FAST LIQUID DIFFERENTIAL SCANNING CALORIMETRY (FLDSC)

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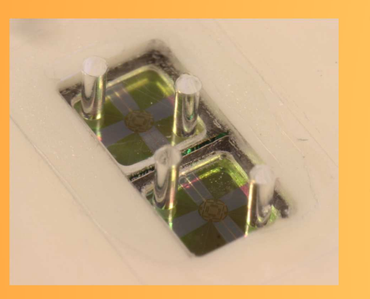
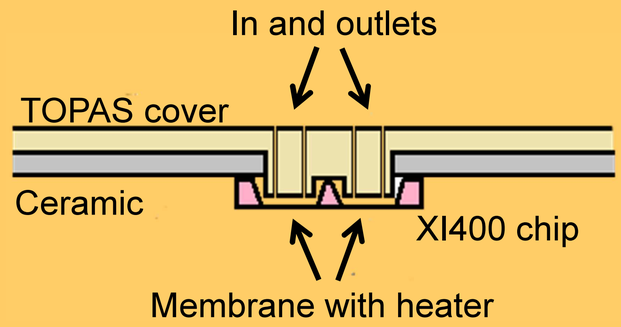
Introduction

Many types of cancer have been distinguished by measuring the thermal denaturation of proteins in blood plasma of patients. While conventional Differential Scanning Calorimetry (DSC) carries out such measurements with scan rates of 1 °C/min, requiring relatively large amounts of sample, Fast Differential Scanning Calorimetry (FDSC) operates at much higher scan rates of up to 1000 °C/s. Besides reducing the measurement time from hours to minutes, this lowers the required sample amount from hundreds to just a single µl.
This poster introduces the new Fast Liquid Differential Scanning Calorimetry (FLDSC) sensor, showing experimental results on lysozyme protein solutions at various fast scanning rates.

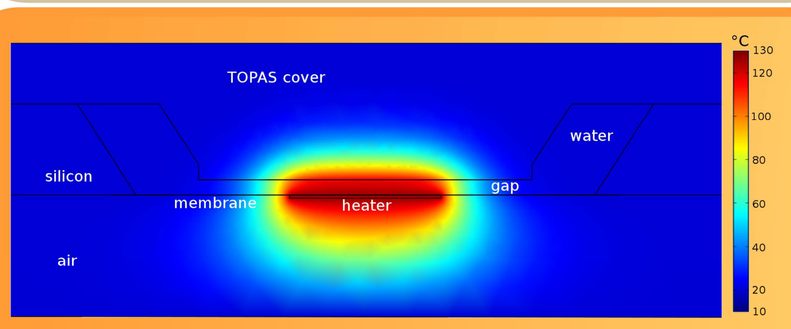
The FLDSC chip



The FLDSC chip is based on the FDSC chip for the Flash DSC1 from Mettler Toledo. This chip contains a reference cell and a sample cell. For this chip a cover, fabricated from TOPAS COC, was developed to prevent evaporation of the liquids. The cover has a liquid inlet and outlet for each cell, so the cells can be filled independently.

