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# SOLID-STATE REACTIONS FROM ISOTHERMAL HEAT CONDUCTION MICROCALORIMETRY
## Theoretical approach and evaluation via simulated data

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## Abstract

Several recent publications from this laboratory have reported developments in the capacity to calculate thermodynamic and kinetic parameters, such as rate constant, enthalpy, order of reaction, from isothermal micro-calorimetric data. To date these developments have all been associated with the calculation of the desired parameters from solution phase reactions. This paper furthers these developments to a theoretical consideration of solid-state reactions and the calculation of the values for the rate coefficient, $k$, the fitting parameters $m$ and $n$, the total number of joules released over the lifetime of reaction, $Q$, and hence either the specific enthalpy or the molar enthalpy of reaction, $H$.

**Keywords:** isothermal microcalorimetry, kinetic and thermodynamic parameters, solid-state reaction

## Introduction

Recent papers from this laboratory [1, 2] have illustrated the development of the equations that can be used to analyse data from heat conduction isothermal microcalorimeters to determine values for reaction enthalpy change, $\Delta_R H$ (hereafter $H$ for simplicity); rate constant, $k$; order of reaction, $n$; Gibbs Function, $\Delta_R G$; entropy change, $\Delta_R S$; activation energy, $E_a$. These equations have been applied to formulated pharmaceutical preparations [3]; raw drug materials [4]; complex reactions [5]; solution phase [6] reactions. In particular they have been applied to the study of long-term stability and compatability of raw drugs and of formulated medicines.

There has also been an attempt [7] to characterise solid-state reactions in these terms. However until the publication in 2001 of the equations described in [1] all data was analysed via an iterative procedure. For solution phase reactions of integral order this procedure appeared to be satisfactory. Indeed [1] really considers the solution phase as the basic system to be analysed. Moreover the problem associated with

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solid-state reactions, and not present in the analysis of both simple and complex solution phase systems where the constituent reactions have integral orders, is that the fitting (not order) parameters expressed in the (modified) Ng equation [8] (Eq. (1)) are not usually integral and that the equations are complex. Other kinetic equations exist [9] in the literature but for the purposes of this paper only the $N_g$ equation is considered. The Ng equation is described as a common equation that defines most solid-state reactions [8].

$$\frac{d\alpha}{dt} = k(1-\alpha)^n(\alpha)^m \quad (1)$$

In the Ng equation $\alpha$ is the fractional extent of reaction at time $t$ (it hence has values that range between 0 and 1) and $k$, here the rate coefficient has, necessarily, the dimensions of $s^{-1}$.

The majority of calorimetric studies, (usually DSC and other techniques), of solid-state systems consider reactions which can be monitored over relatively short times to significant fractional ($\alpha$) extents of completion. Indeed much recent attention [10 and references therein] is given to discussions of 'model-free' interpretation of such data. Furthermore it is regarded as essential to obtain values for the 'kinetic triplet' (apparent Arrhenius activation energy, pre-exponential factor and a conversion function or kinetic model). From such data it is hoped that accurate extrapolations of kinetic behaviour can be made. Galwey and Brown [11, 12] have discussed, at a theoretical level, isothermal kinetic analysis of solid-state reactions using plots of rate *vs.* derivative function of the rate equation. The work reported in this paper seeks to extend the application of isothermal heat conduction microcalorimetry into the area of long, slow, isothermal, solid-state reaction studies. Inevitably, as with solution phase studies, only a small extent of reaction can be observed and the data used for analysis (typically for a solution phase reaction 50 h observation is sufficient [2] to allow determination of $k$, $n$, $H$ for, for example, a reaction with a first order rate constant of $10^{-11}$ $s^{-1}$). Thus, in addition to the development of the appropriate manipulation of the data it will be necessary to use simulated data to test the derived equations. Importantly too, it will be essential to explore what is the minimum data set required that allows proper specification (i.e. recovery of the correct values for the defining parameters, see Simulated Data section) of the simulated solid-state reaction system. To do this no model will be assumed other than that the data will be explored via the Ng equation [8]. Thus the model will arise through appropriate definition of the resulting fitting parameters, and not through an imposed model (other than that noted above).

