The THT micro reaction calorimeter µRC

Titration
calorimetry
isothermal calorimetry
and scanning calorimetry
- all in one instrument

thermal hazard technology

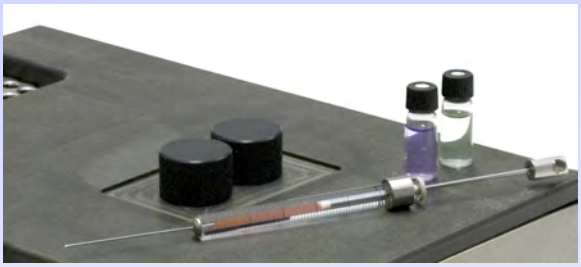
CHEMICAL APPLICATIONS BROCHURE

Introduction and reaction kinetics

The THT Micro Reaction Calorimeter (μRC™) has a wide range of application in the chemical, pharmaceutical and related markets. This brochure shows how using a micro calorimeter can help chemists and engineers in everyday tasks.

Some of the applications detailed within this brochure include:

- Reaction Kinetics
- Process Development
- Scanning Calorimetry
- Thermal Stability
- Heat Capacity Measurement
- Adhesive Curing Reactions
- Waste Management
- End Point Determination
- Hazard Analysis



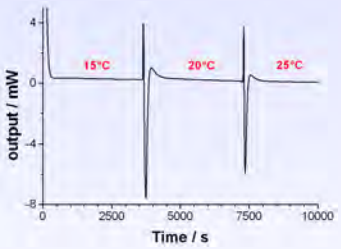
All chemical, physical and biological reactions are accompanied by heat change. These reactions, though sometimes subtle, can be measured using calorimetry. This is the only analysis method that works without modification of the sample or process.

The THT Micro Reaction Calorimeter is based on power compensation technology making it faster in both signal response and temperature variation. Designed for maximum flexibility, the μRC has the capability to measure both kinetic and thermodynamic parameters in both rapid and slow reactions and in solids, liquids or gases.

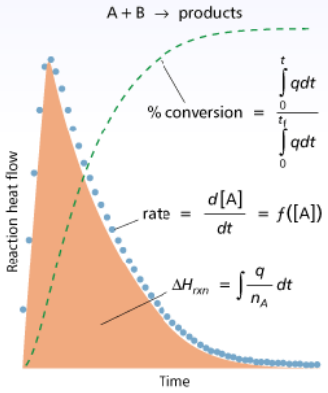
Measurements made by calorimetry are non-destructive and non-invasive making it valuable for initial analyses and for systems where other techniques fail. With the μRC there is minimal sample preparation and no limitation on the physical state of the material. Systems can be studied under ambient or modified environmental conditions.

Kinetics Determination

Kinetic analysis can be tedious and time consuming. The use of micro calorimetry to obtain kinetic parameters has been recognized Internationally and is an essential tool in kinetics research. Since reaction rate is directly proportional to heat-flow, it is possible to utilise the data from a μRC calorimeter to calculate reaction conversion at any point. From here, every data point within the experiment can be used for an "initial-rate" type determination. Fitting of models to the calorimetric data can also be used to elucidate detailed kinetic mechanism.

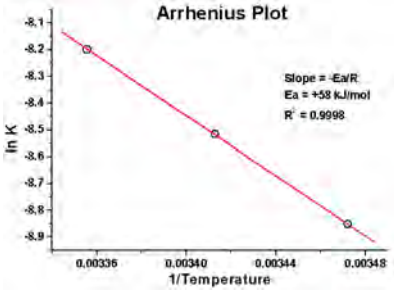


Heat flow vs time at different temperatures hydrolysis of pharmaceutical material



For slower reactions the Micro Reaction Calorimeter can be used as an isothermal (or step-isothermal) calorimeter giving rapid access to traditional kinetic methods.

