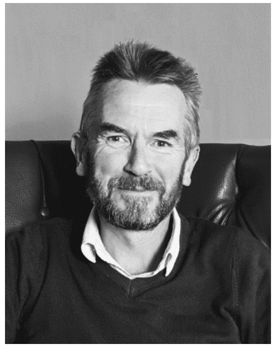
6th Annual Conference & Exhibition
LYOTALK®
EUROPE 2022
19 - 20 May | Amsterdam, Netherlands

What's the point in the end-point?

A determination of the true sublimation end point by Through-Vial Impedance Spectroscopy

Prof. Geoff Smith

School of Pharmacy, De Montfort University, Leicester, UK



DMU LyoGroup

Leicester School of Pharmacy
De Montfort University, The Gateway, Leicester, LE1 9BH, UK
gsmith02@dmu.ac.uk

DE MONTFORT UNIVERSITY LEICESTER

In collaboration with

NIBSC Confidence in Biological Medicines

Overview

- Process analytical technologies for freeze-drying (single vial and batch techniques)
- Introduction to through-via impedance spectroscopy (TVIS)
- Case study : Primary drying end point
  - Separation between sublimation (primary drying) and diffusive desorption (secondary drying)
  - The impact of phase states (crystalline vs amorphous) on the end point profile
- Conclusion that:
  - Existing, vapour and temperature sensing PATs cannot differentiate between source of water vapour (ice or adsorbed water)
  - TVIS provides identification of true sublimation (primary drying) end point

Process Analytical Technology (PAT)

PAT, as defined by the ICH, is "a system for **designing, analysing and controlling** the manufacturing through timely measurement (during the process) of critical quality and performance attributes of raw and in-process materials and the process with the goal of ensuring final product quality"

ICH, 2009. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Topic Q8(R2): Pharmaceutical Development.

Single vial (new) techniques

- Through vial impedance spectroscopy

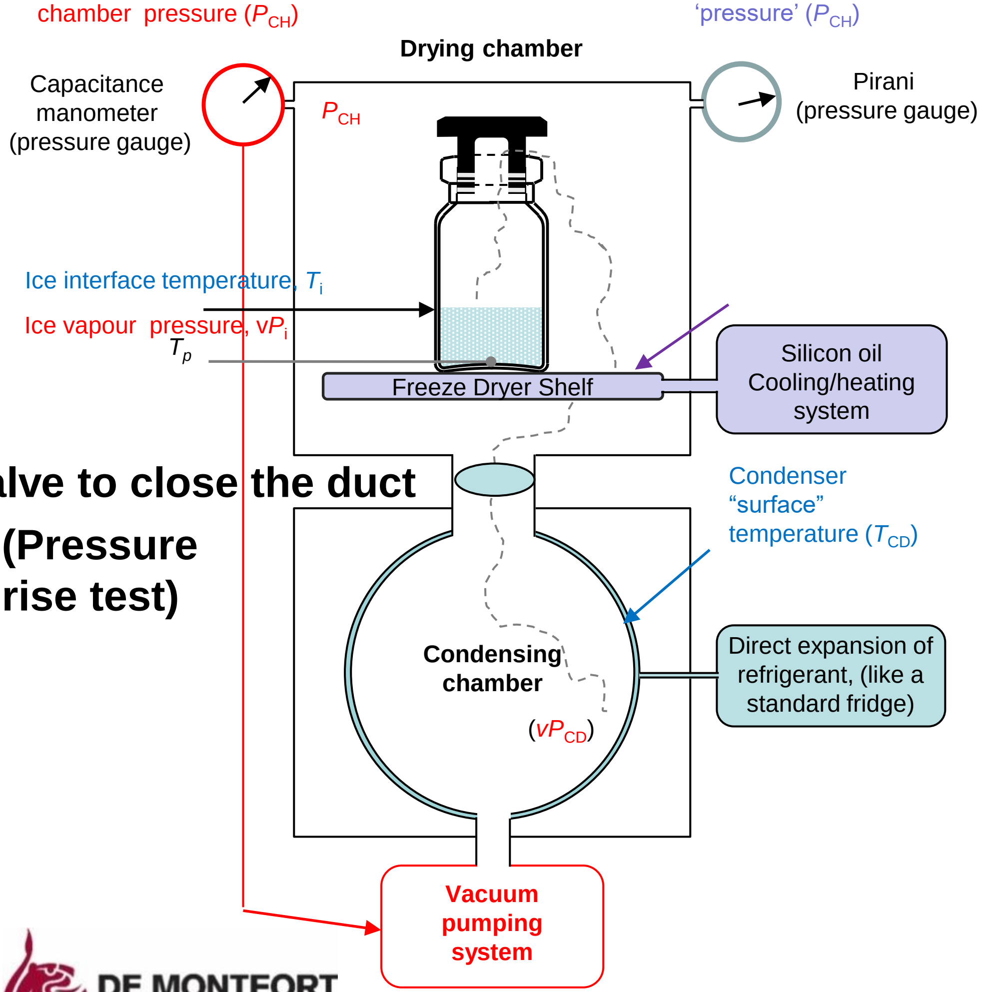
Single vial (existing) techniques

- Temperature probes
- Heat flux transducers
- Microbalance

Batch techniques

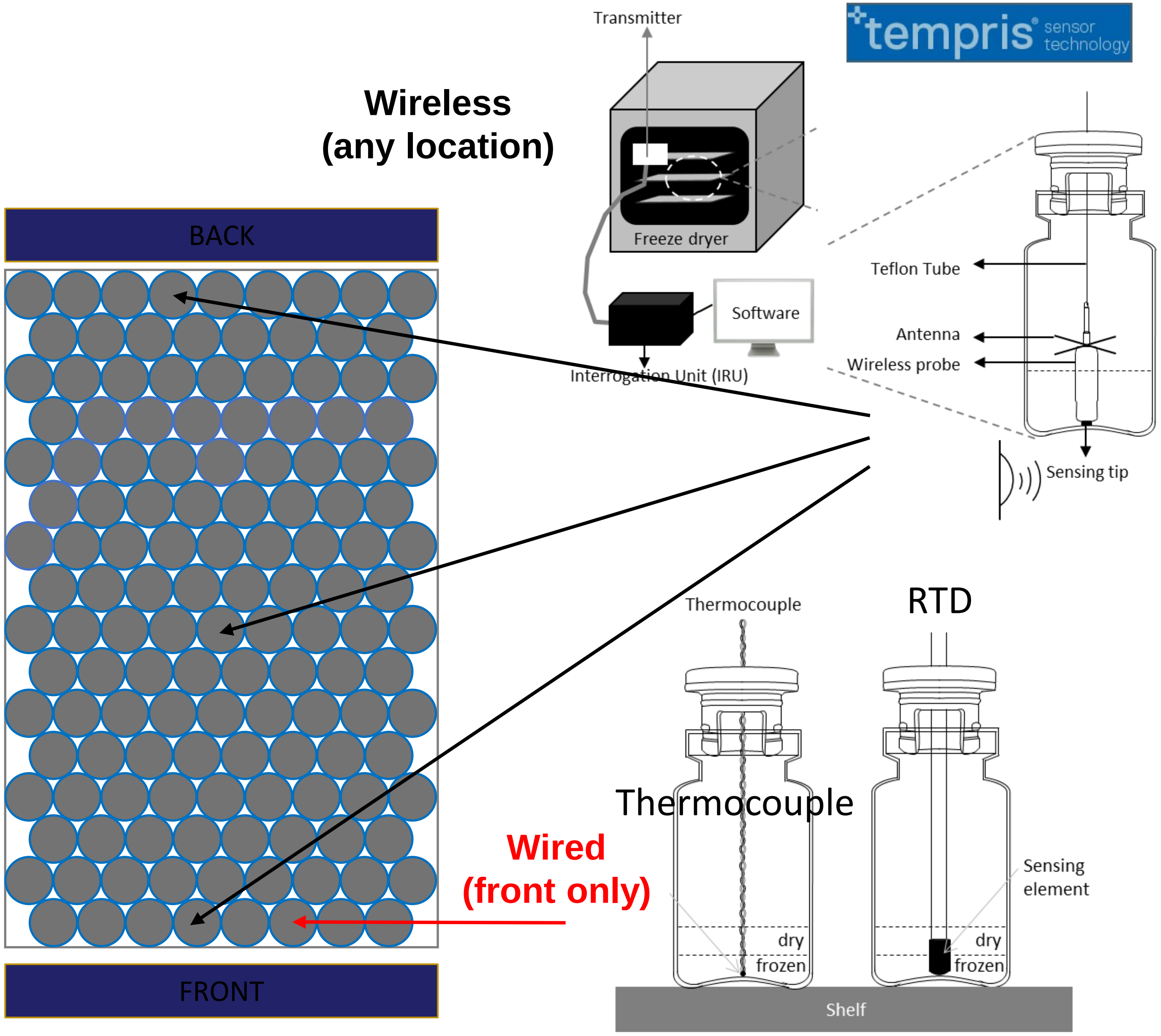
- Pressure rise test (PRT)
- Manometric temperature measurement (MTM)
- Comparative pressure measurement (CPM) – Pirani vs capacitance manometer
- Time domain laser absorption spectroscopy (TDLAS)

Comparative pressure measurement



Valve to close the duct

(Pressure rise test)

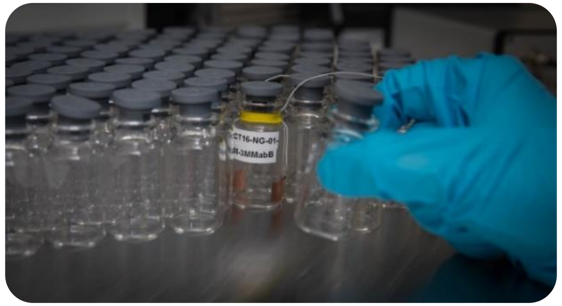


DE MONTFORT UNIVERSITY LEICESTER

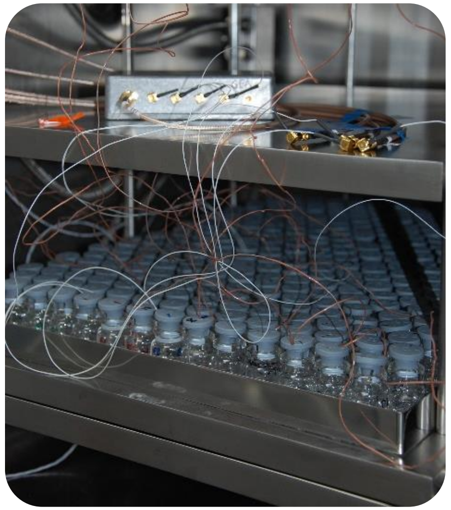
Through Vial Impedance Spectroscopy

Single Vial PAT

Non- perturbing to packing of vials



Multichannel



Thin flexible cables (0.5 - 2 m)

- Stoppering unaffected

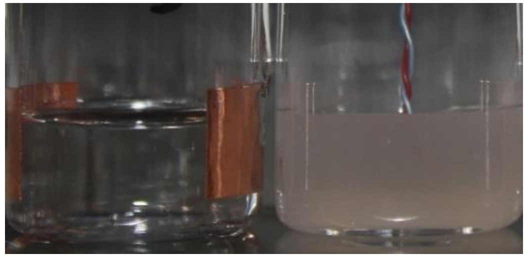
Temperature calibration

- using nearest neighbour vial(s)

Low thermal mass of electrodes

- no interference with heat transfer & drying rates

Plain vial TVIS vial TC vial



Non-sample invasive
no impact on ice nucleation

CASE STUDY

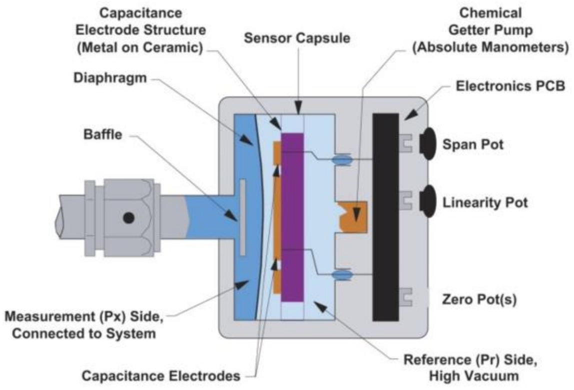
Primary drying end point

Separation between sublimation (primary drying) and diffusive desorption (secondary drying)

The impact of phase states (crystalline vs amorphous) on the end point profile

Comparative pressure measurement (CPM)

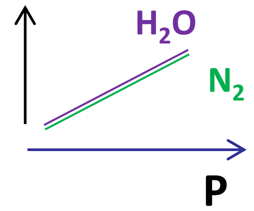
Capacitance manometer



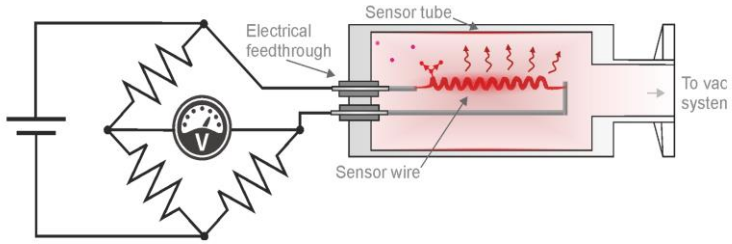
Pressure changes position of a diagraph which alters the electrical capacitance of the system

Sensitive to total pressure

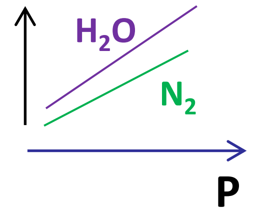
Capacitance



Pirani gauge



Resistance



Gas molecules collide with the element and removes heat changing the resistance

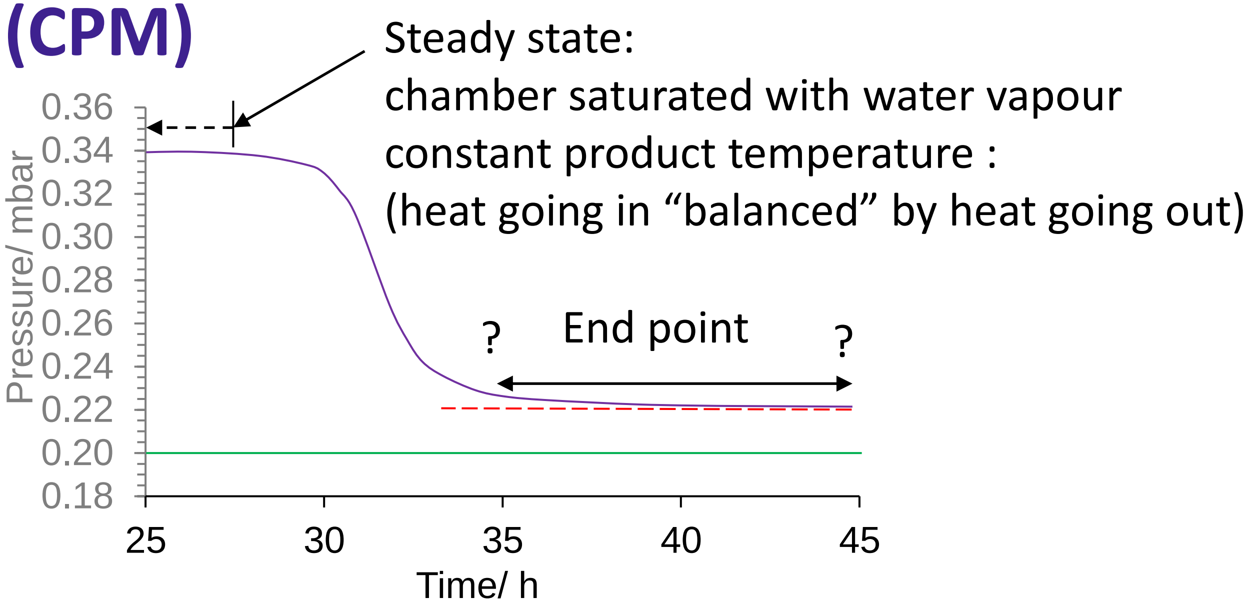
Sensitive to type of gas,

e.g., N_2, H_20

Comparative pressure measurement (CPM)

Pirani

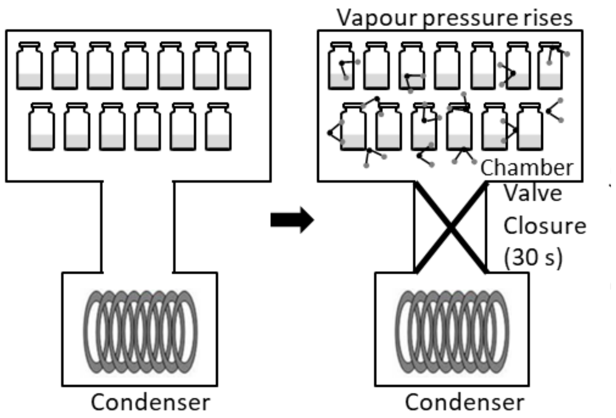
Capacitance manometer

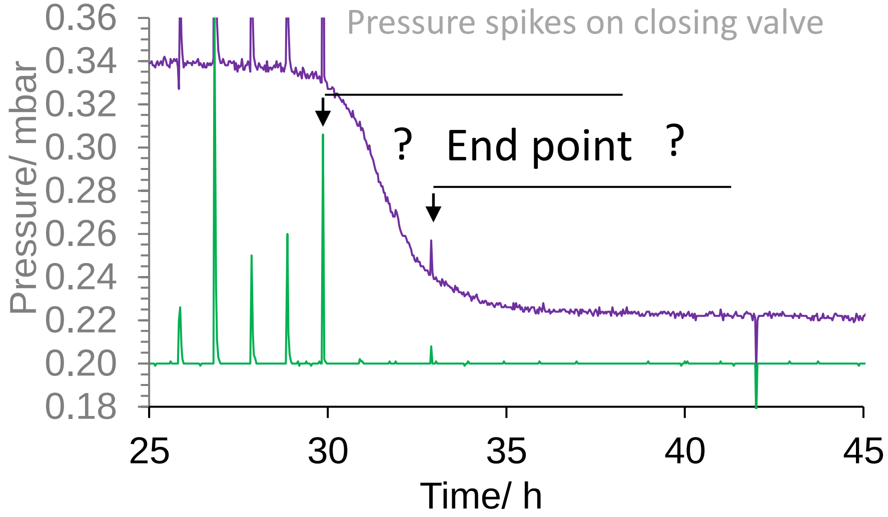


- Comparative pressure measurement (CPM):
  - Capacitance manometer responds to absolute gas pressure
  - Pirani response to water vapour is ~ 1.6 x that of the capacitance manometer
  - Therefore, Pirani output is higher than the CM while water vapour is being generated
- When drying is complete the Pirani converges on the capacitance manometer

But when has an asymptote been reached?
And does the end of sublimation coincide with the asymptote?

Pressure Rise Test (PRT)





- Pressure rise testing (PRT)
  - Brief (up to 30 s) isolation of the valve between drying chamber and condenser
  - Results in spikes (pressure rises) in both Pirani and capacitance manometer readings
  - Reason :
    - water vapour is released from the product during the drying stages
    - Vapour can not vent to the condenser when the valve is closed
    - Pressure rise occurs until the valve is opened again

AAPS PharmSciTech, Vol. 11, No. 1, March 2010 (© 2009)
DOI: 10.1208/s12249-009-9362-7

Research Article

Determination of End Point of Primary Drying in Freeze-Drying Process Control

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3]

Received 9 June 2009; accepted 9 December 2009; published online 8 January 2010

Abstract. Freeze-drying is a relatively expensive process requiring long processing time, and hence one of the key objectives during freeze-drying process development is to minimize the primary drying time, which is the longest of the three steps in freeze-drying. However, increasing the shelf temperature into secondary drying before all of the ice is removed from the product will likely cause collapse or eutectic melt. Thus, from product quality as well as process economics standpoint, it is very critical to detect the end of primary drying. Experiments were conducted with 5% mannitol and 5% sucrose as model systems. The apparent end point of primary drying was determined by comparative pressure measurement (i.e., Pirani *vs.* MKS Baratron), dew point, Lyotrack (gas plasma spectroscopy), water concentration from tunable diode laser absorption spectroscopy, condenser pressure, pressure rise test (manometric temperature measurement or variations of this method), and product thermocouples. Vials were pulled out from the drying chamber using a sample thief during late primary and early secondary drying to determine percent residual moisture either gravimetrically or by Karl Fischer, and the cake structure was determined visually for melt-back, collapse, and retention of cake structure at the apparent end point of primary drying (i.e., onset, midpoint, and offset). By far, the Pirani is the best choice of the methods tested for evaluation of the end point of primary drying. Also, it is a batch technique, which is cheap, steam sterilizable, and easy to install without requiring any modification to the existing dryer.

KEY WORDS: end point; freeze-drying; PAT; primary drying; residual water.

Freeze-dryer: Lyostar II (SP Industries)
Shelves : 3 (total area 0.5 m^2)
Chamber door : sampling thief
Solutions : 5% w/v sucrose; 5% w/v mannitol
Filtered: 0.22-µm membrane
Vials : 240 vials
Fill volume : 3 mL
FD load: center shelf.
Product temperature:
28-gauge copper-constantan (type T) TC
Resolution : ±0.1°C.
TC Position:
Bottom center of edge and center vials.
Sampling: across shelf

AAPS PharmSciTech, Vol. 11, No. 1, March 2010 (© 2009)
DOI: 10.1208/s12249-009-9362-7

Research Article

Determination of End Point of Primary Drying in Freeze-Drying Process Control

The apparent end point of primary drying was determined by comparative pressure measurement (i.e., Pirani *vs.* MKS Baratron), dew point, Lyotrack (gas plasma spectroscopy), water concentration from tunable diode laser absorption spectroscopy, condenser pressure, pressure rise test (manometric temperature measurement or variations of this method), and product thermocouples.

melt. Thus, from product quality as well as process economics standpoint, it is very critical to detect the end of primary drying. Experiments were conducted with 5% mannitol and 5% sucrose as model systems. The apparent end point of primary drying was determined by comparative pressure measurement (i.e., Pirani *vs.* MKS Baratron), dew point, Lyotrack (gas plasma spectroscopy), water concentration from tunable diode laser absorption spectroscopy, condenser pressure, pressure rise test (manometric temperature measurement or variations of this method), and product thermocouples. Vials were pulled out from the drying chamber using a sample thief during late primary and early secondary drying to determine percent residual moisture either gravimetrically or by Karl Fischer, and the cake structure was determined visually for melt-back, collapse, and retention of cake structure at the apparent end point of primary drying (i.e., onset, midpoint, and offset). By far, the Pirani is the best choice of the methods tested for evaluation of the end point of primary drying. Also, it is a batch technique, which is cheap, steam sterilizable, and easy to install without requiring any modification to the existing dryer.

KEY WORDS: end point; freeze-drying; PAT; primary drying; residual water.

