A Bright Future for Thermal Methods

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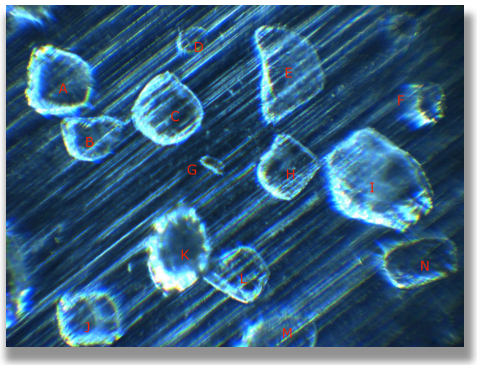
# TASC Applications for Pharmaceuticals

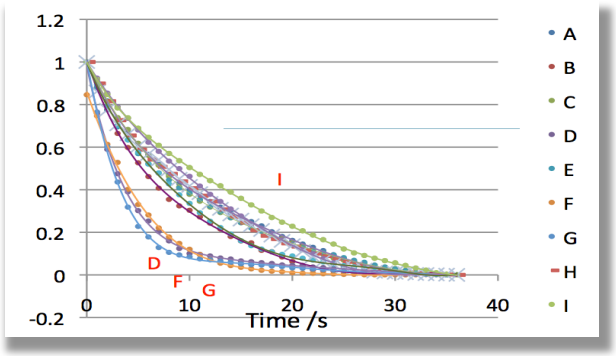
- Thermal Dissolution Analysis
- Glass Transition Kinetics
- Complex Melting
- T-Map Mode
- Histogram of Transition Temperatures

## Thermal Dissolution Analysis

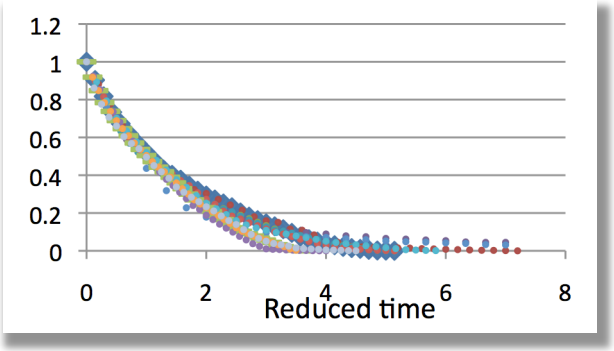
**Right** is an image of a collection of sugar crystals in water in a DSC crucible. The TASC algorithm can follow their disappearance. Graphs of the dissolution of these crystals is shown **below right.**



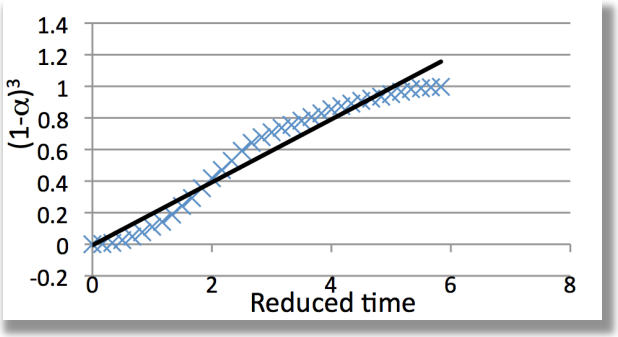

In the graph shown **right**; it can be seen that small crystals D, F and G disappear much faster than the large crystal I. The temperature is clearly a crucial parameter in determining dissolution rate and this is carefully controlled by the Hot Stage. **This is called Thermal Dissolution Analysis or TDA**.



**Right** shows a reduced time plot of all of the crystals and it can be seen that, to a reasonable approximation, they follow a consistent function.