A kinetics fitting and modelling package (μRC-KIN) is available as an option with the Micro Reaction Calorimeter. This software is specifically written for use with the THT μRC and contains automatic data importing, advanced data correction, kinetic fitting and modelling. Complex models may be used to provide fitting to consecutive, non-integral, parallel and auto-catalytic kinetics with highly efficient data optimisation routines.

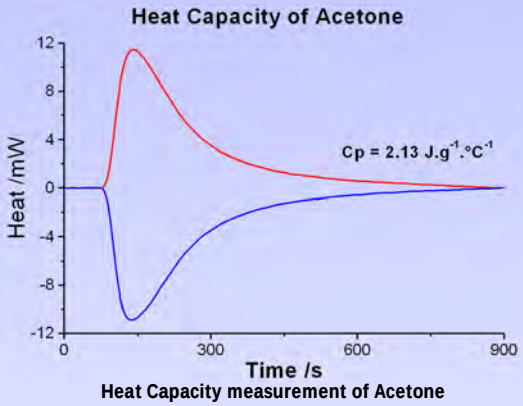


Simple Arrhenius kinetics from micro reaction calorimeter data

Process development & hazard analysis

Heat Capacity Measurement

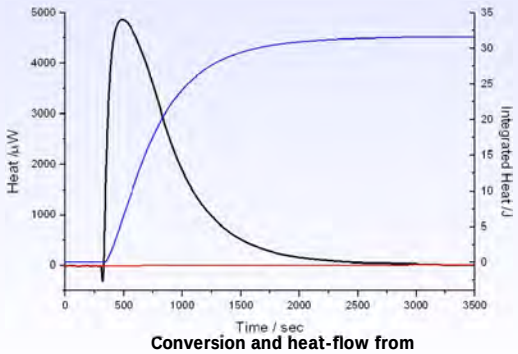
The μRC can be used to rapidly and accurately measure the heat capacity of solids, liquids and mixtures. Applying small temperature steps to the material in question allows the heat required to be measured. Using these data can significantly improve the data measured using larger reaction calorimeters.



Heat Capacity measurement of Acetone
Accuracy better than +/-0.5% of Literature value

Process Hazard Analysis

The Micro Reaction Calorimeter provides hazard analysis with both speed and flexibility. Working with less than 2ml total volume reduces costs, waste and time. The μRC is capable of reducing the time requirement of a reaction calorimetry study on a process from several days to a few hours.



Conversion and heat-flow from hydrolysis reaction

Power compensation calorimetry measures in units of power meaning that calculation of reaction enthalpy is simply performed by dividing heat-flow integral (automatically produced) by quantity. Using the different modes of injection (single, multiple or timed) allows batch and semi-batch processes to be simulated under safe controlled conditions.

Process deviation studies have never been easier. Instead of generating several litres of waste over several hours for each variant considered, the micro calorimeter can generate the same information in a few minutes. This will allow proper consideration of all possible mal-operations where before, time, cost and material availability may have limited the application.

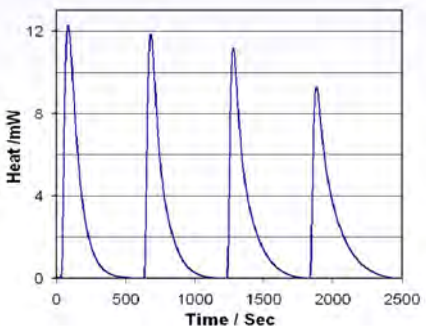
The more considerations of credible mis-operation that are performed the safer a plant and process are. THT aim to re-empower the safety professional by providing new technologies which can considerably improve the way hazard studies are performed.

Additional options such as a pressure handling option and high pressure cells will allow users to monitor pressure and gas formation either as a function of reaction conversion or, in the case of scanning experiments, as a function of temperature. The system can also function with disposable syringes for use with highly aggressive materials.

Process Development

The μRC is easy to use which allows any chemist or engineer the ability to rapidly investigate whatever reaction parameters they desire.