Freeze-dryer: Lyostar II (SP Industries)
Shelves : 3 (total area 0.5 m^2)
Chamber door : sampling thief
Solutions : 5% w/v sucrose; 5% w/v mannitol
mbrane

Product temperature:
28-gauge copper-constantan (type T) TC
Resolution : ±0.1°C.
TC Position:
Bottom center of edge and center vials.
Sampling: across shelf

AAPS PharmSciTech, Vol. 11, No. 1, March 2010 (© 2009)
DOI: 10.1208/s12249-009-9362-7

Research Article

Determination of End Point of Primary Drying in Freeze-Drying Process Control

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3]

Received 9 June 2009; accepted 9 December 2009; published online 8 January 2010

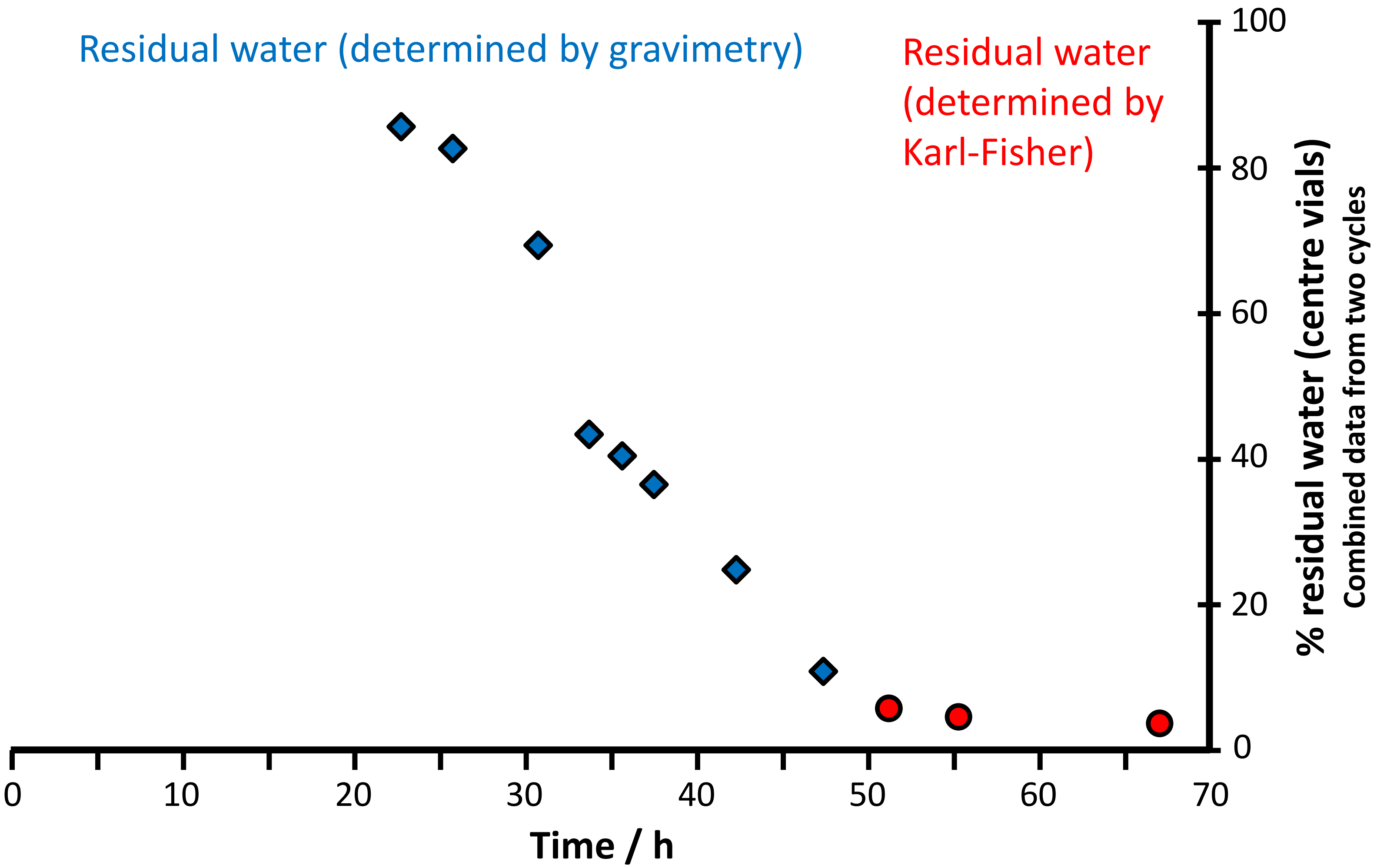
Abstract. Freeze-drying is a relatively expensive process requiring long processing time, and hence one of the key objectives during freeze-drying process development is to minimize the primary drying time, which is the longest of the three steps in freeze-drying. However, increasing the shelf temperature into secondary drying before all of the ice is removed from the product will likely cause collapse or eutectic melt. Thus, from product quality as well as process economics standpoint, it is very critical to detect the end of primary drying. Experiments were conducted with 5% mannitol and 5% sucrose as model systems. The apparent end point of primary drying was determined by comparative pressure measurement (i.e., Pirani *vs.* MKS Baratron), dew point, Lyotrack (gas plasma spectroscopy), water concentration from tunable diode laser absorption spectroscopy, condenser pressure, pressure rise test (manometric temperature measurement or variations of this method), and product thermocouples. Vials were pulled out from the drying chamber using a sample thief during late primary and early secondary drying to determine percent residual moisture either gravimetrically or by Karl Fischer, and the cake structure was determined visually for melt-back, collapse, and retention of cake structure at the apparent end point of primary drying (i.e., onset, midpoint, and offset). By far, the Pirani is the best choice of the methods tested for evaluation of the end point of primary drying. Also, it is a batch technique, which is cheap, steam sterilizable, and easy to install without requiring any modification to the existing dryer.

KEY WORDS: end point; freeze-drying; PAT; primary drying; residual water.

Freeze-dryer: Lyostar II (SP Industries)
Shelves : 3 (total area 0.5 m^2)
Chamber door : sampling thief
Solutions : 5% w/v sucrose; 5% w/v mannitol
Filtered: 0.22-µm membrane
Vials : 240 vials
Fill volume : 3 mL
FD load: center shelf.
Product temperature:
28-gauge copper-constantan (type T) TC
Resolution : ±0.1°C.
TC Position:
Bottom center of edge and center vials.
Sampling: across shelf

Vials were pulled out from the drying chamber using a sample thief during late primary and early secondary drying to determine percent residual moisture either gravimetrically or by Karl Fischer, and the cake structure was determined visually for melt-back, collapse, and retention of cake structure at the apparent end point of primary drying (i.e., onset, midpoint, and offset).

5% sucrose (3 mL in 5 mL tubing vials)



Adapted from …

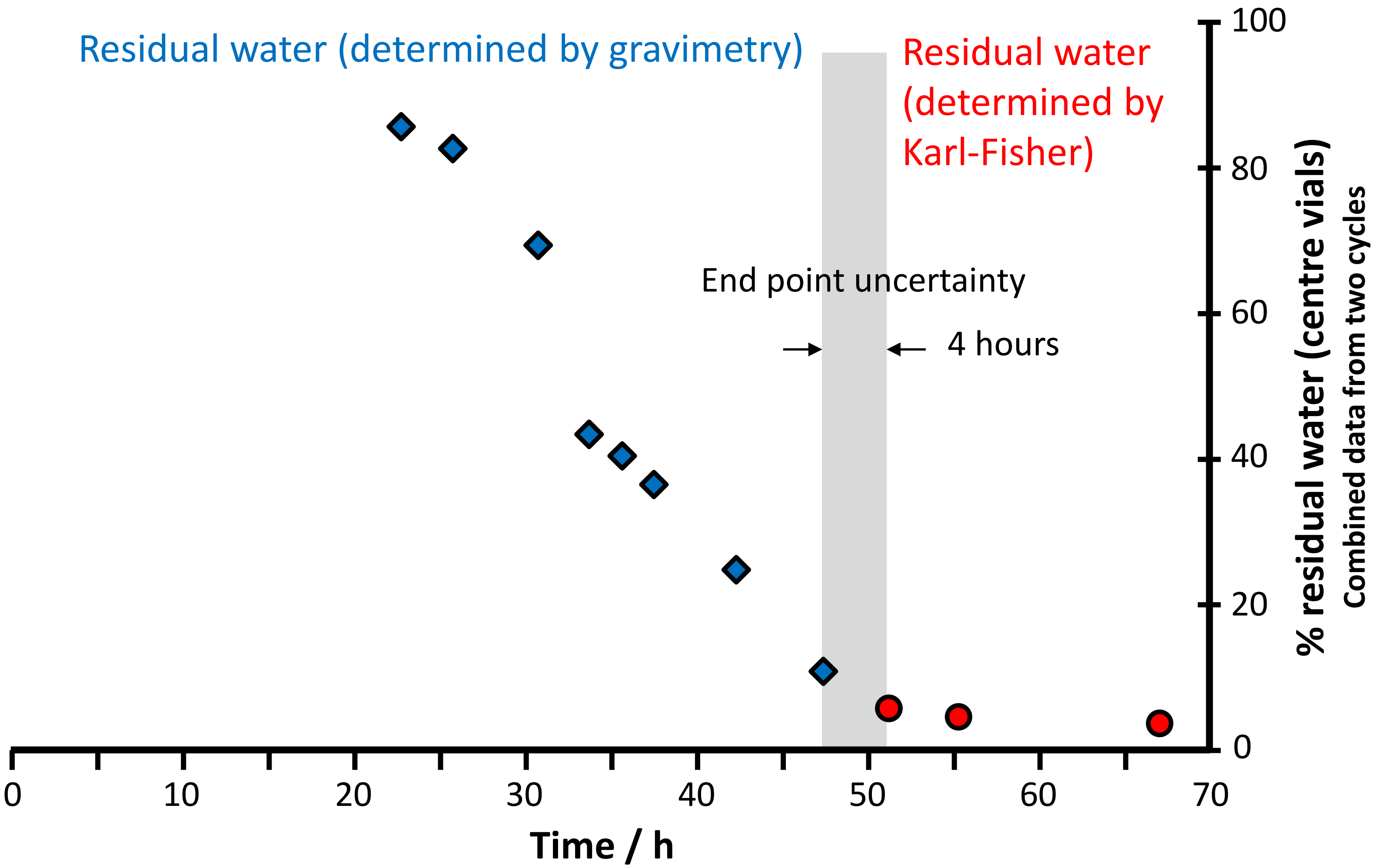
Determination of End Point of Primary Drying in Freeze-Drying Process Control

https://doi.org/10.1208/s12249-009-9362-7

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3]

AAPS PharmSciTech, Vol. 11, No. 1, March 2010

5% sucrose (3 mL in 5 mL tubing vials)

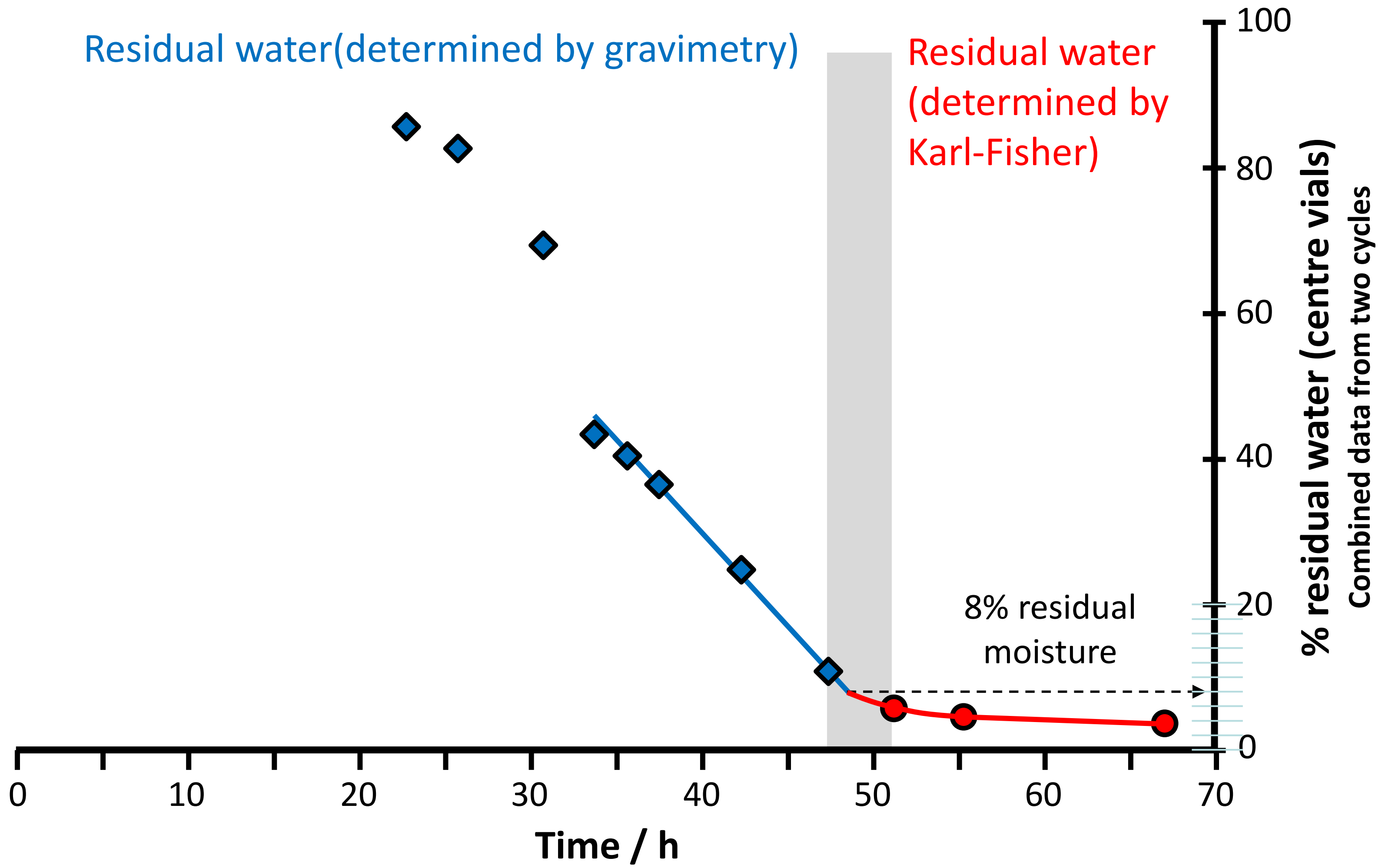


Adapted from …

Determination of End Point of Primary Drying in Freeze-Drying Process Control https://doi.org/10.1208/s12249-009-9362-7

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3] *AAPS PharmSciTech, Vol. 11, No. 1, March 2010*

5% sucrose (3 mL in 5 mL tubing vials)



Adapted from …

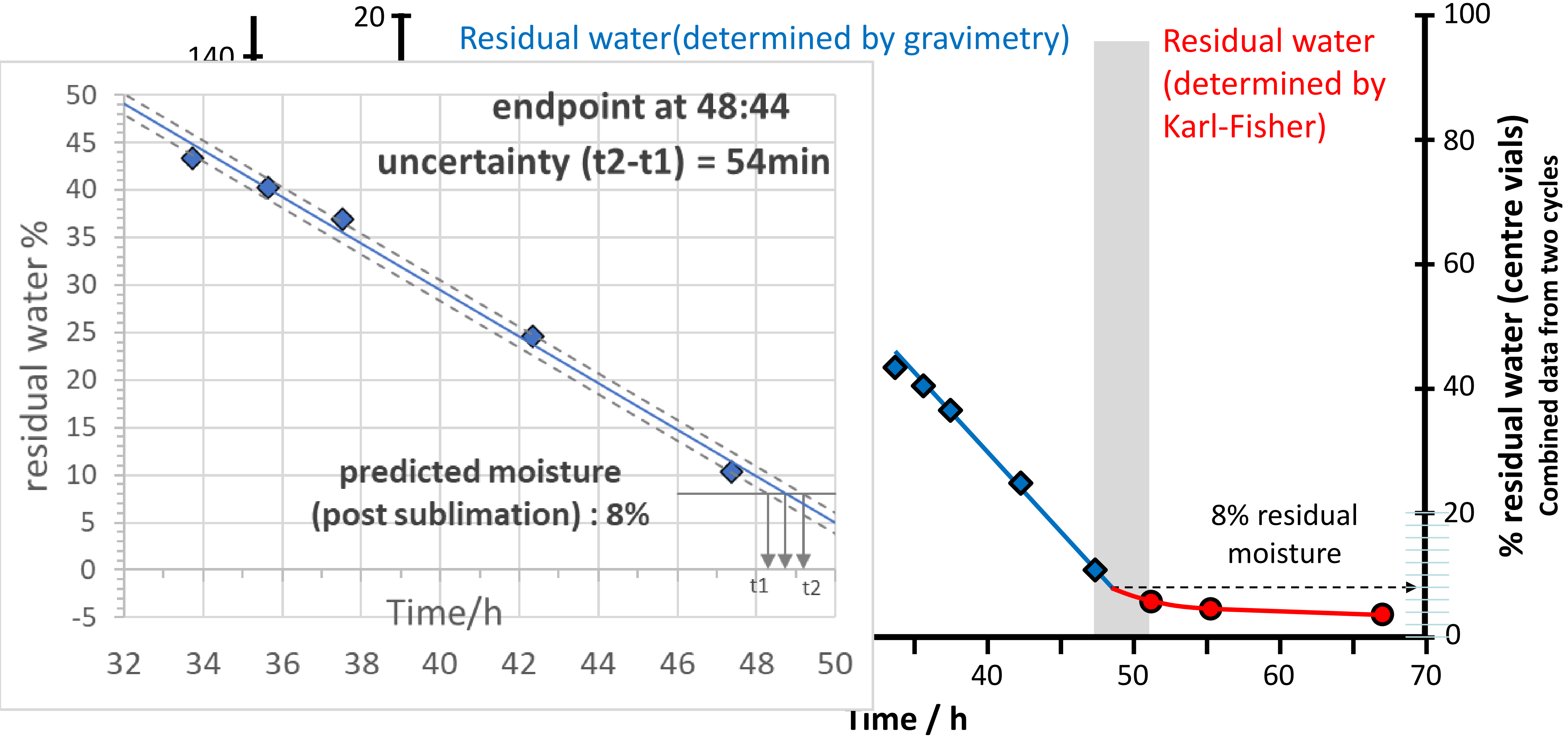
Determination of End Point of Primary Drying in Freeze-Drying Process Control

https://doi.org/10.1208/s12249-009-9362-7

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3]

AAPS PharmSciTech, Vol. 11, No. 1, March 2010

5% sucrose (3 mL in 5 mL tubing vials)

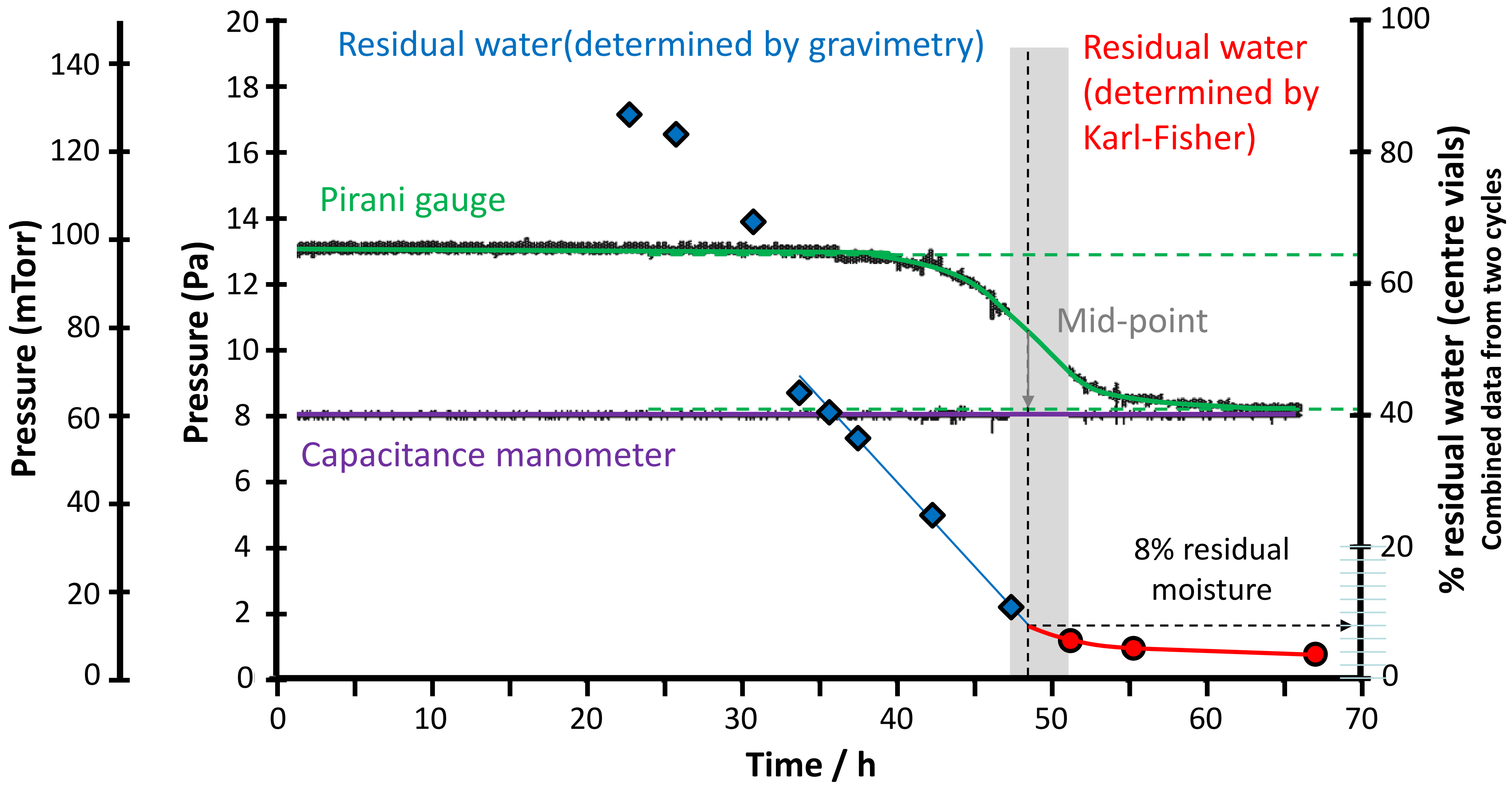


Adapted from …

Determination of End Point of Primary Drying in Freeze-Drying Process Control https://doi.org/10.1208/s12249-009-9362-7

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3] *AAPS PharmSciTech, Vol. 11, No. 1, March 2010*

5% sucrose (3 mL in 5 mL tubing vials)



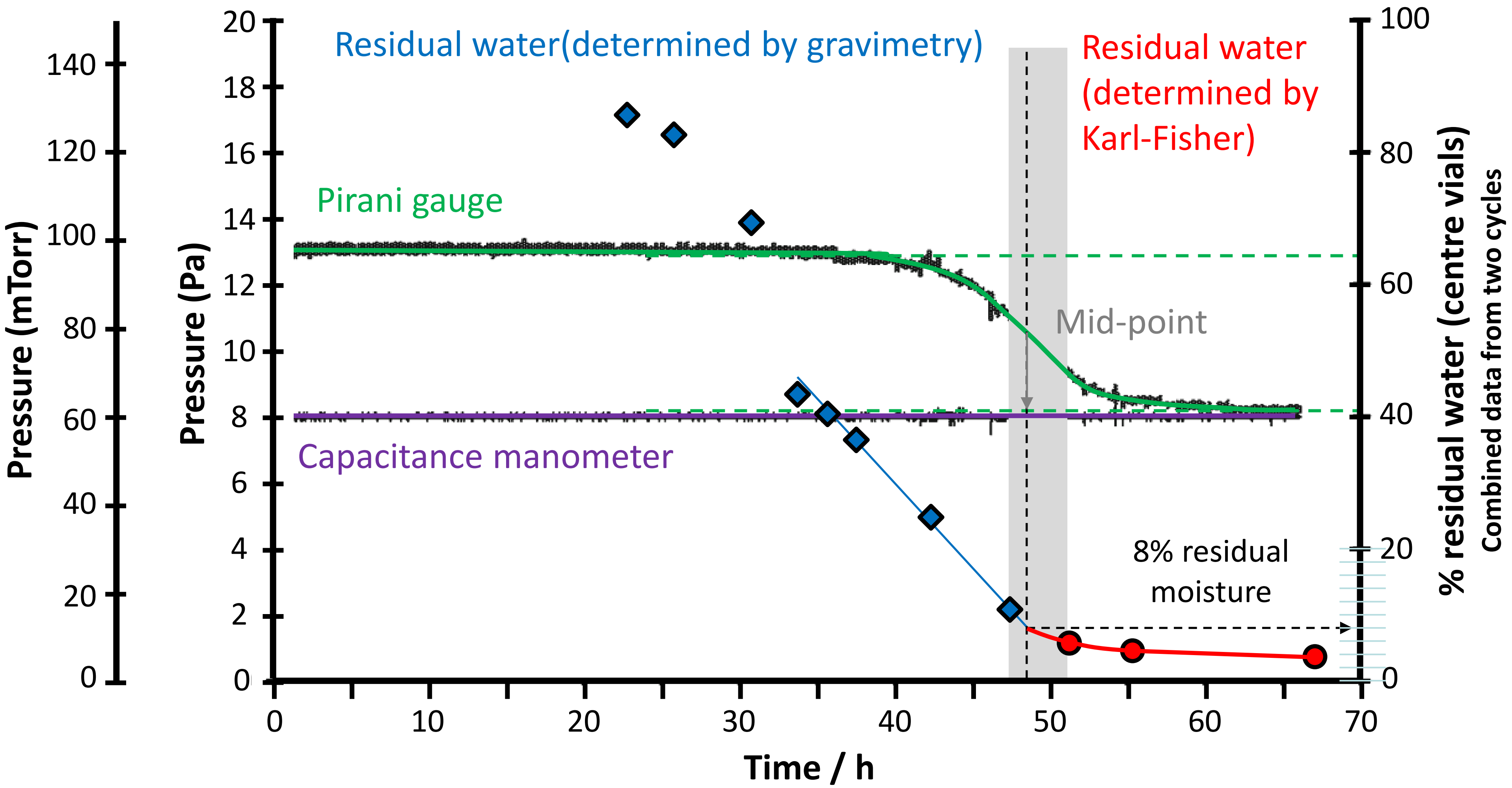
Adapted from …

Determination of End Point of Primary Drying in Freeze-Drying Process Control https://doi.org/10.1208/s12249-009-9362-7

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3] *AAPS PharmSciTech, Vol. 11, No. 1, March 2010*

Amorphous with a high water binding capacity

5% sucrose (3 mL in 5 mL tubing vials)