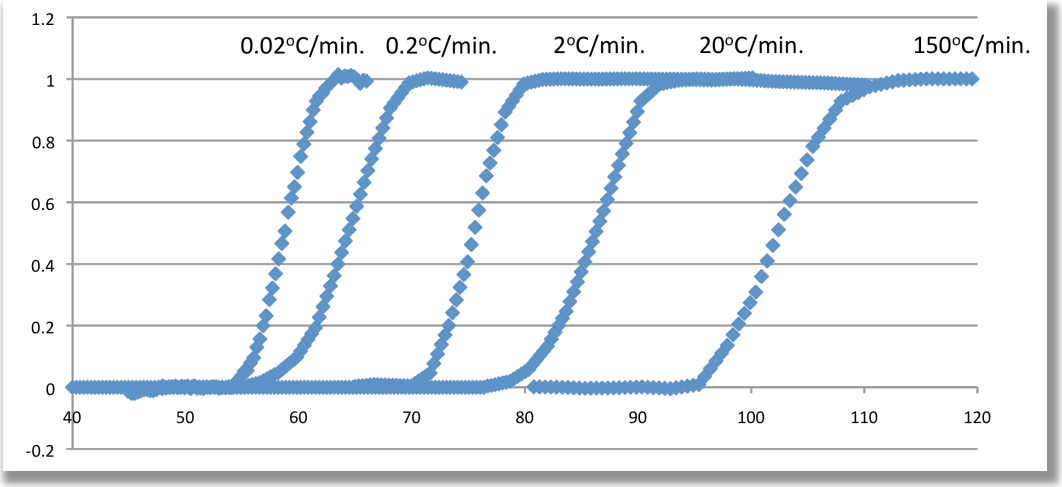


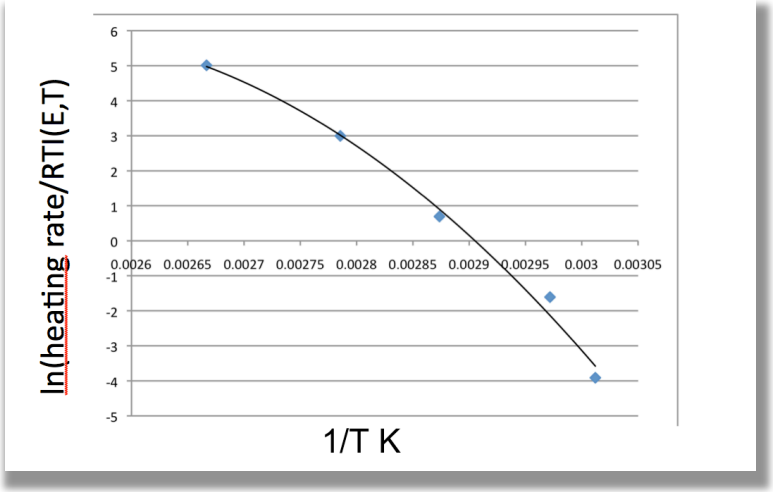

**Right,** averaged data are plotted against $(1-\alpha)^3$, an approximately linear graph is obtained as would be expected for a shrinking 3D object. In other cases a different empirical function might be found.




TDA enables the dissolution kinetics of a wide range of particulate samples to be determined so that, for example, the dissolution rates of drugs with different morphologies in different environments at different temperatures can be characterized**.**

