Temperature Mapping During Freezing and Thawing

within Celsius-Paks

By Gaël Péron, Matthew Olsen, and William Heyn

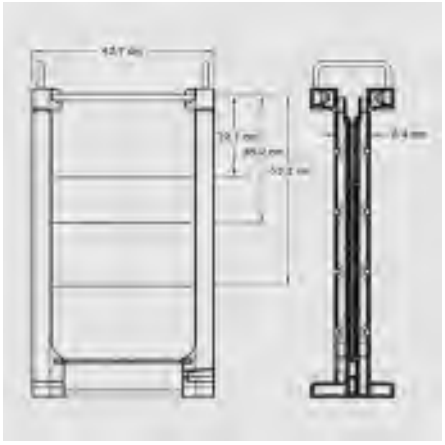

Figure 1: Thermocouple positioning during the experiment.

Sartorius Stedim Biotech is the world leader in controlled Freeze-Thaw technology

Executive Summary

The Celsius system has been designed to produce bi-directional freezing through the two faces of the Celsius-Pak. The controlled freezing operation results in the growth of ice from the sides towards the center as well as from the bottom of the Celsius-Pak towards the top. This freezing pattern has been demonstrated through temperature mapping at different points within the Celsius-Pak during normal Celsius operations. By inducing bottom to top freezing, the Celsius system allows for relief of stresses due to ice growth within the Celsius-Pak into the Celsius-Pak headspace where they can be most easily accommodated through expansion of the solid volume. This document provides data to indicate that the last point to freeze within the Celsius-Pak occurs at the liquid surface at the centerline of the liquid volume.

Introduction

Process development procedures often require the mapping of the temperature within any container that will be frozen and thawed. For the Celsius controlled freeze-thaw technology, the production process is monitored by an RTD positioned at the last point to freeze (LPTF) in each individual Celsius-Pak. This RTD provides freezing and thawing data for one point of the Celsius-Pak which can be considered as the worst-case. However, a comprehensive monitoring program is sometimes desired during initial investigation of the equipment. This application note provides data gathered to support the choice of the LPTF location and provide guidelines to the customer willing to replicate these experiments on their own equipment.

Materials and Methods

A Celsius FT100 with CU5000 system was used to produce the freezing data shown in this document. The system was filled with 5 standard 16.6 L Celsius-Paks and one 16.6 L Celsius-Pak with an extra long thermowell. All Celsius-Paks were filled with deionized (DI) water and pressurized to 0.6 psig. The long thermowell Celsius-Pak allows for measurement of temperature within the Pak at depths below a 10 L fill volume. These Celsius-Paks are not suitable for production manufacturing but are available in small quantities for process development and qualification testing. The long thermowell Celsius-Pak was specially fitted with a thermocouple capable of measuring temperature at multiple points spanning the liquid height. The thermocouple was carefully positioned to attempt to gather data vertically within the Pak. This positioning is critical to the attainment of useful data. Temperatures were recorded as standard for the remaining 5 Celsius-Paks (See TM-0030 for details of standard RTD positioning).

The Celsius-Pak fitted with the multipoint measuring device was placed in the front of Bay A (position A2). The positioning of the thermocouples within the Celsius-Pak is shown in Figure 1 below with measurements shown from the height of the bottom of the standard RTD holder. This is the standard for RTD depth measurements and allows for these measurements to correspond with those reported in TM-0030 which outlines proper height for RTD placement in the Celsius-Pak.

Table 1: Freezing Times of the six Celsius-Paks

	A1	A2	B1	B2	C1	C2	Avg.	Std. Dev.
NFT(h)	1.62	1.51	1.92	1.68	1.85	1.65	1.70	0.15
EFT(h)	2.28	2.17	2.47	2.17	2.50	2.20	2.30	0.15

