

IMPLEMENTATION OF PAT FOR REAL-TIME PRODUCT MONITORING AND CONTROL DURING CONTINUOUS FREEZE-DRYING

Continuous freeze-drying

- Spin freezing of vials; cooling via cold gas
- Infrared-assisted primary and secondary drying
- Thin product layer leads up to **40x shorter** processing time
- **Uniform** drying conditions for **EACH** vial
- **No scale-up issues** (as opposed to batch freeze-drying)
- **100% quality control** at unit dose level

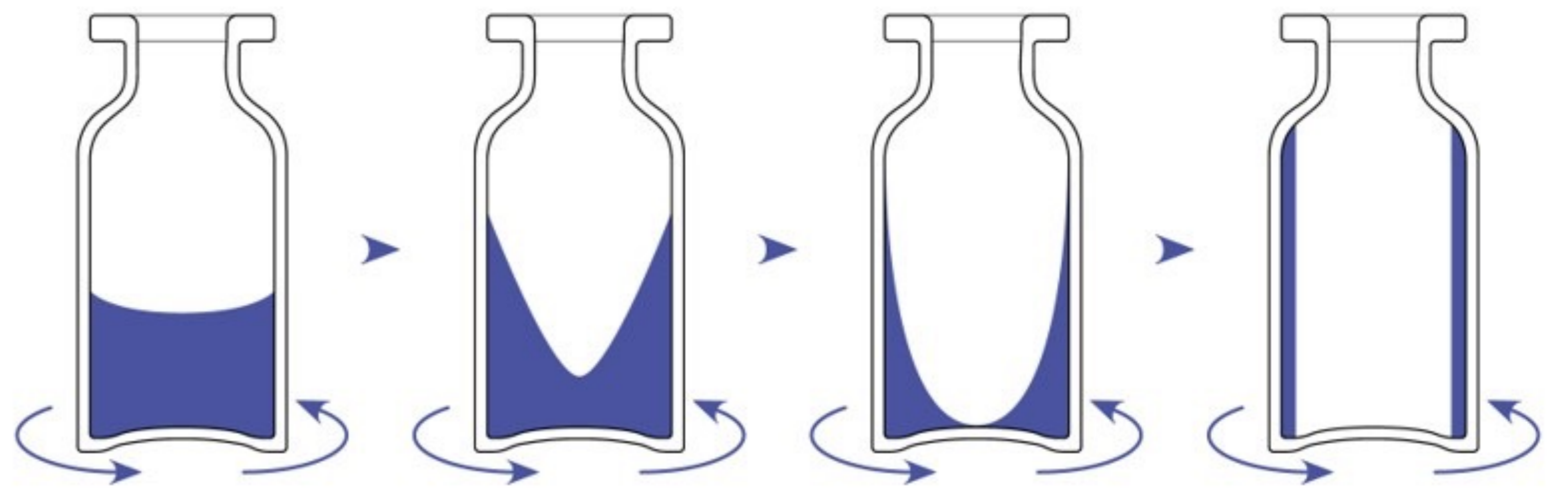


Figure 1: Illustration of spin freezing - Vials rapidly rotated to create a thin frozen product layer spread over the entire vial wall