# Glass Transition Kinetics

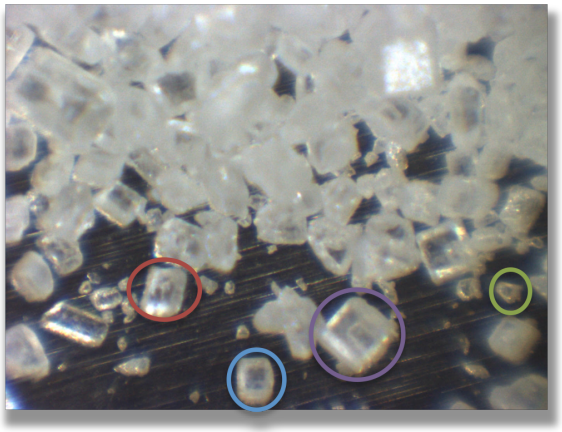


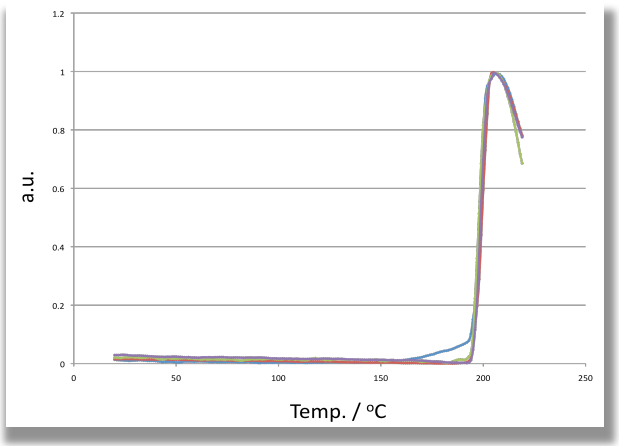




**Above left** is a series of TASC experiments for indomethacin at different heating rates. Results have been obtained over a range of almost five orders of magnitude. **Above right,** Arrhenius plot for the TASC data. The expected non-linear response is clearly seen.

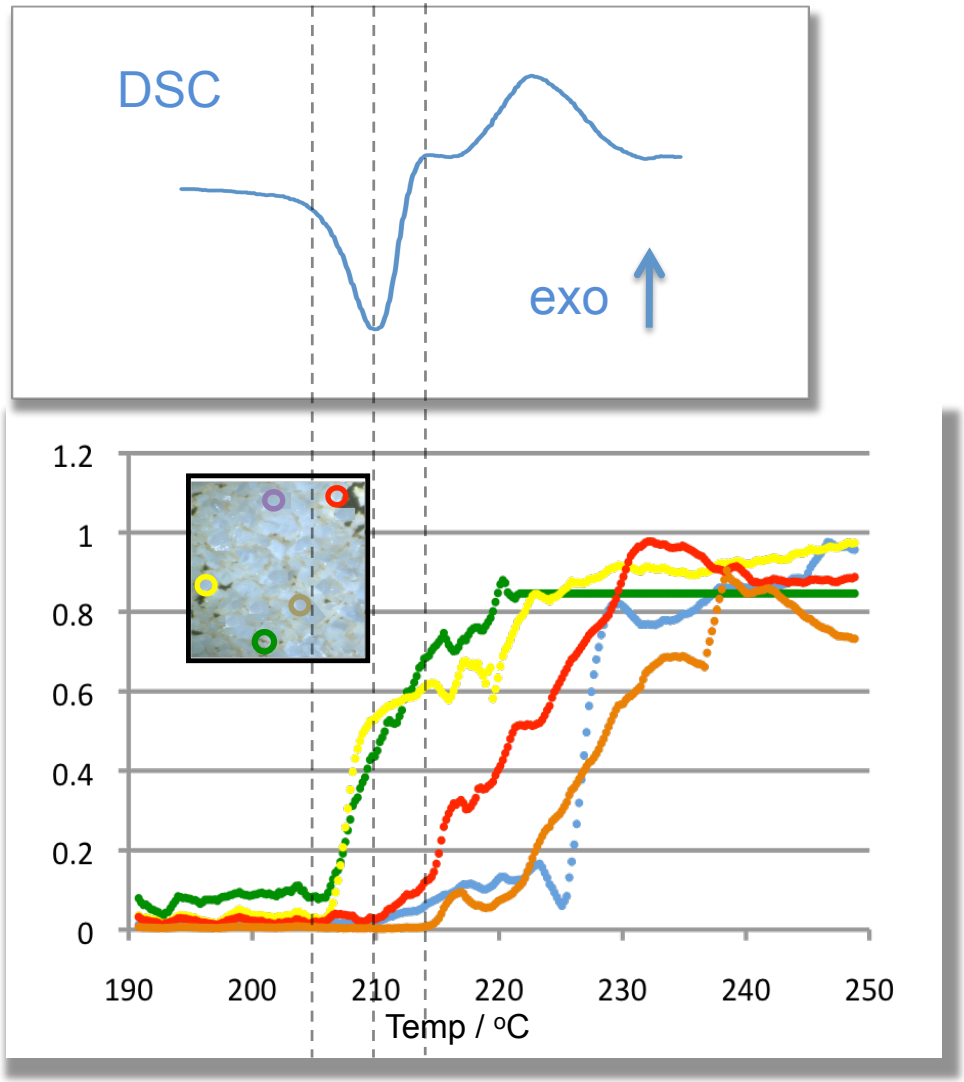
TASC enables a true relaxation measurement to be performed over a broader range of heating rates than any other thermal technique.

