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Multicycle differential scanning calorimetry

Thermophysical procedures for research, development, and quality control of substances and materials

E. Marti · E. Kaisersberger · E. Füglein

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Abstract Multicycle Differential Scanning Calorimetry (MCDSC) is a procedure where repeated temperature cycles are executed and the measured data are superimposed for a selected number of cycles. Temperature cycles with a single sample are executed under selected experimental conditions in one of these procedures, namely, the $\mathrm{MCDSC_s}$. The second one, $\mathrm{MCDSC_m}$ is a procedure in which every identical temperature cycle starts with a new sample of the same substance of a similar mass. The procedure $\mathrm{MCDSC_s}$ using the same sample for a number of cycles is only applicable for substances and materials which are chemically and physically stable under the selected experimental conditions. The application of MCDSC enhances two extremely important qualities of a DSC measurement, namely, the sensitivity and the statistical base, both qualities with respect to the final data elucidated. Another possibility by MCDSC also related to the enhanced sensitivity can lead the discovery of a phenomenon which hitherto has not been observed. The most important result of any MCDSC application is the determination of the mean DSC curve within the temperature interval of interest by superimposing the single curves point by point and by the division of the calorimetric values obtained with the number of scans evaluated. The signal-to-noise-ratio (SNR) for the mean curve can be compared with the value determined for one or even for all the single curves measured yielding the improvement factor achieved with a MCDSC measurement. This experimentally determined improvement of the SNR can be compared with the value given on a statistical consideration by Gauss as the square root of the number of cycles evaluated. The main aims of this article are to prove the practical application of the procedure and the efficiency in case of rather small sample masses. Substances were selected with known enthalpy transitions and, in addition, polystyrene was taken for a determination of the data for the glass transition by MCDSC. Rather small sample masses in the order of micrograms as well as the experimental conditions have been selected for the measurements with 4,4′-azoxyanisole and *n*-hexatriacontane with the expectation to get a value of SNR for the single curves of about unity or even below. Two aims should be achieved with these experiments. First, the multicycle procedures and the data evaluation developed should be capable of establishing, after performing of a certain number of cycles, a mean curve showing an improvement over the SNR with respect to the single curves. Second, we should be able to get a rough estimation of the lower limit of the SNR for a single curve, below the instrumental noise level of the DSC used, necessary to achieve with a MCDSC experiment a mean curve with a clearly visible peak.

Keywords DSC · Multicycle Differential Scanning Calorimetry · Sensitivity · Statistical base · Signal-to-noise ratio · Accuracy · Reversibility · Stability · Weak enthalpic transitions

Introduction

Multicycle Differential Scanning Calorimetry (MCDSC) is a thermophysical and thermoanalytical procedure with wide applications in specific areas, namely, for research

E. Marti (✉)
APCh Marti Consulting, 4054 Basel, Switzerland
e-mail: erwin.marti@apch.ch

E. Kaisersberger · E. Füglein
Netzsch-Gerätebau GmbH, 95100 Selb, Germany

and development, for the thermodynamic characterization of substances and materials, as well as for analysis and quality control, especially in the development of reference materials and validation procedures. Applications for substances and materials may be developed and tested especially for crystalline, semi-crystalline and amorphous solids by using MCDSC. The different facets of MCDSC enlarge the possibilities to increase the sensitivity on the basis of the experimental setup used. Therefore, investigations with MCDSC may be focused on the search for weak or even hitherto not detected caloric transitions for their qualitative or quantitative elucidation.

Our investigations were restricted to DSC; however, the multicycle procedure can be extended to the whole area of thermal analysis, the so-called MCTA. In order to start a MCDSC experiment for a known enthalpic transition it is necessary to get the best sensitivity for a single DSC measurement with regard to the substance or material under investigation. For this, sample mass and conditions of the sample in the crucible, the selected experimental parameters, and the performance of measurements under different heating rates must be considered to obtain the highest sensitivity possible with the DSC instrument in use. Several of these factors are outlined and discussed in the Netzsch Annual 2000 [1].

The sensitivity of any DSC instrument can be increased by use of the new method MCDSC, which is a so-called time-averaging measurement. The procedure requires repeated scans of heating and/or cooling of a sample over a selected temperature interval. The generated signals are added arithmetically by a computerized data collection, and the resulting mean signal can be calculated. The noise contributions, which vary randomly from one scan to another, are more and more compensated with increasing number of cycles. However, in case an enthalpic change for a substance exists within the selected temperature interval, then it will be enlarged within the evaluation procedure independent of its visibility for a single scan.

The aim of the MCDSC which is the essential part of this procedure is an improvement in the signal-to-noise ratio (SNR). The improvement is made according to the theory introduced by Gauss and is calculated as the square root of the number of scans evaluated. A main part of our investigation was to proove quantitatively this approach for SNR below 1 for the single curves measured.