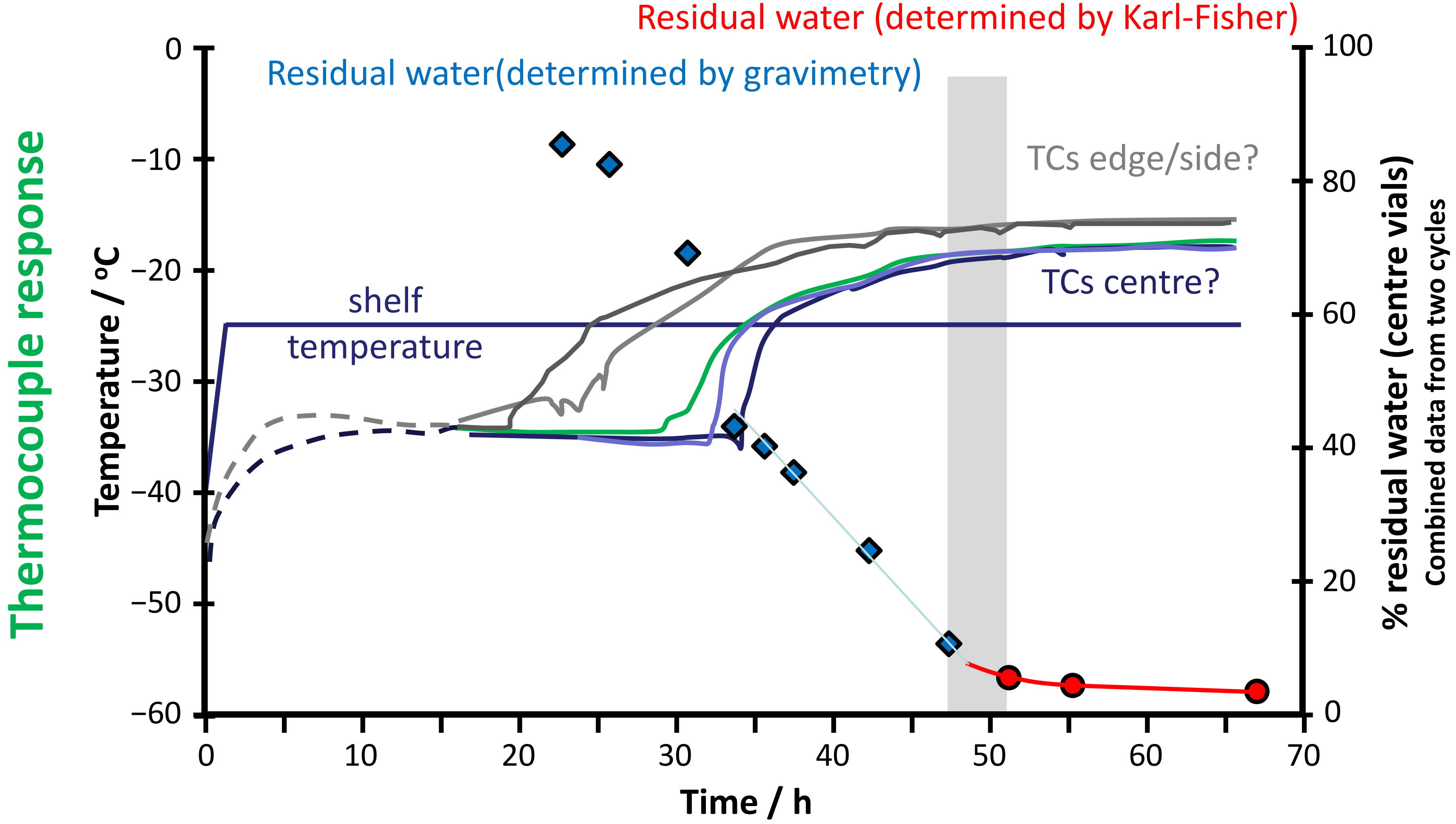


Adapted from …

Determination of End Point of Primary Drying in Freeze-Drying Process Control https://doi.org/10.1208/s12249-009-9362-7

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3] *AAPS PharmSciTech, Vol. 11, No. 1, March 2010*

5% sucrose (3 mL in 5 mL tubing vials)

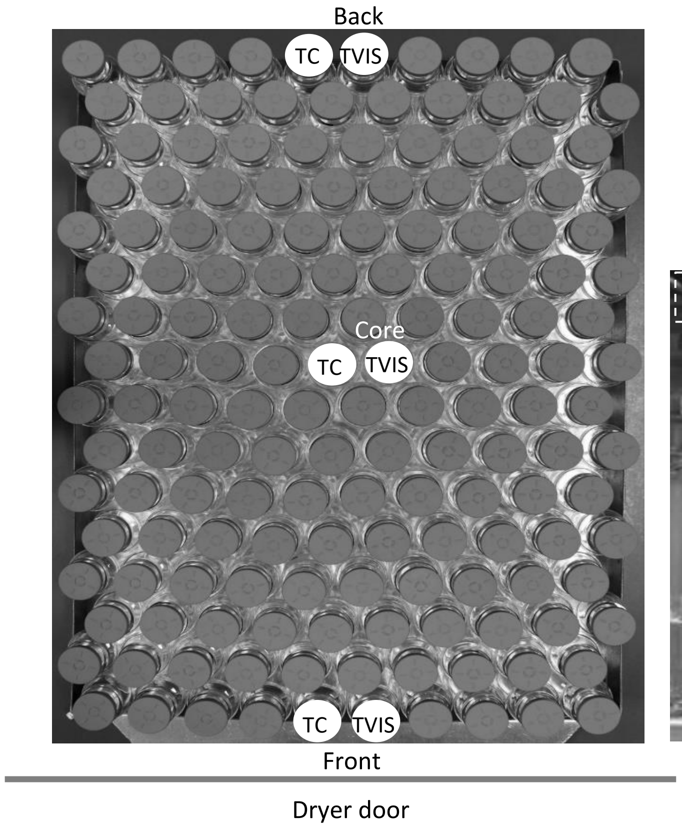


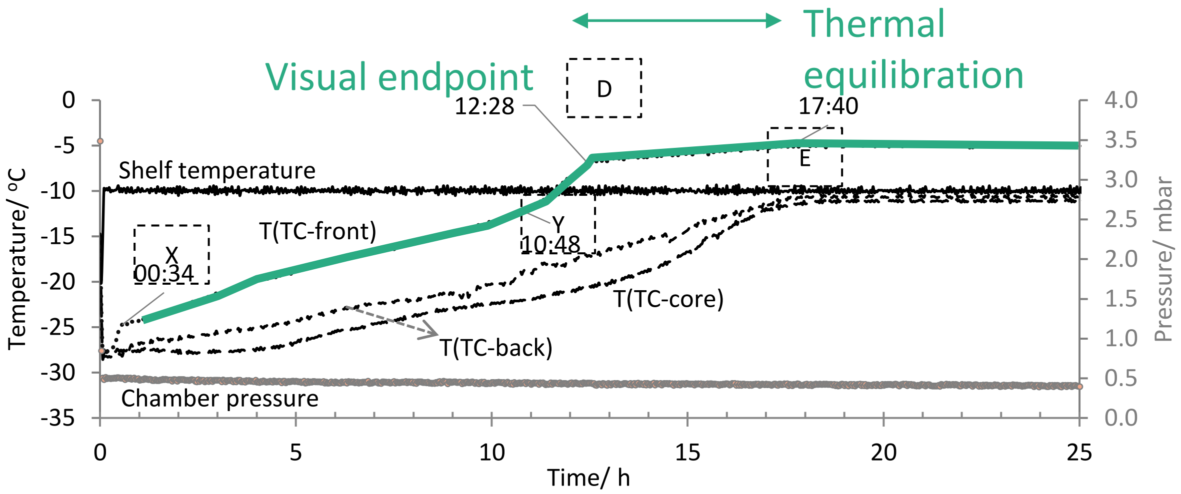
Adapted from …

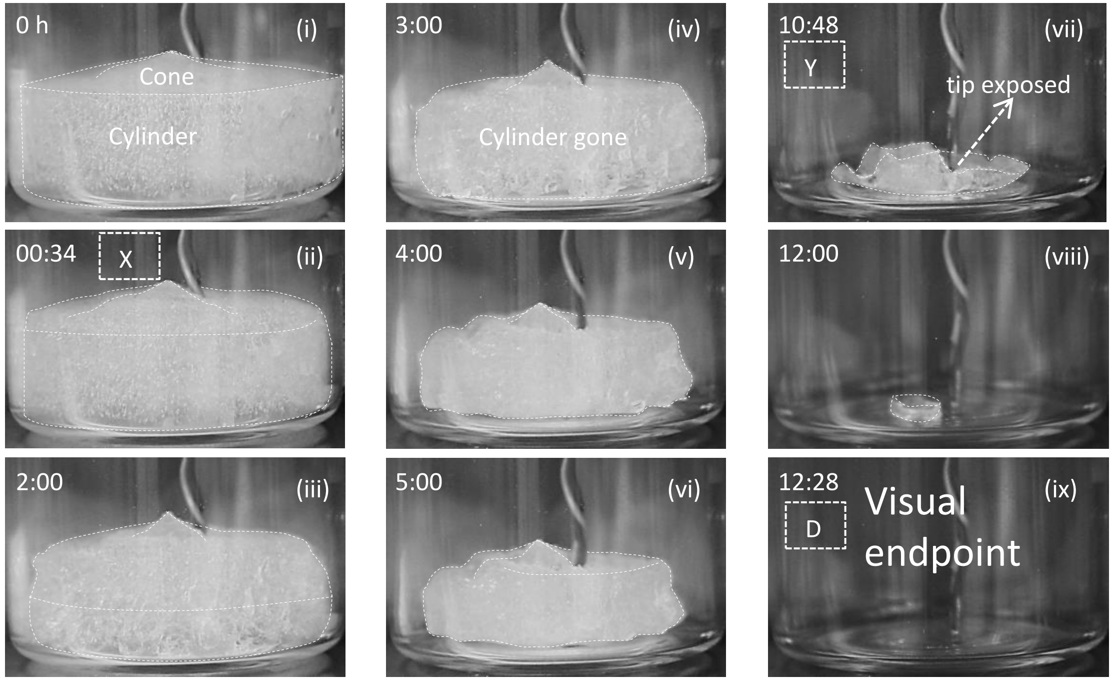
Determination of End Point of Primary Drying in Freeze-Drying Process Control https://doi.org/10.1208/s12249-009-9362-7

Sajal M. Patel,[1] Takayuki Doen,[1,2] and Michael J. Pikal[1,3] *AAPS PharmSciTech, Vol. 11, No. 1, March 2010*

Thermocouple response







Through Vial Impedance Spectroscopy
(nanopure water)
NO SOLIDS FRACTION

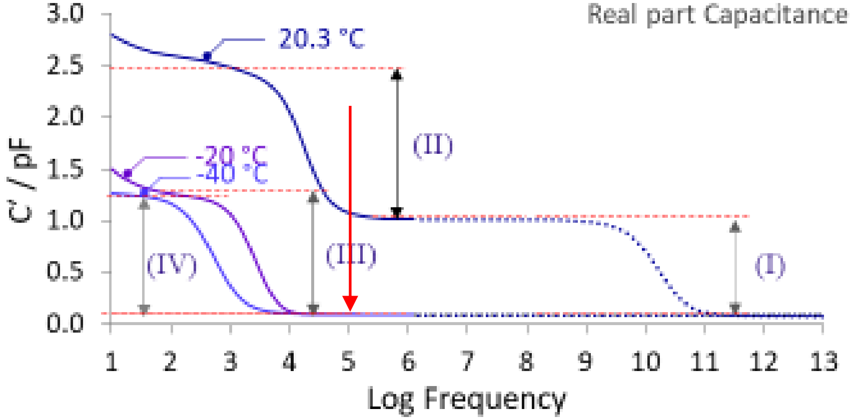
Frozen Water and Dielectric Relaxation of Ice

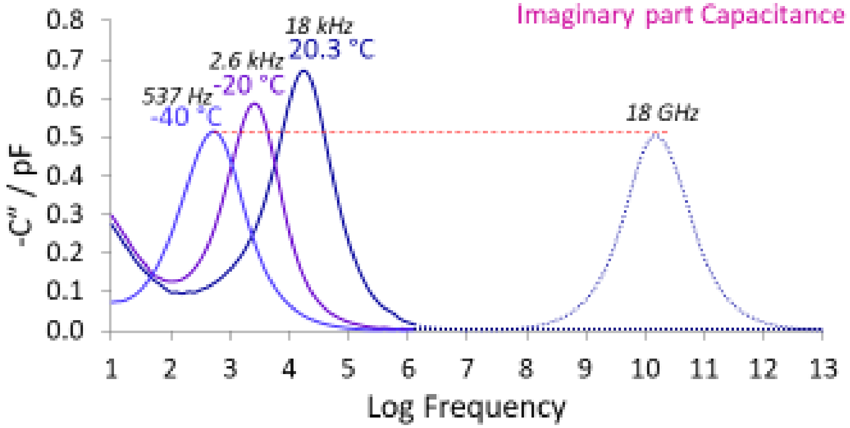
I. : The polarization of the water dipole in liquid water at 20 ˚C, with a dielectric loss peak frequency of ~ 18 GHz

II. : The Maxwell-Wagner (MW) polarization of the glass wall of the TVIS vial at 20 ˚C, with a dielectric loss peak frequency of 17.8 kHz

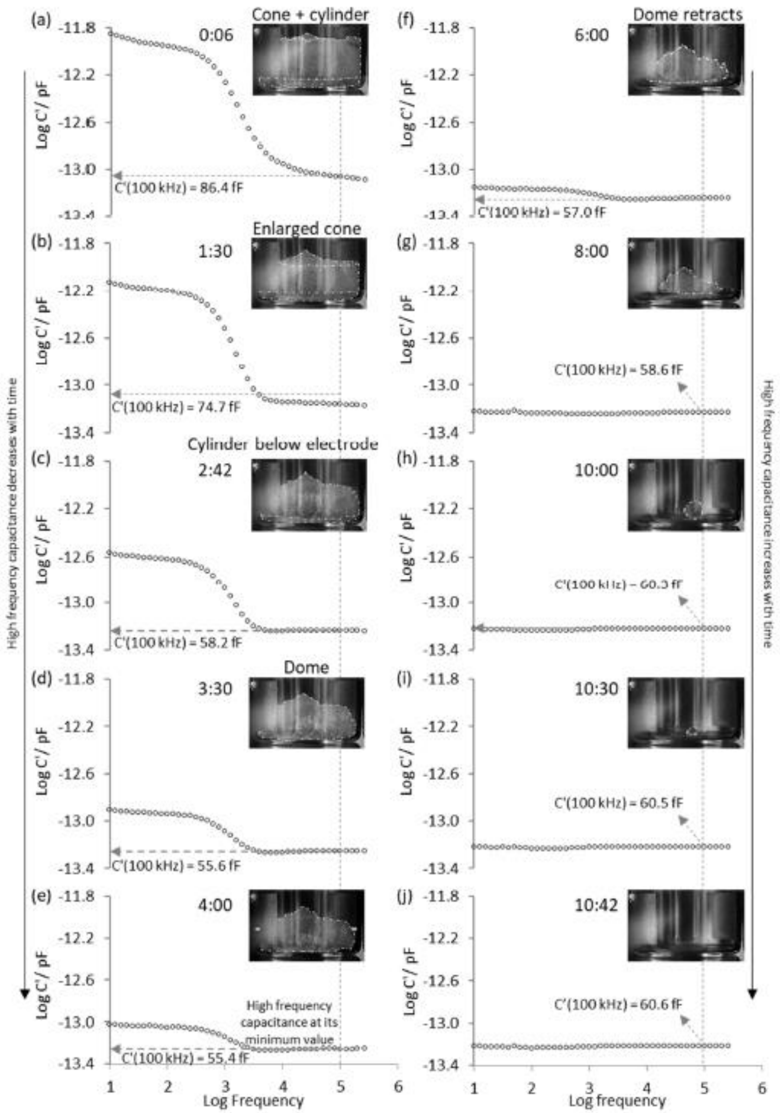
III. : The dielectric polarization of ice at −20 ˚C, with a dielectric loss peak frequencies of 2.57 kHz

IV. : The dielectric polarization of ice at −40 ˚C with a dielectric loss peak frequencies of 537 Hz.

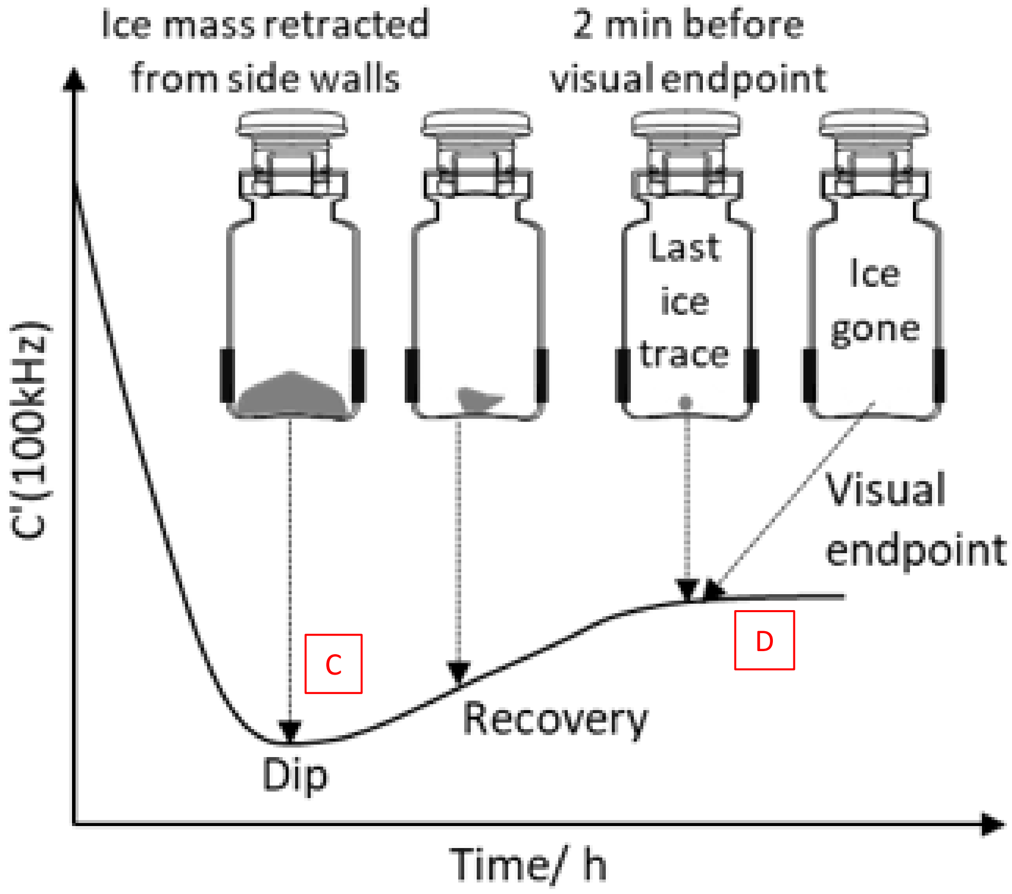


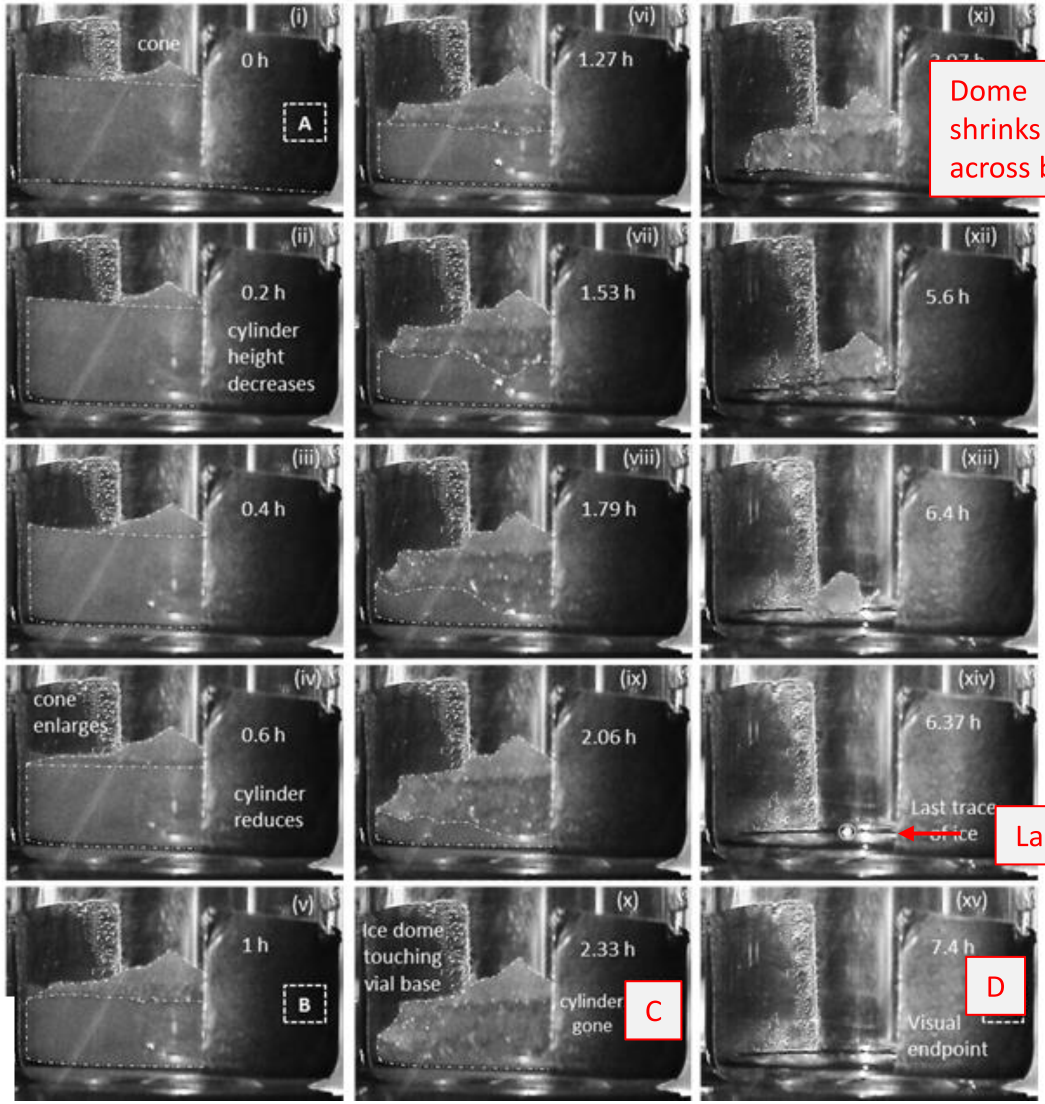


TVIS real-part capacitance spectra



TVIS Sublimation end point

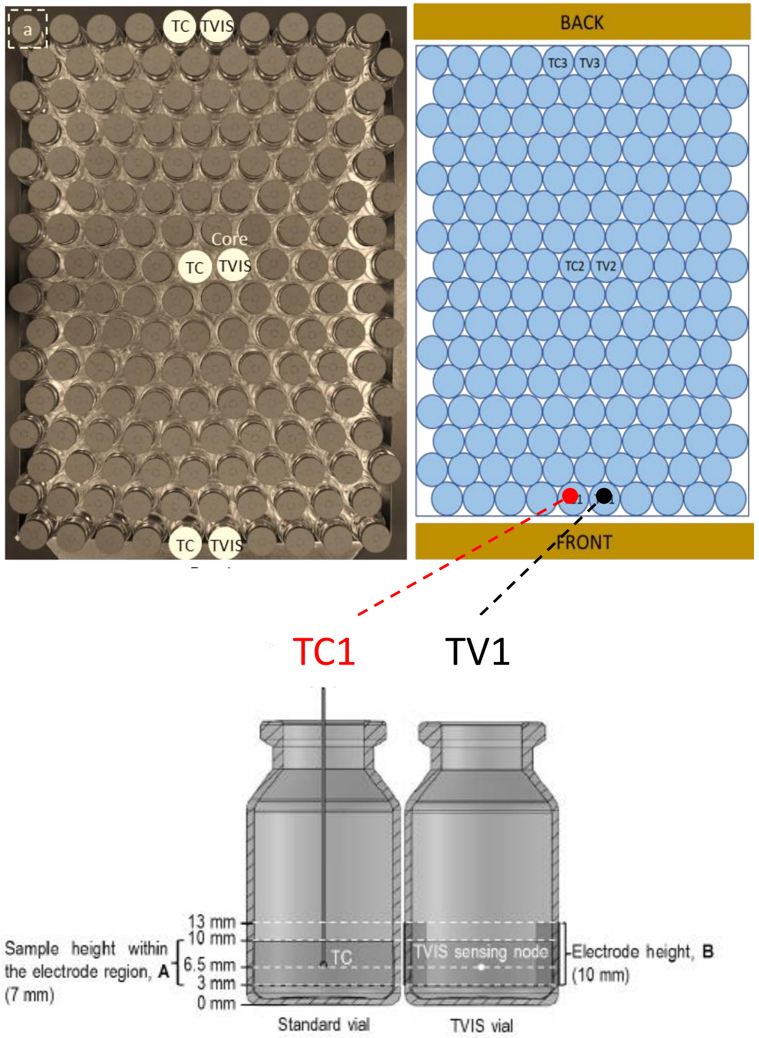


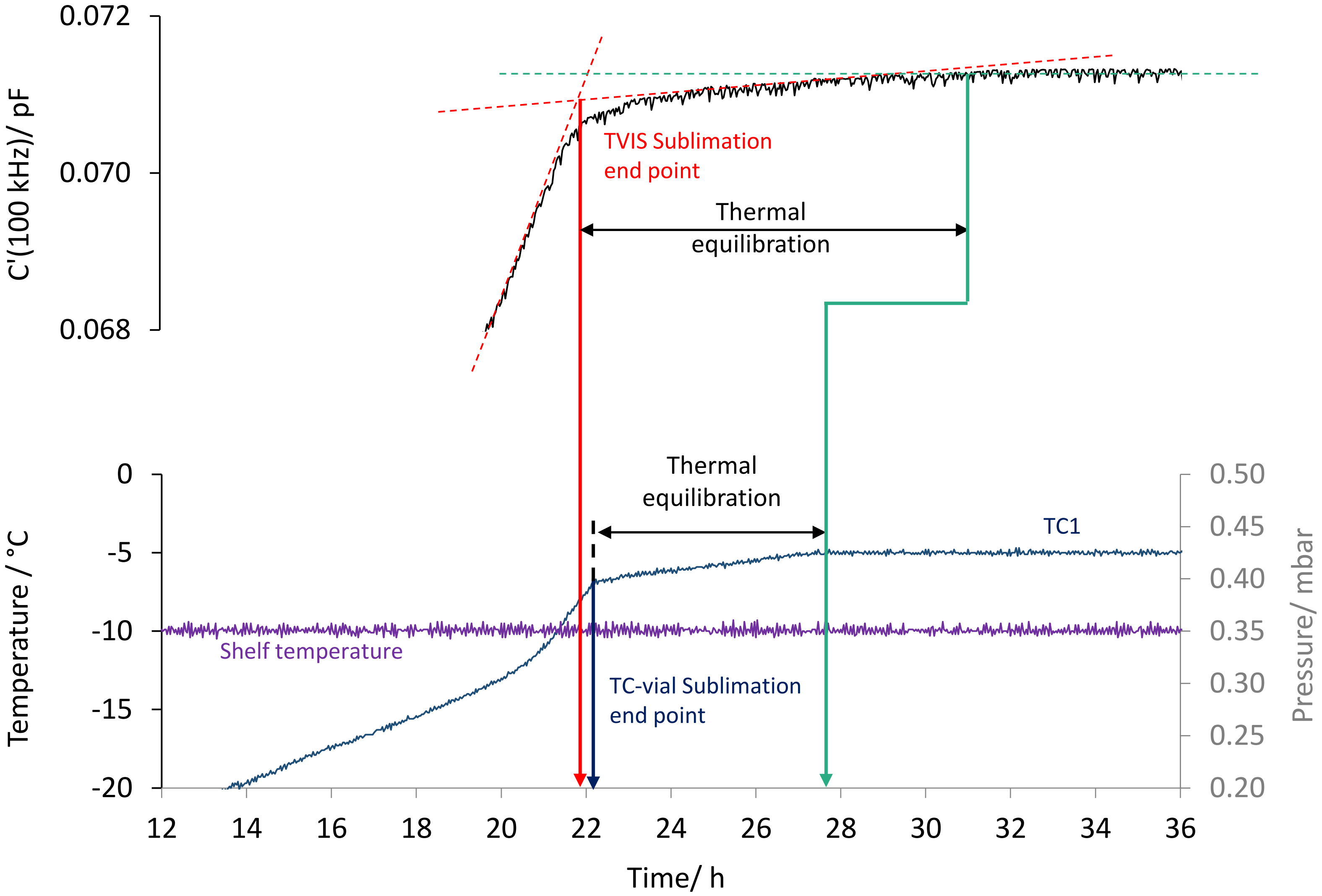


Bhaskar, P., Smith, G., Ermolina, I., Polygalov, E. (2021). Observations on the changing shape of the ice mass and the determination of the sublimation end point in freeze-drying: An application for through-vial impedance spectroscopy (TVIS). Pharmaceutics, 13(11) 1835.
Accepted 13 October 2021, Available online 02 November 2021
https://doi.org/10.3390/pharmaceutics13111835

