Freezing Point Depression Measurement using a built Temperature Logging Device

Aston University

Sandra B. Donohoe

Andrew J. Ingham

School of Life & Health Sciences, Aston University, Birmingham, B4 7ET

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Introduction

Temperature is a critical parameter monitored in Freeze-Drying production and manufacturing processes to ensure reproducible product quality, process efficiency and productivity. Research is carried out into the development of methods and control systems that can acquire accurate low temperature measurements for commercial use. In freeze-drying applications this research could be used to determine solute concentrations within vials, the time at which complete solidification is obtained during the freezing stage of the process and information on crystal morphology. The objective of this project is to monitor very low freezing points because of a direct relationship to osmolality of a system. A high speed data acquisition system (DAQ) for remote low temperature recording has been illustrated for its ability to acquire freezing point values in the range 0°C to -21°C suitable for deployment within a freeze-dryer. The feasibility of calibrating the system against freezing point profiles is also discussed.

Materials and methods

The block diagram of the device (Figure 1) used to obtain the freezing point depression profiles of 0 % w/v, 0.9 % w/v and 23.3% w/v sodium chloride solutions.

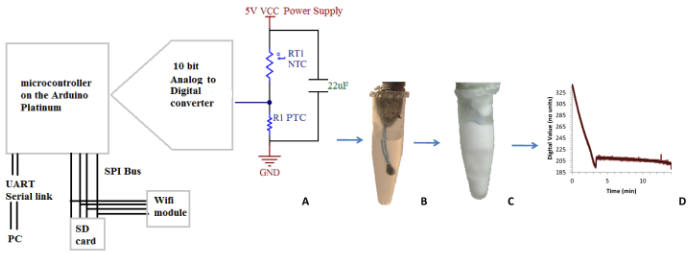

Figure 1: (A)Block diagram of the logging device and the analogue linearization circuit, (B) temperature sensor placed into eppendorf and into -68°C, (C) frozen sample, (D) recorded freezing point profile of sample.

A negative temperature coefficient (NTC) thermistor was connected in series to a positive temperature coefficient (PTC) resistor. A 22uF capacitor and a 5V reference supply were also used as part of the analogue linearization circuit.

The signal was digitised with a 10bit analogue to digital converter (ADC) prior to being processed by the microcontroller and stored as external memory on board the device.

An optional sampling frequency of 30ms was selected due to the requirement for rapid sampling rates suitable for freezing point depression events.
According to the British Pharmacopoeia, the freezing point of the solution is defined as the maximum temperature observed during the solidification of a supercooled liquid [1].
Calibration of the device is carried by freezing solutions with known freezing point depressions (Figure 2) and osmolalities.
The following relationship is present between osmolality and temperature:

$\varepsilon = (\Delta T / 1.86) \; x \; 1000 \; mosmol/kg$ [1]

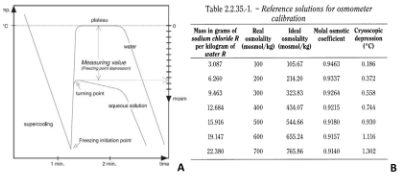

Table 2.2.35-1. - *Reference solutions for osmometer calibration*

Mass in grams of sodium chloride R per kilogram of water R	Real osmolality (mosmol/kg)	Ideal osmolality (mosmol/kg)	Molal osmotic coefficient	Cryoscopic depression (°C)
3.087	100	105.67	0.9463	0.186
6.269	200	214.20	0.9337	0.372
9.463	300	323.83	0.9264	0.558
12.684	400	434.07	0.9215	0.744
15.916	500	544.66	0.9180	0.930
19.147	600	655.24	0.9157	1.116
22.380	700	765.86	0.9140	1.302

Figure 2: (A)Water and aqueous solution cooling curves and freezing point depression [2], (B) reference solutions [1].

The thermistor was placed into 1ml of each solution and frozen to -68°C.
The system was often used real time through direct monitoring of the Universal Asynchronous Receiver/Transmitter (UART) and data stored on external memory space.

Results and Discussion

Initiation of nucleation sites were formed over the temperature range -2°C to -7°C for 0.9%w/v NaCl solution using epoxy coated thermistor sensor (Figure 4). Factors known to influence this include the quantity of "foreign impurities" [3] both those of the container and contaminants in solution.

Freezing point depression was recorded as increasing with increasing NaCl concentration (Figure 6).

