) Determination of equilibrium constants for reactions with small constants by the continuous titration method was first published in 1965 [11,12], and was later applied to proton ionization from sugars [3], from guest–host complexes of cyclodextrins [13] and crowns [14], absorption of solutes by suspended solids [15], and to multiple equilibria systems such as metal-ligand [7,14,16,17] and protein-surfactant binding [18]. All of these applications made use of the ability of the method to characterize a titration curve with around 100 data points obtainable during an experiment taking only 1–2 h. Processing the massive amounts of data generated required the use of electronic computers which also first became available in the early 1960s. Producing the first equilibrium constants from continuous titration data for two test systems, ionization of HSO_4^- and reaction of OH^- with HPO_4^{2-}, required months of programming effort during which, on my own, since there was no one to teach me, I gradually learned to read the poorly organized and very opaque IBM FORTRAN manuals of the day.

The success of these techniques was primarily due to their ability to provide data that was timely for illuminating extant questions in organic chemistry, biochemistry, guest–host chemistry, and air pollution. Organic chemistry needed good data on acid–base chemistry to understand substituent effects on reaction mechanisms, biochemistry and guest–host chemistry needed data on weak interactions to make sense of the wealth of structural information just becoming available, and environmental chemists needed simple methods to identity and measure the chemical species present in very complex and highly variable mixtures.

3. Isothermal power-compensation calorimetry

During the late 1960s a power-compensation solution calorimeter was developed at BYU [19] and a commercial version was marketed by Tronac. Although the solution calorimeter as such never found much of an application niche, a line of flow calorimeters developed from the concept found an application in determining heats of mixing of organic liquids as a function of temperature and pressure [20]. These calorimeters all operate on the principle of balancing a constant power loss from either a Peltier cooler or a controlled ΔT with power from an electrical heater. The heater power required to maintain an isothermal condition is the calorimetric measurement.

The successful commercialization of these flow calorimeters was due to their ability to rapidly provide data on mixtures as a function of composition, p, and T at a time when the chemical industry needed such data to develop predictive models of the properties of homogeneous mixtures.

4. Heat conduction calorimetry

The first foray of the BYU group into heat conduction calorimetry resulted from a need for a method to predict the useful life span of batteries used to power heart pacemakers. Pacemakers with an expected lifetime of 10 years inside a patient had become available because of advances in materials and electronics. However the batteries approved for use at that time only had a lifetime of about 2 years. As it would be unreasonable to wait 10 years or more for shelf studies to be completed, a predictive method was sought. Accelerated aging at higher than body temperature was found to be unreliable. Calorimetry was thus suggested as a means for measuring the rate of energy loss from candidate batteries. With a 1-year, US $5000 Grant from Wilson Greatbatch, Roger Hart and I accepted the challenge. A quick calculation showed that making the required measurements was indeed going to be a challenge. To make the required prediction over a 10-year span on a 1.5 A h battery required knowing the rate of energy loss within a fraction of a microwatt. At the time, the lowest detection limit that had been reported for a calorimetric measurement was 10 μW obtained with a heat conduction calorimeter designed and built in the thermochemistry laboratory at Lund, Sweden.

Our best efforts over several months convinced us the lowest possible baseline noise with an isothermal, power-compensation calorimeter was about 100 μW. The problem rested there until nearly the end of the grant period when Roger visited the labs in Lund and personally viewed a disassembled heat conduction calorimeter. On his return we decided to make another attempt using the Lund technology. With the better temperature control provided by a Tronac water bath and by carefully avoiding noise sources from improper grounding and the electrical circuit we thought we could achieve the necessary reduction in baseline noise. Within 3 weeks we had constructed a calorimeter and achieved a short-term noise of 0.1 μW superimposed on a 1 μW peak-to-peak diurnal cycle. After much trial and error over several months, the source of the 1 μW noise, which was only present with a battery in the calorimeter, was discovered to be thermal coupling to room temperature by the 30 cm long sewing thread we were using to lower and raise batteries into the calorimeter chamber. A description of the calorimeter was first published in 1978 [21]. A calorimeter with a baseline reproducible to 0.1 μW for making measurements on heart pacemaker batteries was shortly thereafter marketed by Tronac, and later, a line of calorimeters for studying other batteries of various sizes and shapes was marketed by Hart Scientific. Many battery chemistries, including that in the lithium batteries used to power the Mars Rover, have since been characterized in these calorimeters [22].

Another application of heat conduction calorimetry that took advantage of the ability of these calorimeters to directly measure rates of very slow processes was determination of the kinetics of degradation reactions in pharmaceutical products. These products must be assigned an expiration date that guarantees the potency. Expiration dates are required to be assigned on the basis of shelf-life tests that of necessity must last as long as the shelf life, often for several years. Short-term measurements predictive of the outcome of the shelf-life tests were needed to avoid the time consuming consequences of problems arising during the shelf-life tests. Accelerated testing at temperatures above room temperature is frequently done, but can be misleading. For example, if testing is done at a temperature above the isokinetic temperature (which is commonly around 50–60°C for oxidation of organics), compounds will be ranked in the opposite order of their stability at room temperature. Direct analytical methods are also slow because of the necessity of waiting for sufficient reaction products to accumulate for an accurate analysis. The problems in these methods are avoided in the calorimetric method because heat conduction calorimetry measures an instantaneous rate and has sufficient sensitivity to often measure the rate at room temperature. Thus, during the period from 1984–1989, working with Merck Sharp and Dohme, methods for determining the nature and rate law of the degradation reaction were demonstrated [23], short-term calorimetric measurements were shown to be a viable method for predicting shelf-life [24], and the methods were used to study drug-excipient interactions (unpublished data). These methods have become widely used since then [25], but the limitations of the method, which are often instrument dependent [26], and the complexities of relating the measured heat rate to the chemistry [27] are often not appreciated.