# Analysis of Complex Melting Behavior



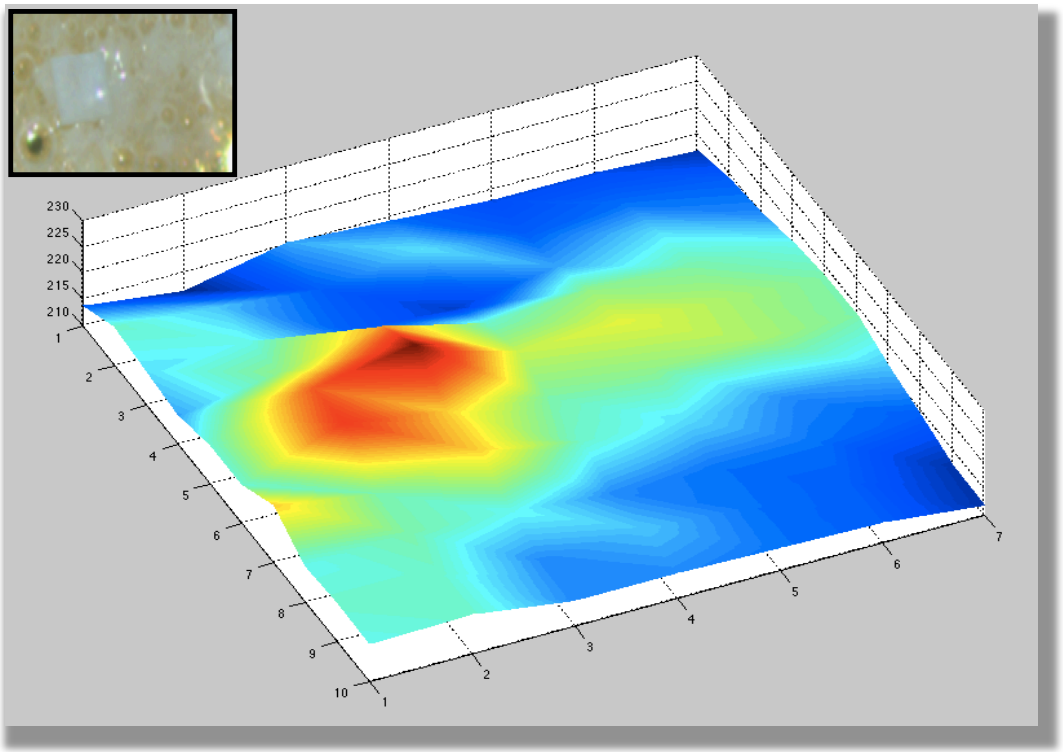



The melting of sucrose crystals, shown **above left**, can be considered as complex because it shows a heating rate dependence. However, the TASC data, **above right** show that each crystal behaves the same so the sample behaves in a homogeneous manner in this respect. It can be seen that the TASC measurement is highly reproducible.




**Above,** the inset photograph shows a sample of zoledronic acid. A series of TASC measurements are shown from different locations following the color coding given by the circles in the inset photograph. It is clear that there is a broad range of melting temperatures from 205°C to 225°C. The melting endotherm, see the DSC plot, has an onset temperature of 205°C, peak temperature of 210°C and offset temperature of 217°C. This endotherm is then followed by an exotherm attributable to a decompositions reaction. The TASC results show complex behavior because they demonstrate that melting continues during this exotherm.

# T-Map Mode




**Above** Is a 3D image created by mapping transition temperatures within the region shown in the inset photograph of zoledronic acid undergoing melting. In the photograph It can be seen that there is an unmelted crystal surrounded by bubbling molten material from crystals that melted at lower temperatures. In the 3D image this crystal appears as red because of its higher melting temperature. The T-Map vividly illustrates the inhomogeneous nature of the sample. The bubbling is due to decomposition and the DSC trace shows an exotherm at this point. This confirms the observations made above.

# Transition Temperature Histograms

The T-Map data can be used to create a histogram of the distribution of transition temperatures shown **right**; this characterizes the inhomgeneity of the sample in a way not possible by other means.