Greater supercooling occurred with a glass bead coated sensor (Figure 5). This was hypothesised to have occurred due to the smoother surface, reducing the initiation of nucleation (increased supercooling).

The expected deviation of the freezing points was observed as the concentration was increased (Figure 6). This occurs due to:

- Different salt-water phases being formed in saline solutions during solidification. The solvent separates by forming pure solid ice crystals amongst a concentrated solute phase [3].

The freezing artefact caused by an ice insulation barrier (Figure 5) has still to be overcome.

Figure 6 allows calibration of the sensor, where the digital values (Table 1) correspond to the known freezing points of the solution.

	Distilled water, 0°C freezing point, (0mosm)	*0.9% NaCl (300mosm), freezing point depression of 0.558°C [1]*	*23.3% sodium chloride solution with a freezing point of 251K [4]*
Epoxy coated thermistor	217.4 digital units	210.3 digital units	80.6 digital units
Glass coated thermistor	313.9 digital units	308.2 digital units	143.5 digital units

Table 1: Calibration points for the temperature measurement device

Typical freezing point characteristics of saline solutions are illustrated in figure 3.

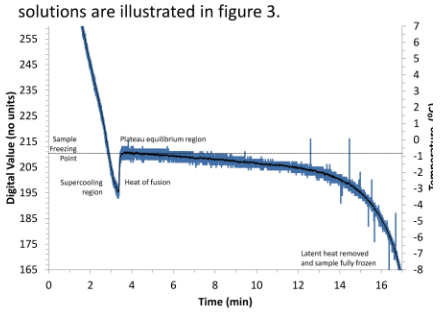

Figure 3: Freezing characteristics of 0.9% w/v NaCl (300mosm), 100kohm epoxy thermistor, at *5 deg°C/min cooling rate*. Representative trace showing freezing point depression characteristics.

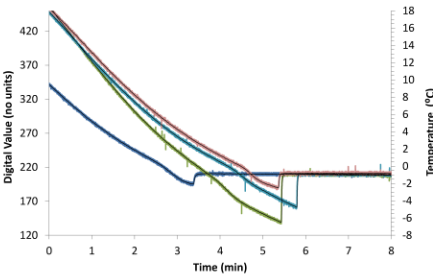

Figure 4: Freezing characteristics of four samples of 0.9% w/v NaCl (300mosm), *5 deg°C/min cooling rate, (*n=8), 100kohm epoxy thermistor.

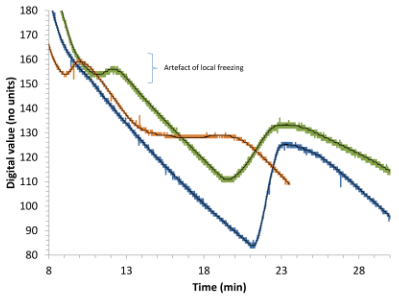

Figure 5: Three freezing point depression curves of 23.3% w/v sodium chloride (eutectic point and temperature is 251K [4]), n=6, using a 1.65kohm glass bead thermistor.

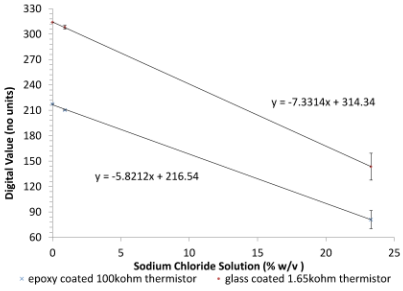

Figure 6: Calibration graph showing the freezing point digital value means ± SD for 0% w/v, 0.9% w/v and 23.3% w/v NaCl solutions.

Conclusions

To conclude, the device has shown potential for use in the high speed data acquisition and data storage of low temperatures. A wireless logging system capable of measuring in excess of -20°C has been developed in order to progress to much lower values. Resolution of 3 model systems: distilled water, NaCl 0.9% w/v and NaCl 23.3% w/v has been performed with digital separation of over 100 arbitrary units of precision. Future work would investigate different methods of controlling ice nucleation to promote uniform freezing to allow accurate calibration of the system against freezing points.

erences:
BRITISH PHARMACOPOEIA COMMISSION OFFICE 2013. *British Pharmacopoeia Volume V- Appendix V N. Osmolality,* London, Stationery Office.
LOSER MESSTECHNIK 2008. Loser Manual Micro-Osmometer Type 6.