# Virtual Thermocouple: A Non-Invasive Product Temperature Measurement Approach for Controlled Lyophilization

A non-invasive system uses an external probe and simulation to accurately monitor product temperature and sublimation front during lyophilization, replacing traditional thermocouples and reducing product loss.

Researchers at Purdue University have developed a non-invasive method of measuring product temperature during lyophilization. Lyophilization is a freeze-drying method extensively used by pharmaceutical companies. Monitoring the product temperature is important to avoid slow or incomplete drying or collapse of the product. The current best-practice for measuring product temperature during lyophilization is via a thermocouple. However, using a thermocouple changes the freeze-drying conditions; it creates a surface for nucleation of ice crystals, heats the product, and can potentially contaminate the product. It is also difficult to control the exact position of the thermocouple. The Purdue researchers' method involves attaching a temperature probe to the external wall of the vial and using COMSOL Multiphysics simulation to predict product temperature throughout the vial. The system also allows prediction of the location of the sublimation front. This technology allows for a more accurate and less invasive approach for temperature monitoring during lyophilization, increasing the quality of the final product along with decreasing losses caused by product collapse.

**Technology Validation:** The researchers' system has a temperature probe with 5 temperature sensing elements, and the Multiphysics simulation accounts for process parameters and material properties. This system accurately predicts experimentally determined temperatures, which eliminates the need for thermocouples.

## Advantages:

- Non-invasive
- Accurate

## **Technology ID**

2021-ALEX-69270

## Category

Pharmaceuticals/Biopharmaceuti Biotechnology & Life Sciences/Analytical & Diagnostic Instrumentation

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# Applications:

- Measuring product temperature during lyophilization

**TRL:** 2

# **Intellectual Property:**

Provisional-Gov. Funding, 2020-11-06, United States | PCT-Gov. Funding, 2021-11-05, WO | NATL-Patent, 2021-11-05, Europe | NATL-Patent, 2023-05-01, United States | CON-Gov. Funding, 2025-08-18, United States

**Keywords:** Non-invasive temperature measurement, lyophilization temperature monitoring, freeze-drying temperature, COMSOL Multiphysics simulation, product collapse prevention, sublimation front prediction, pharmaceutical freeze-drying, temperature probe, vial temperature sensing, thermocouple alternative, freeze drying, Lyophilization, Pharmaceuticals, Process Analytical Technology (PAT), Product temperature, Simulation