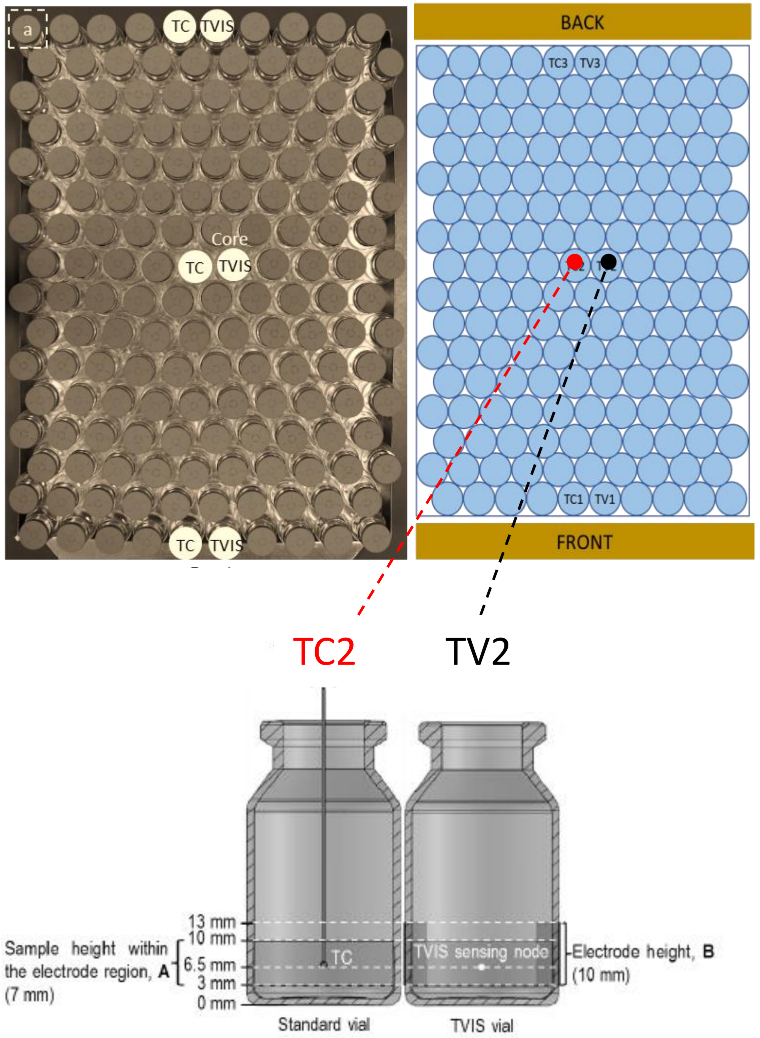
C: Ice mass no longer in contact with the side wall

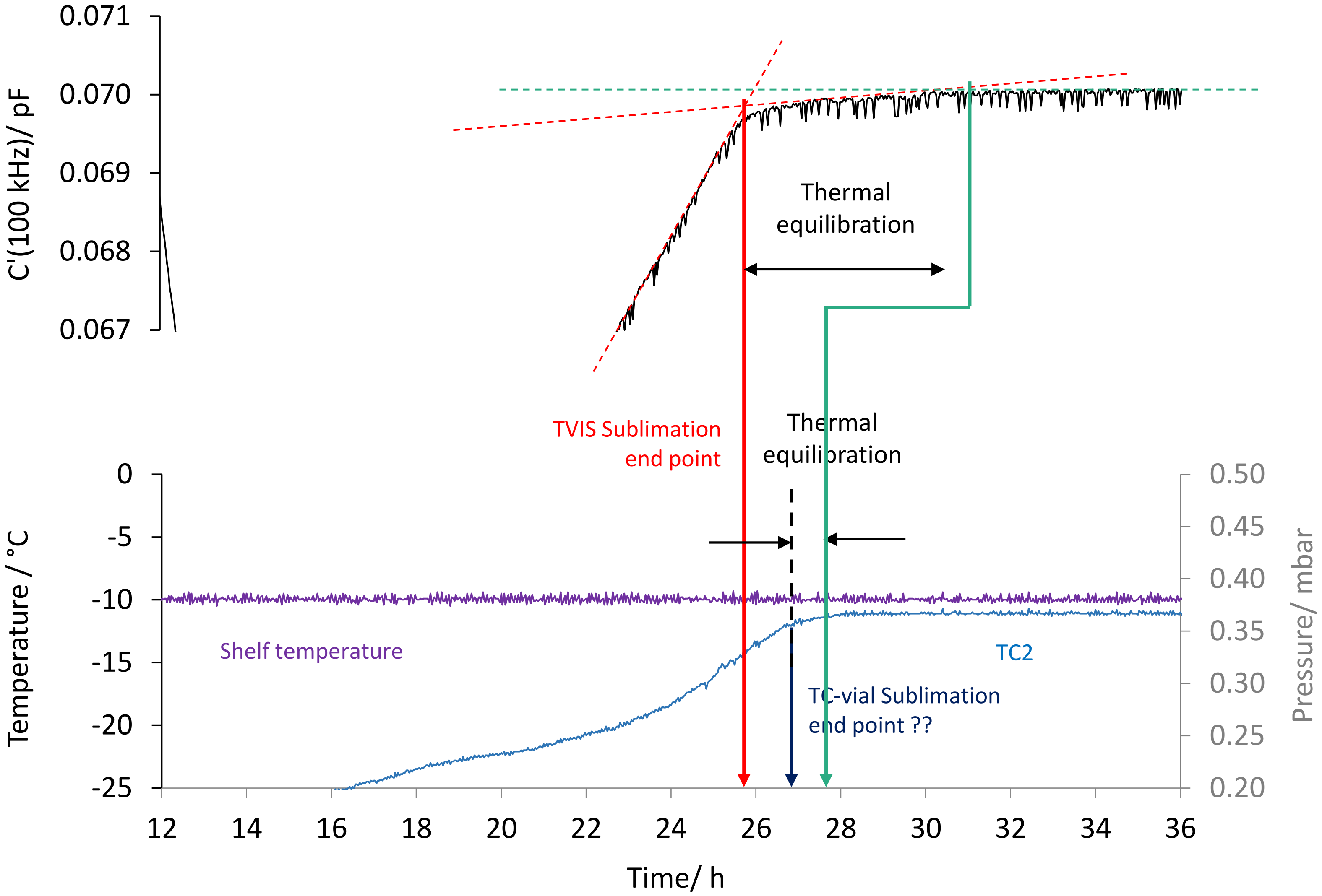
Nano-pure water



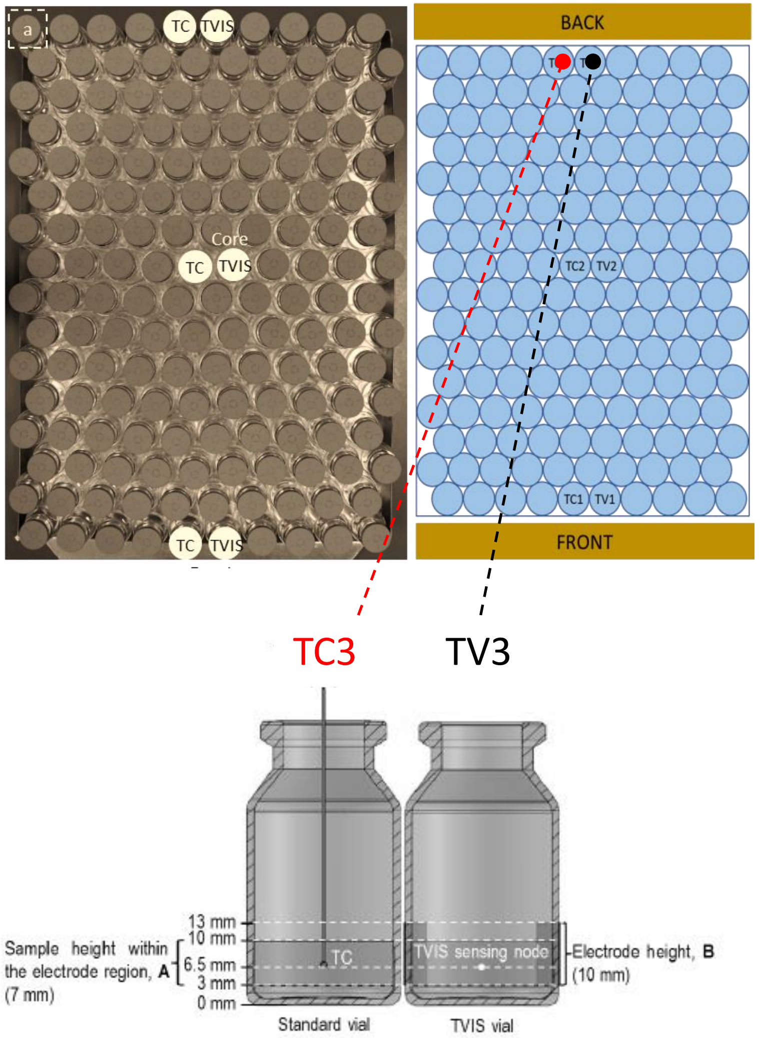


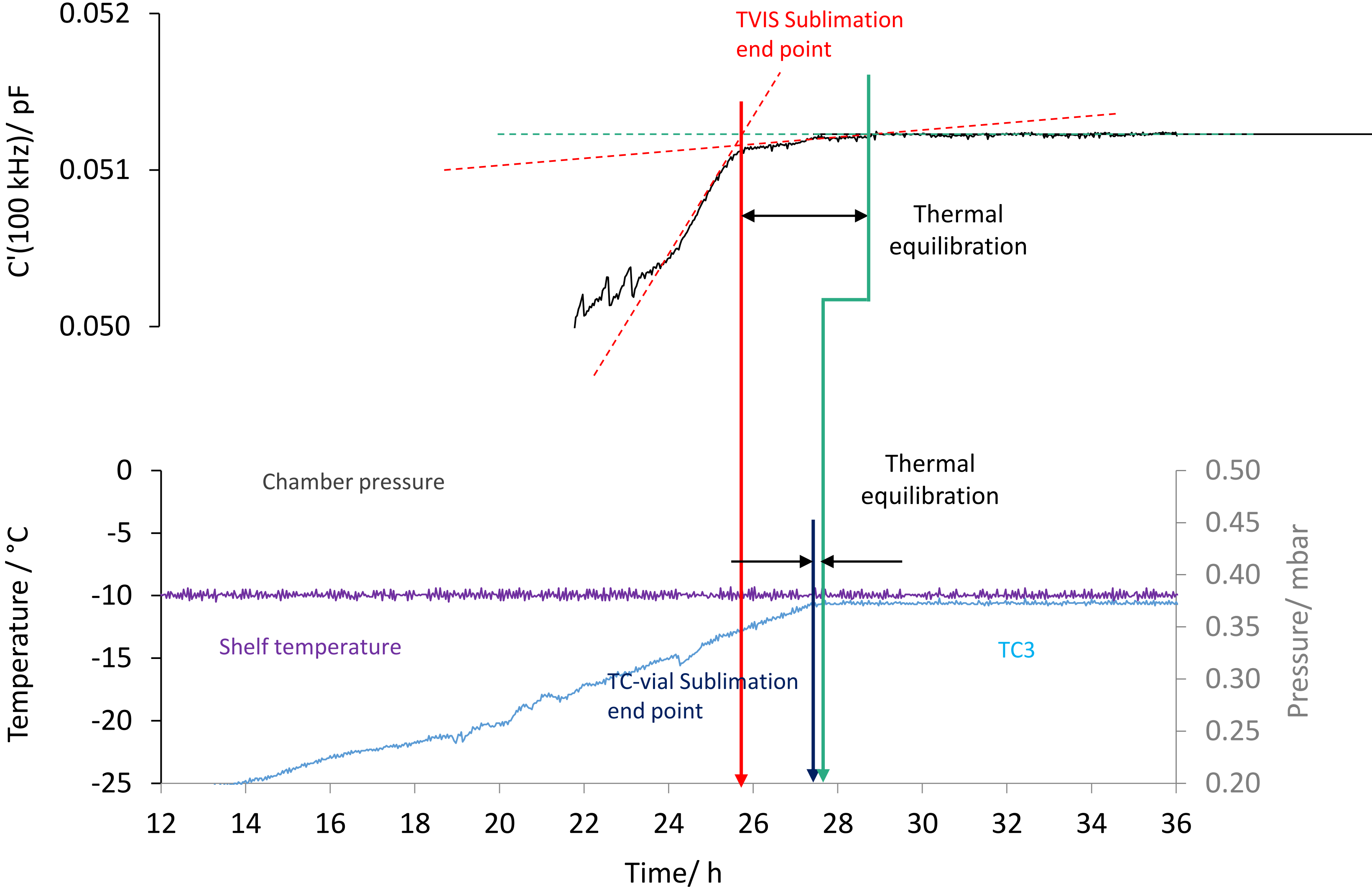
Nano-pure water





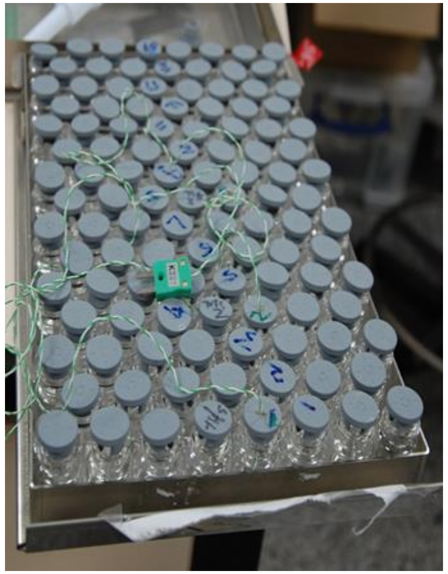
Nano-pure water

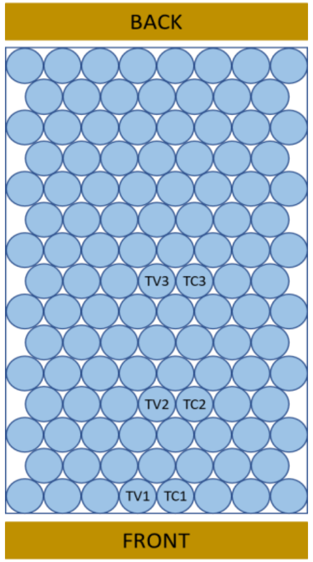


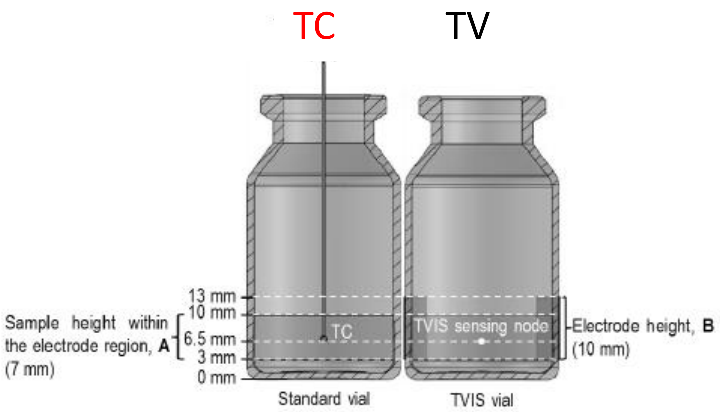


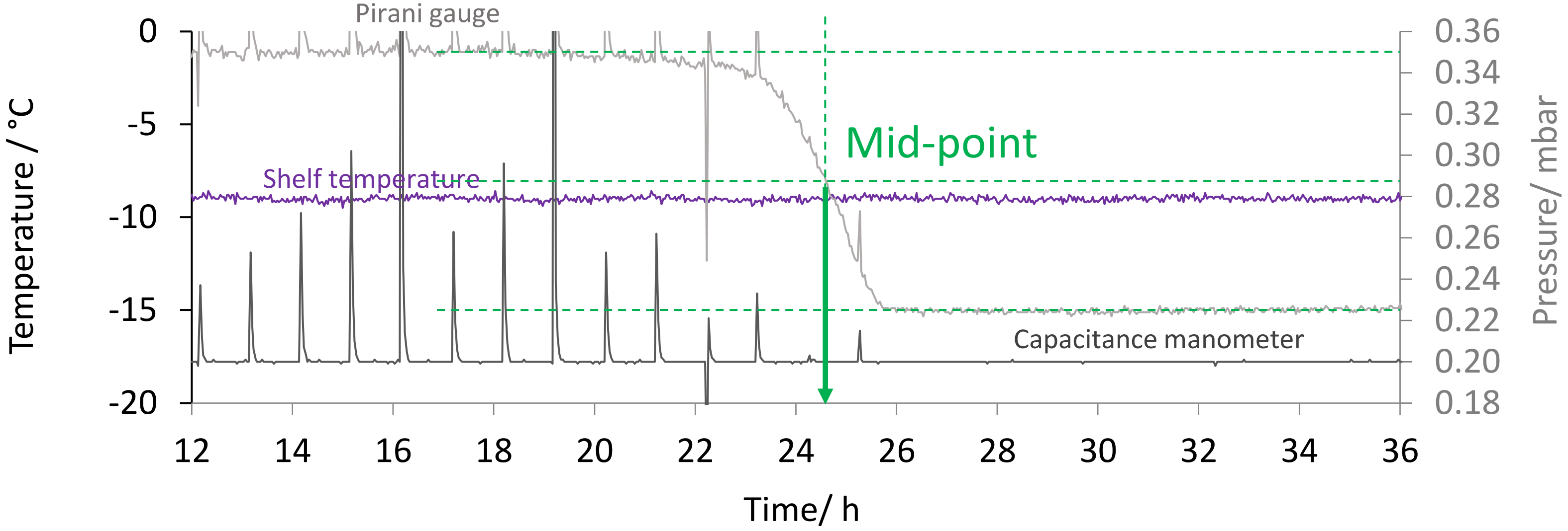
Through Vial Impedance Spectroscopy
(5% mannitol)
CRYSTALLINE SOLIDS FRACTION

