The Micro Reaction Calorimeter can operate in number of different modes and is more versatile than larger volume systems:

1. Incremental titration
2. Single shot addition
3. Calibration (heater pulse)
4. Isothermal mode (stability and storage measurements)
5. $C_p$ Measurement
6. Temperature Scanning
7. Pressurised cell (Hydrogenation)

The integrated addition syringe means that all liquid-liquid reactions can be conducted with walk-away operation minimising the users time requirement. But the instrument is not restricted to liquids.
How does small scale reaction calorimetry work?

Active control of sample temperature, sample temperature precisely controlled. Sensors are Peltier elements

Advantages:
Short time constant
Very rapid response
Stable calibration, valid for months not days
Most stable sample temperature μ°C
Measurement in true power units
At equilibrium, the temperature of both cells will be equal and no additional power is added or removed. An exothermic sample causes the temperature of the sample cell to increase. In response to this increase, the control algorithm removes power from the sample cell to return and maintain its temperature to that of the reference cell. The power added to or removed from the sample cell during this control procedure is equal to the power absorbed or produced by the sample.

The μRC Peltier modules control the sample temperature over the temperature range of −5 to 170°C requiring no external chillers or liquid nitrogen cooling.
- Temperature Range: -5°C to 170°C
- Thermal Stability: +/- 0.0001°C
- Baseline Noise: +/- 5μW
- Cell Volume: 2 ml removable vial
- Injection Volume: 1 μl – 250μl
- Pressure Range: up to 10 Bar
- Stirring: up to 500rpm
- Scanning Rate: up to 2 °C/min
- Small Footprint: 15 x 30 x 45 cm
• Instrument connects via standard USB port.
• Windows 7 or XP based instrument control and analysis software
• μRC utilises disposable sample cells in the form of standard HPLC vials. Crimp top or solid phenolic vial lids used for work above 120°C.
Software

- Select the appropriate tab for your desired experiment
Calibration

- The Micro Reaction Calorimeter contains an inbuilt calibration routine using a heater attached to the sample cell.

- Using empty cells, no vials. Calibrations are carried out using a number of identical heat pulses (usually at least 3) at a chosen temperature.

- In order to build a polynomial equation for the calibration constant it is necessary to have at least 3 calibration values over a range of temperature.
Step-Isothermal Measurement

• THT μRC has the ability to rapidly change temperature and re-equilibrate. This makes the system ideal for screening experiments over a range of temperatures.

• Examples of these type of experiments are excipient compatibility screening and isothermal kinetics determination.
Excipient compatibility

- Screening of excipient-drug formulations for incompatibility information
- Stressed/Unstressed systems can be easily tested over a wide temperature range with rapid yes/no results
• Incompatibility easily observed using accelerated rate generated by step-isothermal technique

• THT μRC has the ability to rapidly change temperature and equilibrate. This makes the system ideal for screening experiments over a range of temperatures.
Scanning Mode

- Measurement of Crystallization / Amorphous content

Low amorphous content not seen if not enough sample. μRC dynamic range and larger sample loading allows to detect low levels of amorphous content.

μRC Scan 15-120°C at 2°C/min

100% amorphous

100% crystalline
Isothermal Measurement

- Measurement of Crystallization

Measurements at elevated humidity by placing a saturated salt solution in the calorimeter cell with the sample. Different particle sizes Lot A, B and C have same total heat generated (area), but hydrate impurity formed more rapidly at smaller particle size.
Solid Addition

- Teflon plunger/plug arrangement to add solid to liquid under temperature control
Solid Addition

Results

The test was repeated. The results are given in the table below, with a literature value for the enthalpy of solution also quoted. The results show good agreement with the literature value $^1$

<table>
<thead>
<tr>
<th>KCl Mass (mg)</th>
<th>Heat (J)</th>
<th>Enthalpy of Solution (J/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>34.3</td>
<td>-7.58</td>
<td>+221.0</td>
</tr>
<tr>
<td>21.4</td>
<td>-4.85</td>
<td>+226.6</td>
</tr>
<tr>
<td>27.3</td>
<td>-6.28</td>
<td>+230.0</td>
</tr>
<tr>
<td>43.0</td>
<td>-9.69</td>
<td>+225.3</td>
</tr>
</tbody>
</table>

**Average, (J/g)**

+225.7

**Literature Value (J/g)**

+231.0

Figure 1: heat signal for 20.9 mg KCl injected into 1.5 ml H$_2$O
Solid Addition

- Using heat of solution to determine relative stability of polymorphs
Titration

- Titration experiments require the motorized titration tower to be attached to the instrument.
- Raise the syringe arm to its top position using the ‘Syringe Move’ button in the ‘Syringe’ tab.
Titration

• Next, load the glass syringe. Syringes come in two sizes, 100µl, 250µl

• The tower is comprised of two parts: these parts simply unscrew. Place the needle through the metal piece then screw the metal and the PTFE parts together.
Titration

- A Teflon stir bar is placed in the sample vial and the vial loaded into the chamber.