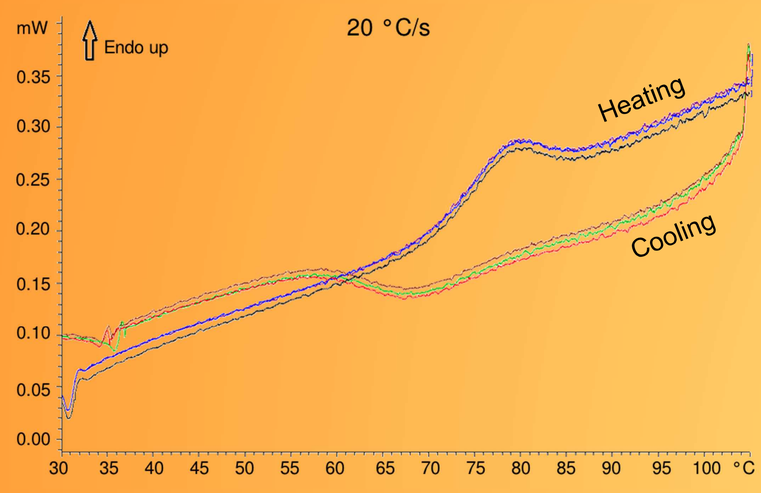


Simulation of heat transfer in the FLDSC chip

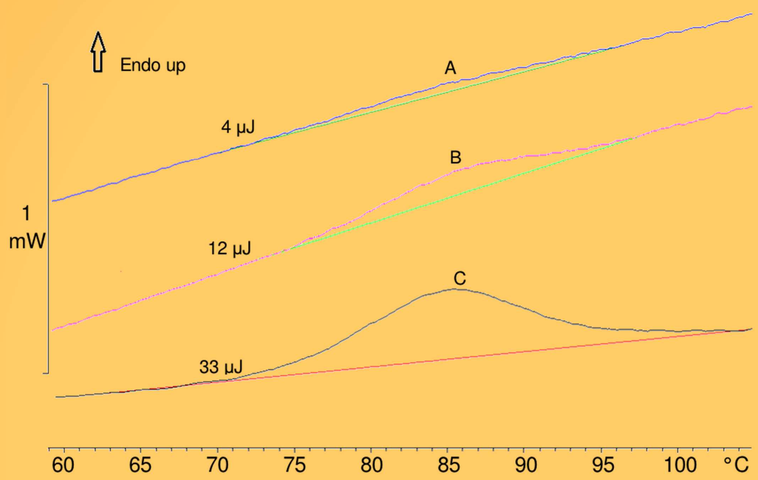


Simulation of heat transfer in the FDSC chip with a gap size of 50 µm. In 70 ms around 50 % of the sample in the gap on top of the heater is heated up from ambient temperature to 125 °C. This 70 ms is enough to heat up to 100 °C at 1000 °C/s scan rate. With smaller gaps higher scan rates can be achieved.

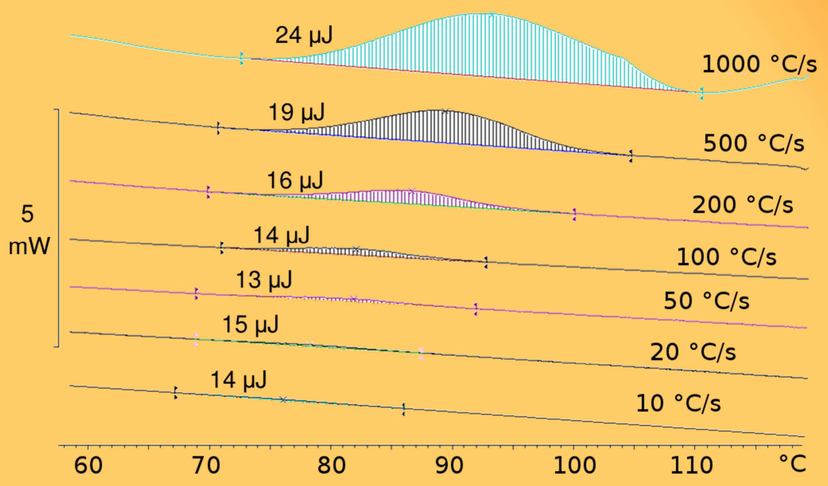
FLDSC measurements with lysozyme



Measurements of a 10 % lysozyme-in-water solution.
In the heating curves the protein unfolding peak can be seen between 70 °C and 90 °C. In the cooling curves protein refolding can be seen between 80 °C and 55 °C.



Heating curves of 1 % (A), 3 % (B) and 10 % (C) lysozyme-in- water solutions at 100 °C/s.
The protein unfolding peak appears between 70 °C and 100 °C, with a peak temperature at 85 °C .
The chip gap size is about 60 µm.



Heating curves of a 10 % lysozyme-in-water solution measured at scan rates between 10 °C/s and 1000 °C/s.
As expected the protein-unfolding peak becomes bigger at higher scan rates, and shifts to higher temperatures.
The chip gap size is about 30 µm.

Conclusions

The new Fast Liquid Differential Scanning Calorimetry sensor introduces revolutionary performance in liquid scanning calorimetry with off-the-shelf instruments, enabling experiments on a single µl sample that are finished in minutes.
Lysozyme experiments show that protein unfolding can be recorded at scan rates of up to 1000 °C/s, and for lysozyme concentrations of 1 % and probably even down to 0.1%.

Acknowledgments

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