

The effects of experimental parameters and calibration on MTDSC data

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Abstract

To produce accurate and artefact-free MTDSC data it is necessary to choose suitable experimental parameters (i.e. modulation period, temperature amplitude, sample mass and pan type). A poor choice of parameters can result in distortion of the modulation and inaccurate heat capacity data and can also affect the result of the deconvolution procedure. This paper aims to review these effects and to offer some guidance on how to achieve optimum results. In particular, it is suggested that the modulation parameters should be chosen to ensure that the sample can follow the programme without thermal gradients developing and also that at least six modulations should take place during any thermal transition. Two methods of calibration are discussed; a one-point method is sufficient in most cases but a temperature-dependent method should be used when more accurate data are required or for sub-ambient experiments. © 1999 Elsevier Science B.V. All rights reserved.

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1. Introduction

Modulated temperature differential scanning calorimetry (MTDSC) is a development of the conventional differential scanning calorimetry (DSC) technique which uses a sinusoidally oscillating temperature programme instead of the usual linear temperature ramp. The benefits of this method have been shown to include the abil-

ity to separate overlapping thermal transitions which differ in their reversing and non-reversing behaviour, the improved identification of thermal processes and the accurate measurement of heat capacity (Reading et al., 1992; Reading, 1993; Boller et al., 1994). Early investigations with the MTDSC technique were mainly concerned with the characterisation of thermoplastics, such as poly(ethylene terephthalate), but applications for food and pharmaceutical materials are increasingly being developed. Recent MTDSC papers on such samples include the study of foodstuffs, frozen sucrose solutions, HPMC, spray dried lactose, progesterone-loaded poly(lactic acid) micro-

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spheres and amorphous drugs (Bell and Touma, 1996; Izzard et al., 1996; Royall and Craig, 1997; Thomas and Aubuchon, 1997; Hill et al., 1998a,b; Royall et al., 1998).

As experience of using MTDSC has increased, it has become apparent that the ability to produce accurate and artefact-free data relies on the operator developing a sound understanding of the effects of the experimental parameters on the results obtained. It is well known that when using conventional DSC, a number of factors such as heating rate, pan type and sample mass, can affect the quality of the data produced. In MTDSC the use of a sinusoidally oscillating temperature programme introduces two extra parameters (period (s) and temperature amplitude (°C)) to the heating method which increases the complexity of choosing experimental parameters. The MTDSC method also requires an extra calibration procedure to correct heat capacity measurements. The aim of this paper is to review the ways in which the chosen experimental parameters may affect the resulting data and to offer some guidance on how to achieve optimum results, particularly for analysts who are new to the technique. All the results presented in this paper were obtained using a TA Instruments heat flux DSC but the issues raised should also be considered when using other makes of DSC instrumentation.

2. Materials and instrumentation

Aluminium oxide (99.9%, – 100 mesh, Aldrich and 99.99%, fused, – 6 + 12 mesh, Aldrich) and spray dried lactose were used for the investigation of the experimental parameters. The method of preparation of the spray dried lactose has been detailed previously (Hill et al., 1998a). Cyclohexane (99.9%, Riedel-de Haën), indium (99.999%, Aldrich, Gillingham, Dorset, UK) and tin (99.999%, Aldrich) were used for temperature calibration.

All MTDSC and conventional DSC measurements were made using a DSC 2920 equipped with a refrigerated cooling accessory (RCS) (TA Instruments, New Castle, DE). The DSC was calibrated for baseline using empty pans of

matched mass and for temperature using the temperature standards listed above. The DSC cell was purged with 30 ml/min nitrogen unless otherwise stated. The RCS was purged with 150 ml/min helium when equilibrating at sub-ambient temperatures and with 150 ml/min nitrogen while heating the sample. All measurements were made using pairs of sample and reference pans which had been matched by mass to either ± 0.1 or ± 0.02 mg. Analyses were performed using several types of pan; open pans, non-hermetically sealed pans and hermetically sealed pans. Hermetically sealed pans were purchased from both TA Instruments and Perkin Elmer and are referred to in the text as ‘hermetic (TA)’ or ‘hermetic (PE)’ respectively. The heat capacity results are shown uncalibrated so that the effects of experimental parameters on the measurement could be investigated. The experimental methods that were used are detailed with the relevant results.

3. Results and discussion

Poorly chosen experimental parameters can affect the data in a number of ways, some of which are inter-related. In this study, such effects have been grouped into four main categories; distortion of the modulation, inaccurate heat capacity measurements, factors affecting the outcome of the deconvolution procedure and effects caused by the pan type. All the problems discussed can be avoided by choosing suitable experimental parameters. The options available for calibration are also discussed.