The discussion of the noise is restricted in this article to the technique of time averaging, introduced in thermal analysis in the form of MCDSC. The procedure was introduced in the 1960s in physical chemistry for the application to instruments with a rather low sensitivity as well as for the investigation of substances and kinetic intermediates at low concentrations. Ernst introduced the time-averaging procedure for the high-resolution NMR spectroscopy [2]. He received for his comprehensive contributions to the NMR spectroscopy the Nobel Price for Chemistry in 1991. Johnston developed since 1960 the molecular modulation kinetic spectroscopy in applying also the time-averaging data collection. Gas phase kinetics with the formation of intermediates in low concentrations with rather short lifetimes far below one second were measured using all major spectroscopic methods. He was the first to understand the radical processes in the interaction of halogenated hydrocarbons with ozone in the stratosphere [3, 4]. Another application published in literature is the multiscanning chromatography for the determination of a high enantiomeric purity of substances. The task here was to find enantiomeric impurities as traces [5].

The technique is applied for DSC instruments with another aim, namely, for the determination of the repeatability for the baselines as well as for the repeatability of calorimetric peak areas measured with reference materials [6].

The question that arises is “what is new in techniques of MCTA and MCDSC?” New within the application of these multicycle procedures within thermal analysis are the anticipated aims:

- To reveal that with DSC measurements it is possible to increase the sensitivity as well as the statistical basis
- To focus on the aspects of the physical chemistry of substances and materials in research and development
- To determine basic physicochemical phenomena, such as the reversibility of substances and materials, and the stability as well as the compatibility of multicomponent systems
- To search for transitions with weak enthalpy changes, or transitions which hitherto have not been observed.

Two different experimental procedures under the heading of MCDSC are proposed in this article. The first procedure, the $\mathrm{MCDSC_s}$ is applied to substances and materials remaining rather stable with respect to physical and chemical changes under the selected experimental conditions. The second procedure, the $\mathrm{MCDSC_m}$ is applied to samples for which instability or evaporation allows only the measurement of one cycle. Multicycle DSC is achieved by repeating identical measurements using every time a new sample with similar mass.

Examples from research, development, and technical areas where MCTA and MCDSC could play an outstanding role are numerous and exceed the frame of our investigations.

The two MCDSC procedures which will be presented here are defined as follows:

- Multicycle Differential Scanning Calorimetry using a single sample ($\mathrm{MCDSC_s}$) is a procedure where repeated temperature cycles are performed for a substance or a material using one single sample mass for one multicycle experiment. Data of the measured curves are superimposed, and a mean curve is calculated.

- Multicycle Differential Scanning Calorimetry using multisamples ($\mathrm{MCDSC_m}$) is a procedure where one temperature cycle is executed for a given sample mass, and this experiment is repeated under equal conditions for similar sample masses of the same substance or material. Data of the measured curves are adjusted for the mean of all sample masses, and the recalculated data are superimposed to a mean curve.

The first procedure, namely, $\mathrm{MCDSC_s}$, should be applied in case a substance or a material is investigated for the first time. Of course, for each temperature interval selected and also for any different condition selected, the reversibility must be asserted again. The outcome could be that the sample is reversible under the selected experimental conditions. In this case, the number of cycles could be kept rather high, depending on the anticipated research and development problem. An investigation about an analytical quantification might require a number of cycles which may be far high over hundred. Now, the question arises on the issue of the time required for so many cycles. Depending on the existing problem to be solved, one can minimize the temperature interval for which the cycles must be executed. Even then the heating and cooling rates as well as the chosen time interval eventually selected as waiting time at the highest and lowest temperature count for the overall time required for such an experiment with the procedure $\mathrm{MCDSC_s}$.

The outcome of the single sample procedure applying multicycles also could not be an ideal one and might reveal a more or less heavy irreversibility for any selected condition. A marked irreversibility could be caused by a number of properties of a substance or a material under investigation. Two different pathways are open depending on the results for the observed irreversibility. The first is a complete irreversibility of a substance or material within the temperature interval under the selected conditions, which mainly also depends on the chosen heating rate. This is the case for samples which undergo a strong chemical reaction or a strong decomposition. An example for such a drastic irreversibility is ranitidine hydrochloride in the melting region presented and discussed in [1]. The decomposition of this substance in a DSC experiment is significant even when applying a heating rate of $100\ \mathrm{K\ min^{-1}}$. Such an instable substance, as ranitidine hydrochloride, with regard to the melting region is no candidate, either for the $\mathrm{MCDSC_s}$, or for the $\mathrm{MCDSC_m}$. The determination of the melting points and the enthalpy of fusion, especially for the existing crystal modifications of ranitidine hydrochloride on a reasonable accuracy level must be undertaken by a procedure with classical DSC instruments outlined in the cited literature [1]. Of course, specialized instruments allowing extreme high heating rates such as developed by C. Schick could be the state-of-the-art technique for substances which are highly instable [7].