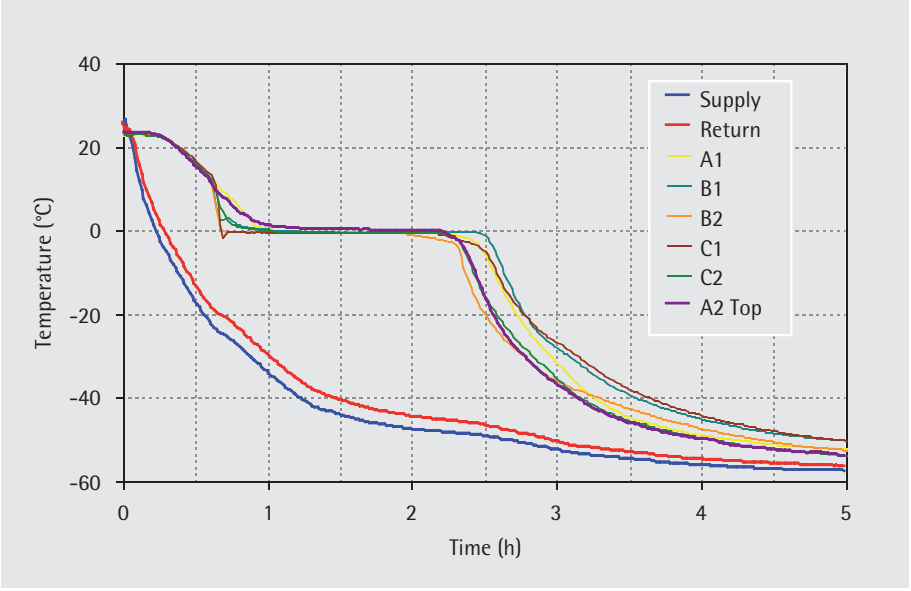

Fig 2: Freezing Temperature Profiles from different Celsius-Paks

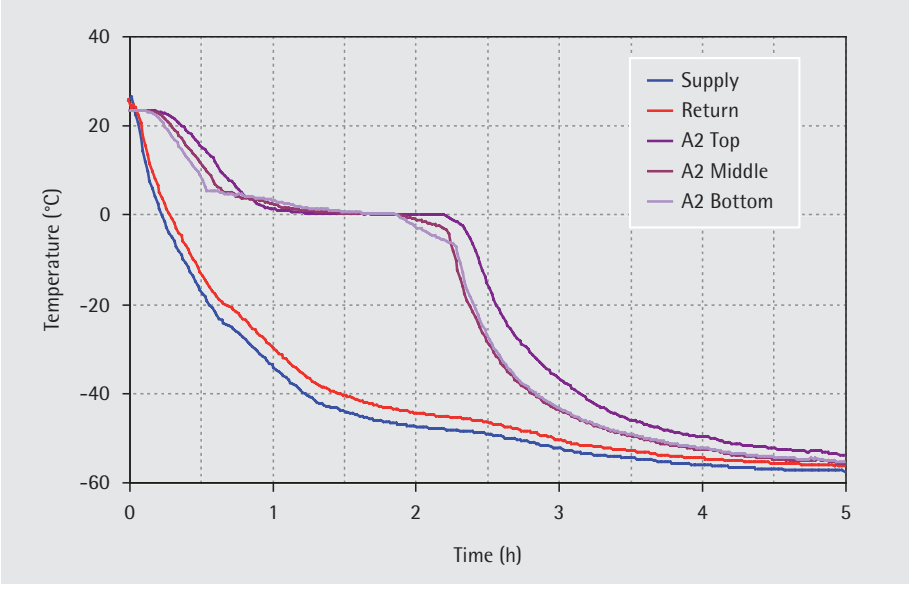

Fig 3: Freezing Temperature Profiles from different points within Celsius-Pak A2

Results And Discussion

The Celsius system underwent a standard freezing process which produced the data shown in Figure 2. Data collected from the thermocouple and the RTDs used for the first experiment are converted to quantitative measures of the freeze as shown in Table 1.

The average fusion time measured by the Nominal Freeze Time (NFT) is 1.7 hours and the average process time measured by the Effective Freeze Time (EFT) is 2.3 hours. The NFT is defined as the time required for the product to change from +3°C to –5°C at the LPTF. The EFT is defined as the time required for the product temperature to change from +10°C to –30°C at the LPTF. The low dispersion of the six freezing temperature curves can be seen in Figure 2 below and is also illustrated by the 0.15 hours standard deviation obtained in both NFT and EFT values.

The data shown in Figure 3 supports a bottom-up effect during the freezing process. This is also supported by the data shown in Table 2 below in which a 22 minute difference is observed between the completion of the fusion at the bottom of the Celsius-Pak and that observed at the top.

Table 2: Freezing Times of the six Celsius-Paks

	A2 Top	A2 Middle	A2 Bottom
NFT (h)	1.50	1.32	1.14

The data collected from the top shows a sharp transition from the temperature plateau at the freezing point to the portion of the curve where the temperature is descending below the freezing point. This type of sharp departure from the freezing point temperature is characteristically seen for temperatures measured near the last point to freeze and is evidence of the proper positioning of the uppermost thermocouple.

After the final portion of liquid within a given volume is frozen, the temperature of the entire volume can descend quickly below the freezing point producing the sharp descent seen in Figures 3. However, for all other points within the volume, the descent from the freezing point is more gradual until such time as all the liquid within the volume has frozen. This effect can be seen in the curves collected from the bottom and middle heights of the Celsius-Pak. The temperatures present at all points within the Celsius-Pak volume at any given time during the freezing process will be distributed between the temperature at the heat exchange plate walls (represented by average of HTF Supply and Return temperatures) and the central width of the Celsius-Pak.

The thawing data show in Figure 5 demonstrate that the melting starts from the top of the Celsius-Pak and progresses to the bottom until buoyancy forces the last piece of ice to float to the top of the Celsius-Pak. This phenomenon causes a small transitory dip in temperature which can be observed in Figure 4 at a process time of around three hours. This brief temperature change is useful to determine the complete thawing time shown in Table 3.