3.1. Distortion of the modulation

3.1.1. Period

The MTDSC software aims to produce a sinusoidally oscillating temperature programme. However, if the chosen modulation parameters require heating and cooling rates that are beyond the capability of the instrument this may result in distortion of the sine wave. The level of distortion was assessed for a range of periods from 10 to 80 s using a 10.079-mg fused aluminium oxide sample. The sample was analysed quasi-isothermally

Table 1
Summary of the amount of sine wave distortion for various periods^a

	Period (s)							
	10	20	30	40	50	60	70	80
N ₂ purge, isotherm at 50°C	D	D	SD	no D	no D	no D	no D	no D
N ₂ purge, isotherm at 150°C	D	no D	no D	–	–	–	–	–
He purge, isotherm at 50°C	D	no D	no D	–	–	–	–	–
He purge, isotherm at 150°C	SD	no D	no D	–	–	–	–	–

^a D, distorted; SD, slightly distorted; no D, no distortion.

at 50 and 150°C with either nitrogen or helium gas (30 cc/min) used as the cell purge. The RCS was purged with 150 cc/min of nitrogen for all the experiments and the modulation amplitude setting was kept constant at 0.5°C. Non-hermetic pans were used. The method was allowed to run for approximately 10 cycles at each period so that the oscillation would have time to stabilise, then the modulated heat flow was studied for any distortion of the sine wave. The symmetry of the sine wave was visually assessed by tracing one cycle of the modulation on to paper and then rotating and reflecting the paper. The level of distortion determined for each set of conditions is summarised in Table 1.

It was found that the distortion was most pronounced for short periods and low temperatures. With these conditions, it is difficult for heat from the furnace to transfer to the sample and then be removed by the RCS at the rate required to maintain the modulation. It was also noted that when the oscillation was found to be asymmetrical, the distortion usually occurred in the lower part of the sine wave. This corresponded to the heating segment of the modulation cycle during which the furnace was trying to overcome the constant cooling of the RCS. The amount of distortion produced may depend on the type of cooling accessory used so that different limits could be expected for an instrument using a liquid nitrogen cooling accessory (LNCA). Changing the purge gas from nitrogen to helium was found to make shorter periods possible. This is thought to be due to the higher thermal conductivity of helium, which may improve the transfer of heat in and out of the sample.

3.1.2. Lissajous figures

A preferable way to monitor the distortion to the sine wave is to plot the raw data in the form of a Lissajous figure (TA Instruments, 1996; Varma-Nair and Wunderlich, 1996). Lissajous figures are composed of two sinusoidally oscillating signals plotted against each other and are commonly used to investigate the response of a system to an applied modulated stimulus. The shape of the figure produced depends on the frequency and phase of the two signals. Examples of Lissajous figures can be produced by plotting,

$$x = a \times \sin(2\pi ft) \quad (1)$$

$$y = b \times \sin(2\pi ft + \varepsilon) \quad (2)$$

where a and b are amplitudes, f is frequency, t is time and ε is a phase difference (Gough et al., 1996). The resulting curve shapes are shown in Fig. 1 for various y -curve frequencies and phase differences relative to the x -curve. In MTDSC

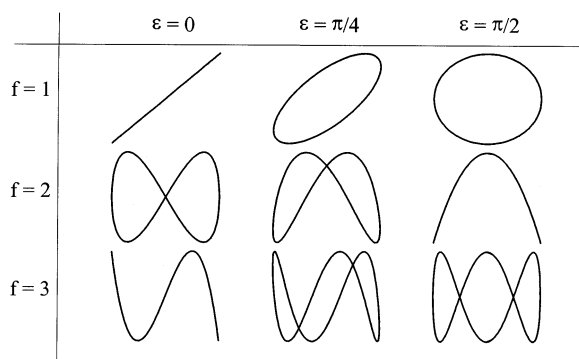


Fig. 1. Examples of the Lissajous figures produced by plotting sine wave oscillations of various frequency ratios and phase differences.

experiments, the modulated heating rate and heat flow signals have the same frequency and there is usually a non-zero phase lag between them, so that an ellipse is formed when they are plotted against each other. When no sample transitions are taking place, the amplitude of each signal and the phase lag between them remain constant so that each cycle of the ellipse will superimpose on the previous one. Any distortion of the ellipse will indicate a corresponding distortion of the sine wave due to loss of steady state; parameters that cause this should then be avoided.

To illustrate the applicability of such a method, a spray dried lactose sample was analysed in hermetic (PE) pans using a range of periods from 10 to 90 s and a temperature modulation of 0.5°C. The sample was held quasi-isothermally at 20°C for 20 min at each period and several cycles from each analysis is shown in Fig. 2. The distortion to the ellipse caused by shorter periods can be easily

seen using this method, confirming that this is a convenient method for assessing the sine wave.

3.1.3. Temperature amplitude

As for the period, the choice of temperature amplitude may be limited. The heat capacity data are calculated from the ratio of the amplitude of the heat flow oscillation (A_{HF}) to the amplitude of the heating rate oscillation (A_{HR}) i.e.

$$C_p = K_c A_{HF} / A_{HR} \quad (3)$$

where K_c is a heat capacity calibration constant. Therefore, large amplitudes are recommended as these increase the heat capacity precision by reducing noise (Boller et al., 1994). However, the maximum temperature amplitude that can be obtained in practice is limited by the heating and cooling capability of the instrument.