The irreversibility is an expression for a physical and/or chemical instability of any product. In other words, behind such a finding of a product lies a vast area of hidden phenomena which could be, according to the research situation, a significant task to be elucidated. As an example, the irreversibility can play an immense key role in the area of risk assessments.

Differential Scanning Calorimeters are characterized by a certain number of properties and parameters. The basic set of properties and parameters is the same for all DSC instruments; however, additional parameters are existing for special types, such as Photo-Calorimeters, Temperature-Modulated DSC, and also for several types of coupled DSC. A list of the rather heterogeneous properties and parameters are given in [8]. Lists of essential specifications are available for commercially available DSC expressed by numerical values for the characteristic parameters and features. These significant parameters are as follows: caloric sensitivity, temperature resolution, noise, short-time noise, heating and cooling rates under controlled conditions, temperature and caloric accuracy, repeatability, linearity of the heat flow rate, data acquisition rate for the temperature, and the heat flow rates.

The selection of the optimal parameters for a DSC investigation is not always very straightforward task, but is crucial for obtaining the highest sensitivity for a single scan. The properties of the substances and materials as well as the research and development aims anticipated must be taken into consideration. In addition, analytical demands to reach the required quality control are also part of this selection process. The mutual interrelations of the main parameters of DSC instruments are presented in Table 1.

The advantages gained by MCDSC are certainly depending on the phenomena investigated and the specific quantitative analytical procedure under development. The practical examples obtained with the MCDSC technique can only be regarded as preliminary in regard to this new procedure for the planning and performance of further research and development work.

Multicycle differential scanning calorimetry and data evaluation

MCDSC is a segment of methods aimed at increasing the SNR by an experimentally based procedure. A great

Table 1 Interrelations of main parameters of DSC instrument procedures

DSC instrument parameters	Temp. resolution	Caloric sensitivity	SNR
DSC single measurement	Depending on design	Depending on design	Depending on design
MCDSC$_s$, MCDSC$_m$	Significant improvement for SNR < 100, Increased statistical base	Significant improvement for SNR < 100, Increased statistical base	Improved
Sample mass	Inverse proportional	Independent within certain limits	Proportional
Heating cycles	Reversibility	Independent	Improved
Heating rate	Inverse proportional	Independent	Independent
Noise	Independent for Heat flow[a] $\geq 10^2 \cdot$ pp[b]	Independent for Heat flow[a] $\geq 10^2 \cdot$ pp[b]	Inverse proportional

[a] Heat flow at peak height of the signal under investigation

[b] pp means peak-to-peak noise

number of different theoretical or mathematical methods of data collection and data transfer exist to achieve this aim. The broadest applications of the different theoretical approaches are in the high frequency regions.

A different possibility is to measure one single DSC curve and to apply a smoothing procedure on the measured data by formation of a sliding mean over a selected temperature interval. This latter procedure bears handicaps. One effect is that a weak signal becomes even weaker.

The frequencies of the short-time noise in DSC instruments are in a very low and narrow interval of about 10^{-1} to 10 Hz. A transfer of physical theories successfully used to increase the SNR in the high-frequency region (MHz to GHz) to DSC seems practically impossible. The crucial question arises how to reduce the low frequency noise of DSC instruments, whether by a theoretical or an experimental approach? In this article, experimental procedures are proposed, namely, MCDSC$_s$ and MCDSC$_m$.

There are three different values possible to characterize the noise level, namely, peak-to-peak noise, absolute peak noise, or the so-called root-mean-square noise (RMS). In the presented investigations, only the peak-to-peak noise has been used.

The selection of the substances and of the measured phenomena for the experiments presented was made while considering different aspects:

- Transitions with a low enthalpy change.
- First order transitions as well as transitions of a higher order, e.g., glass transitions and also transitions from a liquid crystalline phase into an isotropic liquid.

Measurements with extremely low sample masses have been chosen to simulate phenomena with low enthalpy change.

The evaluation of a multicycle experiment with an enthalpic peak showing a value of SNR above about 100 for a single curve can be made in a straightforward way. In this case where the range of variation of the SNR for all single curves measured is rather small, one needs to take only one SNR randomly selected to assess the outcome.

However, a statistical evaluation of the SNR for all single curves measured is necessary to get a mean value, especially for a multicycle experiment with SNR below about 100.

The first step of a detailed evaluation is the determination of the SNR for all evaluated single curves $(S/N)_S$. This evaluation includes the determination of the peak height and the position of the baseline for the signal as well as the noise level below and above the transition.