- A vial containing buffer is loaded into the reference chamber.

- Finally the syringe tower is placed into the sample position.
When the “identical injections” boxes is ticked, all injections will be carried out at the same temperature and using the same injection size. There are also the stirring on/off and stirring speed options.

In Test Information the syringe volume is set. Other fields are available for the basic information such as sample ID, sample name and concentration.
Titration

- Select the folder to save the data and ‘Start Test’

- The μRC software will use the automated baseline tracking feature to initiate the injections. This ensures that the instruments baseline is stable before the titrant is injected.
Binding study (Supramolecular, Host-Guest Chemistry)

- Binding of 18-Crown-6 ether to Barium ions
- Decrease of reaction heat with increasing 18-Crown-6 shows the binding equilibrium
- Integrated heats, changing with amount added.
- Binding equilibrium constant, heat of binding and stoichiometry all can be obtained easily from these data.
Heat Capacity

• The measurement of heat capacity is achieved by making a “step-change” in the temperature of the cell in comparison to an empty vial.

• Before measuring the Cp of a material. A ‘blank’ should be run using empty vials in the sample and reference position (to account for any differences in the heat capacities of the two vials (sample and reference).

The machine will carry out temperature steps of the required magnitude around the required temperature. The temperature listed in the left column is not the start of the temperature step, but the middle of the step. For example, a 1°C temperature step at 25oC will begin at 24.5°C and end at 25.5°C.
Heat Capacity

‘Blank’ Temperature and Heat data
Heat Capacity

• The analysis software incorporates a wizard to subtract the blank data from the experimental data. The heat capacity is then calculated in J/°C/g
Pressure Option

• Addition of a pressure transducer and stainless steel pressure cells allow measurements up to 10bar. *Hastelloy cells available upon request.*
Simultaneous Titration & Pressure measurement

- Modification to µRC Tower

µRC Syringe Tower injection of 250µl HNO₃ to Bicarbonate of Soda
Heat of reaction under controlled gas flow

• The option has been used to good effect to study Carbon Capture involving the exothermic reaction that occurs when CO₂ gas is absorbed by an amine solution.

• The GFO consists of a flow controller to regulate the flow rate of CO₂ into the cell containing the amine solution.

• Weighing the vial before and after the test is used to calculate the rate of CO₂ uptake.
Methylethanolamine (MEA) was added to water in 30% concentration by weight CO₂ absorption was monitored at three different flow rates.
Absorption of CO$_2$ into MEA

**Enthalpy calculated by:**

\[
\text{Enthalpy of Absorption} = \frac{\text{Heat}}{\text{Number of moles of CO}_2 \text{ absorbed}}
\]

\[
\Delta H_{\text{abs}} = \frac{222.4 \text{ J}}{\left( \frac{0.12}{44.01} \text{ mol} \right)} = 81.55 \text{ kJ/mol}^{-1}
\]

<table>
<thead>
<tr>
<th>Sample</th>
<th>Flow rate of CO$_2$ feed (ml/min)</th>
<th>CO$_2$ Absorbed (g)</th>
<th>CO$_2$ Absorbed (mmol)</th>
<th>Energy released (J)</th>
<th>Enthalpy (kJ/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEA 0.3 (wt)</td>
<td>0.98</td>
<td>0.12</td>
<td>2.7</td>
<td>222.4</td>
<td>81.55</td>
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<tr>
<td></td>
<td>1.11</td>
<td>0.12</td>
<td>2.7</td>
<td>226.0</td>
<td>82.87</td>
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<tr>
<td></td>
<td>0.56</td>
<td>0.12</td>
<td>2.7</td>
<td>209.0</td>
<td>83.60</td>
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<td></td>
<td>0.26</td>
<td>0.12</td>
<td>2.7</td>
<td>224.0</td>
<td>82.13</td>
</tr>
<tr>
<td>Average</td>
<td>0.73</td>
<td>0.12</td>
<td>2.7</td>
<td>220.4</td>
<td>82.54</td>
</tr>
</tbody>
</table>
The uRC

- High Sensitivity
- Low volume (2ml)
- Removable cell with stirring
- Titration, step-isothermal and scanning
- Low cost
- Small footprint