Heat conduction calorimetry has a long history of use to determine metabolic heat rates of living organisms, but very little work of this type was done at BYU until about 1987 when a program to apply calorimetry to plant metabolism was initiated with co-workers at the University of California at Davis. Simultaneous measurements of heat and CO_2 rates of dark respiration in plant tissue as functions of temperature have proven to be very informative about plant metabolic responses to environmental conditions [28–47], have led to faster means for tree improvement [48–53], and are changing some fundamental paradigms in plant biology [54–56].

Although direct calorimetry has been used to measure metabolic rates of living organisms since the beginning of modern chemistry [57,58], data interpretation has been mostly phenomenological. Relating the thermal signal to the biochemistry of the organism, as Lavoisier did, holds much more promise because fundamental insights into cellular energetics can thus be obtained. For example, the work of Kemp and co-workers [59] has provided information on the division between aerobic and anaerobic processes in animal cells and our work on plant metabolism has shown how respiratory properties of plant tissues are related to growth rates and how these properties have evolved to match the environmental requirements for ectotherms.

5. Characteristics of past successes

Past successes of calorimetry appear to have two things in common. (a) An immediate need by an industry or academic community for data that can only be obtained or can be obtained much more rapidly by calorimetry. (b) The ability to immediately supply commercial calorimeters to obtain the desired data, even if that means making significant advances over or changes in previous instrumentation. These past successes have depended on the existence of close ties between industry, instrument manufacturers, and academics. This network will likely cease to exist within the next decade. When calorimeters were designed and constructed within university laboratories, those labs provided a steady supply of graduates trained in the science of calorimetry who made their way into industry and academics. But, because of the current paucity of graduate students who are interested in calorimetry, and because people who were trained in calorimetry before the period of rapid commercialization are now retiring and are not being replaced by scientists with the skills necessary to do good calorimetry, there is no longer an adequate supply of trained people.

As evidence for the general lack of understanding of the fundamentals of calorimetric measurements amongst the community of physical scientists, one only has to read some of the literature on ‘cold fusion’ whose practitioners glibly claim violations of fundamental laws of thermodynamics and nuclear physics on the basis of measurements in improperly calibrated and inadequately tested ‘calorimeters’ that would not be acceptable in a student chemistry lab. The weak public response of the community of knowledgeable calorimetrists to the ‘cold fusion’ fiasco is a further indication of the rapid loss of well-trained people in calorimetry. Thus, it is uncertain who will build the calorimetric instrumentation of the future.

However, I will predict that there will always be a need for new instruments with new or different capabilities and for someone to apply calorimeters to new problems. Such a prediction can be made because of the centrality of calorimetric measurements as a means for obtaining thermodynamic data. Despite this fundamental necessity for calorimetry in characterizing materials and processes, studies in thermodynamics and calorimetry are poorly funded, probably because they are commonly perceived as ‘old’ sciences. Furthermore heat, in the quantities measured in a calorimeter, unlike a laser beam or mutant mouse or cloned sheep, is not photogenic, nor does it usually have an easily understood immediacy. Funding and recognition are thus two key problems in attracting new people into calorimetry.

The most likely areas for new applications for calorimetry in the next decade will be in materials science and in the energetics of living systems. New materials are constantly being synthesized in the search for new or better electromagnetic and structural properties, e.g. semiconductors, superconductors, magnetic materials, polymers, and composites. Temperature scanning calorimeters will certainly be important for characterizing and understanding these materials. Calorimetric instruments capable of simultaneously scanning p, V, and T, such as those developed by Randzio [60], will also be very useful. Calorimeters with capability for simultaneous spectroscopic or diffraction measurements will also be particularly useful in these applications. In the other area, there is currently a need for understanding energy flow in living systems, from single-celled organisms, to plants and animals of all sizes, to ecosystems, to the entire biome of earth (gaia). Although the need for data is well-recognized, the ability of calorimetry to supply the necessary data is not. Many existing models for energy flow in living systems are based on faulty assumptions that often violate the laws of thermodynamics [55,56,61]. In this area, nonequilibrium thermodynamics should be very helpful, but is not yet developed to where it is useful. Also, none of the commercially available calorimeters are optimal for many of the biological systems that need to be studied. As large numbers of samples will need to be run, and because calorimetric measurements are inherently slow, calorimeters with many sample chambers for parallel, simultaneous measurements will be needed.

In conclusion, calorimetry will always be a significant contributor to new science, but significant challenges and difficulties will beset the field in the near future.

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