The second step is the determination of the mean value and its standard deviation ($\sigma^n_{s,\mathrm{mean}}$) for all SNRs of the single curves. The mathematical expression Eq. 1 to evaluate MCDSC is based on the statistics of the Gaussian distribution:

$$\left(\frac{S}{N}\right)^n_{s,\mathrm{mean}} = \sum \frac{1}{n}\left(\frac{S}{N}\right)^i_S \tag{1}$$

where $i = 1, \ldots n$, and $n =$ number of cycles.

The determination of the mean DSC curve is the third step. In order to obtain the mean curve, all the single curves selected for evaluation are superimposed by a point to point addition of the measured data and by dividing the obtained superimposed heat flow values by the number of cycles. The SNR for the enthalpic peak of the mean curve is given by $(S/N)^n_{\mathrm{mean}}$ together with the standard deviation σ^n_{mean}.

The fourth step is the calculation of the experimentally determined improvement factor α_{exp} in respect of the observed peak which is defined as follows:

$$\alpha_{\mathrm{exp}} = \frac{\left(\frac{S}{N}\right)^n_{\mathrm{mean}}}{\left(\frac{S}{N}\right)^n_{s,\mathrm{mean}}} \tag{2}$$

The improvement factor can be expressed in terms of the error limits and the error propagation given by Eq. 3

$$\alpha_{\text{exp}} = \frac{(a \pm \Delta a)}{(b \pm \Delta b)} \tag{3}$$

Eq. 3 can be approximated as follows:

$$\alpha_{\text{exp}} \approx \frac{a}{b} \pm \frac{1}{b^2} \cdot \{a \cdot \Delta b + b \cdot \Delta a\} \tag{4}$$

Eq. 4 is simplified in case the error of the enthalpic peak of the mean curve (Δa) can be disregarded:

$$\alpha'_{\text{exp}} \approx \left(\frac{a}{b}\right) \cdot \left\{1 \pm \frac{\Delta b}{b}\right\} \tag{5}$$

The experimentally determined improvement factor according to Eq. 2 may be compared with the improvement factor given by the theory as the value which is an upper limit for any multicycle experiment performed. This theoretical improvement factor is given by

$$\alpha_{\text{theo}} = \sqrt[2]{n} \tag{6}$$

The efficiency of the multicycle procedure is determined as a relative value ($e_{\text{f,rel}}$) given by the expression:

$$e_{f,\text{rel}}(\%) = \left(\frac{\alpha_{\text{exp}}}{\alpha_{\text{theo}}}\right) \cdot 100 \tag{7}$$

Instruments, materials, and methods

The instrument used in the following experiments is the heat flow DSC 204 F1 Phoenix® from Netzsch-Gerätebau GmbH, Selb, Germany, equipped either with the μ-, the tau-, or the standard sensor. The glass transition curves were evaluated with the Proteus® software provided with the DSC 204. Materials and experimental details are explained for each of the presented investigation.

The uncertainty throughout this article is given as the standard deviation of the mean.

Experiments and results

MCDSC$_\text{S}$ of 13.6 µg 4,4′-azoxyanisole

A multicycle experiment on a single sample has been performed to test the principle of a multicycle determination using a DSC instrument. A rather low sample mass (13.6 ± 0.3) µg of 4,4′-azoxyanisole was enclosed in an aluminum crucible with pierced lid. In addition, a transition with a rather low enthalpy change typical for a transition from nematic to isotropic liquid phase was selected. This transition between 134 and 136 °C is endothermic, and the enthalpy of transition is 0.52 kJ mol^{-1} [8, 9]. The enthalpy change according to the literature for the given sample mass is, therefore, (27 ± 1) µJ. The enthalpy change was measured by MCDSC$_\text{s}$ using the μ-sensor. The atmosphere was static air, and 22 cycles were executed with the same sample. These identical cycles were performed between 120 and 140 °C with a heating rate of 4 K min^{-1} and a cooling rate of 1 K min^{-1}, and with a constant time interval of 5 min at the lowest and the highest temperature of each of the cycles. An instability with increasing number of cycles could be observed, and, therefore, the evaluation was restricted to the first 12 cycles. The SNR for all the selected single curves and the mean value together with the standard deviation of the mean were determined. The lowest and the highest value for the SNR for the 12 single curves measured were 6.40 and 8.52. The mean value for the 12 single curves was calculated as 7.5 ± 0.20. The point-to-point calculation of the data was made based on the data acquisition rate of 300 pts min^{-1}.

The mean curve was determined for all the data points by adding the heat flow data for the 12 DSC curves on heating between 133 and 136.5 °C, as shown in Fig. 1 together with the 8th heating curve. The SNR for the transition peak from the nematic to isotropic liquid phase was determined for the mean curve as 25.4 ± 0.9. The error of the SNR for the mean curve, the error of the peak height, and the error of the base line have all been estimated. The improvement factor according to Eq. 2 of this multicycle experiment is (25.4 ± 0.9)/(7.5 ± 0.2) = 3.4 ± 0.2.