In the next set of experiments, the aim was to determine the maximum temperature amplitude that could be achieved for a selection of periods and temperatures. The 10.079 mg fused aluminium oxide sample was re-analysed and a helium cell purge was used. Quasi-isothermal experiments were performed at underlying temperatures of -50 , -30 , 50 and 150°C with periods of 10, 20 and 30 s being used at each temperature. The temperature amplitude set in the modulation method was then gradually increased until the observed amplitude could no longer reach the set value. The previously measured amplitude was then recorded as the maximum that could be obtained for those conditions. These values are shown in Fig. 3.

It was found that larger amplitudes could be obtained using longer periods and at higher temperatures. Although it was possible to increase the observed temperature amplitude above these values by entering an amplitude larger than required in the method, it was decided to avoid this as failure of the observed signal to match the programmed signal implies loss of modulation control. It was also noted that for the experiments with a 30-s period, the sine wave started to become distorted before the amplitude failed to meet the set value. This would indicate that monitoring the sine wave for distortion is a more important measure of the acceptability of the

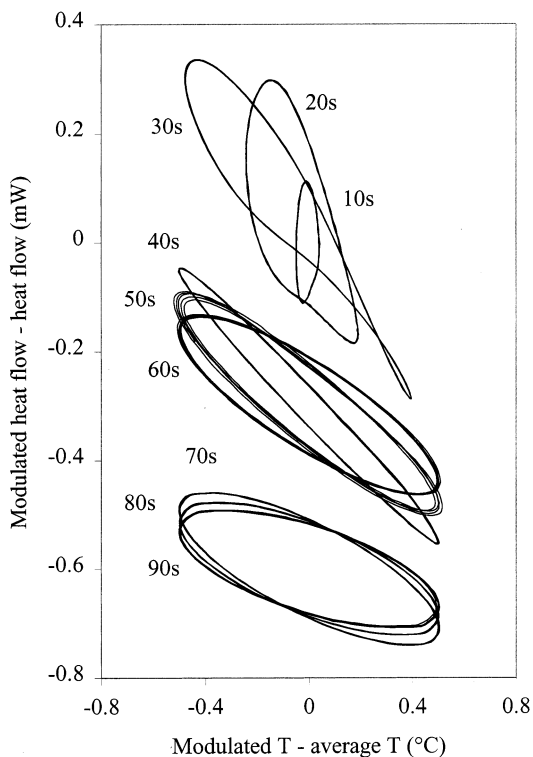


Fig. 2. Lissajous figures for quasi-isothermal experiments on spray dried lactose using a range of periods.

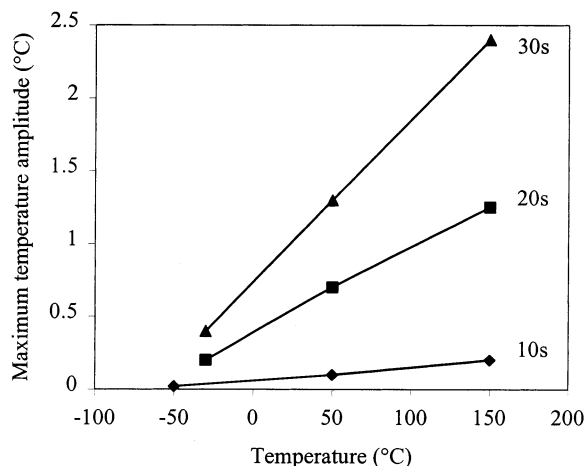


Fig. 3. Maximum temperature amplitudes measured for periods of 10, 20 and 30 s and at a range of temperatures.

modulation than checking that the amplitude is correct.

It should be noted the maximum amplitude that can be used at each period will depend on the cooling accessory used and may also be affected by the choice of purge gas. In this case an RCS was used and a helium cell purge but different values could be expected if the liquid nitrogen cooling accessory (LNCA) or a nitrogen purge were used. It has also been suggested that the thermal conductivity of the sample should be considered when determining the maximum temperature amplitude because temperature modulations may not be transmitted through samples of low thermal conductivity (Sauerbrunn and Blaine, 1994). However, in general, only small sample masses were to be used in this study so the thermal conductivity effect was not investigated further. It has also been recommended that small temperature amplitudes ($< \pm 0.03^\circ\text{C}$) are not used as these are difficult to detect and control (TA Instruments, 1993).

3.2. Factors affecting the measurement of heat capacity

It is important to determine the influence of the experimental parameters on the heat capacity as this signal is used to calculate the reversing heat flow, which in turn is used to calculate the non-re-

versing heat flow. Thus, any error or artefact in the heat capacity signal will be carried through to these other signals. In the following set of experiments, the cell constant (E) and heat capacity calibration constant ($K(C_p)$) were set to 1 (i.e. no calibration) so that the uncorrected heat capacity values could be compared to literature values for the material used.

