MAKING SCIENCE WORK

UCONN
UNIVERSITY OF CONNECTICUT

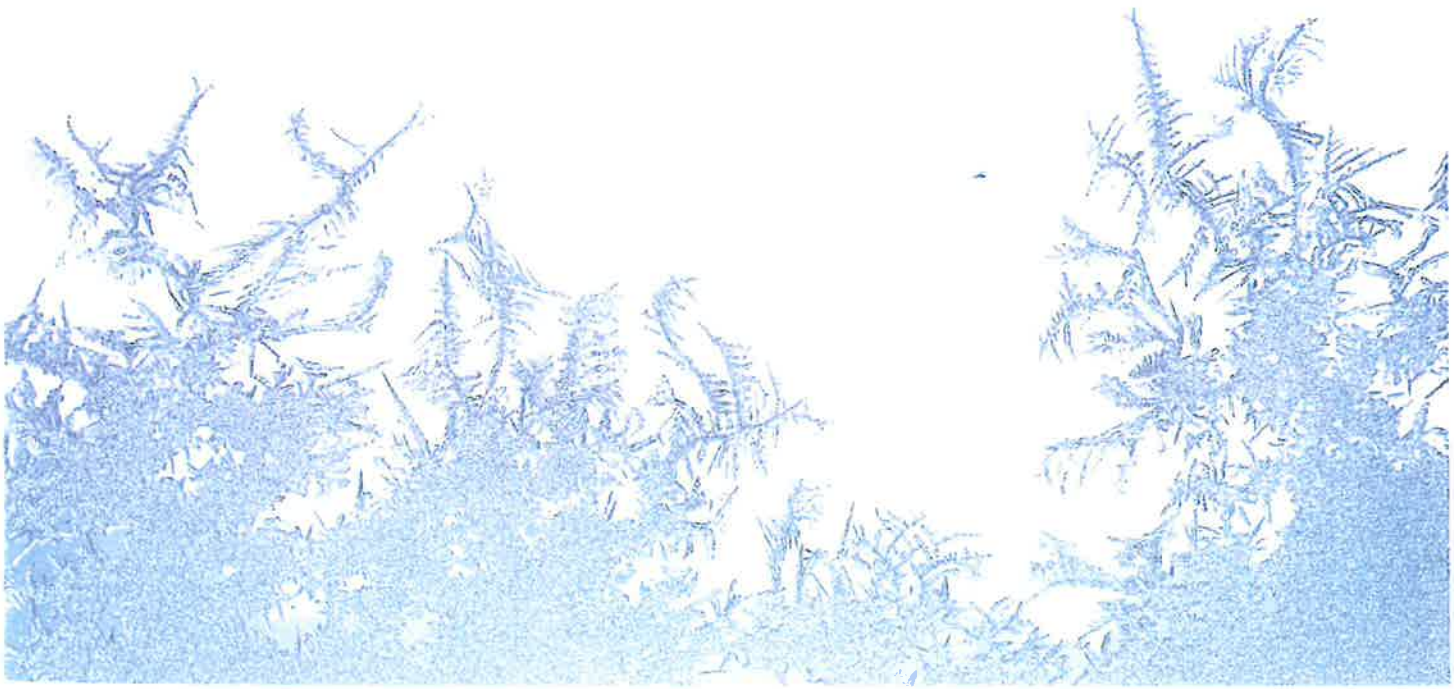
LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

FREEZE DRYING OF PHARMACEUTICALS & BIOLOGICALS

September 16 – 19, 2025

Dorint Hotel
Garmisch-Partenkirchen, Germany

CONFERENCE BOOKLET



Conference Organization

Freeze-Drying of Pharmaceuticals and Biologicals

Organization:

APV Mainz
LMU München
University of Connecticut

Organization Comittee:

Alina Alexeenko
Purdue University
alexeenk@purdue.edu

Jean-Rene Authelin
Sanofi
Jean-Rene.Authelin@sanofi.com

Bakul Bhatnagar
Pfizer
bakul.bhatnagar@pfizer.com

Robin Bogner
University of Connecticut
robin.bogner@uconn.edu

Wolfgang Friess
University of Munich
wolfgang.friess@lrz.uni-muenchen.de

Arnab Ganguly
Amgen
agangu02@amgen.com

Steven L. Nail
Purdue University
stevennail@mac.com

Sajal Patel
AstraZeneca
kpds708@astrazeneca.net

Ingo Presser
Boehringer Ingelheim
ingo.presser@boehringer-ingelheim.com

Edward Trappler
Lyophilization Technology, Inc.
etrappler@lyo-t.com

Gerhard Winter
University of Munich
gerhard.winter@lrz.uni-muenchen.de

Investigating the Role of Thermal Interactions during Freezing on the Morphology of Freeze-Dried Products

Vincenzo Massotti[1], Fiora Artusio[1], Antonello A. Barresi[1], Roberto Pisano[1]

[1]Department of Applied Science and Technology, Politecnico di Torino, Corso Duca degli Abruzzi 24, 10129 Turin, Italy

Corresponding author: roberto.pisano@polito.it, +39-011-0904679

PURPOSE

The solidification of water into ice is initiated by a stochastic phenomenon called nucleation. Since the phase change is an exothermic process, the heat released by nucleation in a vial can delay nucleation in the neighbouring ones. The combination of these two phenomena causes each vial to have a unique thermal profile. Since the ice crystal size depends on the thermal history of the solution, the morphology of the final product results to be heterogeneous. In this work, experiments were coupled with a mathematical model to assess the influence of thermal interactions during freezing on the morphology of freeze-dried products.

METHODS

A 5% sucrose-mannitol (1:1) was freeze-dried in different loading conditions, with vials in an interacting or a non-interacting configuration. The nucleation times of 10x20 vials were recorded by two video cameras placed above the shelf. The thermal profiles recorded by thermocouples were used to estimate the equipment-to-vial and the vial-to-vial heat transfer coefficients. These pieces of information were used as input in a mathematical model to compute the thermal profile of each vial in the batch. From these profiles, the model extracts information on the product morphology and the resulting drying times.

RESULTS

Thermal interactions led to a decrease in the average nucleation temperature characterised by a broader distribution. Moreover, the average freezing front rate increased, and in this case as well, resulted to be highly variable within the batch. Therefore, when interactions were present, the average pore size resulted to be lower and more variable than the non-interacting case. The resulting drying times resulted to be higher due to the increased resistance to the vapour flow.

CONCLUSION

The mathematical model suggested that thermal interactions affect the product morphology. The pore size distribution had a lower average value and a higher variability compared to non-interacting cases, slowing down the drying step. These results evidenced the importance of considering thermal interactions in the design and the optimisation of freeze-drying cycles.

REFERENCES

1. Pisano, R., Semeraro, J., Artusio, F., Barresi, A.A., 2024. Insights into thermal interactions in frozen pharmaceutical vials: effects on ice nucleation times and inhibition. Pharm. Res. 41 (1), 1285–1297. https://doi.org/10.1007/s11095-024- 03713-2

2. Massotti V., Artusio F., Barresi, A.A., Pisano, R., 2025. Mathematical modelling of thermal interactions during freezing: Effects on product morphology and drying behaviour. European Journal of Pharmaceutical Sciences 210, 107112. https://doi.org/10.1016/j.ejps.2025.107112