Drying of 5% mannitol







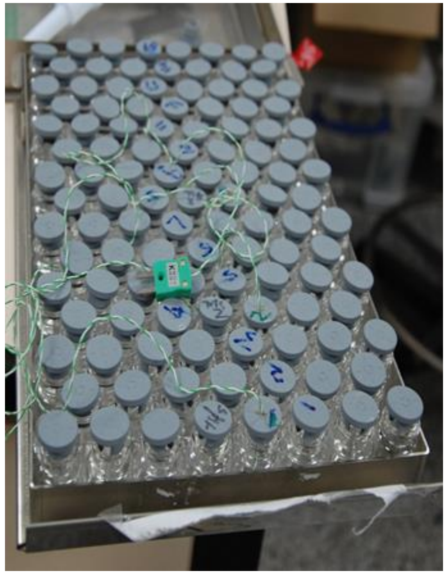


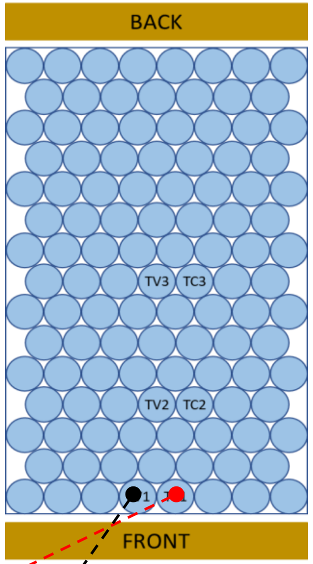
DE MONTFORT UNIVERSITY LEICESTER

NIBSC Confidence in Biological Medicines

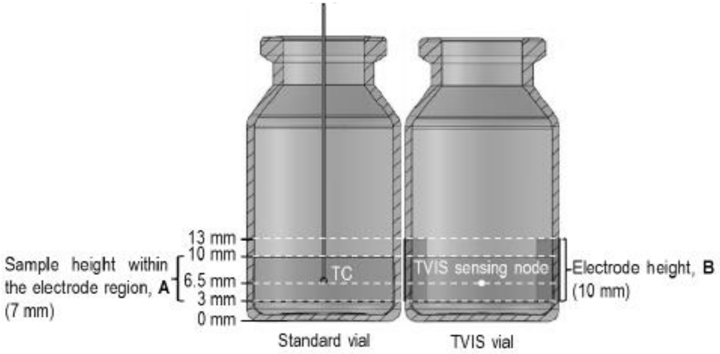
DMU LyoGroup

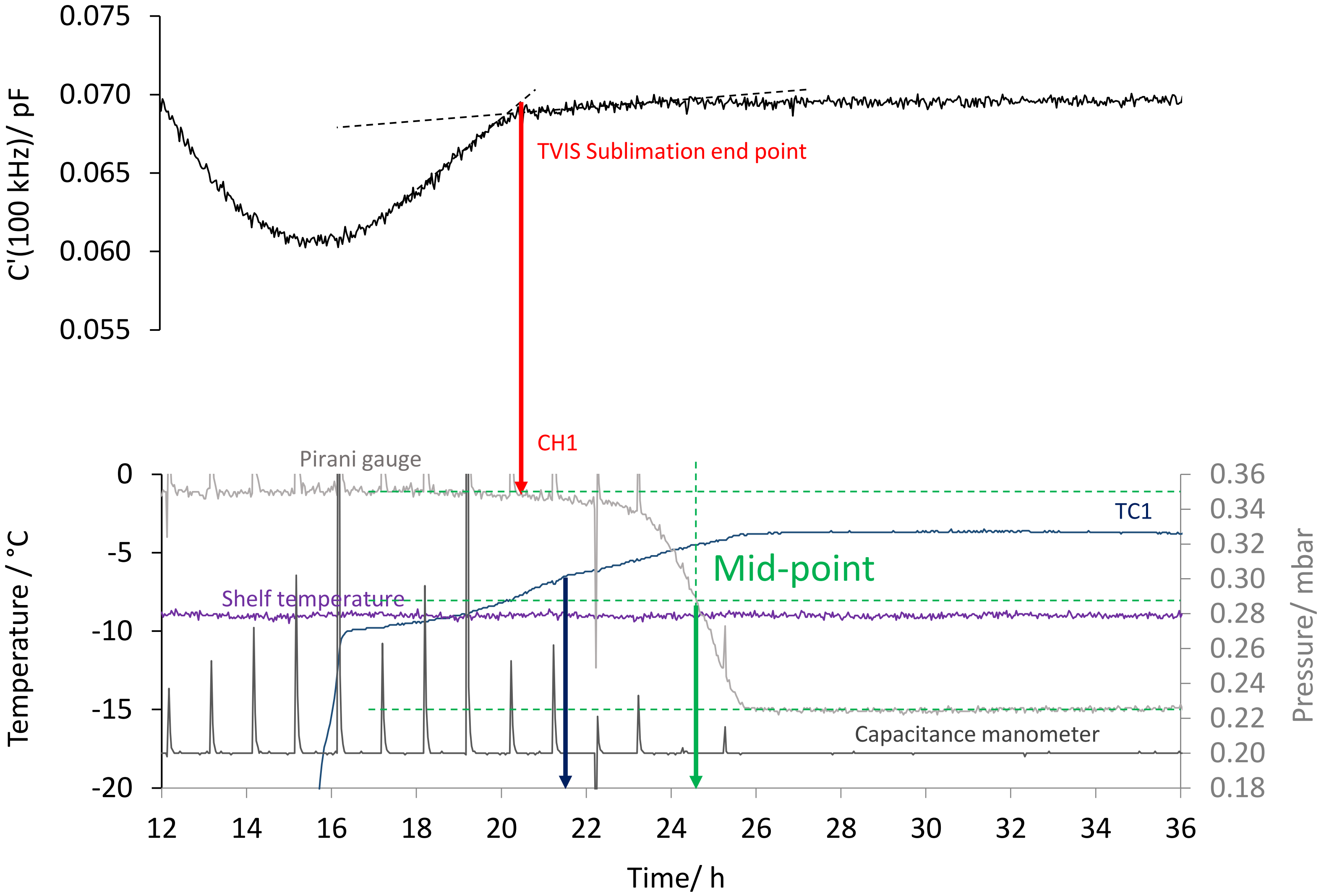
Drying of 5% mannitol



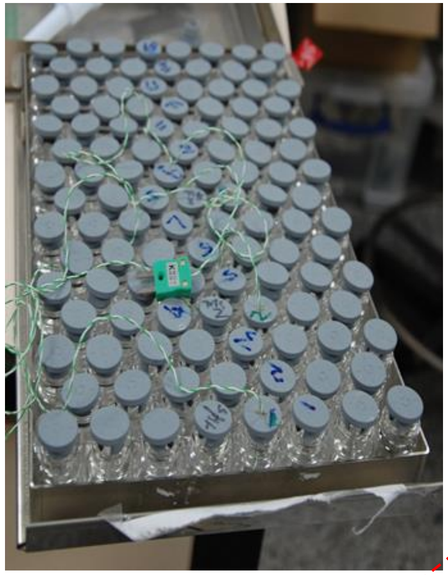


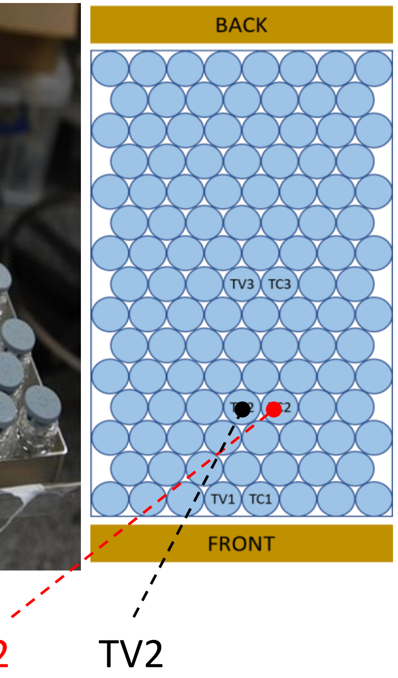
TC1 TV1

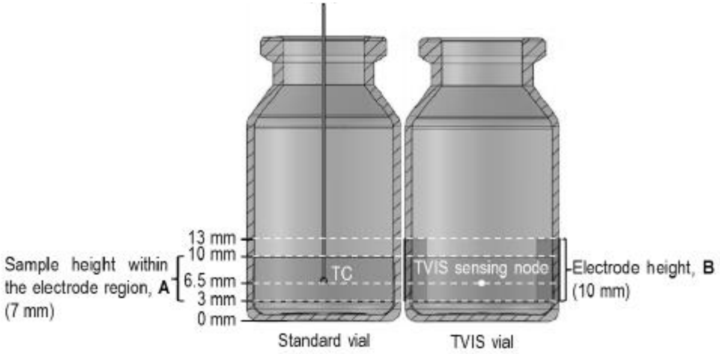


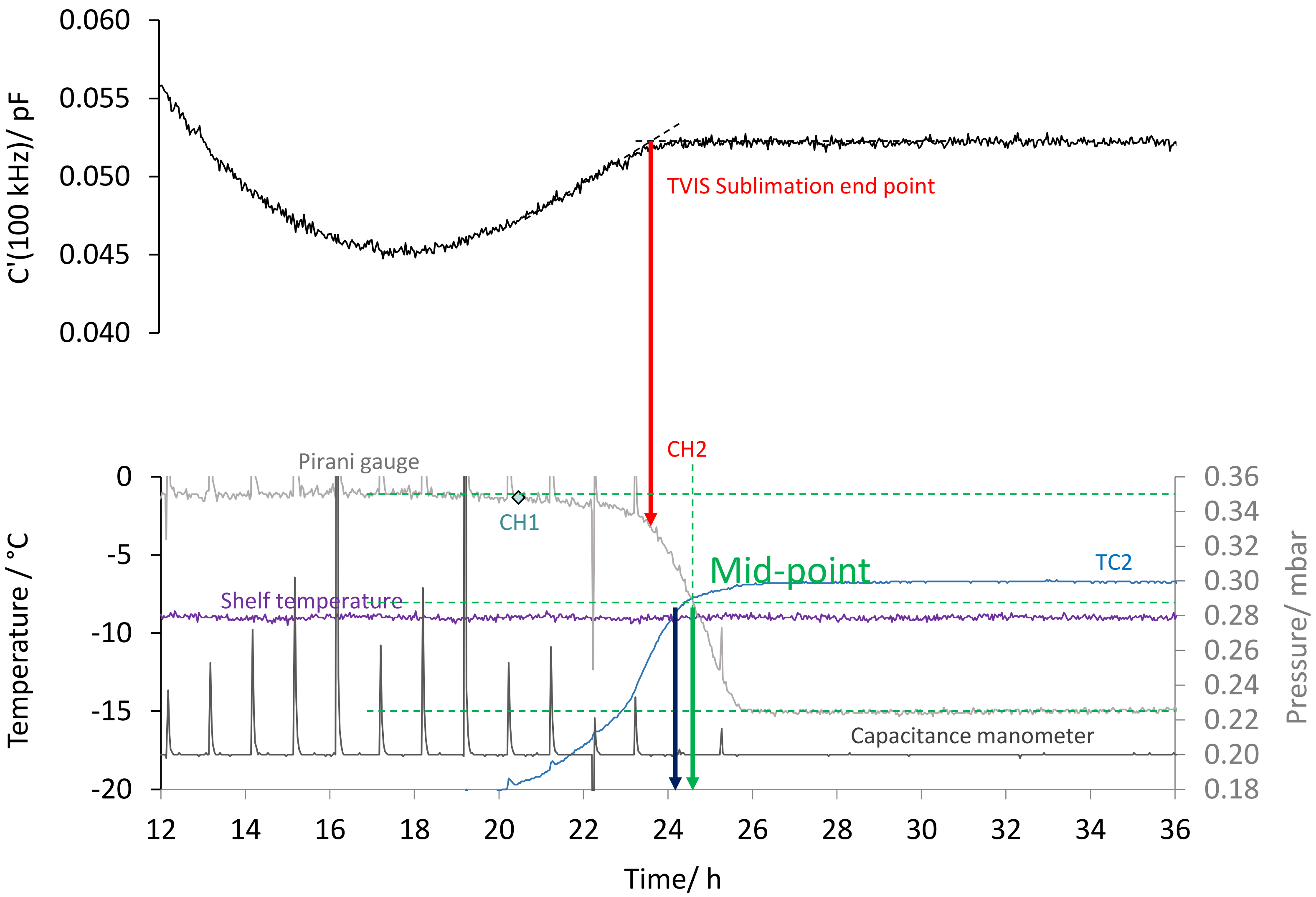


Drying of 5% mannitol







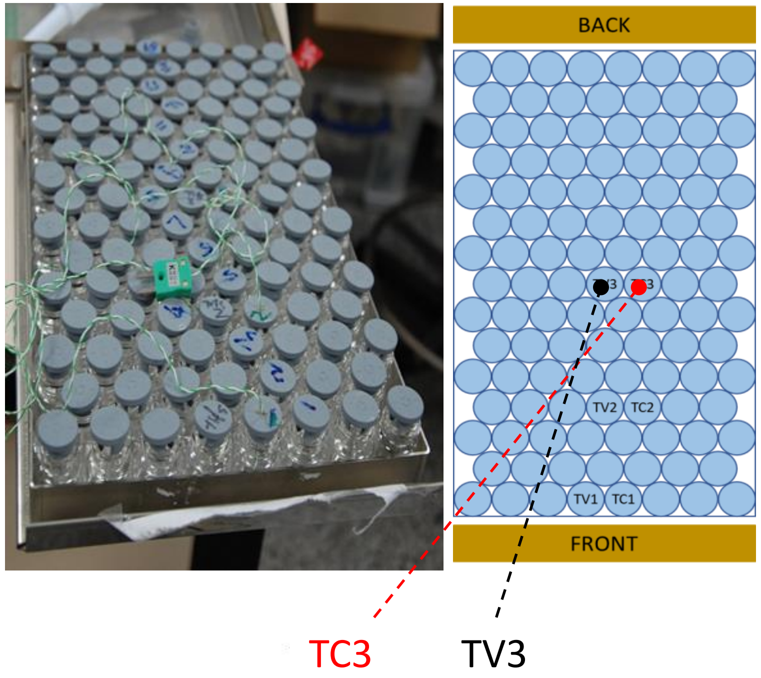


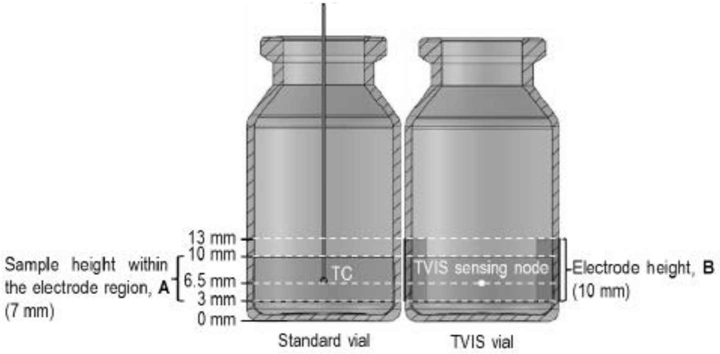
DE MONTFORT UNIVERSITY LEICESTER

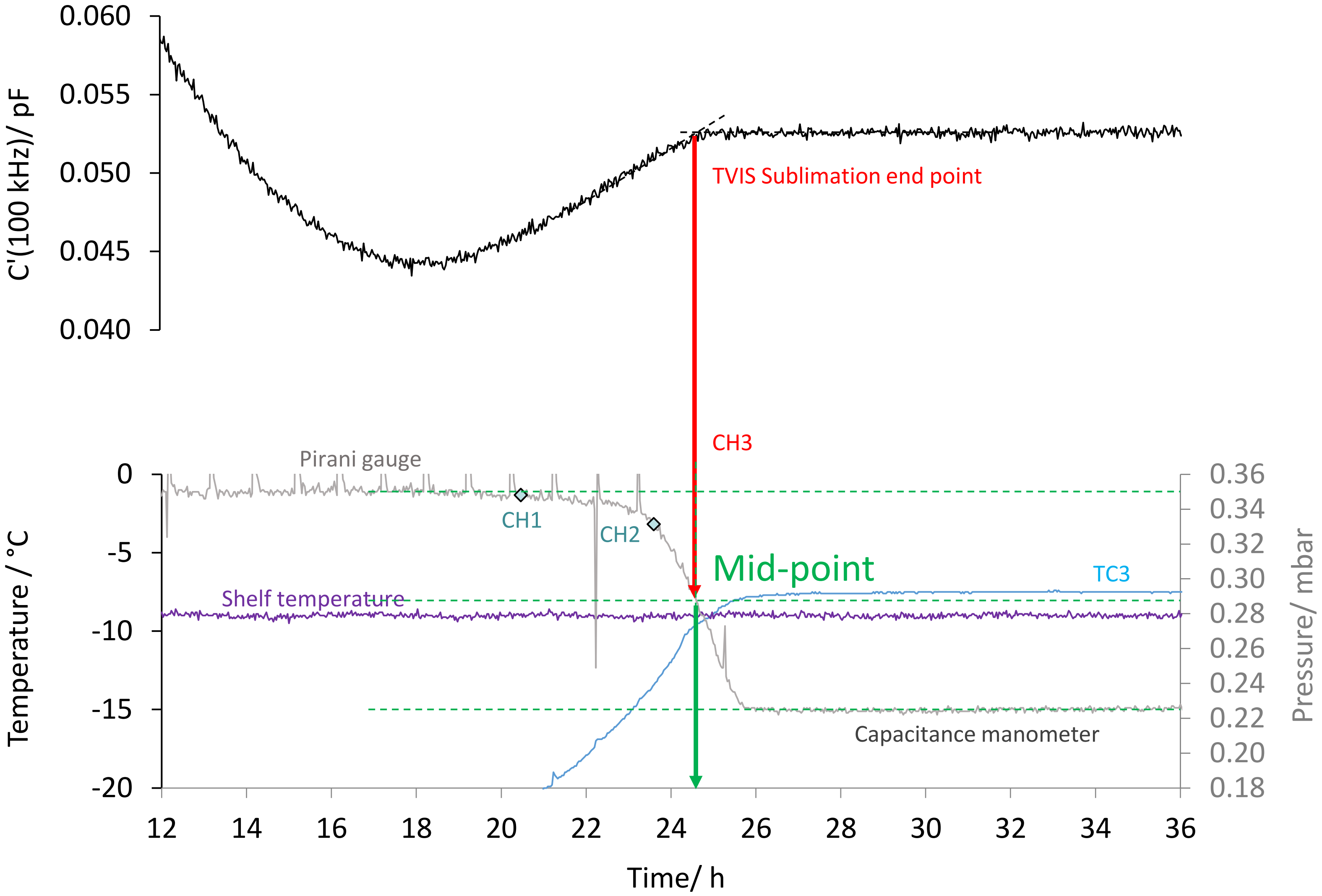
NIBSC Confidence in Biological Medicines

DMU LyoGroup

Drying of 5% mannitol



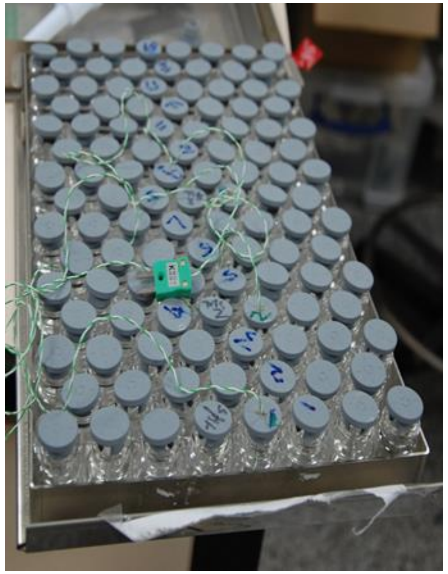


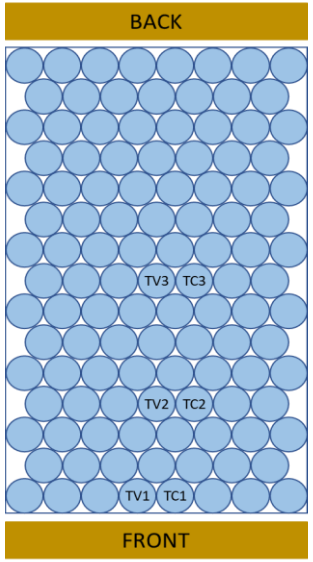


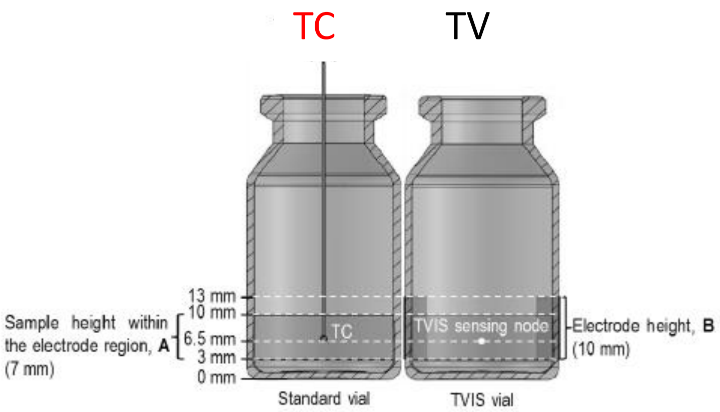
DE MONTFORT UNIVERSITY LEICESTER

NIBSC Confidence in Biological Medicines

Drying of 5% mannitol





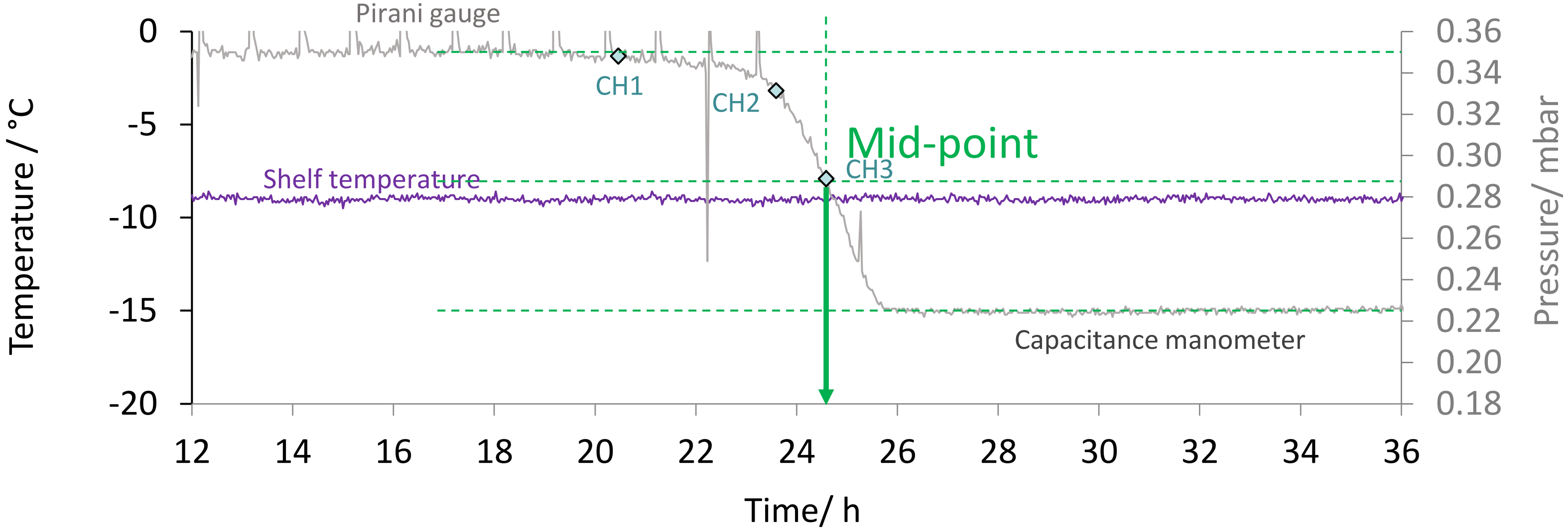


Key observation:

(1) All TVIS vials have sublimation end points either before, or coinciding with the mid-point of the Pirani curve

(2) The end point for the front vial coincides with the beginning of the step down in the Pirani profile

(3) The end point for the middle vial coincides with the mid point of the step down in the Pirani profile



DE MONTFORT UNIVERSITY LEICESTER

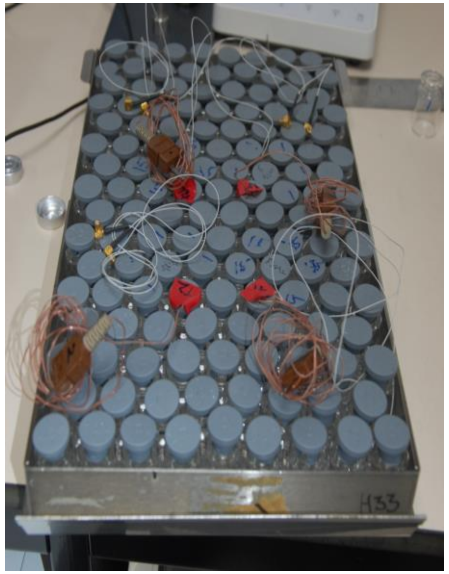
NIBSC Confidence in Biological Medicines

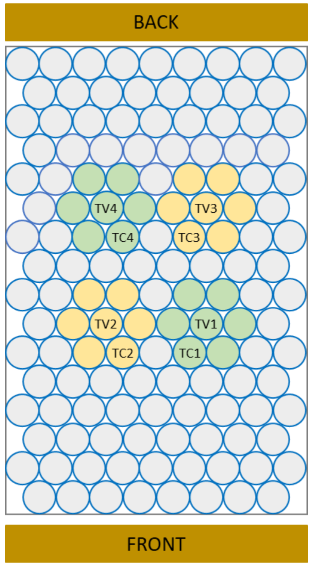
DMU LyoGroup

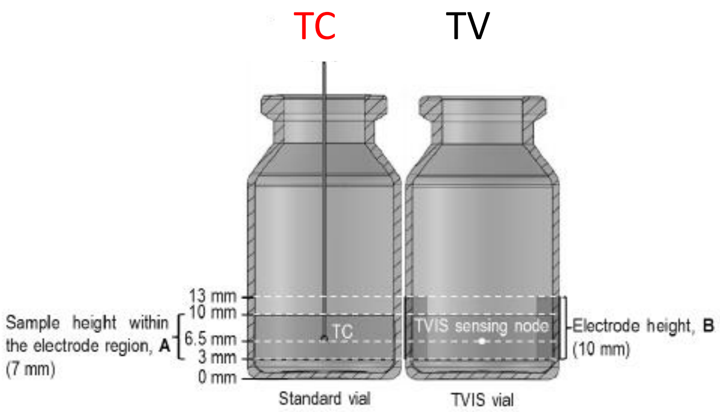
Through Vial Impedance Spectroscopy

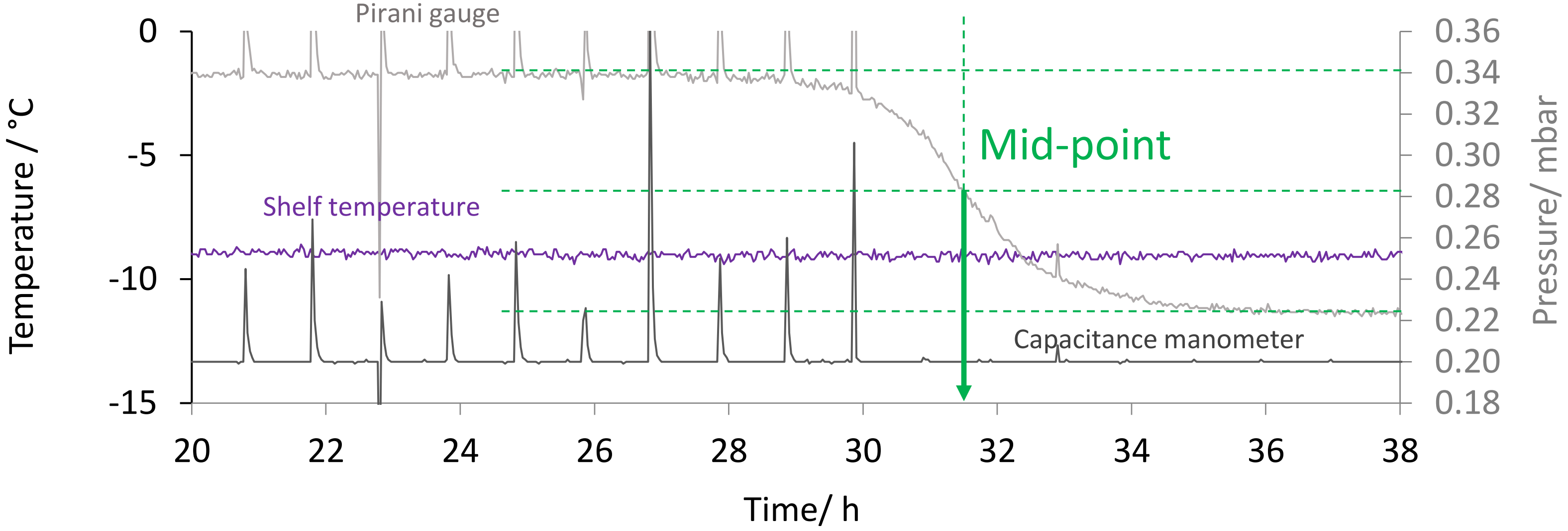
(15% IgG, 1% Sucrose, 4% Mannitol, 20 mM Histidine, 0.01% Tween 20)