3.2.1. Cell purge gas

The first factor to be considered was the cell purge gas. A gas is passed through the DSC cell to provide an inert atmosphere (which prolongs the lifetime of the cell) and to prevent contamination of the constantan disk. The two most commonly used gases, nitrogen and helium, were compared whilst measuring the heat capacity of a 61.308 mg aluminium oxide disk obtained from a DSC calibration kit. A heating rate of $2^\circ\text{C}/\text{min}$, period of 60 s, amplitude of 0.32°C and non-hermetic pans were used. The sample was run twice in both purge gases.

Fig. 4 shows the measured heat capacity for the sample compared to literature values (Archer, 1993). It can be seen that at high temperatures the use of a nitrogen purge results in uncalibrated values that are close to the literature values. It is thought that this is due to the higher thermal conductivity of the helium gas which may alter

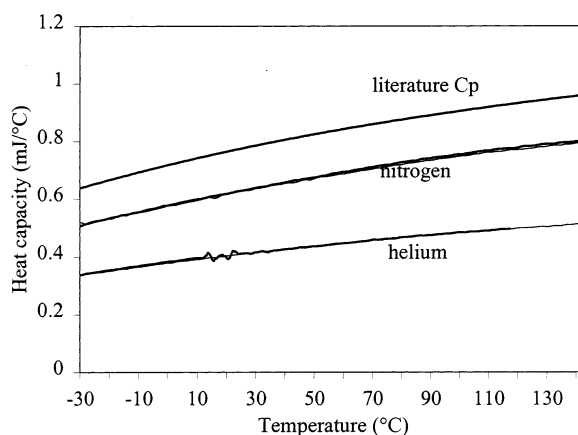


Fig. 4. Uncalibrated heat capacity measured for aluminium oxide when using nitrogen and helium cell purges. The literature values are also shown (Archer, 1993).

the heat transfer characteristics of the cell. It is possible that the gas conducts heat away from the sample causing a temperature gradient to build up. This would then cause low heat capacity measurements, as not all the sample would be following the temperature modulation. It may be possible to remove this effect by calibrating the cell while using the same purge gas but it should be noted that the equations used to represent the heat flow in the DSC are based on the assumption that the primary heat transfer path is through the constantan disk. If, therefore, the use of a highly conductive gas caused a secondary path through the purge gas to become significant, this could invalidate the assumption. However, the relatively low purge flow rates used may prevent this from becoming likely.

Although the use of a helium purge has been found to produce low heat capacity measurements, its use brings the advantage that shorter periods can be obtained without distortion of the modulation and this may be a more important consideration for samples that exhibit narrow transitions. It has also been suggested that smoother data are produced when using a helium purge (Cser et al., 1997). The cell constant, E , measured during calibration has been shown to be more sensitive to the purge flow rate for helium gas compared to a nitrogen gas, so it is important to keep the flow rate constant from run to run (TA Instruments, 1997).

3.2.2. Sample mass

When using conventional DSC, it is recommended that large sample masses are chosen if precise heat capacity data are required as this increases the ΔT and heat flow signals. However, the MTDSC technique may impose a limit on the maximum mass of sample that can be used successfully as it has been found that large sample masses can cause low heat capacity readings (Boller et al., 1994). This effect can be explained by considering that thermal gradients build up in large samples, so that not all the sample is following the modulation. Effectively, only the heat capacity due to part of the sample is being measured which causes an error when the total sample mass is used to calculate the specific heat capacity values. In the study by Boller et al. (1994), the sapphire standard analysed was in

the form of a solid machined disk. It is likely that the physical form of the sample (solid, powder, liquid, etc.) may affect the heat transfer characteristics and so could be expected to impact on the ability to modulate the sample. Therefore, the effect of the sample mass on the measured heat capacity was assessed using a fine grained aluminium oxide powder.

A number of samples were prepared with masses between 5.103 and 40.127 mg (which was the maximum that could be packed into the pan). The non-hermetic sample and reference pans were matched in mass to ± 0.1 mg. The samples were analysed using modulation parameters of a $2^\circ\text{C}/\text{min}$ heating rate, an 80 s period and a 0.42°C temperature amplitude which produced the specific heat capacity values, measured at 100°C , shown in Fig. 5. At least two measurements were made of each sample mass. The heat capacity values are lower than the expected literature value ($0.907\text{ J/g per }^\circ\text{C}$ at 100°C (Kaye and Laby, 1995)) as they are shown uncalibrated.

