



e-MicroCalorimetry News

Volume 8 Issue 2 Summer 2008

Ultrasensitive Calorimetry for the Life Sciences™

Welcome

Summer may conjure up images of lazy days, relaxing by the pool and sipping cool drinks. However, MicroCal has not been relaxing this summer. Instead, we've been working overtime to introduce the latest advance in Isothermal Titration Calorimetry (ITC), the Auto-iTC₂₀₀.

Combining the performance of the highly successful, ultrasensitive iTC₂₀₀, with full automation to run up to 75 samples per day unattended, the Auto-iTC₂₀₀ is designed to address the needs of today's life science researchers, particularly those in drug discovery and development. To learn more about this exciting new product, please see the article below.

As always, we welcome your comments and suggestions. Please email us at info@microcal.com

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New Book Available from MicroCal

MicroCal has had the honor and privilege of participating in the biennial Applications in Biocalorimetry Conference series and the Current Trends in Microcalorimetry Conference series for over ten years. Once highly sensitive microcalorimeters, both Differential Scanning Calorimeters (DSC) and Isothermal Titration Calorimeters (ITC), became commercially available, acceptance of the technology and technique grew rapidly and there was great interest in exploring the capabilities, limitations and applications for microcalorimetry. These meetings provided, and still provide, a wonderful forum for this exchange of information, knowledge, ideas and questions.

MicroCal was pleased to sponsor the 2007 Current Trends in Microcalorimetry meeting held in Boston in July and we were delighted by the size and quality of the scientific program, the attendance and the highly interactive participation of the presenters and attendees. There were 23 podium presentations and 33 poster presentations. Based on the substantive and diverse scientific content presented at this meeting, we decided to publish the "Proceedings of the 2007 Current Trends in Microcalorimetry Conference." Please contact your local sales representative to reserve your copy.

Personnel Update

MicroCal is pleased to welcome Steve Zisk as the Account Manager for the mid-Atlantic states. Steve will be covering New Jersey, New York, Pennsylvania and Delaware. Steve comes to MicroCal with years of experience in selling capital equipment and reagents to institutions in the mid-Atlantic states for companies such as Amersham Biosciences, GE Healthcare and Whatman. Steve can be reached at szisk@microcal.com or by telephone at 610-908-7574 or 413-570-1586.

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Advancing Research

Stability Screening During Biopharmaceutical Manufacturing

Biopharmaceuticals, such as therapeutic antibodies, are manufactured by pharmaceutical and biotechnology companies, as well as contract manufacturing organizations (CMOs) worldwide. Production at a manufacturing scale involves protein expression in tens of thousands of liters of cell culture, followed by purification using chromatography columns which are hundreds of liters in size. This results in kilograms of purified product, which is formulated and dispensed for sale to doctors and hospitals. The final drug product must be stable for at least 2 years and this is tested and controlled.

Biopharmaceutical companies are constantly optimizing their manufacturing processes, to improve product yield, speed up the purification process, and improve stability of the final product. A single manufacturing run can result in millions of dollars of drug product, so any improvement in final yield is important to the economics of manufacturing. Conversely, a failure in any step of the production, resulting in decreased yield and/or stability, can result in a large financial loss. Stability is an important property of a biopharmaceutical protein. Stability is characterized during process optimization, as part of lot release, as well as during the shelf-life stability studies of the drug. Stability is also used to assess at the biocomparability of drugs after any modifications were made in the manufacturing process, or manufactured at a different site. Differential Scanning Calorimetry (DSC) measures the transition temperature (the T_m), which is an indication of thermal stability – the higher the T_m , the greater the thermal stability.

DSC is used during manufacturing to:

- Quickly assess the impact of manufacturing processes to the drug product including: purification, protein expression, scale-up
- Easily determine guidance for optimal storage conditions before making critical decisions
- Intervene during critical steps during the manufacturing process resulting in financial savings
- Quickly and easily assess the biocomparability of a drug product before shipment

Other bioanalytical assays for stability, such as SEC-HPLC, require storage of sample for hours, days, or even weeks and months. DSC provides results at the start of the process, and DSC stability data correlates well with other protein stability assays.