## Theoretical development

Calorimetric forms of the Ng equation have been written [2] and analysed [7] through an iterative procedure i.e. values for the fitting parameters $n$ and $m$ were sought in addition to those for $H$ and $k$ (recall for solid-state reactions $k$ is the rate coefficient). In

Eq. (2), $Q$ is the total number of joules involved in the reaction to time, $t = \infty$ and $q$ is the number of joules involved up to any time $t$. Thus $\alpha$ can be set equal to $q/Q$ and Eq. (1) becomes:

$$\frac{\mathrm{d}q}{\mathrm{d}t} = \phi = kQ\left[1-\left(\frac{q}{Q}\right)\right]^{n}\left(\frac{q}{Q}\right)^{m} \tag{2}$$

The need to determine $n$ and $m$ in addition to $H$ (through knowledge of $Q$: note that in the case of solid-state reactions it may not be possible to specify the number of moles of reaction and in such an instance $Q$ could be used to determine a specific enthalpy, that is J $g^{-1}$) and $k$ unsurprisingly increased the demand upon the iterative procedure (effected through the Origin® software programme (Microcal, USA)).

Following from the capacity to deal with solution phase reactions by direct calculation [1] we next turned our attention to the problem of the direct calculation of the target parameters for solid-state reactions. This paper presents the equations developed and their application to simulated data (constructed in MathCad® software). Use of simulated data allows us to examine utility of the outlined procedures and hence to specify the accessible range.

The first problem [1] in the analysis of microcalorimetric data is the determination of the order or, in the cases considered here, the fitting parameters $m$ and $n$. A recent procedure described [13] by some of us now permits these values to be determined from a method which relies only on the knowledge of values of $\phi$ and $q$ for paired time points throughout the power-time curve ($\phi$–$t$) recorded during the observation period a subsequent paper [14] will describe in detail experimental methods for the determination of $m$, $n$, $k$ and $Q$. Note that here, and in the following development, the observation period is not set equal to $t = \infty$, *i.e.* $Q$ is not experimentally measured. Now, given that $m$ and $n$ can be calculated from paired $\phi$–$t$ values then, from inspection of Eq. (2), the issue remaining is to determine, not measure, the value of $Q$. This again can be achieved through paired data points. Writing Eq. (2) for two data points and forming the ratio between them yields Eq. (3);

$$\frac{\phi_1}{\phi_2} = \frac{\left(1-\frac{q_1}{Q}\right)^{n}\left(\frac{q_1}{Q}\right)^{m}}{\left(1-\frac{q_2}{Q}\right)^{n}\left(\frac{q_2}{Q}\right)^{m}} \tag{3}$$

If now the values of $q_1$ and $q_2$ are selected such that $q_2$ is a known factor of $q_1$ e.g. that $q_2$ is equal to $cq_1$ and hence $q_2/q_1 = c$ and setting $R$ as:

$$R = \left(\frac{\phi_1}{\phi_2}(c)^{m}\right)^{\frac{1}{n}} = \frac{\left(1-\frac{q_1}{Q}\right)}{\left(1-\frac{cq_1}{Q}\right)} \tag{4}$$

then Eq. (4) is solvable for $Q$ viz.

$$Q=\frac{q_1(cR-1)}{(R-1)} \tag{5}$$

Possession of values for $m$, $n$ and $Q$ permits calculation of $k$ for each value of $\phi$. Thus the arithmetic appears straightforward and the remaining issue is the range of application of the equations.

Firstly all ranges of values for $m$ and $n$ (they each range from 0 to 1, and the particular combination of values describes [8] the mechanism of the process under study) are determined [13] from the proposed method. The issue is how much data is required in order to fully determine $Q$ and hence $\alpha$ (equal to ($q$/$Q$)) at any time $t$ then to determine $k$, the rate coefficient, and hence the reaction lifetime. Clearly determination of both $\alpha$ and of $k$ allows calculation of an appropriate shelf life for, for example, a pharmaceutical product.

## Data simulation and manipulation

Simulated data has been used as noted in the Introduction to establish the minimum value for $\alpha$ (i.e. ($q$/$Q$)) for given values of $n$ and $m$ that allows characterisation of the model system. As previously done [1] for solution phase reactions programmes were written in MathCad® to allow data simulation however in this instance these data were exported to Microsoft Excel® for calculation of values of $Q$ and $k$. Comparison of the set values with the calculated values allows the minimum range of $\alpha$ to be specified.