It was found that the measured heat capacity was fairly constant over the mass range 5–40 mg and that large masses did not decrease the accuracy of the data. However, it should be noted that non-hermetic pans were used in these experiments. When open or hermetic pans are used, in which there may be no contact between the top of the sample and the lid, the heat transfer may

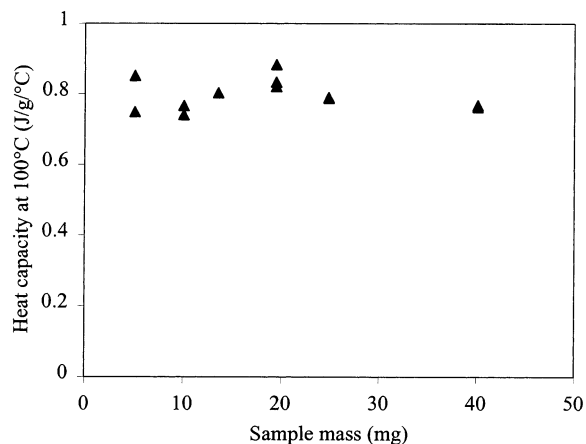


Fig. 5. Effect of mass on the measured specific heat capacity of aluminium oxide.

become more difficult for large samples. The heat transfer will also be affected by the thermal conductivity of the sample, so that the maximum mass that can be used without causing low heat capacity data may be smaller for samples of low thermal conductivity.

It was also observed that there was quite a large variation in the values obtained on repeating the analyses and this was found to relate to the positioning of the pans in the cell. When a pan was not moved between runs, the second measured value was very close to that obtained on the first analysis (as seen for the top two of the three 5-mg results). For the rest of the experiments, the pans were removed and then replaced in the cell between runs. Although it was attempted to reposition the pans symmetrically and reproducibly each time, it would appear that even small variations in position and thermal contact can alter the measurement. It may be possible to overcome this problem by using a robotic loading accessory (Autosampler) to load pans and by making sure the pans are completely flat.

3.2.3. Period

In the above experiment, a relatively long period was used so as to give the sample plenty of time to respond to the changing temperature programme. If thermal lags develop in the sample they would be expected to become larger at shorter periods. To test this assumption, two of the aluminium oxide samples (24.838 and 40.127 mg) were re-analysed using a heating rate of 2°C/min, periods of 20, 30, 40, 50, 60, 70 and 80 s, and amplitudes calculated to keep the minimum heating rate zero, i.e. the amplitude of the derivative modulated temperature was constant. The instrument sensitivity is dependent on this amplitude so keeping it constant allows the period effect to be studied alone.

Fig. 6 shows the heat capacity values measured at 100°C for each period. It is seen that the measured heat capacity decreases as the period is reduced and that this effect is more pronounced for the larger mass. This is consistent with the assumption that thermal gradients build up across the sample. A similar decrease in measured heat capacity with period has been observed for an

indium sample and was also attributed to heat transfer effects (Cao et al., 1997). Other studies on a calibration standard (aluminium oxide) have also found low heat capacity readings to be measured at short periods, resulting in high calibration constants (Sauerbrunn et al., 1994; Varma-Nair et al., 1994). This strong dependence between heat capacity and period makes it very important that all calibration experiments are performed at the same period as subsequent sample analyses. It should also be noted that short periods may allow faster heating rates to be used, while maintaining a specific number of cycles through a transition and this should also be considered when choosing parameters.

3.2.4. Pan mass

The heat capacity measured by MTDSC is dependent on the difference in mass on the sample and reference positions. If the empty sample and reference pans weigh exactly the same, the measured heat capacity should be zero. When a sample is added, the measured heat capacity is then due solely to the mass of the sample. However, in practice the pans are not usually identical in mass and so the mass difference will cause an error on the measured heat capacity which will be particularly significant for small sample masses. Thus, the empty pans should be matched by mass as closely as possible. TA Instruments recommends

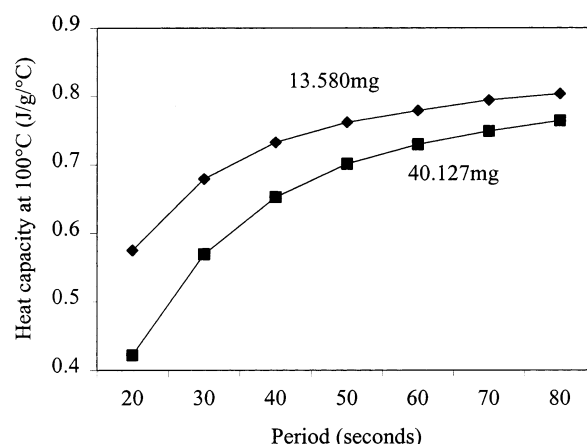


Fig. 6. Effect of period on the measured specific heat capacity for two masses of aluminium oxide.

that the pans be selected so that the difference in mass be ± 0.1 mg or less, although it is usually possible to exceed this without having to weigh a large number of pans (± 0.02 mg is practicable). Sauerbrunn et al. (1994) have found that heavier pans produce larger heat capacity calibration constants. Therefore, if very accurate heat capacity data are required, the same mass pans should be used for both the calibration and sample analyses and also the pans should be as light as possible.

3.3. Factors affecting the result of data deconvolution

Ideally, the total heat flow from a MTDSC experiment should be identical to the heat flow obtained from a conventional DSC experiment at the same underlying heating rate. In most cases this has been found to be true and when differences are seen they can usually be explained by the choice of experimental parameters.