DSC is also used for:

- Identify the most stable construct from protein engineering
- Screen multiple liquid biopharmaceutical formulations to quickly select the most stable candidates to move forward

- Optimize bioprocessing conditions during process development

Reviewed by Verna Frasca, Technical Services Scientist

The Auto-iTC200 in Small Molecule Drug Discovery

We are all excited about the Auto-iTC₂₀₀ arriving in laboratories around the globe. It has been amazing for those of us who are used to running 4 or 5 experiments a day to see this automated iTC₂₀₀ deliver a full thermodynamic profile on up to 75 samples in 24 hours unattended. The new software also provides a wizard to simplify experiment design. We believe that this combination of automation, reduction in protein consumption and ease of method development, will accelerate the use of ITC in drug discovery research, where it can now be applied earlier in the pipeline. This will allow researchers to make the best decisions, quickly, about which compounds to select to move forward through the process of hit to lead selection, lead optimization and ultimately to candidate selection. This platform is also well suited for fragment-based screening where it can be employed for assessing the affinities of weak binding fragment libraries.

ITC is considered to be the **"Gold Standard 'K_dometer'"**, but until now its use has been restricted because of sample consumption and throughput limitations. However, the low sample consumption and improved throughput of the Auto-iTC₂₀₀ extends the application of this technology into routine screening, as well as provides the detailed 'Mechanism of Action' and SAR data so important for successful discovery programs. The Auto-iTC₂₀₀ has been designed with both new users and experts in mind. For example, there are "prepacked" methods for cleaning and binding experiments that should be suitable for all users needs, but there is also the flexibility for those who want to develop their own methods from the ground up. An automatic post-run data analysis package has been included which will minimize the time spent on the analysis of large volumes of data, and improve the ease of data transfer.

ITC has never been so fast and easy to use. The Auto-iTC₂₀₀ can be used to generate up to 75 **"Gold Standard"** K_ds in 24 hours. We believe that both new and expert users alike will enjoy the benefits of this latest development from MicroCal.

Reviewed by Ronan O'Brien, Application & Research Manager, MicroCal

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Inside Story - q & a, tips and practical advice

Question:

I understand that the iTC₂₀₀ needs less protein than the VP-ITC. Does this mean I can use lower protein concentrations?

Answer:

No, the protein concentration is identical to the one used for the VP-ITC. Less protein would mean less protein amount (expressed in micrograms); this is due to a decrease of the cell volume.

Question:

I bought the iTC₂₀₀ last year and I would be interested in the Auto-iTC₂₀₀. Is there an upgrade program?

Answer:

Your instrument can be upgraded to the automated version easily, please discuss the upgrade process with your local sales representative.

Question:

I am pleased to see I can run hundreds of compounds with the Auto-iTC₂₀₀, but the data analysis will require too much time for me. Any comments?

Answer:

The data will be automatically analyzed by the Auto-iTC₂₀₀ software and the thermodynamic parameters are presented in an Excel spreadsheet.

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 [Calendar](#) - shows, seminars and other events

Meetings	Dates	Locations
American Chemical Society (ACS)	Aug 17-21	Philadelphia, PA
ICBL 2008	Aug 26-30	Maastricht, Netherlands
National Enzyme Conference	Aug	TBD
XXth International Symposium on Medicinal Chemistry (EFMC-ISMC 2008)	Aug 31-Sep 4	Vienna, Austria
The Malaysian Society for Biochemistry and Molecular Biology (MSBMB)	Aug 27 - 28	Kuala Lumpur, Malaysia
AUC and Hydro 2008	Sep 11-12	Newcastle, UK
BioProcess International Conference	Sep 23-26	Anaheim, CA

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We welcome your comments. Please email info@microcal.com with your thoughts and suggestions.

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