Drying of a protein formulation







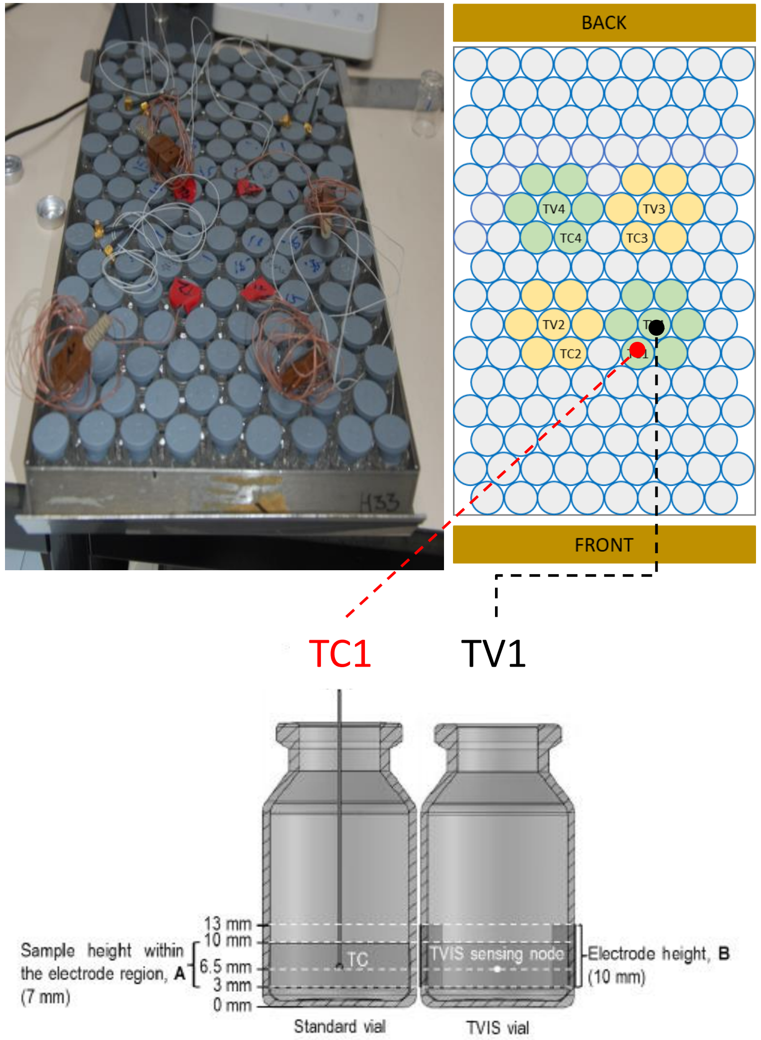


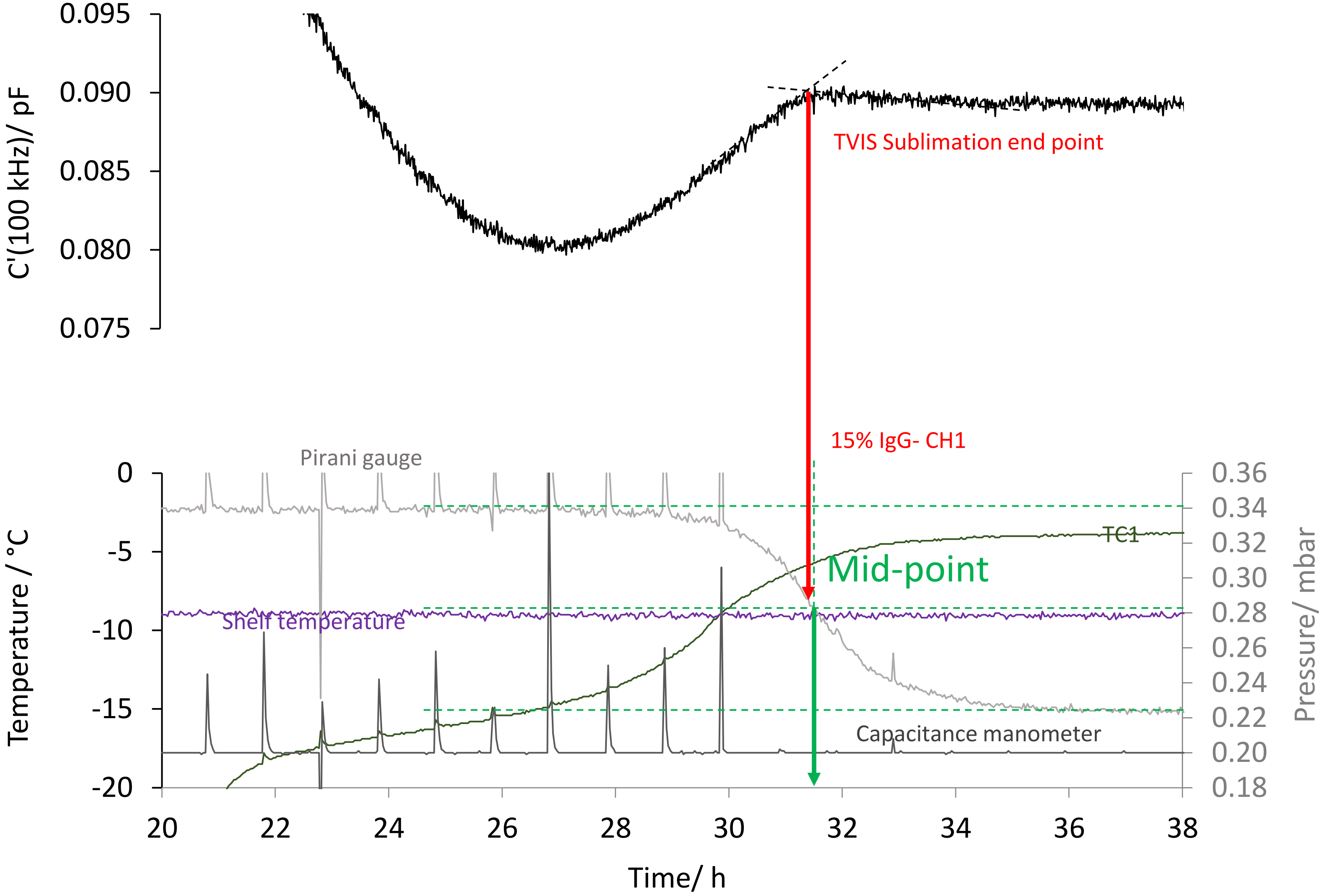
DE MONTFORT UNIVERSITY LEICESTER

NIBSC Confidence in Biological Medicines

DMU LyoGroup

Drying of a protein formulation 15% IgG, 1% Sucrose, 4% Mannitol, 20 mM Histidine, 0.01% Tween 20



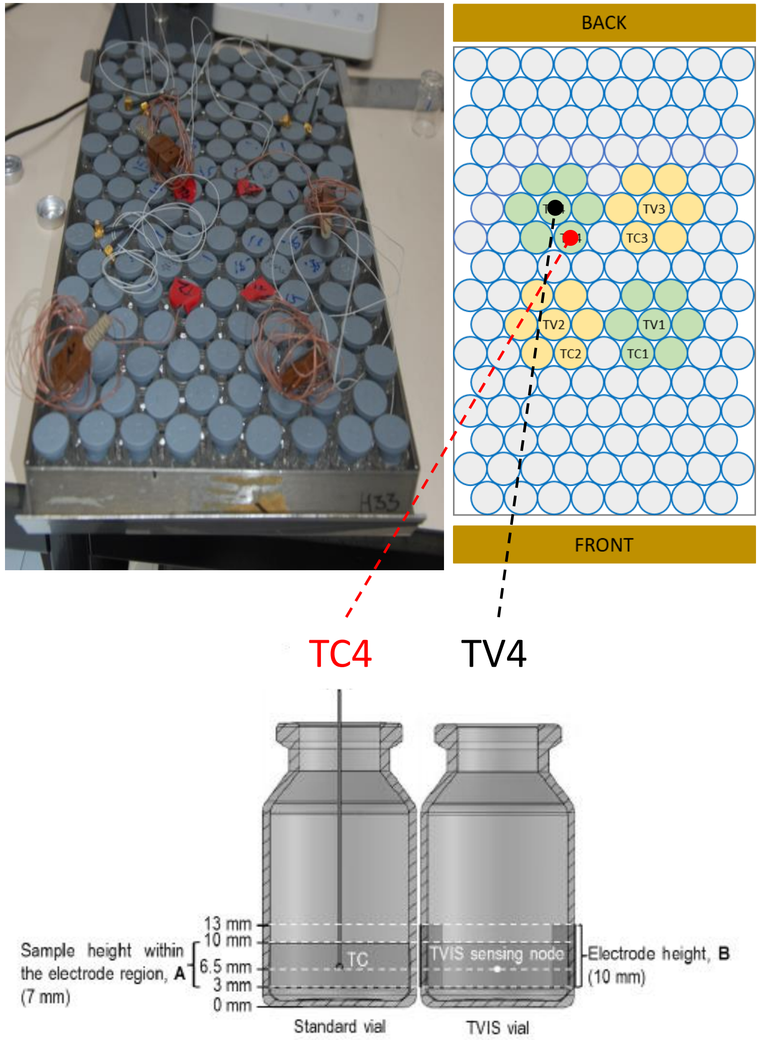


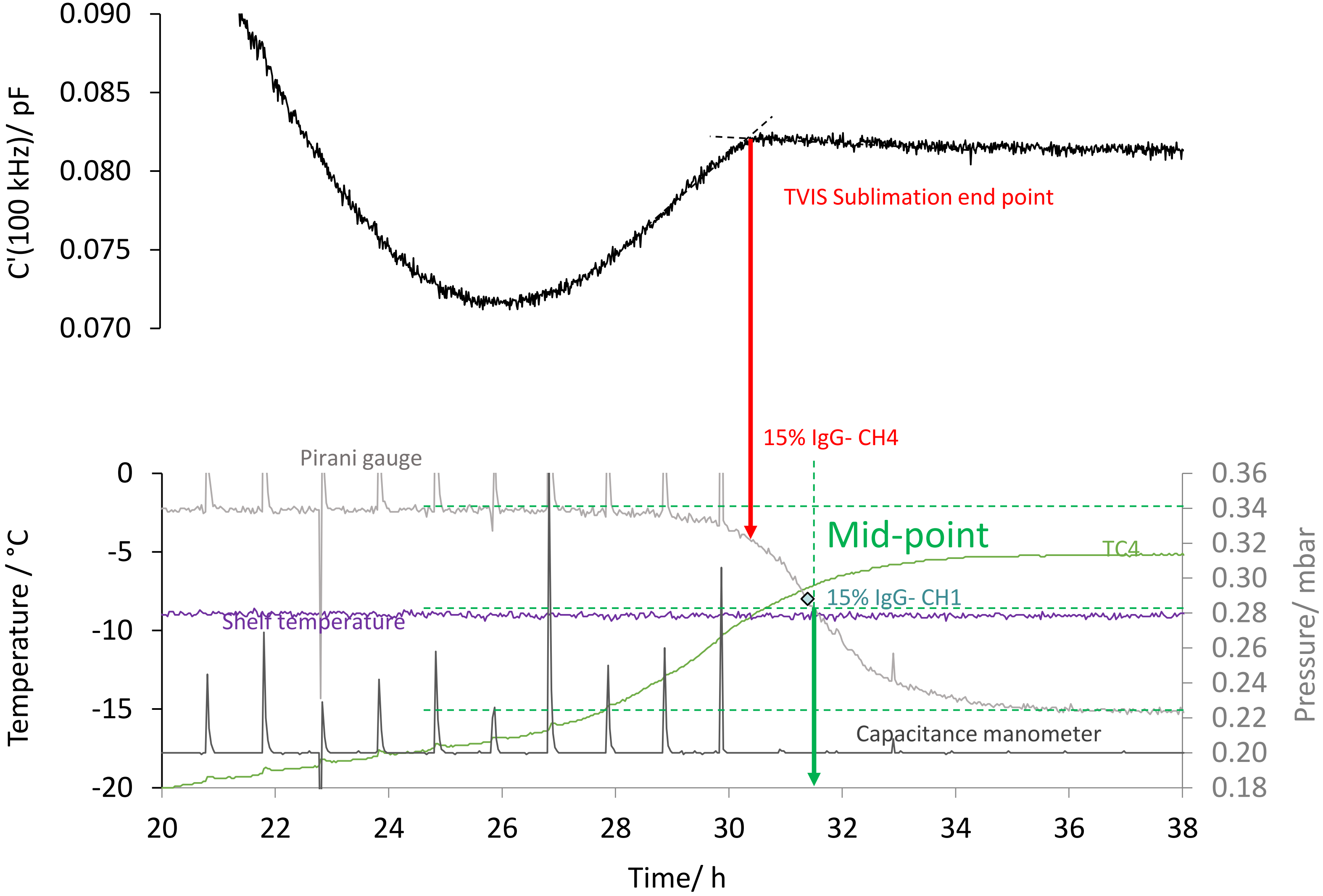
DE MONTFORT UNIVERSITY LEICESTER

NIBSC Confidence in Biological Medicines

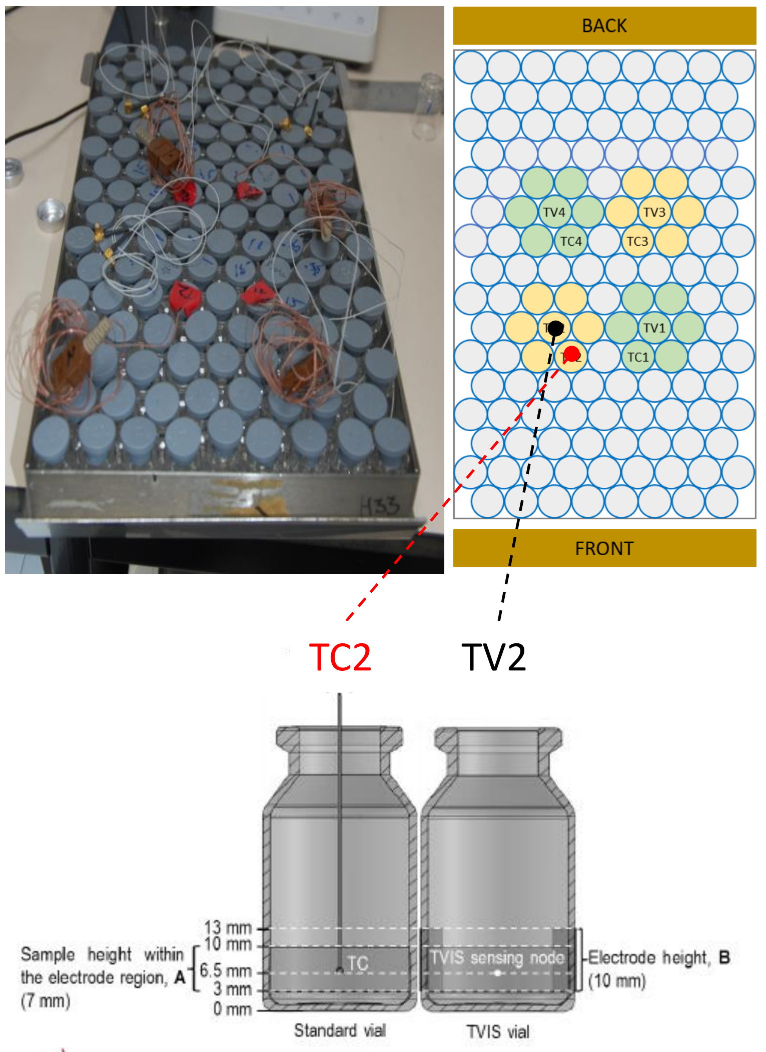
DMU LyoGroup

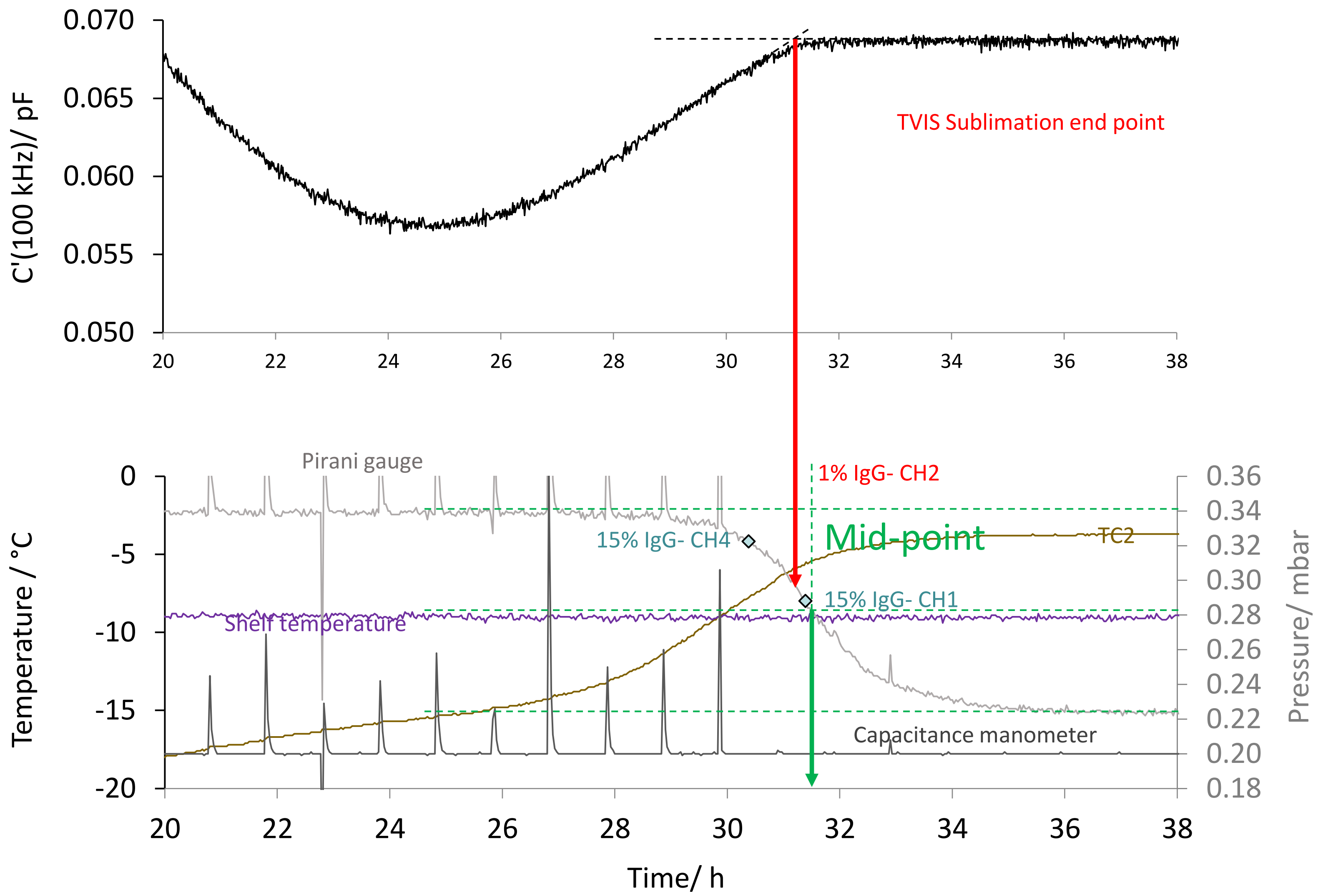
Drying of a protein formulation **15% IgG, 1% Sucrose, 4% Mannitol, 20 mM Histidine, 0.01% Tween 20**



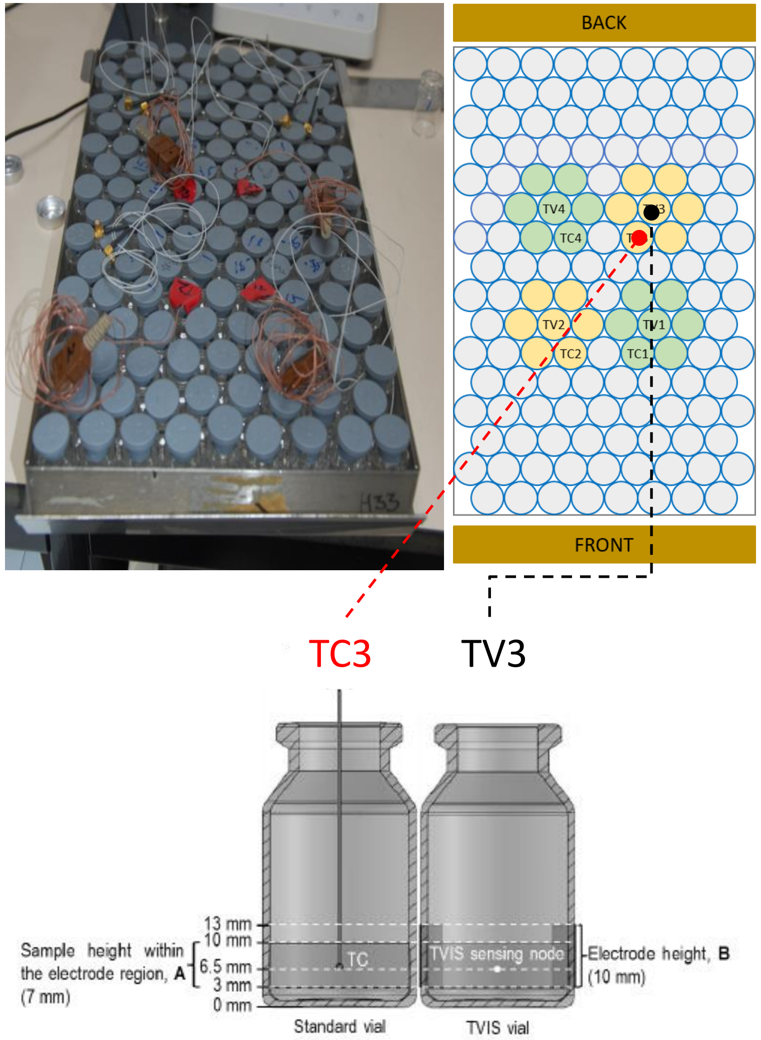


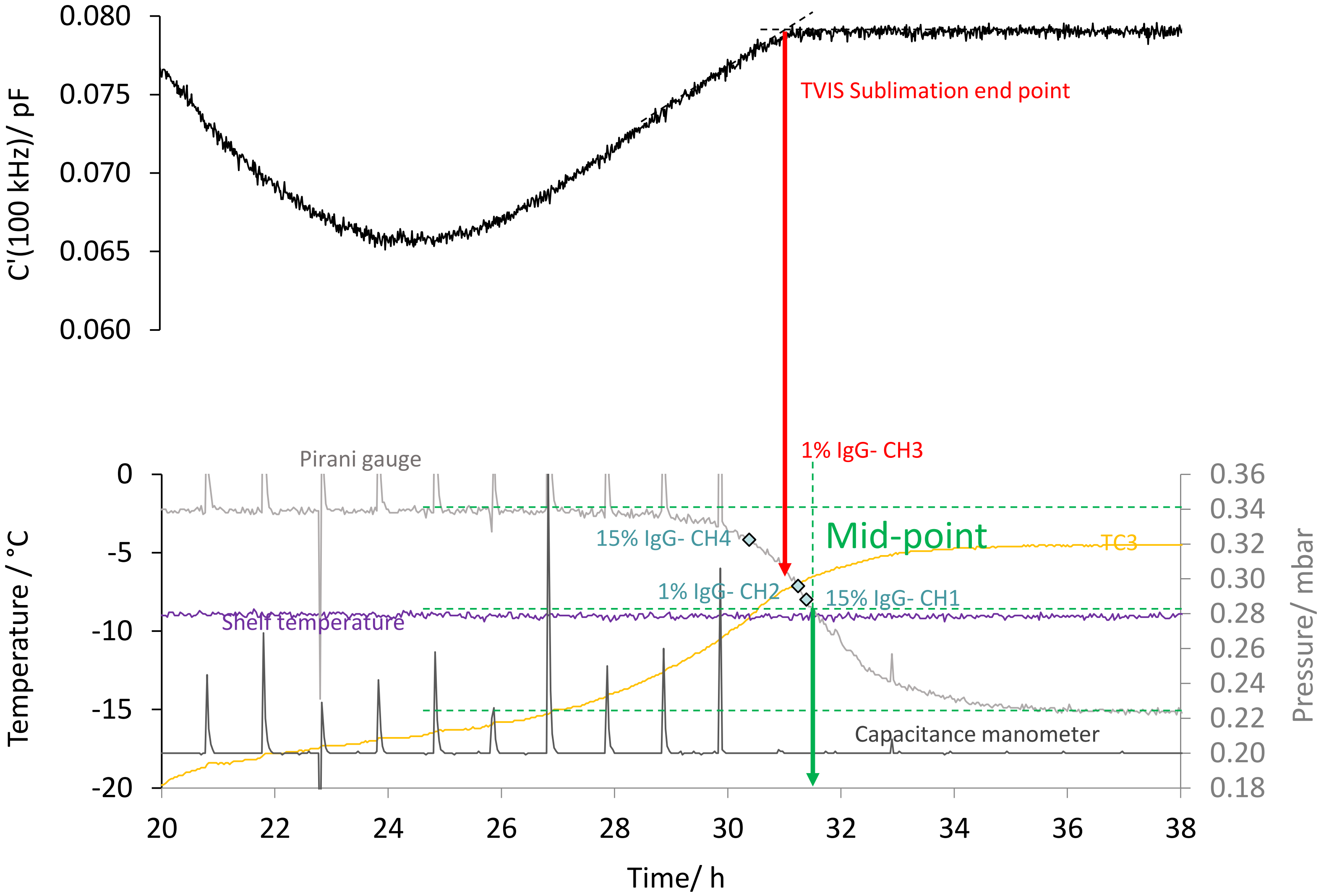
Drying of a protein formulation 1% IgG, 1% Sucrose, 4% Mannitol, 20 mM Histidine, 0.01% Tween 20