3.3.1. The number of modulations through a transition

One possible cause of differences seen between DSC and MTDSC heat flow data is having an insufficient number of modulations through the transition in the modulated experiment. This can be illustrated using the recrystallisation exotherm seen on heating spray dried lactose (Hill et al., 1998a). The sample was analysed using hermetic (TA) pans, a $2^\circ\text{C}/\text{min}$ heating rate and a range of periods from 10 to 80 s. The modulation amplitude was adjusted in each case so that it was the maximum value possible without inducing cooling as part of each cycle. As Fig. 7a shows, the total heat flow becomes shorter and broader as the period is increased. The software deconvolution process uses data from one complete cycle of modulation to calculate each data point and this appears to have a smoothing effect when there are only a few cycles through the peak (Fig. 7b).

As well as influencing the size and shape of the peak in the total heat flow, an insufficient number of cycles was also found to affect the heat capacity results (Fig. 7c). When short periods were used, the signal was slightly noisy during the temperature region of the crystallisation peak but

no transition was seen. As the period was increased, a peak was seen in the heat capacity signal. It appears that when there are only a few modulations through a peak the rapid rise in underlying heat flow, which takes place over only one or two modulations, is registered as a change in amplitude. This causes an increase in the apparent heat capacity.

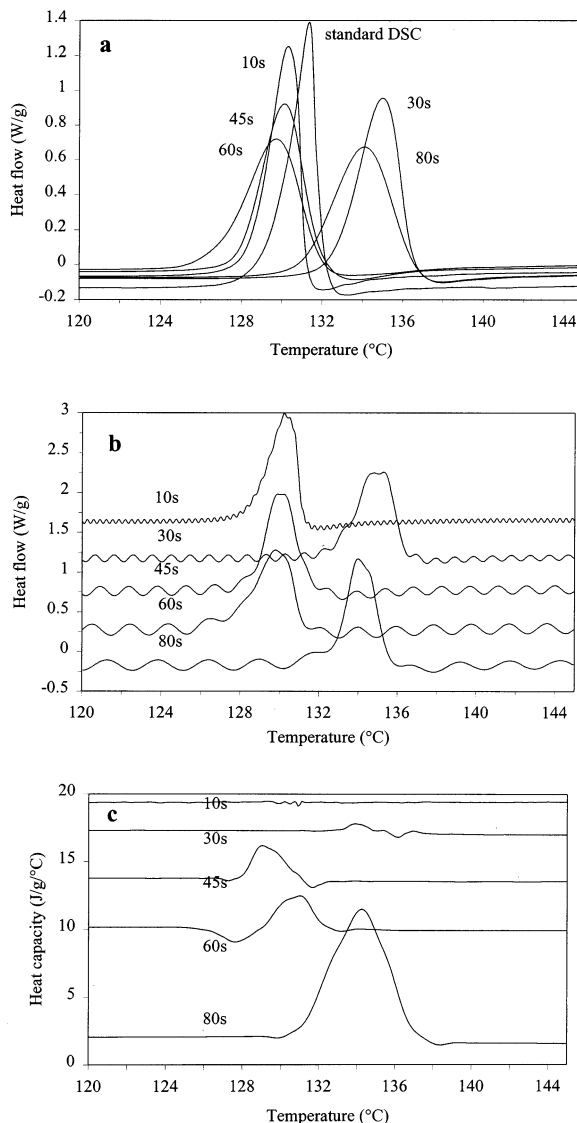


Fig. 7. (a) Total heat flow; (b) corresponding modulated heat flow and (c) heat capacity for analysis of a spray dried lactose sample using various periods.

These results would imply that short periods should be selected as they will give more modulations through a transition and so produce heat flow data similar to conventional DSC. However, it has already been shown that short periods make distortion of the sine wave more likely, reduce the maximum temperature amplitude that can be achieved and result in low heat capacity values. Therefore, for samples that exhibit narrow transitions it will be necessary to either choose a compromise in the parameters or to consider stepwise quasi-isothermal methods.

3.3.2. Cooling during the modulation

The use of large temperature amplitudes may produce cooling as part of each modulation cycle even when the underlying heating rate is positive. It is possible that this cooling section of the cycle may influence melting and crystallisation processes, compared to a conventional (linear heating) experiment. Such discrepancies can be avoided by choosing an amplitude so that the minimum heating rate is never less than zero. The maximum amplitude in this case is found using the expression (TA Instruments, 1993),

$$\text{amplitude} = (\text{heating rate} \times \text{period}) / 2\pi \times 60 \quad (4)$$

3.4. Pan type

There are a range of pan types available for use in the DSC, some of which are illustrated in Fig. 8, and the type chosen may affect the heat transfer to the sample. Open pans do not compress the sample onto the base of the pan which may exacerbate the problem of low heat capacity readings for large samples. The non-hermetic pans improve heat transfer by compressing the sample

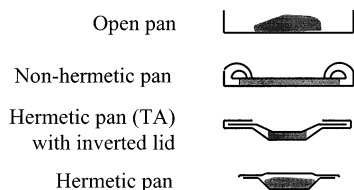


Fig. 8. Illustration of some of the pan types available for use in a DSC.

and also because the sample contacts with the lid. Hermetic pans do not normally touch the top of the sample, although for some makes of pan the lid can be inverted to improve contact. With each type of pan it is important to make sure the base of the pan is completely flat.