The theoretical value which can be achieved under ideal conditions for the improvement of the SNR for this multicycle experiment with 12 scans is the square root of 12, which yields 3.46. The efficiency of the multicycle procedure for this experiment is (98 ± 6)%.

MCDSC$_\text{S}$ of 3.0 µg 4,4′-azoxyanisole

Multicycle experiments have been performed with the DSC 204 Phoenix® equipped with a μ-sensor on a sample of 3.0 µg of 4,4′-azoxyanisole. The sample was investigated

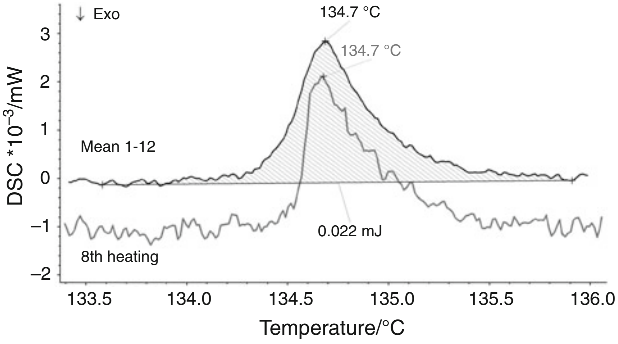

Fig. 1 MCDSC$_\text{s}$ of 4,4′-azoxyaniosole, sample mass 13.6 µg, comparison of the 8th heating curve with the mean curve from the evaluated 12 heatings; heating rate 4 K min^{-1}, under static air atmosphere

using an aluminum pan with a pierced lid and air atmosphere. Identical temperature cycles ($n = 23$) were executed with the same sample between 126 and 140 °C with heating and cooling rates of 1 K min^{-1}. Isothermal segments of 5 min were maintained between each heating and cooling. The sample mass (3.0 ± 0.3) µg was calculated by the determination of the enthalpy of transition from the solid into the nematic liquid phase, measured for this specific sample during a separate heating at the rate of 10 K min^{-1} between 100 and 126 °C. The enthalpy for this transition was taken from literature as 31 kJ mol^{-1} [8, 9].

The heating curves have been individually evaluated for the SNR at the nematic to isotropic liquid transition peak within the temperature interval of 132–136 °C. The mean value for the 12 evaluated single curves has been found as 0.65 ± 0.12. The mean curve for the same 12 heatings is an arithmetic mean with a point by point calculation based on a data acquisition rate of 300 pts min^{-1}. In Fig. 2, two single curves of the multicycle experiment are presented together with the mean curve of 12 heating curves. No transition peak could be observed for the 2nd and the the 9th heating. The 12th heating gave an SNR of 0.5. The highest value observed for the 5th heating curve was 1.37.

The literature value for the transition temperature from the nematic to the isotropic liquid phase is 134–136 °C [8, 9], and our evaluation of the mean curve yields a value of 134 °C.

The SNR was also determined for the mean curve with the same procedure as described above and the value obtained is 2.5 ± 0.4. The improvement factor of this multicycle experiment for the 12 individual heatings gave a value of (2.5 ± 0.4)/(0.65 ± 0.12) = 3.8 ± 1.3.

The theoretical value for the improvement of the SNR for this experiment with 12 scans is equal 3.46. The relative efficiency of the improvement is (110 ± 34)%.

$\mathrm{MCDSC_S}$ of 1.7 µg *n*-hexatriacontane

A multicycle experiment has been performed with the DSC 204 equipped with tau-sensor on a sample mass of 1.7 µg *n*-hexatriacontane. The sample was investigated using an aluminum pan with a pierced lid under nitrogen atmosphere with a volume flow of 20 mL min^{-1}. A total of 31 equal temperature cycles were executed with the identical sample between 73.5 and 76 °C with a heating rate of 0.05 K min^{-1} and a cooling rate of 1 K min^{-1}. No isothermal segments were introduced between each cycle. The sample mass (1.7 ± 0.3) µg was calculated from the melting effect investigated during a separate heating with a heating rate of 1 K min^{-1} between 70 and 80 °C. The literature value for the enthalpy of melting of *n*-hexatriacontane was taken as 82 kJ mol^{-1}, and the melting point as 75.0 °C [8].