Combining modern DOE approaches to experimental design of calorimetry tests can provide users with information on reactant conversion, material accumulation, competitive reactions, inhibition and catalysis.



Kinetic controlled reaction in μRC

Automated addition of materials allows unattended, walk-away operation and the options of disposable reactors and syringes keeps costs to the minimum when conducting many reactions.

Catalysts, cements, & pharmaceuticals

Catalyst Screening

Although many reactions run better when catalysed it is very difficult to know the best catalyst to use. A recent survey of catalyst manufacturers suggested that in excess of 1000 versions of alumina supported platinum exist. The question of which the best system is and what the best conditions

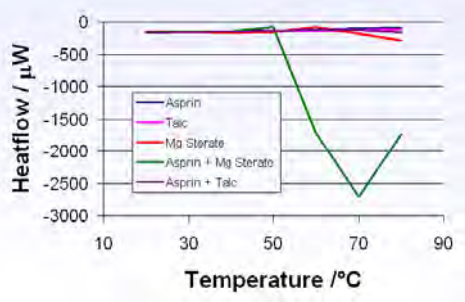
The ability to measure both kinetics and thermodynamics simultaneously allows users to select the parameters which are important to their process and monitor those as the catalyst is changed.

High pressure vessels (up to 20bar) now available with the Micro Reaction Calorimeter allow gas phase reactions (e.g. hydrogenation) to be examined. The µRC can be supplied with a high pressure transducer for direct measurement of gas uptake during reaction or gas evolution measurement.

The new µRC-KIN, dedicated kinetics package gives users the ability to easily import data directly into a specialist kinetics analysis software and then to model the reaction using a wide range of purpose designed systems. µRC-KIN is compatible with the CISP software products which allows full-scale models of reactions to be implemented for reactor modeling, runaway prediction and other useful parameters.

Excipient Compatibility Screening

The three temperature modes of the µRC make it a very useful and flexible tool for excipient compatibility assessment. Using the device in an isothermal mode allows auto-catalytic and slow reactions to be monitored.



Comparison of the thermal response between Aspirin and two standard excipients, Talc and Magnesium Sterate

Step-isothermal calorimetry will provide an accelerated method by which thermal stability assessments can be reduced from weeks to hours. Temperature scanning can also be used to detect reaction onset. Working as a macro-scale DSC, the µRC can provide onset information where lack of material consistency requires the use of larger volumes of material.

To meet the needs of the compatibility assessment market, THT have launched a new multi-cell calorimeter designed to simplify the testing of drugs, excipients and packing materials in abstract and designed environmental conditions. This, eight cell calorimeter allows users to run complete investigations in a single experiment negating concerns of reproducibility over extended periods.

The four-cell variant of the µMC

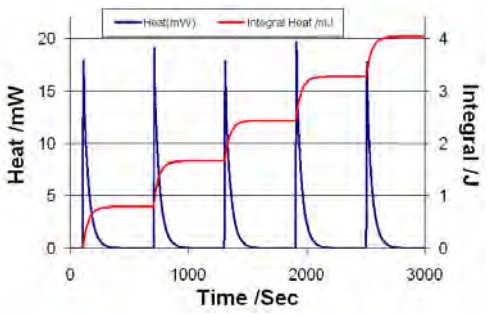
The multi-cell calorimeter (µMC) will operate in isothermal, step-isothermal or slow-scan modes and with 1.5ml or 4ml vials gives users the ability to have predetermined humidity within the system.

Adhesive Curing

Materials studies including adhesive curing, cement hydration and other such processes can be easily studied using the micro reaction calorimeter. The disposable vials make the system an ideal tool for chemistries where materials harden, set or gel. Being able to study these processes as a function of temperature is an ideal way of gaining valuable thermokinetic data which is otherwise unavailable.

Waste Management

The ever increasing pressure on natural resources means that the optimisation of waste handling is becoming more important. Combining of waste streams and batches may reduce volumes, costs and handling issues but safety dictates that these simple operations must be fully investigated as unexpected reaction may occur.