It has been found that the type of pan used can also affect the reproducibility of baselines measured for empty matched pans. Fig. 9a–d shows baselines produced by open, non-hermetic, hermetic (TA) and hermetic (PE) pans while using modulation parameters of a heating rate of 2°C/min, a period of 30 s and an amplitude of 0.16°C. The open, non-hermetic and hermetic (PE) pans were found to give relatively good reproducibility but the reproducibility for the hermetic (TA) pans was found to be poor. This was at first thought to be due to poor thermal contact between the pan and cell so two methods of improving this contact were assessed. The first involved lightly sanding the base of the pan to make sure it was smooth. The second involved flattening the base of the pan with a specially made metal die before crimping on the lid. However, neither method was found to improve the reproducibility to the extent expected. It has been suggested by the manufacturer that a heat conducting paste can be used to stick the pan to the constantan disk in the cell. However, this introduces the difficulty of matching the mass of the paste on the sample and reference positions and also the cell would have to be cleaned between each run which is not ideal.

Results presented by other MTDSC users (Varma-Nair et al., 1994; Varma-Nair and Wunderlich, 1996) have also described difficulties with the hermetic (TA) pan type in making accurate heat capacity measurements and it is thought that the difficulty could be due to the large mass of these pans (typically 56–58 mg). This may indicate that large mass pans, which are a necessity for some applications, for example measuring large volumes of liquid, may present problems for MTDSC measurements unless the modulation parameters are very carefully chosen. Alternatively, it may be the shape of the pan which causes problems and this issue has yet to be resolved.

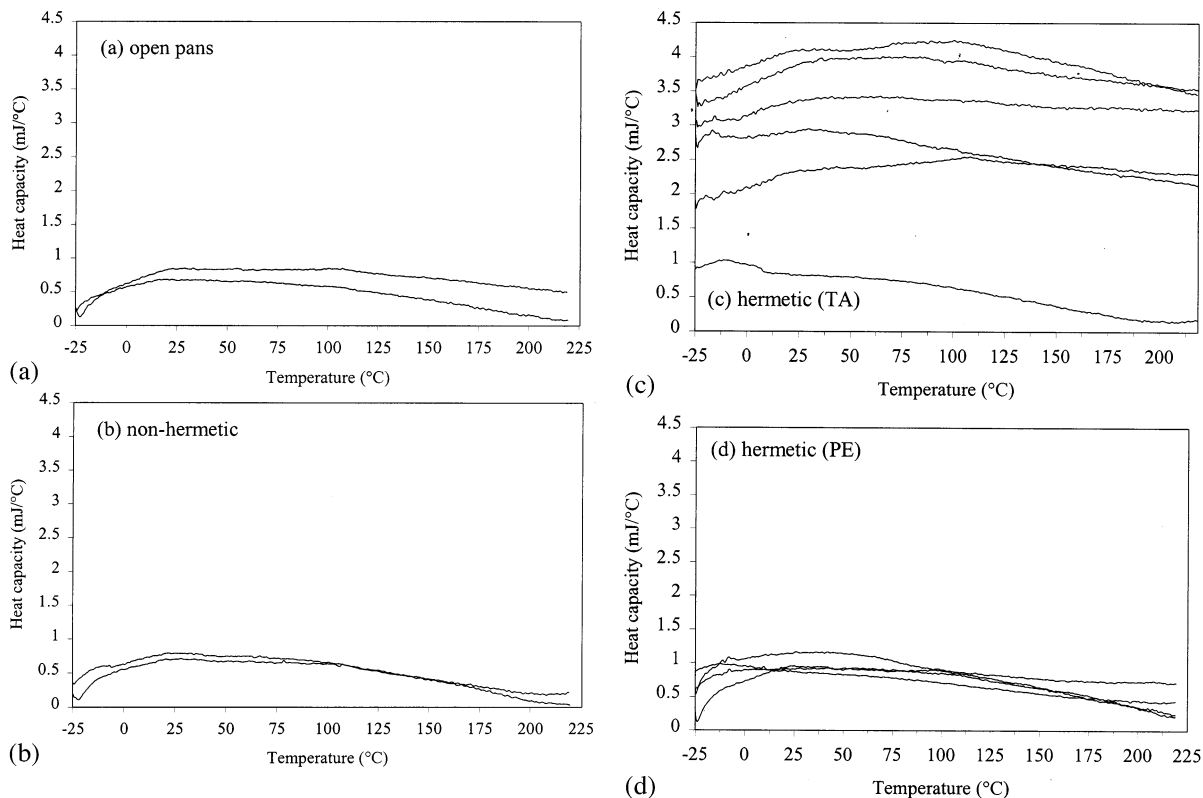


Fig. 9. Baselines measured using (a) open pans (b) non-hermetic pans (c) hermetic (TA) pans (d) hermetic (PE) pans.