The first heating cycle has been omitted. All other heating curves have been individually evaluated for the SNR at the melting peak, and the mean value of 0.52 ± 0.04 has been found. The mean curve of 30 heatings is an arithmetic mean with a point by point calculation based on a data acquisition rate of 300 pts min^{-1}. Figure 3 compares two single heatings with the mean curve of 30 heatings. The 11th heating curve revealing the highest SNR, namely, 0.79, and the 28th heating indicating no detectable melting signal are presented. The mean of the 30 heatings has been calculated in the melting region and the thermodynamic data, namely, the melting point of 75.2 °C and the enthalpy of fusion of 80 kJ mol^{-1}, respectively, have been determined.

The SNR was determined for the mean curve with the same procedure as described above and the value obtained was 2.8 ± 0.1. The improvement factor for the 30 individual heatings gave a value of (2.8 ± 0.1)/(0.52 ± 0.04) = 5.4 ± 0.6.

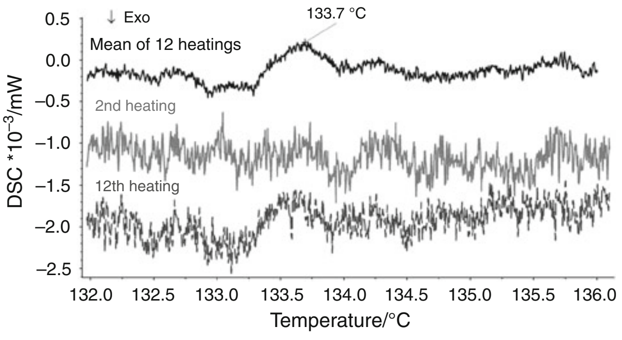

Fig. 2 $\mathrm{MCDSC_s}$ of 3 µg of 4,4′-azoxyanisole with 23 heating cycles in the temperature range of the nematic to isotropic liquid transition; 2nd and 12th heatings shown as well as the mean curve from the first 12 heatings; heating rate 1 K min^{-1}, under static air atmosphere

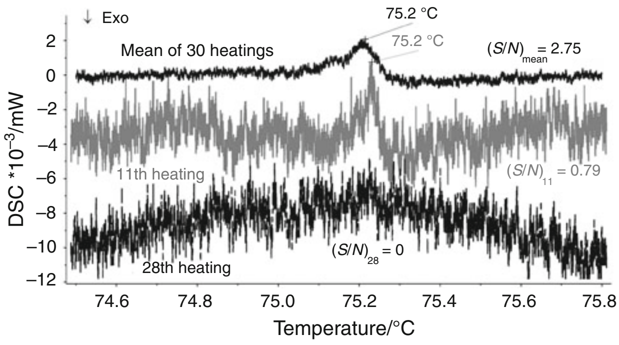

Fig. 3 $\mathrm{MCDSC_S}$ of 1.7 µg *n*-hexatriacontane, the 11th and 28th heating curves are compared with the mean of 30 heatings, heating rate 0.05 K min^{-1}, under nitrogen atmosphere

The efficiency of the multicycle procedure according to Eq. 7 is (99 ± 11)%.

MCDSC$_S$ of 462 μg polystyrene

A MCDSC$_S$ experiment has been performed using a sample mass of polystyrene of (462 ± 2) μg, measured under nitrogen atmosphere (20 mL min^{-1}) with the DSC 204 Phoenix® equipped with a standard sensor, and applying the heating and cooling rates of 10 K min^{-1}. The sample of polystyrene used in this experiment is the reference material SRM 705a from NIST [10, 11]. Multicycles were executed with 24 cycles in the temperature range between 30 and 130 °C and with a data acquisition rate of 100 pts min^{-1}.

The evaluation of the glass transition was done with the Proteus® software. The temperature range between 80 and 128 °C was selected for these evaluations. The evaluation of the characteristic values of a glass transition, namely, the mid-point temperature and the corresponding change of the heat capacity was performed with the classical procedure. The tangents below and above the glass transition were determined within the temperature intervals of 80–90 °C as well as within 118 and 128 °C by formation of the appropriate linear heat capacity functions within these intervals. Such a selection of the temperature intervals is a prerequisite for a consistent analytical evaluation of scans performed under identical experimental conditions. The glass transition data determined from 23 heatings in omitting the first one are as follows: The glass transition temperature as a mean from the 23 single measurements $T_{\mathrm{g,mid\text{-}point}} = 104.5$ °C. The corresponding standard deviation of the mean is ±0.1 °C. The standard deviation of a single measurement for the glass transition temperature is ±0.5 °C. Accordingly, the change of the specific heat as a mean value from the 23 single measurements is $\Delta c_{\mathrm{p,mid\text{-}point}} = (0.293 \pm 0.006)$ Jg^{-1} K^{-1}, and the corresponding standard deviation for a single measurement is ±0.027 Jg^{-1} K^{-1}. The highest and the lowest values of the change of the specific heat at the glass transition for the 23 single measurements are 0.328 Jg^{-1} K^{-1} for the 18th and 0.233 Jg^{-1} K^{-1} for the 2nd heating cycle, respectively.