The data from this experiment shows that the last point to freeze is near the top of the Celsius-Pak at the center of the 8.4 cm width of the Celsius-Pak. Sartorius Stedim Biotech recommends placement of the Product RTD 2 cm below the liquid level in the centreline of the Celsius-Pak since temperature measured at this point is representative of the last point to freeze and provides consistent and reliable temperature process information as demonstrated in all data shown in this document.

Table 3: Thawing times of the six Celsius-Paks

	A1	A2	B1	B2	C1	C2	Avg.	Std. Dev.
TT (h)	3.38	3.45	2.38	2.98	2.75	2.97	2.99	0.40

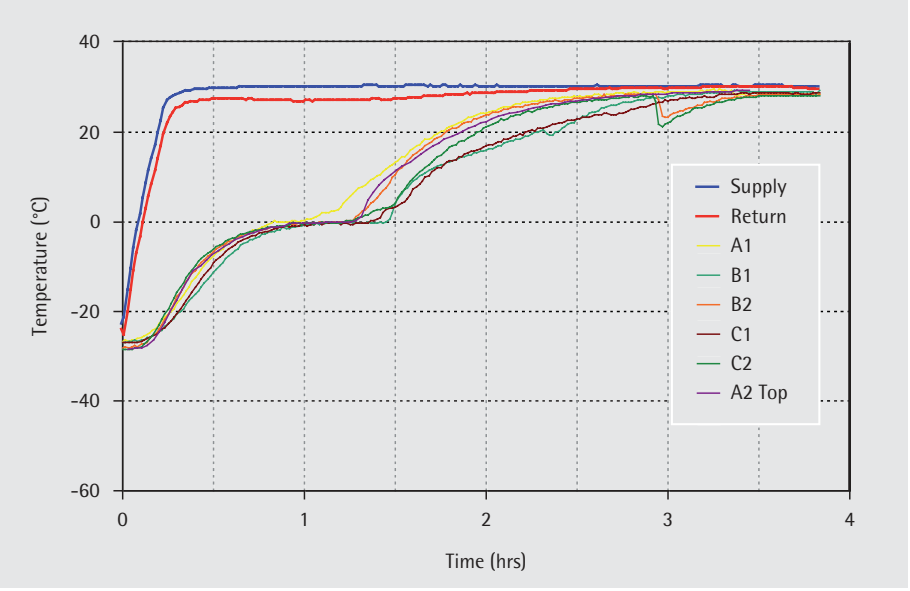

Fig 4: Thawing Temperature Profiles from different Celsius-Paks.

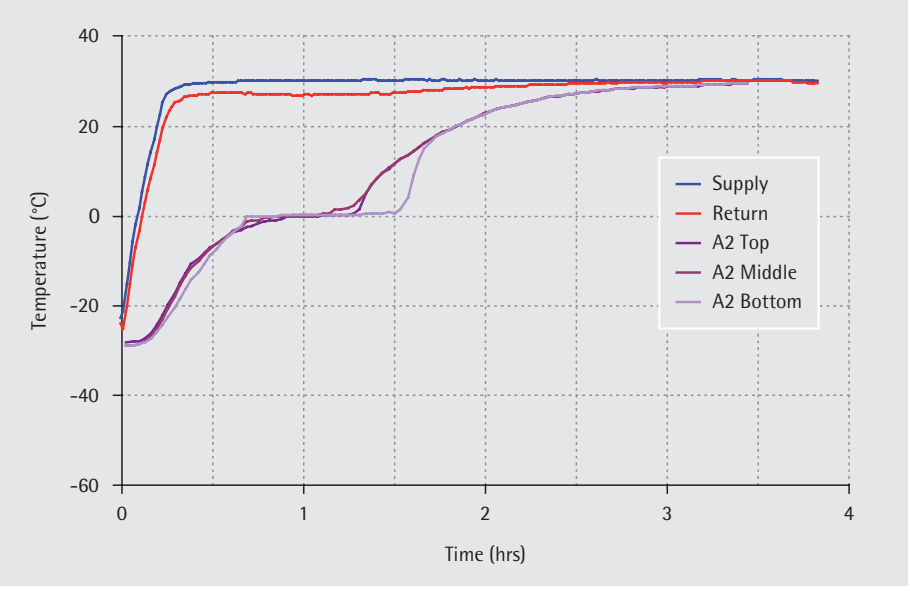

Fig 5: Thawing Temperature Profiles from different points within Celsius-Pak A2

Conclusions
The Celsius system has been shown to provide bottom to top freezing in this study. The last point to freeze is located at the liquid surface within the Celsius-Pak and at the center of the width of the Celsius-Pak.

Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen, Germany

Phone +49.551.308.0
Fax +49.551.308.3289
www.sartorius-stedim.com

USA +1.800.3687178
UK +44.1372.737100
France +33.442.845600
Italy +39.055.634041
Spain +34.91.3586102
Japan +81.3.37405407

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