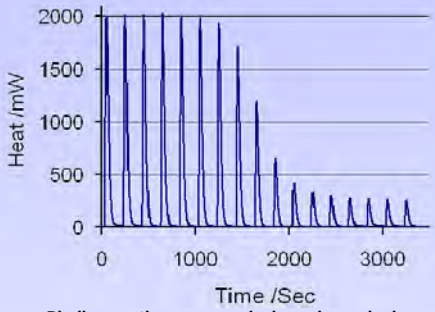


Interaction of Propan-2-ol and water

Titrations, scanning, solids addition and dissolution

End Point Determination

The ability of the μRC to measure small heats of reaction means that it can be used to detect subtle changes in heat output (and therefore reaction) where other indicators may prove unavailable or unreliable. The titration function of the micro calorimeter can be used to determine the exact stoichiometric quantities of reactants required to achieve full conversion.

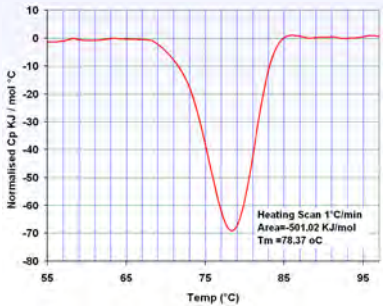


Binding exotherms as equivalence is reached

As well as binding exotherms titrations can be conducted with traditional acid-base type experiments to determine acidic concentration and other parameters where traditional colorimetric determination is not possible (in highly coloured solutions).

Scanning Calorimetry

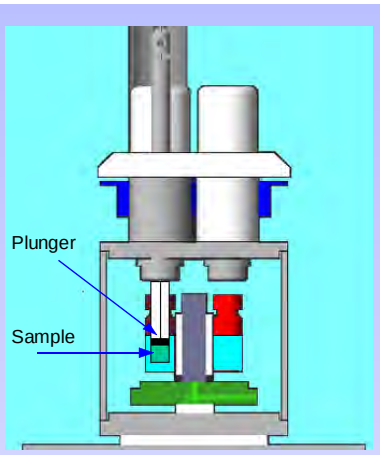
The power compensation system used in the μRC means that temperature scanning may be used as a means of determining many process variables. From reaction onset to melting and crystallisation points the μRC has the ability to detect chemical and physical processes as a function of temperature.



Endothermic result from temperature scan at 1°C/min

Solid Additions

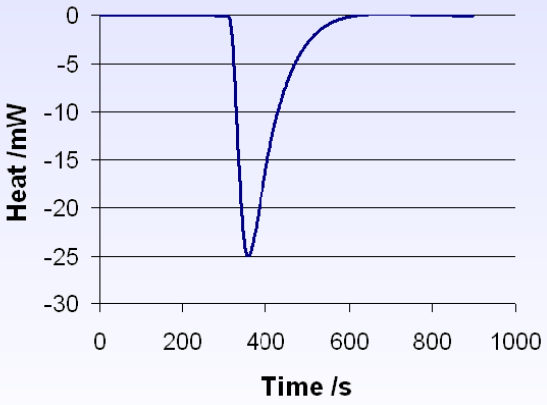
Although the liquid titration system supplied with the micro reaction calorimeter is very efficient to use and very useful sometimes, it is necessary to add solids into a liquid. THT have now developed a specialised system for the addition of solids to the μRC during an experiment. The image shown below illustrates the operation of the system.



Schematic of calorimeter cell & sample insert

Dissolution Experiments

The enthalpy of solution is an important parameter in both chemistry and pharmaceutics. Using the new Solid Addition System, heats of solution can be measured reliably and repeatedly without error. The solid is loaded into the addition system and the base of the system sealed using Parafilm™. The plunger is then lowered at the appropriate time in order to introduce a well-equilibrated material into the solution.