Drying of a protein formulation 1% IgG, 1% Sucrose, 4% Mannitol, 20 mM Histidine, 0.01% Tween 20



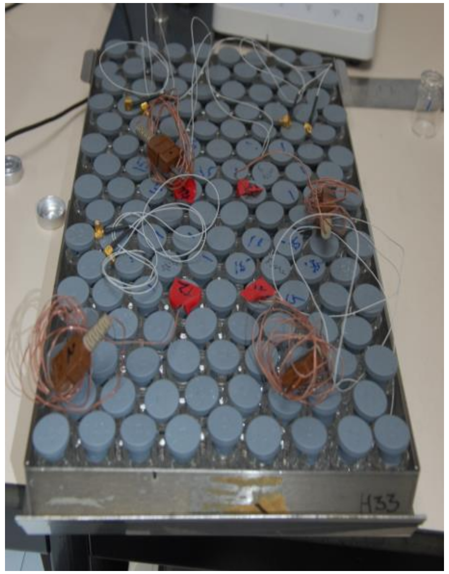


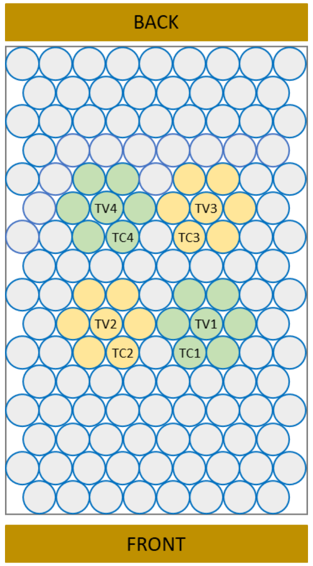
DE MONTFORT UNIVERSITY LEICESTER

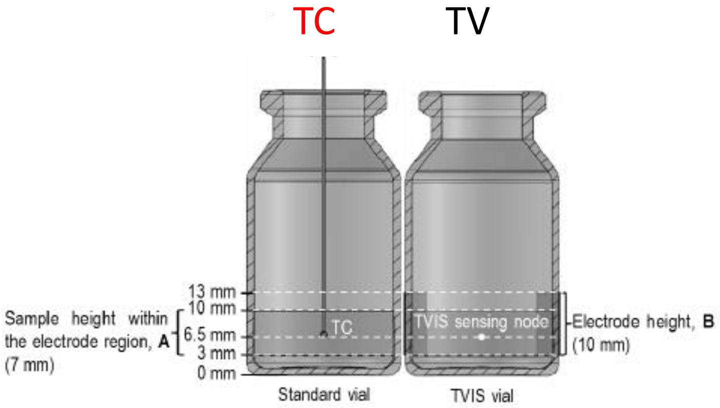
NIBSC Confidence in Biological Medicines

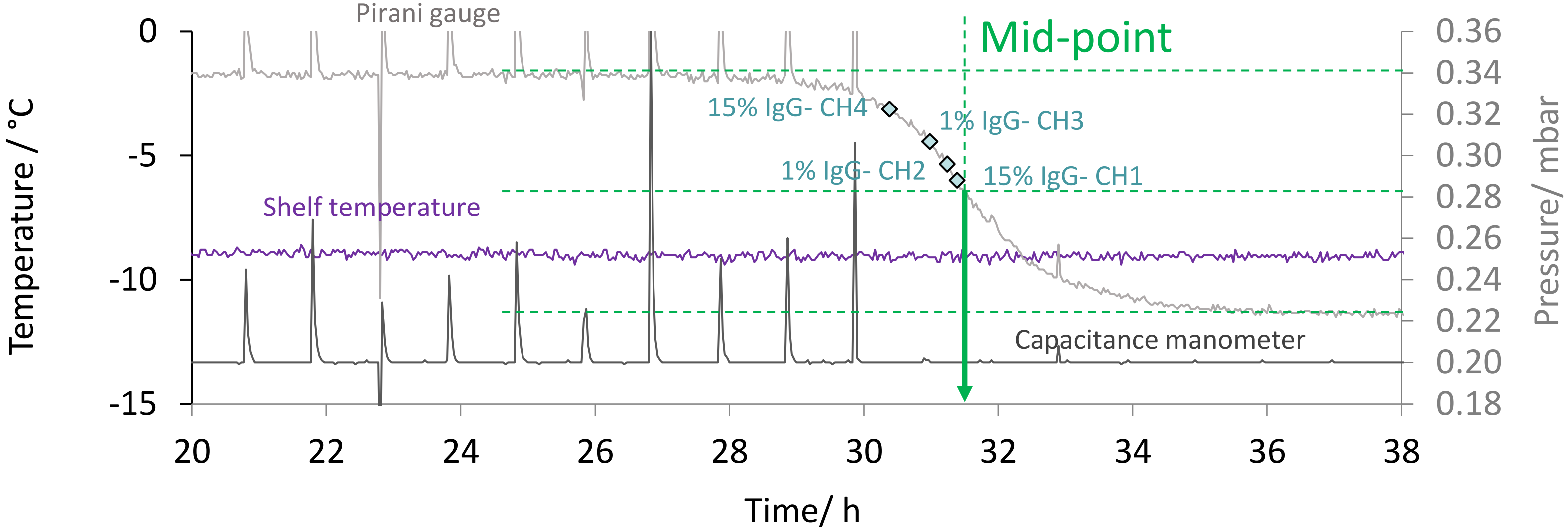
DMU LyoGroup

Drying of a protein formulation

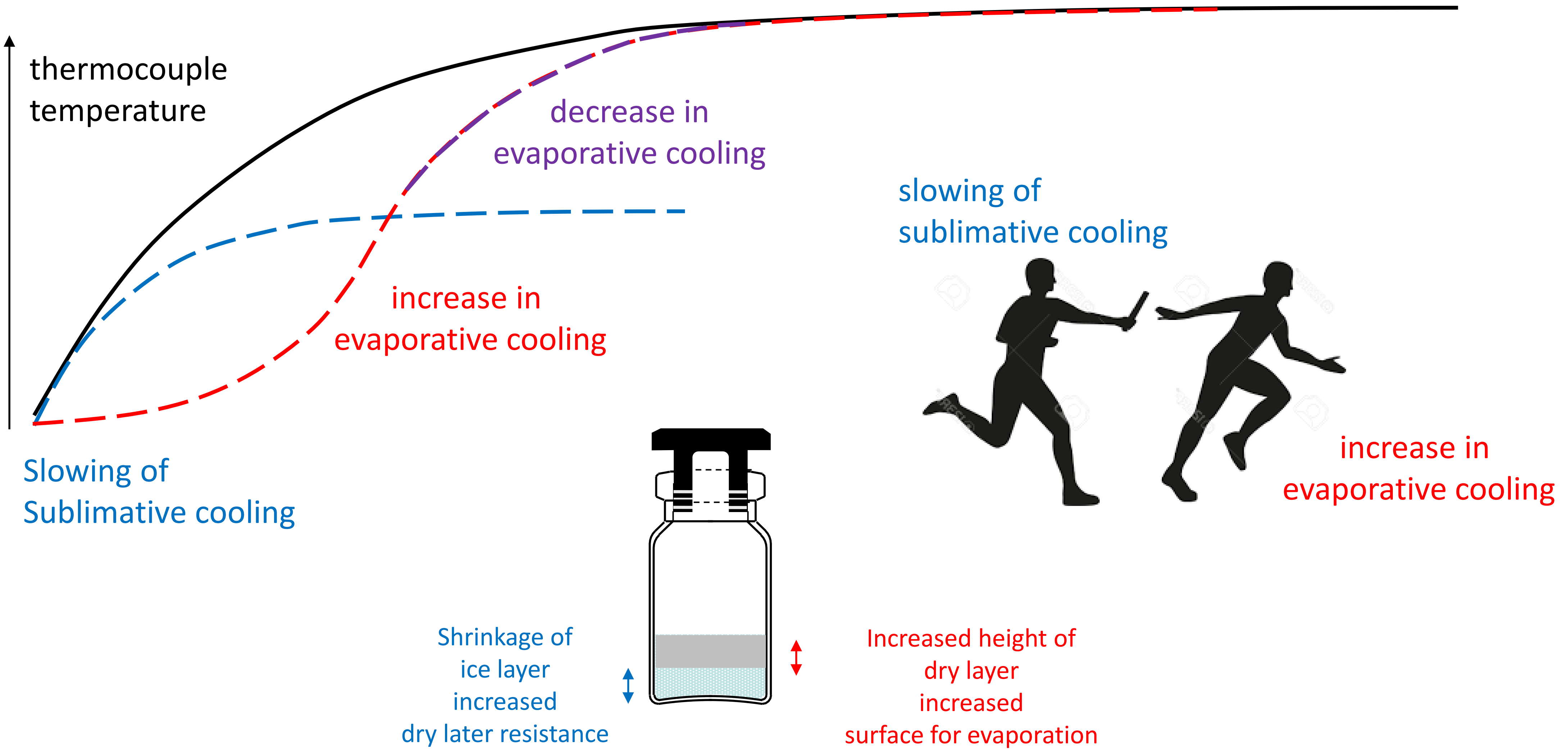




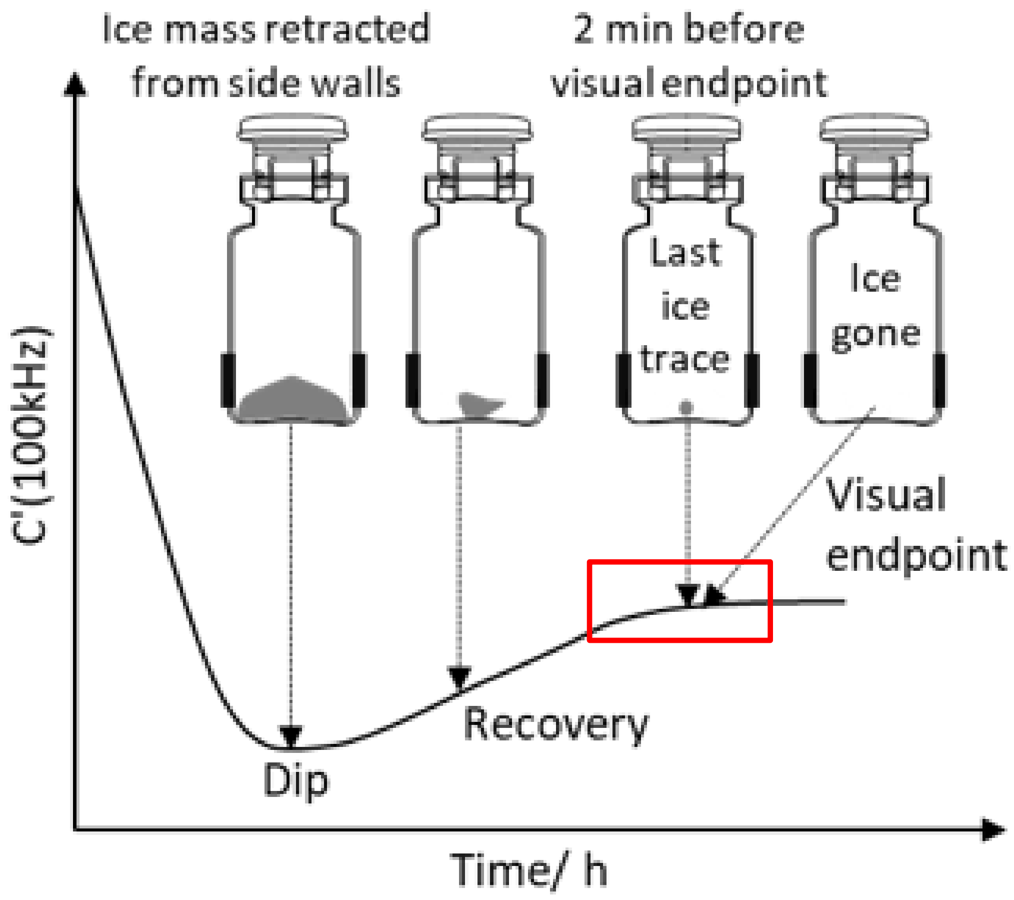


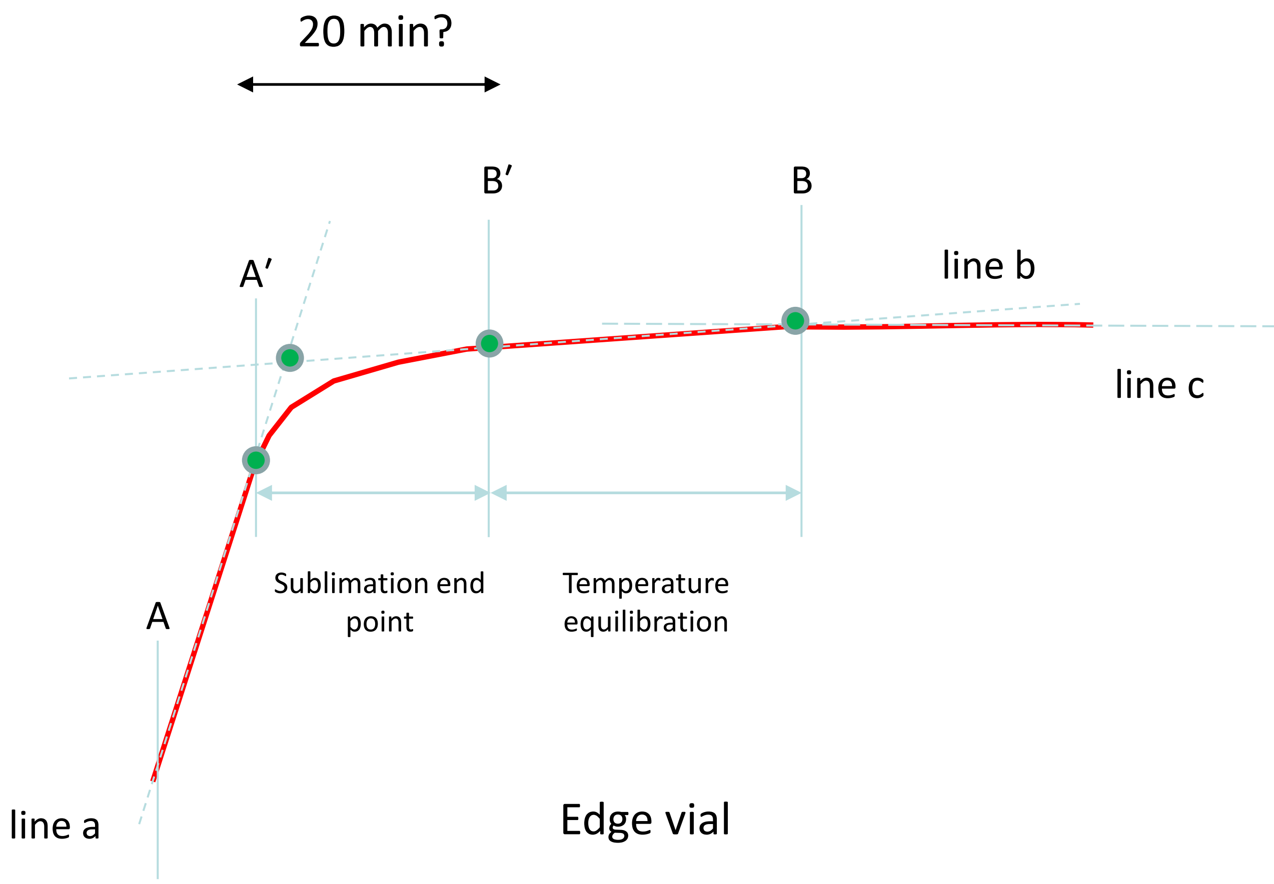


Over-lapping processes (e.g. TC data) = broad/imprecise end-point



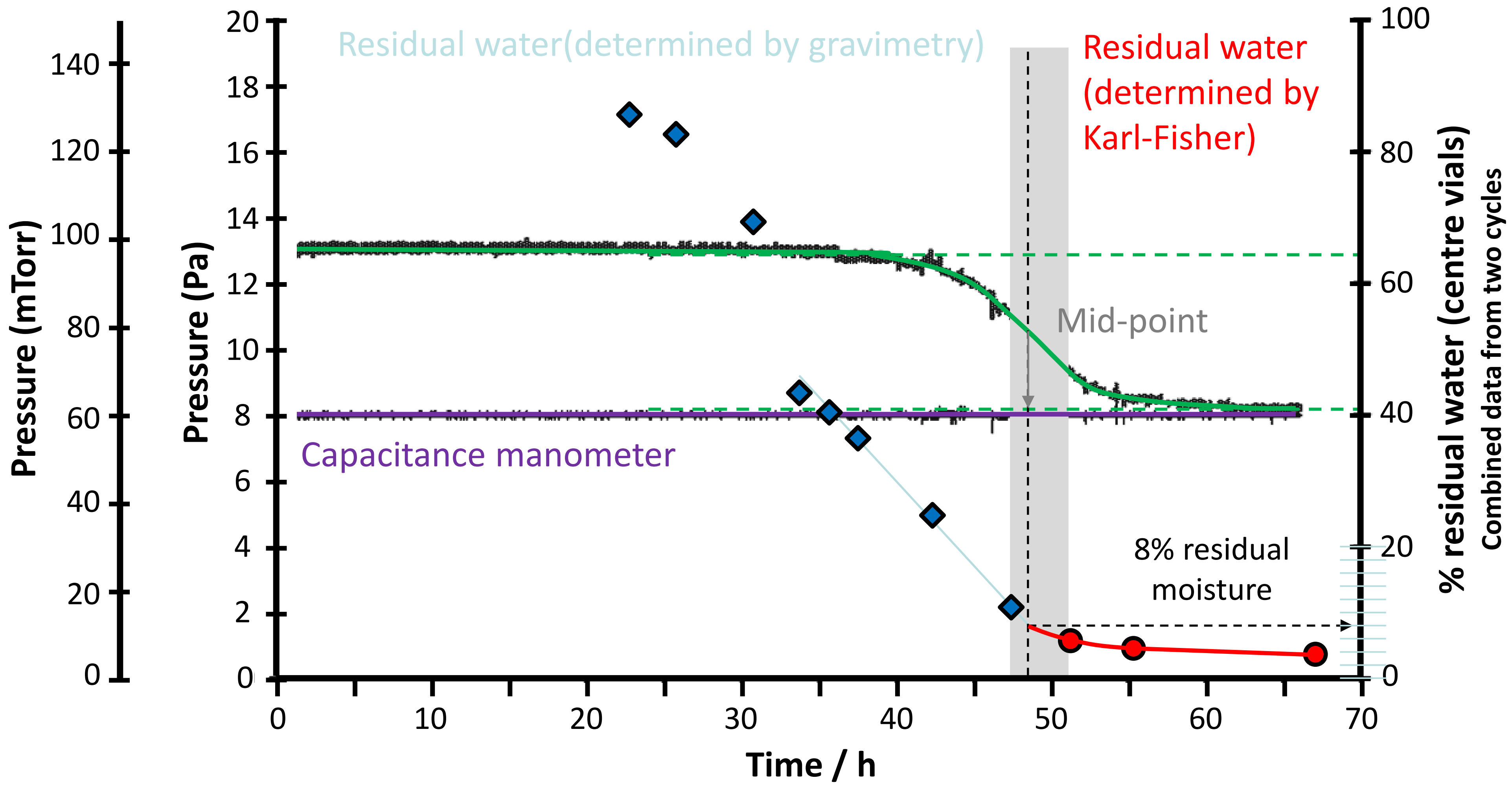
Single? process (TVIS data) – ignoring thermal equilibration