The mean curve for the 23 single measurements was calculated point by point according to the same procedure as described above. The thermodynamic results for the glass transition of the mean curve of polystyrene evaluated within the same temperature interval as applied for the single curves are as follows: Δc_{p} at mid point = 0.297 Jg^{-1} K^{-1} and $T_{\mathrm{g,mid\ point}} = 104.5$ °C.

The Fig. 4 compares the mean curve with two single curves, namely, the 3rd and the 18th heating of the polystyrene sample used.

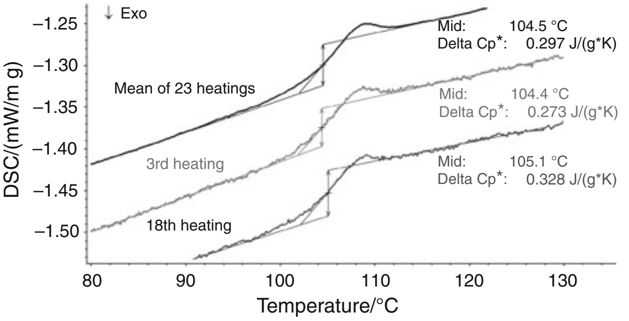

Fig. 4 MCDSC$_S$ to obtain the glass transition of a polystyrene (NIST SRM 705a) sample of 462 μg; heating and cooling rates 10 K min^{-1} in nitrogen atmosphere. The 3rd and 18th heating curves are compared with the mean of 23 heatings

Discussion

The MCDSC$_s$ experiments with 4,4′-azoxyanisole were planned to study the basic principle of this procedure. The experimental conditions and the results obtained for the two measurements of 4,4′-azoxyanisole are displayed in Table 2.

The results of the experiments reveal the fact that it is possible to increase the SNR by a multicycle experiment practically according to the theory, certainly in regard to the existing uncertainty. Taking the uncertainty into consideration seems necessary if the sample mass used in the experiments is reduced to a level which is by a factor of 10^3 lower than normally applied in the classical DSC experiments. In addition, the enthalpy of transition for this change from the nematic to the isotropic liquid phase is only 0.52 kJ mol^{-1}. This enthalpy is about two orders of magnitude smaller compared to first order transitions of organic molecules.

Only the first 12 single curves were evaluated out of 23 curves measured. 4,4′-azoxyanisole is not chemically stable in air at the temperature of the transition. In addition, the liquid crystal transition is not a first-order transition and, therefore, the nematic to isotropic liquid transition cannot be regarded as ideally reversible. As another possibility, for transitions not ideally reversible, one could further improve the SNR by a factor of about 2 by a mixed experiment of MCDSC$_s$ and MCDSC$_m$ using four samples of 3 μg and performing 12 cycles with each sample.

The enthalpy of transition was determined for the mean curve of the 12 heatings for the sample with 13.6 μg 4,4′-azoxyanisole (see Fig. 1). The enthalpy obtained was (22 ± 2) μJ, a value which corresponds reasonably with the literature value (27 ± 1) μJ.

The main findings of a MCDSC$_s$ experiment with *n*-hexatriacontane and a sample mass of 1.7 μg are displayed in Table 3.

Table 2 MCDSC$_s$ for the transition of 4,4′-azoxyanisole from the nematic to the isotropic liquid phase in air with the DSC 204 F1 Phoenix® equipped with the μ-sensor: number of cycles is 12; evaluation interval from 132 to 138 °C

Sample Mass/µg	Enthalpy of transition/µJ	Heating rate/ (K min^{-1})	Mean SNR for single curves	Mean curve SNR	Improvement factor from experiment for SNR	Improvement factor theory for SNR	Efficiency of improvement/%
13.6 ± 0.3	27 ± 1	4	7.5 ± 0.2	25.4 ± 0.9	3.3 ± 0.2	$\sqrt{12} = 3.46$	95 ± 6
3.0 ± 0.3	6 ± 0.6	1	0.65 ± 0.12	2.5 ± 0.4	3.8 ± 1.3	$\sqrt{12} = 3.46$	110 ± 38

The transition is at 134 to 136 °C with an enthalpy of transition of 0.52 kJ mol^{-1} [8, 9]

Table 3 MCDSC$_s$ experiment of (1.7 ± 0.3) µg *n*-hexatriacontane, 30 heating cycles at 0.05 K min^{-1} were evaluated

Sample mass/µg	Enthalpy of transition for sample mass/µJ	Heating rate/ (K min^{-1})	Mean SNR for single curves	Mean curve SNR	Improvement factor from experiment for SNR	Improvement factor from theory for SNR	Efficiency of improvement/%
1.7 ± 0.3	275 ± 50	0.05	0.52 ± 0.04	2.8 ± 0.1	5.4 ± 0.6	$\sqrt{30} = 5.48$	99 ± 11

The melting peak at 76 °C was measured with an enthalpy of fusion according to literature, 82 kJ mol^{-1} (162 J g^{-1}) [8]

The melting of *n*-hexatriacontane as a first-order transition is reversible [8]. Therefore, for this substance, there is practically no limit for the number of cycles. In applying the same experimental conditions as those used for *n*-hexatriacontane the value for the SNR may be estimated to end up for the mean curve in a SNR of 2 (see Fig. 3). A multicycle experiment with 100 cycles would result in a SNR of 0.2 for the single curves. Obviously, the probability to see an enthalpic signal in one of the single curves out of the 100 curves measured is practically zero.