3.5. Calibration

The calibration procedure for MTDSC data is basically the same as for conventional DSC data except that an extra constant is needed for calibration of the heat capacity signal. As in conventional DSC, the temperature signal is calibrated within the instrument software using the observed and literature melting temperatures of up to five calibration standards. The baseline slope is corrected using the manufacturer's method. All calibration experiments are performed using the same experimental parameters as will be used in subsequent MTDSC analyses.

3.5.1. One-point calibration

The version of MTDSC software currently available only allows for one cell constant (E) and one heat capacity constant ($K(C_p)$) to be entered into the software. The conventional DSC method

for enthalpy calibration, in which the measured heat of fusion of a standard material (e.g. indium) is compared to the literature value, is used to produce the cell constant. This value (usually between 1 and 1.1 for a nitrogen purge or higher for a helium purge) is entered into the instrument software and used to adjust the heat flow.

The heat capacity constant, $K(C_p)$, is calculated in a similar manner by dividing the literature heat capacity of a standard material (such as aluminium oxide) by the measured heat capacity. The calibration material should be chosen to be as close as possible to the subsequent sample in terms of thermal conductivity and form (i.e. powder, liquid, etc.). Only one heat capacity calibration constant can be entered into the software so the operator must choose whether to use a value calculated at the centre of the temperature range, or at the temperature of a particular sample transition or to use a value representing an average of

values calculated over the whole range. While this method has the advantage of being simple and quick, it has the disadvantage that $K(C_p)$ values are temperature-dependent. In particular, it has been found that $K(C_p)$ decreases rapidly with temperature below 300 K (Varma-Nair et al., 1994). Therefore, for highly accurate heat capacity data a temperature-dependent calibration constant should be used.

3.5.2. Temperature-dependent calibration

In this method, the calibration material is analysed over the same temperature range as will be used for the subsequent samples. The data are then exported into spreadsheet software and each data point is compared to the literature value for that temperature to produce both enthalpy and heat capacity calibration constants. These temperature-dependent constants can then be used to correct the corresponding data points in the sample data file.

The method can also be adapted to include a baseline correction. In an ideal cell the heat capacity should be zero when there is no sample. In practice, this is not the case because of small asymmetries in the cell which produce a thermal imbalance on either the sample or reference side. This causes a small heat capacity signal to be measured when the empty cell is heated. Determination of the size of this signal is important as it has been found that the heat capacity constant, $K(C_p)$, changes with the size of the thermal imbalance. A cell with a large thermal imbalance (4.4 mJ/°C) was found to give low $K(C_p)$ values (< 1) indicating that the measured heat capacity values were higher than the literature values (Varma-Nair et al., 1994; Varma-Nair and Wunderlich, 1996).

In cases of a large thermal imbalance, it will be necessary to perform a baseline correction, using the data from an experiment on empty pans of matched mass, to achieve accurate heat capacity values. This procedure is routinely used in conventional DSC measurements of heat capacity to correct for the small positive or negative heat capacity signals measured when empty pans are analysed. In MTDSC experiments, the thermal imbalance heat capacity is always positive because

it is calculated from the amplitudes of the modulated signals. Therefore, the phase lag between the modulated heat flow and derivative modulated temperature signals is used to determine if the imbalance is biased towards the sample or reference side (TA Instruments, 1996). If the phase lag is positive, there is sample bias and the measured heat capacity should be subtracted from all subsequent runs. If the phase is negative, the bias is on the reference side and the heat capacity should be added to subsequent runs. The adoption of this temperature-dependent calibration procedure will result in accurate heat capacity data over a wide temperature range but has the disadvantage of being quite time consuming.

4. Conclusions

It has been shown that a number of factors can influence the data produced by MTDSC experiments and so new users of this technique should consider the following points when beginning an investigation.

- Choosing modulation parameters which exceed the heating and cooling capability of the instrument results in distortion of the sine wave. It is recommended that a Lissajous figure be used to check whether a particular combination of parameters will cause distortion before making a full sample analysis.
- Use a medium sample mass (10–15 mg) and try to keep the sample as flat as possible in the pan. It may be necessary to increase the sample mass if detection of very small transitions is difficult. In this case, it is useful to make a set of measurements over a range of sample masses to see if there is any reduction in heat capacity for large masses. Such an experiment will determine the largest mass that can be used.
- Long periods should be used as these allow the sample to follow the applied temperature modulation and prevent thermal gradients building up within the sample. However, it is also important to make sure that there are at least six modulations through any transition.

- The sample and reference pans should be matched by mass as closely as possible.
- Avoid modulation which includes cooling when analysing melting and recrystallisation phenomena.

As regards which calibration procedure is adopted, the choice must be made in light of the aim of the investigation. If accurate heat capacity data are required over a wide temperature range or at sub-ambient temperatures, then the temperature-dependent method should be used. However, if the MTDSC analysis is being undertaken to aid in the interpretation of transitions by revealing their reversing or non-reversing nature or as the preliminary investigation of a material then the one-point calibration will usually be sufficient.

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