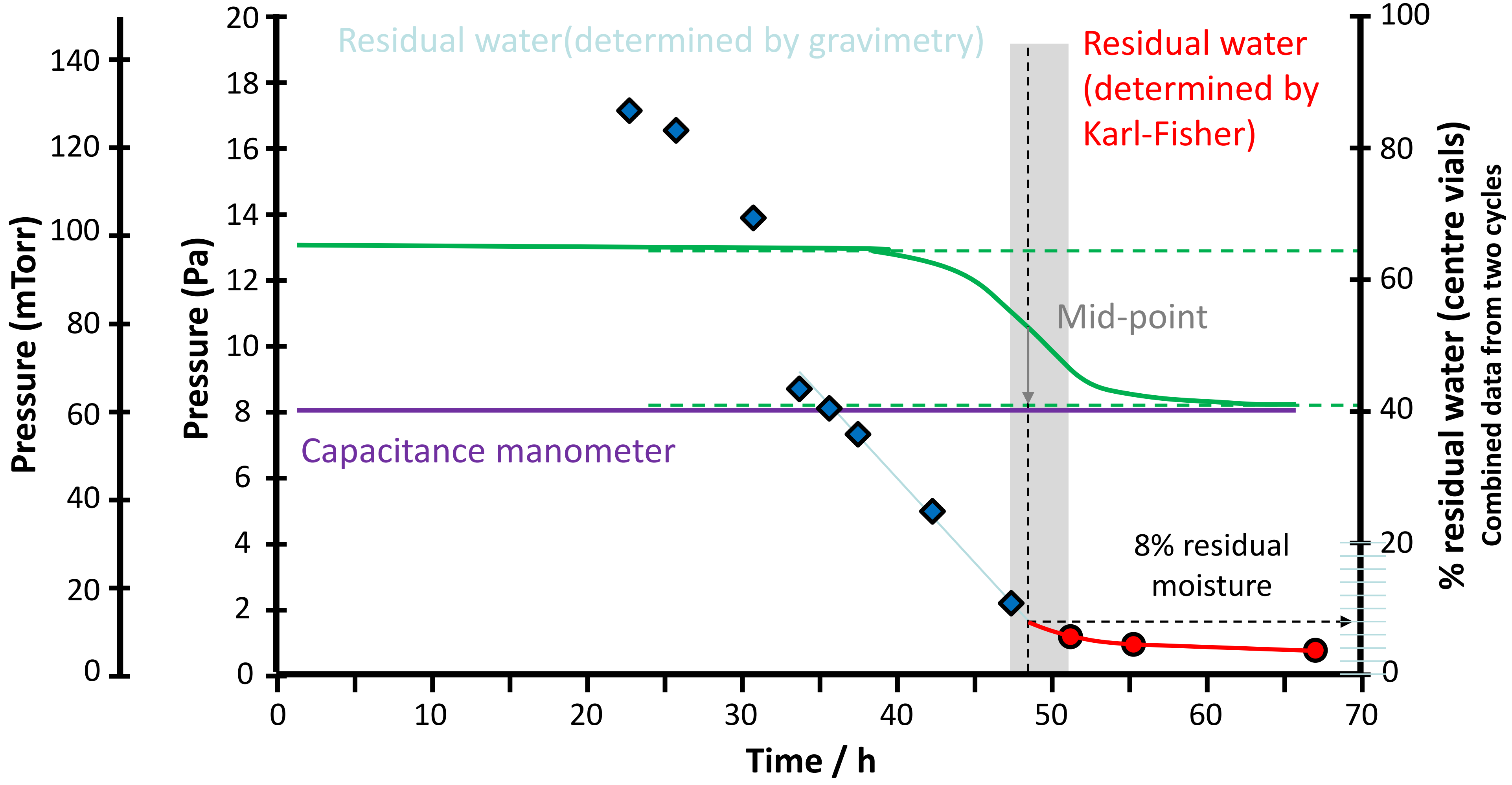


Comparison of Pirani profiles

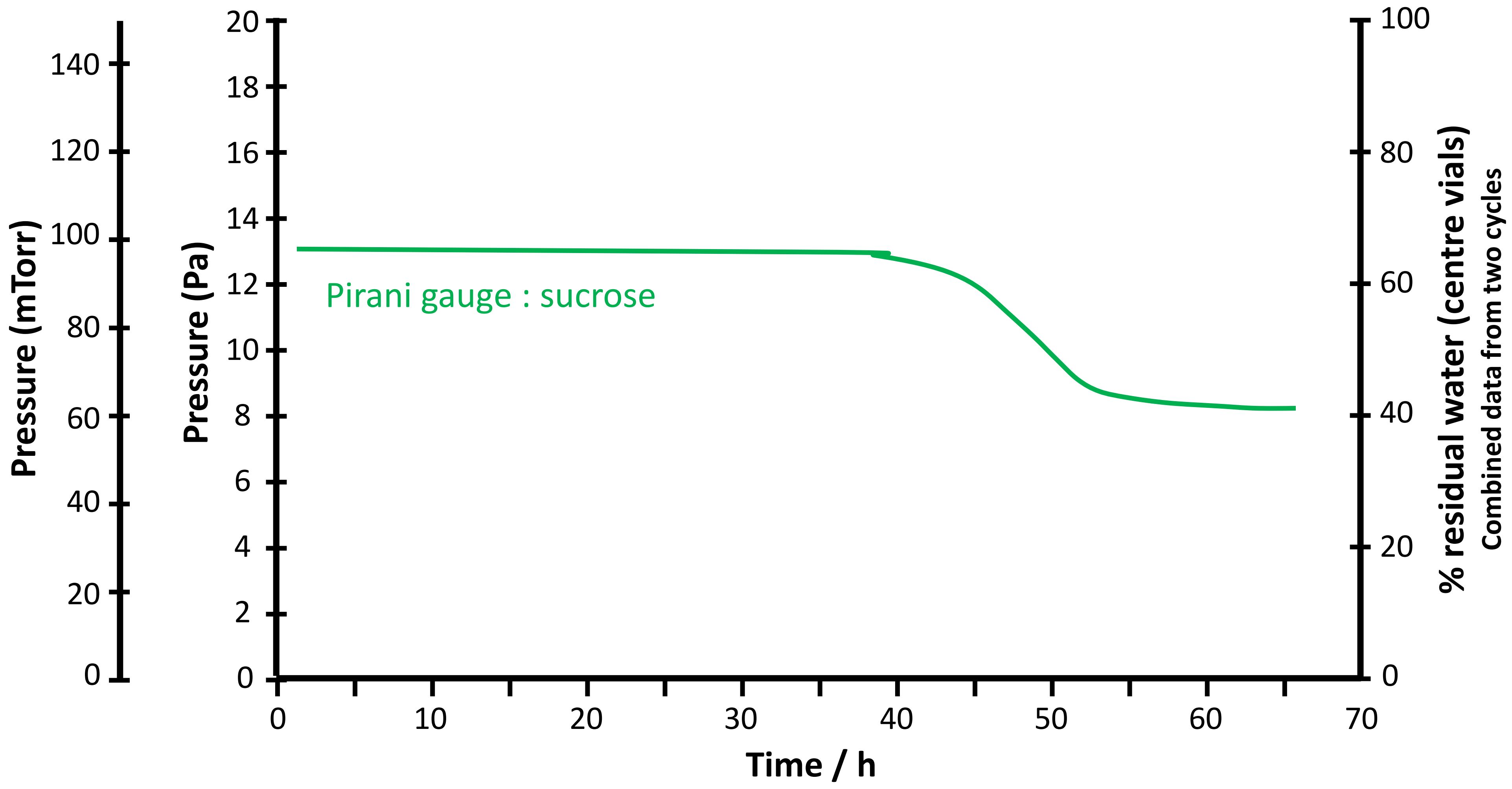
Comparison of Pirani profiles



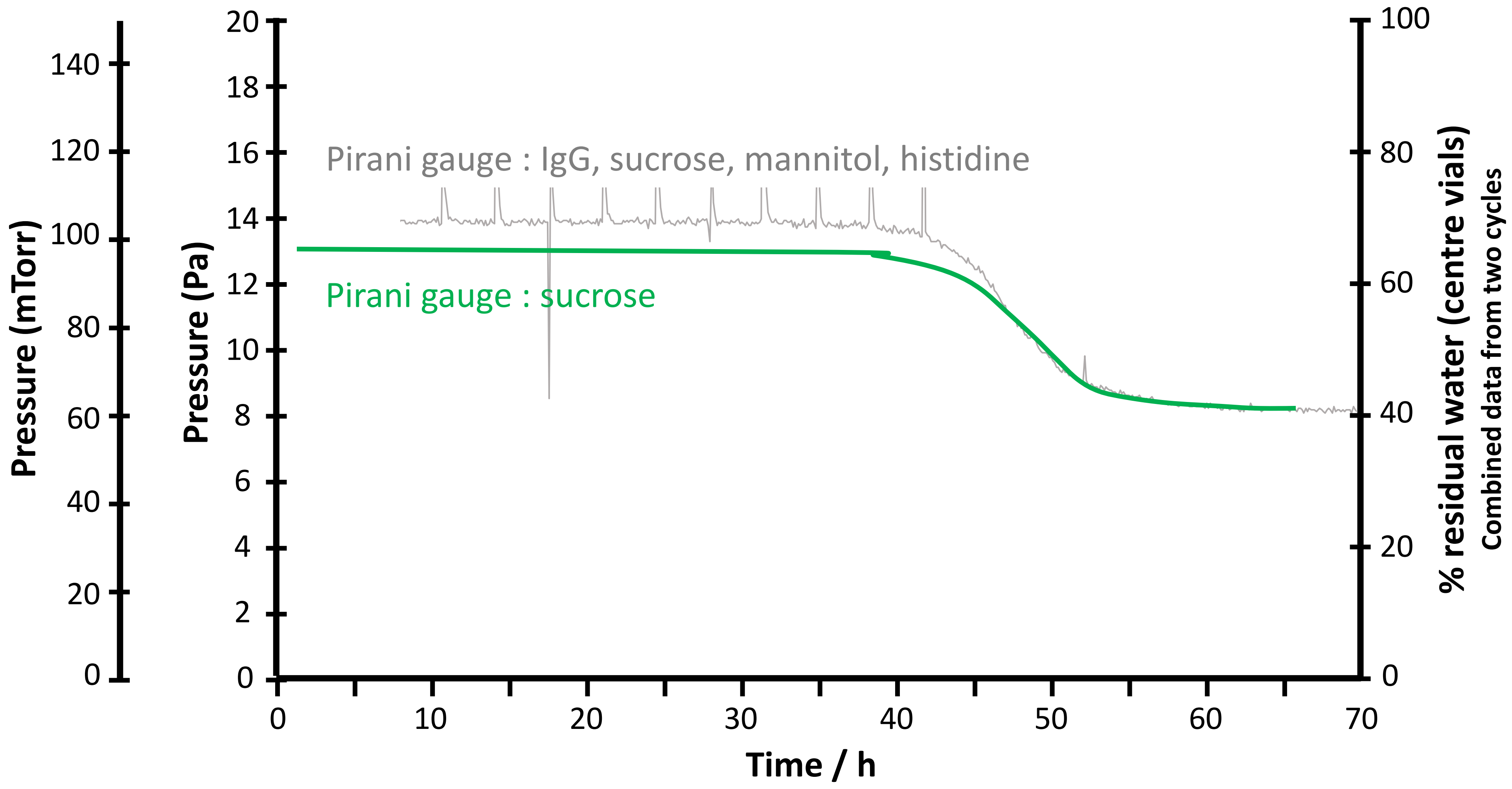
Comparison of Pirani profiles



Comparison of Pirani profiles

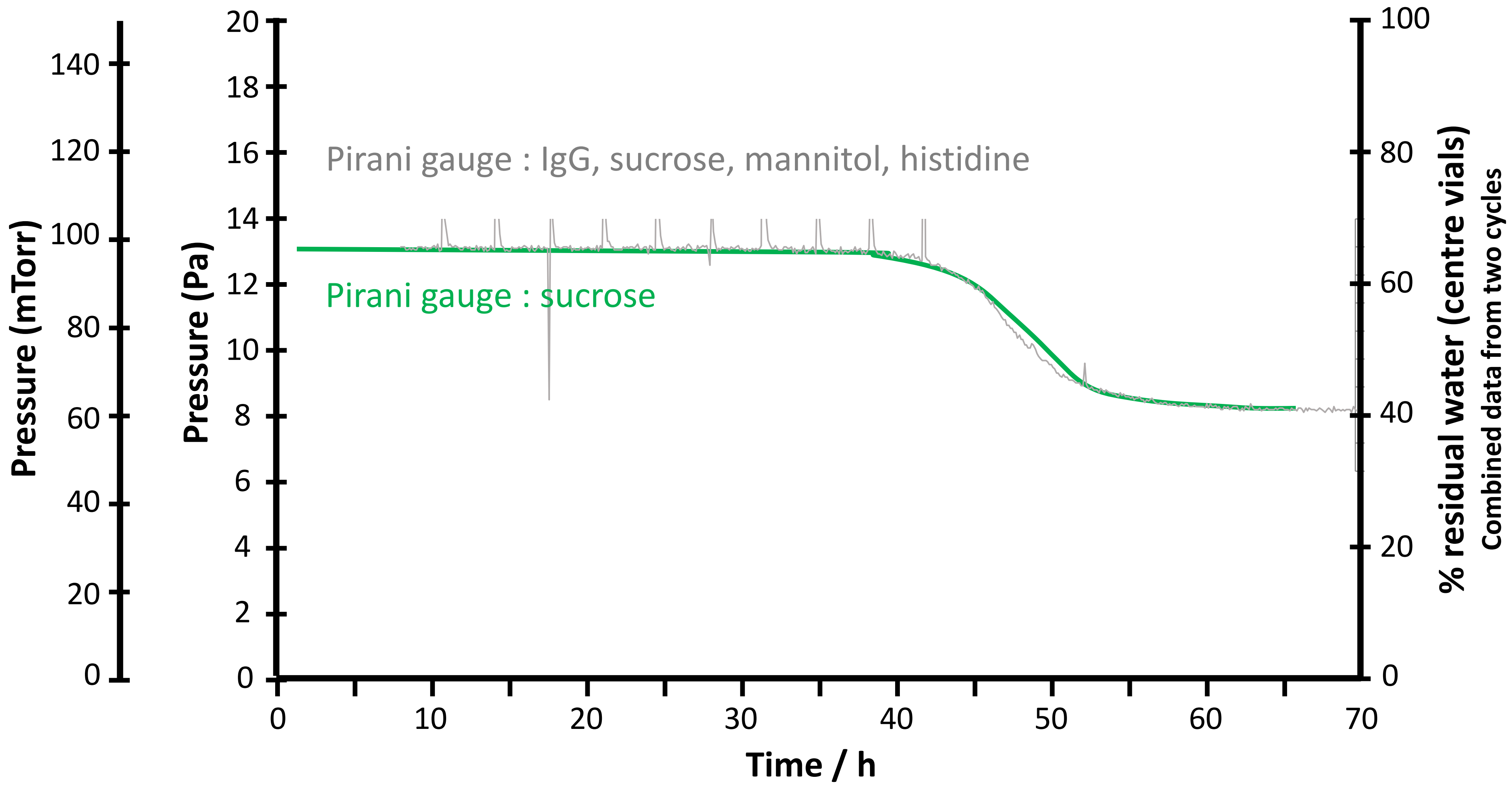


Comparison of Pirani profiles

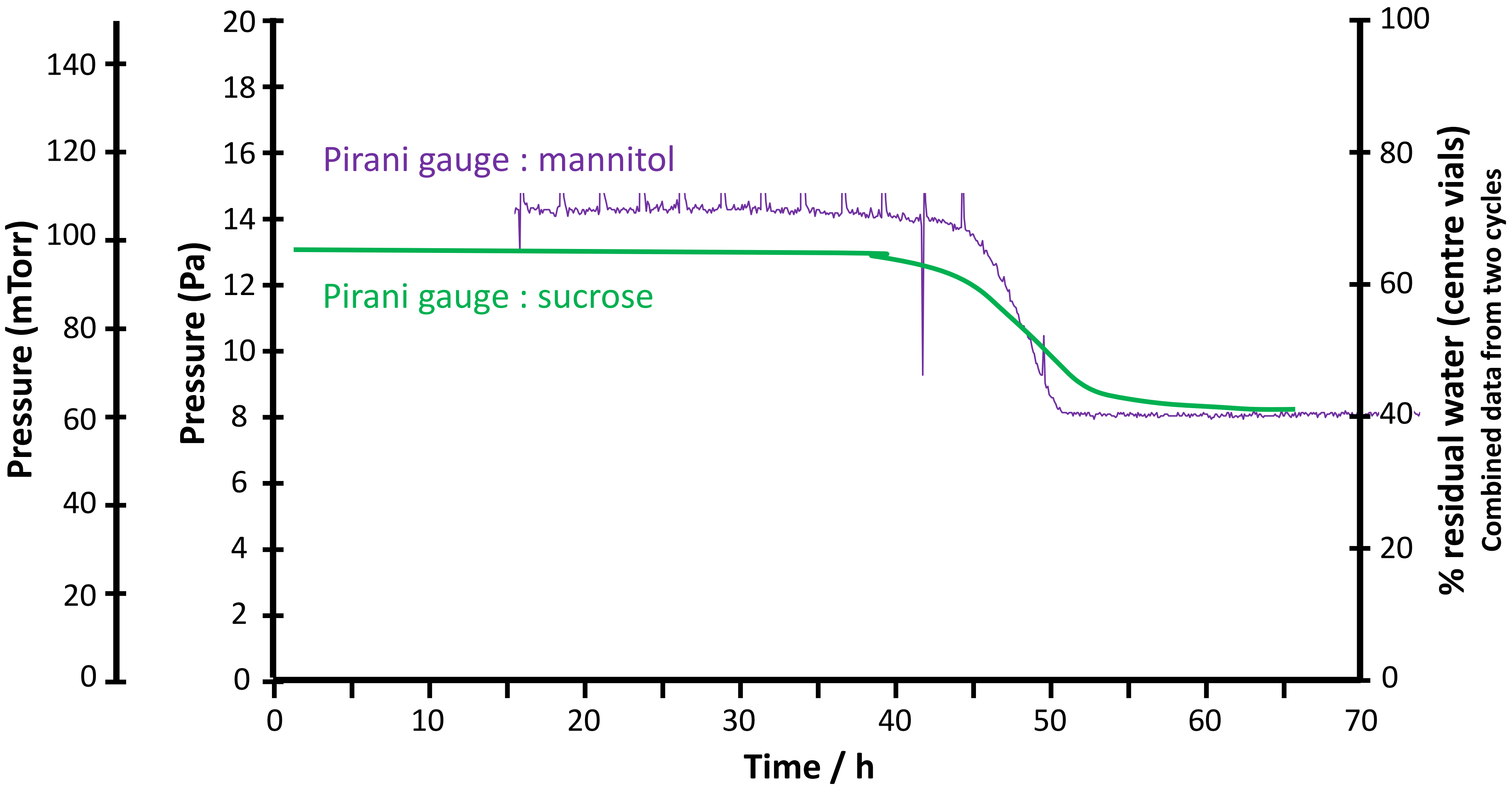


DE MONTFORT UNIVERSITY LEICESTER

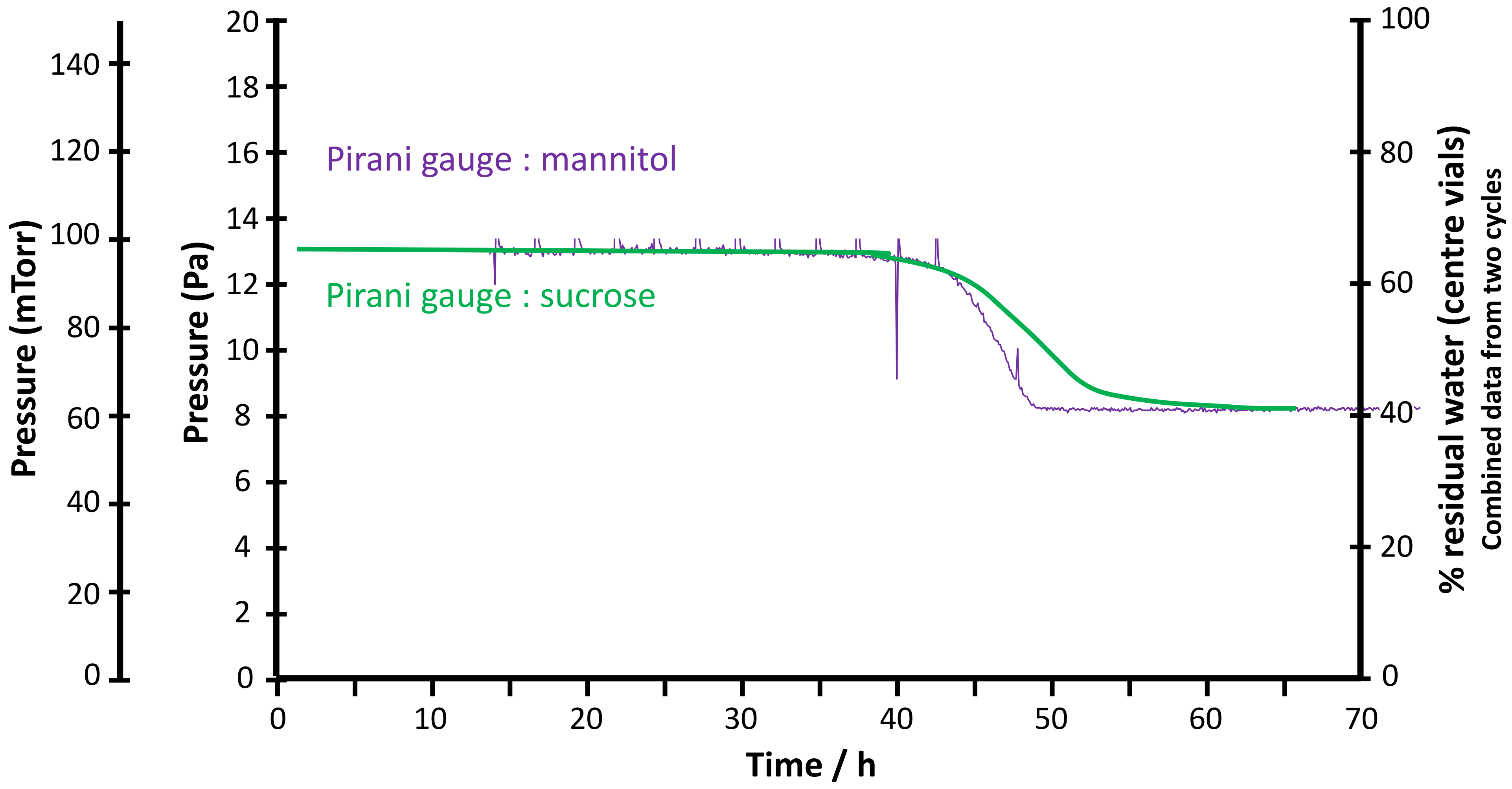
Comparison of Pirani profiles



Comparison of Pirani profiles



Comparison of Pirani profiles



Take home messages from this talk

Pirani and thermocouple measurements can not differentiate between water vapour evolved from ice sublimation and water vapour evolved from moisture desorption

- Vapour sensing technologies, such as CPM, can not differentiate between source of water vapour (ice or adsorbed water)
- Thermal measurements can also detect cooling from desorption of water adsorbed in the unfrozen fraction

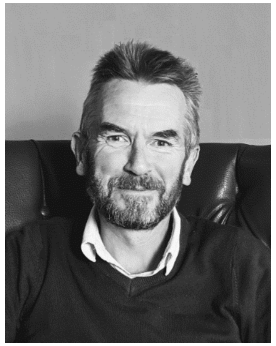
TVIS provides ….

- Identification of true sublimation (primary drying) end point

Summary of Applications (not covered in talk)

Dielectric loss peak		Dielectric constant	
Log peak frequency (F_{PEAK})	Temperature calibration (ice phase) Spatial measurements of ice temperature possible with multiple nodes	**Low frequency (100 Hz)**	Ice nucleation onset time and temperature
Peak amplitude (C''_{PEAK})	Ice mass & sublimation rate Annealing end-point	**High frequency (100-200 kHz)**	Ice solidification end point Glass transition temperature Devitrification Sublimation end point

Thank you for listening ……….



DMU LyoGroup

Feel free to email me if you have any further questions :

gsmith02@dmu.ac.uk

Prof. Geoff Smith

School of Pharmacy, De Montfort University, Leicester, UK

Acknowledgements

Evgeny Polygalov
Physicist and Inventor of TVIS
1952-2020

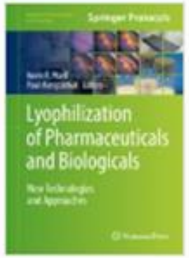
Dr Paul Matejtschuk
Head of Standardization
Science in the Analytical &
Biological Sciences Division

Pathum Wijesekara
PhD student, School of Pharmacy
De Montfort University Leicester

NIBSC
Confidence in Biological Medicines

DE MONTFORT UNIVERSITY LEICESTER

Further Reading



Lyophilization of Pharmaceuticals and Biologicals pp 241-290 | Cite as

Through Vial Impedance Spectroscopy (TVIS): A Novel Approach to Process Understanding for Freeze-Drying Cycle Development

Authors | Authors and affiliations

Geoff Smith, Evgeny Polygalov

- Introduction to TVIS theory
- Description of the measurement principles
- Dielectric loss and relaxations mechanisms (liquid and frozen states)

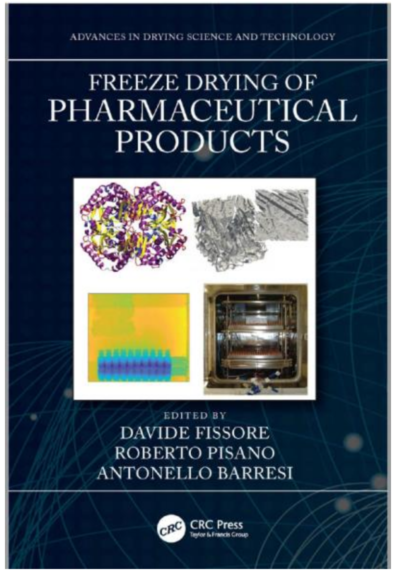
Further Reading

Chapter 5 Through Vial Impedance Spectroscopy (TVIS) A New Method for Determining the Ice Nucleation Temperature and the Solidification End point

CRC Press
Taylor & Francis Group

About Us | Resources | Textbooks | Featured Authors

Home / Pharmaceutical Science / Manufacturing & Engineering / Freeze Drying of Pharmaceutical Products



Freeze Drying of Pharmaceutical Products

1st Edition

Davide Fissore, Roberto Pisano, Antonello Barresi

Hardback
£118.00

CRC Press
November 13, 2019 **Forthcoming**
Reference - 214 Pages - 4 Color & 66 B/W Illustrations
ISBN 9780367076801 - CAT# K405807
Series: Advances in Drying Science and Technology

TVIS publications

www.dmu.ac.uk/TVIS

- Bhaskar, P., Smith, G., Ermolina, I., Polygalov, E. (2021). Observations on the changing shape of the ice mass and the **determination of the sublimation end point in freeze-drying**: An application for through-vial impedance spectroscopy (TVIS). Pharmaceutics, 13(11) 1835. Accepted 13 October 2021, Available online 02 November 2021 https://doi.org/10.3390/pharmaceutics13111835
- Jeeraruangrattana, Y., Smith, G., Polygalov, E. and Ermolina, I. (2020) Determination of ice interface temperature, sublimation rate and **the dried product resistance**, and its application in the assessment of microcollapse using through-vial impedance spectroscopy. European Journal of Pharmaceutics and Biopharmaceutics, 152, pp. 144-163 doi.org/10.1016/j.ejpb.2020.04.015
- Smith, G., Jeeraruangrattana, Y., Ermolina, I. (2018). The application of dual-electrode through vial impedance spectroscopy for the determination of ice interface temperatures, **primary drying rate** and vial heat transfer coefficient in lyophilization process development. European Journal of Pharmaceutics and Biopharmaceutics, 130, pp. 224-235 doi.org/10.1016/j.ejpb.2018.05.019
- Smith, G., Arshad, M.S., Polygalov, E., Ermolina, I., McCoy, T.R., Matejtschuk, P. (2017). Process Understanding in Freeze-Drying Cycle Development: Applications for Through-Vial Impedance Spectroscopy (TVIS) in Mini-pilot Studies. Journal of Pharmaceutical Innovation, 12 (1), pp. 26-40 doi.org/10.1007/s12247-016-9266-5 **Key observation was the potential to measure temperature non-invasively**
- Arshad, M.S., Smith, G., Polygalov, E., Ermolina, I. (2014). Through-vial impedance spectroscopy of critical events during the freezing stage of the lyophilization cycle: The example of the impact of sucrose on the **crystallization of mannitol**. European Journal of Pharmaceutics and Biopharmaceutics, 87 (3), pp. 598-605 doi.org/10.1016/j.ejpb.2014.05.005
- Smith, G., Arshad, M.S., Polygalov, E., Ermolina, I. (2014). Through-Vial Impedance Spectroscopy of the **Mechanisms of Annealing** in the Freeze-Drying of Maltodextrin: The Impact of Annealing Hold Time and Temperature on the Primary Drying Rate. Journal of Pharmaceutical Sciences, 103 (6), pp. 1799-1810 doi.org/10.1002/jps.23982
- Smith, G., Arshad, M.S., Polygalov, E. and Ermolina, I. (2013) An application for impedance spectroscopy in the characterisation of the **glass transition** during the lyophilization cycle: The example of a 10% w/v maltodextrin solution. European Journal of Pharmaceutics and Biopharmaceutics, 86 (3 Part B), pp. 1130-1140 doi.org/10.1016/j.ejpb.2013.08.004

6th Annual Conference & Exhibition

LYOTALK®

Largest Conference on Freeze Drying / Lyophilization

EUROPE 2022

19-20 May Amsterdam

An Event By

BIOTRAINS

Connect Collaborate Evolve