A sample of 462 µg polystyrene SRM 705a from NIST was used for the determination of the glass transition with a multicycle experiment [10–12]. The glass transition is generally assigned as a second-order transition. Thermal history of the sample material as well as kinetic effects of heating and cooling through the glass transition and/or mechanical stress may alter the temperature, the change of the heat capacity, as well as the shape of the glass transition curve. The reversibility is not ideal and therefore one must proceed and evaluate the experiment in a strict way.

The measurements of glass transitions afford rather large temperature intervals, in our case over 100 K. Therefore, short and long time noise has influence on the quantitative results.

The results obtained for polystyrene with MCDSC$_s$ shall be compared with the data obtained by the evaluation of a single curve and with restriction to the change of the specific heat at the glass transition. As a first step, we compared the accuracy of the evaluation of such a DSC curve with the mean value obtained from the 23 cycles measured. The spread of the values for the single curves is from 0.233 Jg^{-1} K^{-1} to 0.328 Jg^{-1} K^{-1} or 33% in relation to the mean value of 0.293 Jg^{-1} K^{-1}. The standard deviation of this mean value for a single measurement is ±0.027 Jg^{-1} K^{-1}. The performance of 23 measurements and evaluation increased the accuracy to a relative value of ±9%. The next question is open, namely, has the formation of a mean curve out of 23 single curves using the same sample of polystyrene any effect on the accuracy? The value from this mean curve determined by MCDSC$_s$ is (0.297 ± 0.006) Jg^{-1} K^{-1}. The standard deviation of the mean is now reduced to ±2%. The second important fact as the benefit of MCDSC$_s$ is revealed by the excellent agreement of the change of the specific heat for polystyrene at the glass transition determined from the mean curve with the literature data (0.303 ± 0.002) Jg^{-1} K^{-1} [11].

Conclusions

MCDSC is a procedure which offers the possibility to increase the sensitivity of any DSC instrument by reduction of the short- and long-time noise. Simultaneously, the statistical basis of any qualitative and quantitative determination is improved.

The application of the two different procedures, namely, the MCDSC$_s$ and MCDSC$_m$, enables us to create valuable and prospective insights into the thermodynamic behavior for a great number of substances and materials. The latter procedure enlarges the application areas to substances and materials having a restricted reversibility or a stability allowing only one heating or cooling within the temperature interval and the additional conditions selected. MCDSC enlarges the application areas to the exploration of weak enthalpic transitions in substances and materials, perhaps even not found until hitherto, or perhaps only described with other methods.

The question of the work load of investigations for the safe introduction and application of substances or materials must be considered with respect to the probability of occurrence of a drastic event and its consequences.

One example shall be mentioned, because the crucial property was the glass transition of a material classified by the NASA for its application as a Critical 1 Component of the Space Shuttle Challenger. The material was an O-ring made from synthetic rubber with the critical property to seal cracks created at the rocket boosters by the extreme forces acting at the start, and the time afforded to seal was less than a second. The required property of this material is the liquid amorphous state at the temperature of the launch. At the beginning of January 1986, the temperature was significantly below 0 °C, and a few seconds after the launch, the functions of the seals were doubtful, and after 73 s the challenger exploded at 15 km altitude. The famous physicist Richard Feynman was demonstrating at the hearing of the commission of the American Congress that the material was at the start in the glassy amorphous state [13]. MCDSC$_s$ would have been certainly a method of choice for a reliable determination of the glass transition temperature of such a material.

Multicycle Differential Scanning Calorimetry is preferably applied for the following areas:

- Discovery of unknown phenomena;
- Investigation of the reversibility of a caloric effect and determination of the physical and chemical stability;
- Improvement of the statistical basis and the accuracy of any thermodynamic determination.

Examples for the above given application areas are among others:

- High-precision data for basic research, material data basis, and standard reference materials;
- Validation procedures and quality assurance for active pharmaceutical ingredients, diagnostics, foods, pharmaceutical products, and medical devices according to good manufacturing practice (GMP) procedures, and guidelines;
- Quantitative analysis and quality control for technical products.

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