Simulation of data for given values of $m$, $n$, $Q$ and $k$: data were simulated using MathCad® for solid-state reactions where $Q$ ranged from 10–10000 J; the rate coefficient, $k$, ranged from $10^{-4}$–$10^{-8}$ $s^{-1}$ and values for $m$ and $n$ between 0 and 1. Data was produced in the form of $\phi$ *vs.* $q$ for a range of values of $\alpha$ up to a maximum of $\alpha$=1. The data were then analysed using an algorithm written in Microsoft Excel® and values of $Q$ calculated for varying ratios of $\phi_2/\phi_1$ (where $\phi_2$ was fixed as the value of $\phi$ when $\alpha$ is at a maximum). It can be shown that from an $\alpha$ value of as small as around 0.01 (when $Q$ is assigned a value of 100 J) it is possible to recover the correct values for the target parameters. Figure 1 illustrates for one simulation study the overall data plot of $\phi$ *vs.* $q$ and the data set required for successful recovery of the target parameters. It should be noted that for successful analysis the ratio of $\phi_2/\phi_1$ should be as large as possible. As the value of $\phi_1$ approaches $\phi_2$ (hence $\phi_2/\phi_1$ approaches 1) the analysis becomes more difficult. The separation required between $\phi_1$ and $\phi_2$ depends on the values of $Q$ and $\alpha$. If Q is small then $\alpha$ must be large enough to allow sufficient separation between $\phi_1$ and $\phi_2$.

The maximum required value of $\alpha$ depends on the value of $Q$; the maximum value of $\alpha$ required for satisfactory analysis is 0.1 for solid-state reactions with values of $Q$ as low as 2 J. That is, long slow solid-state reactions are amenable to study. Without specifying the time base we used data sets of 17.000 points in these analyses. Thus it would appear that, from these simulated data, it should be possible to identify

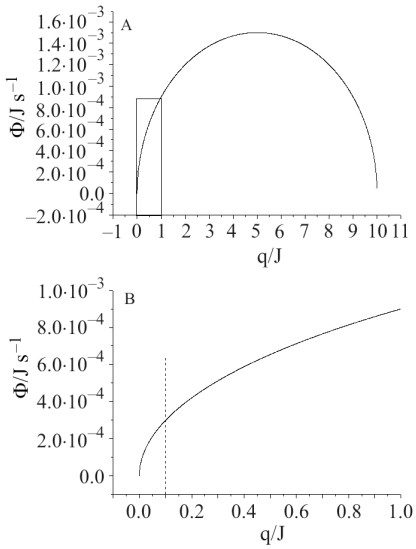


**Fig. 1** A – represents the simulation for the α range 0–1 for $m$=0.5, $n$=0.5, $k$=3·10$^{-4}$ s$^{-1}$, $Q$=10 J. The portion of data enclosed in the box is expanded in B. B – represents that portion of data up to $q$=1 J i.e. α=0.1 and the required data set for successful analysis is that prior to the vertical line at $q$=0.1 J i.e. α=0.01. The whole data set is a representation of 1.7 million data points of which only 17.000 are required for successful analysis. 17.000 data points is equivalent, for example, to recording one data point every 10 s over a 48 h period

appropriate values for $m$, $n$, $Q$ and $k$ for real reaction systems. Moreover the necessary extent of reaction to permit this analysis is very small. This is in contrast to the more 'classical' procedures where for example α values are required [10 and references therein] to range up to 1 (that is the reaction should approach completion). Note the analysis presented here does not rely upon the exploration of particular models of the reaction process (save that the defining equation is the Ng equation [8]). The data analysis returns values for the target parameters which may conform to a model – this approach, therefore, maybe regarded as relatively model free.

## Conclusions

The data presented here demonstrates, from a theoretical development and simulation trials, that it is possible to (1) make direct calculation of values for the target parameters $m$, $n$, $k$, $Q$ and (2) that simulated (ideal) data for fractional extents of reaction as low as α=0.01 will allow such calculations. These outcomes give confidence to pursue the practical (experimental) exploitation of this approach. Such experiments are underway in this laboratory.

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