Enthalpy of solution experiment for KCl

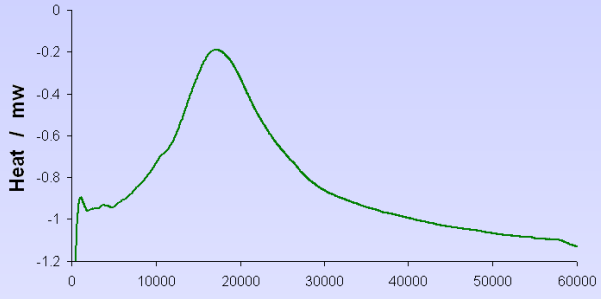
KCl	*Enthalpy of solution(kJ/mol)* = +17.22		
Integral /mJ	*Mass* /mg	*mol*	*Enthalpy*/kJ.mol^{-1}
7690.5	33.5	0.000450	17.10
7915	34.2	0.000459	17.24
7631	32.5	0.000436	17.49
Average			**17.28**
Standard Deviation			**0.20**
% Error (w.r.t Literature)			

Enthalpy of solution results for KCl

Biology education and specification

Biological Applications

The μRC can be used for a wide range of bio-chemical applications including binding studies (of proteins, lipids and enzymes) cell growth, organism metabolism and denaturation. Several features of the μRC make it unique for study of these classes of materials including the incremental titration, temperature scanning, and stirring which, with the removable cells of the micro reaction calorimeter mean that if your experiment precipitates or forms a gel you can simply dispose of the vial and start the next experiment with a clean one.



Growth curve showing bacterial activity in Milk

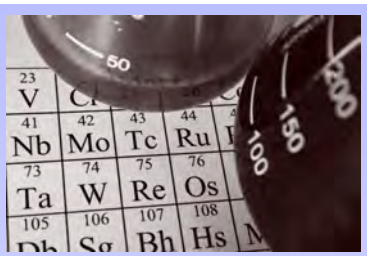
The biochemical applications of the μRC are detailed in a separate applications brochure.

Educational Applications

The Micro Reaction Calorimeter, as can be seen in this brochure, has a very wide range of applications. This versatility makes the μRC the ideal instrument for an academic environment as a range of varied users can perform different experiments on it.

In the teaching laboratory the μRC provides an elegant method of performing kinetics experiments without polystyrene cup calorimeters and watching iodine clock experiments in a water bath. As a research tool the μRC gives a rapid, accurate and unique way of studying a range of parameters which may not be measured by other methods. New applications are being discovered all the time - don't hesitate to enquire.

The μRC benefits from a small footprint, lack of external service requirements (no water bath or chiller) and a simple PC connection (only a USB connection to any PC running Windows XP). The μRC is designed to operate in any chemical or biochemical laboratory and conforms to modern safety standards.



Specification

Baseline Noise	**From 0.5mW RMS [high]**
Dynamic Range	**0.5mW to 10mW [high]**
Temperature Range	**-10°C to 200°C**
Standard Modes of Operation	**Isothermal Step Isothermal Titration**
Optional Modes	**Pressure - pressurise cell up to 10bar Solid Addition Accessory**
Scanning Rate	**Up to 2°C/min**
Isothermal Stability	**+/- 0.0001°C**
Cell Volume	**1.5 ml**
Cell Type	**Removable glass vial**
Time Constant	**30-40 seconds [high]**
Injection Volume	**1 to 250 µl**
Temperature Control	**Peltier based**
Stirring Speed	**0 - 400 rpm**
Measurement Principle	**Power compensation**
Connection to PC	**via USB cable**
Footprint (width x depth x height)	**15 x 40 x 35 cm**

Certain other specifications may be possible by discussion. Contact us with your exact requirements.

Options

The μRC is available with a range of options. These vary from changes to the specification (for high sensitivity application, rapid response or large heats) to specific cell types (dissolution cells, high pressure cells, low tau cells) and others (external pump options, pressure handling systems).

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