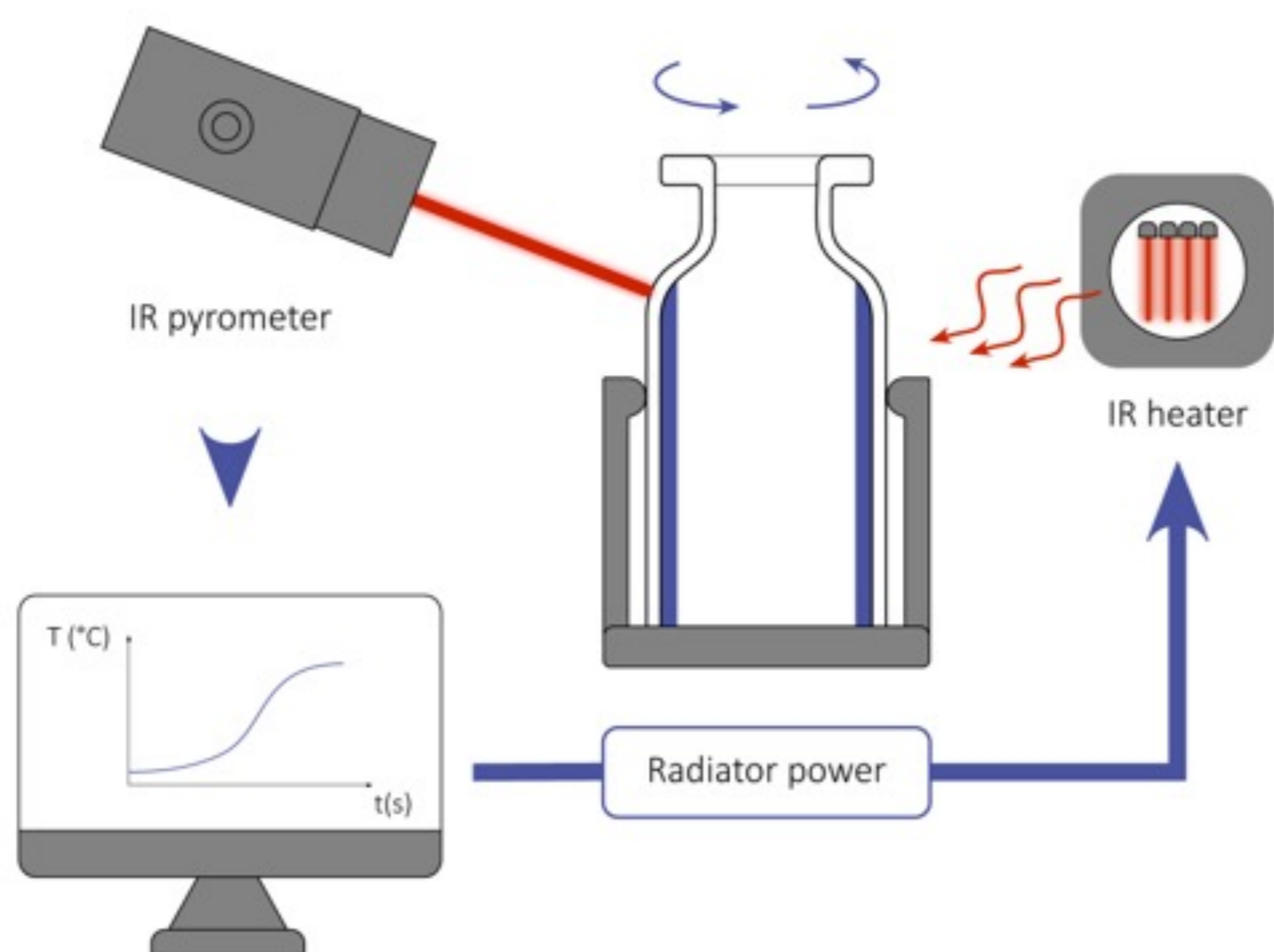


Figure 2: Illustration of closed feedback loop to control the freezing and drying process

Opportunity

- **Optimized and customized** cooling & drying for each product
- **Direct control** of product temperature at individual vial level
- **Identical** freezing & drying conditions for each vial
- Same quality from pre-clinical to production – **no scale-up issues**
- **Fast formulation and process development** with limited material

Implementation & Demonstration

- Closed loop control system during freezing and drying:
 - In **Single Vial Continuous Freeze-Dryer (SVU)**:
 - Product cycle development and optimization
 - Formulation screening
 - In **Industrial Scale GMP Continuous Freeze-Dryer (GMP Flex)**:
 - Product temperature control during production facilitating real-time release
- **In-line NIR spectroscopy** for residual moisture monitoring during the secondary drying step



Figure 3: Single Vial Continuous Freeze-Dryer (SVU)

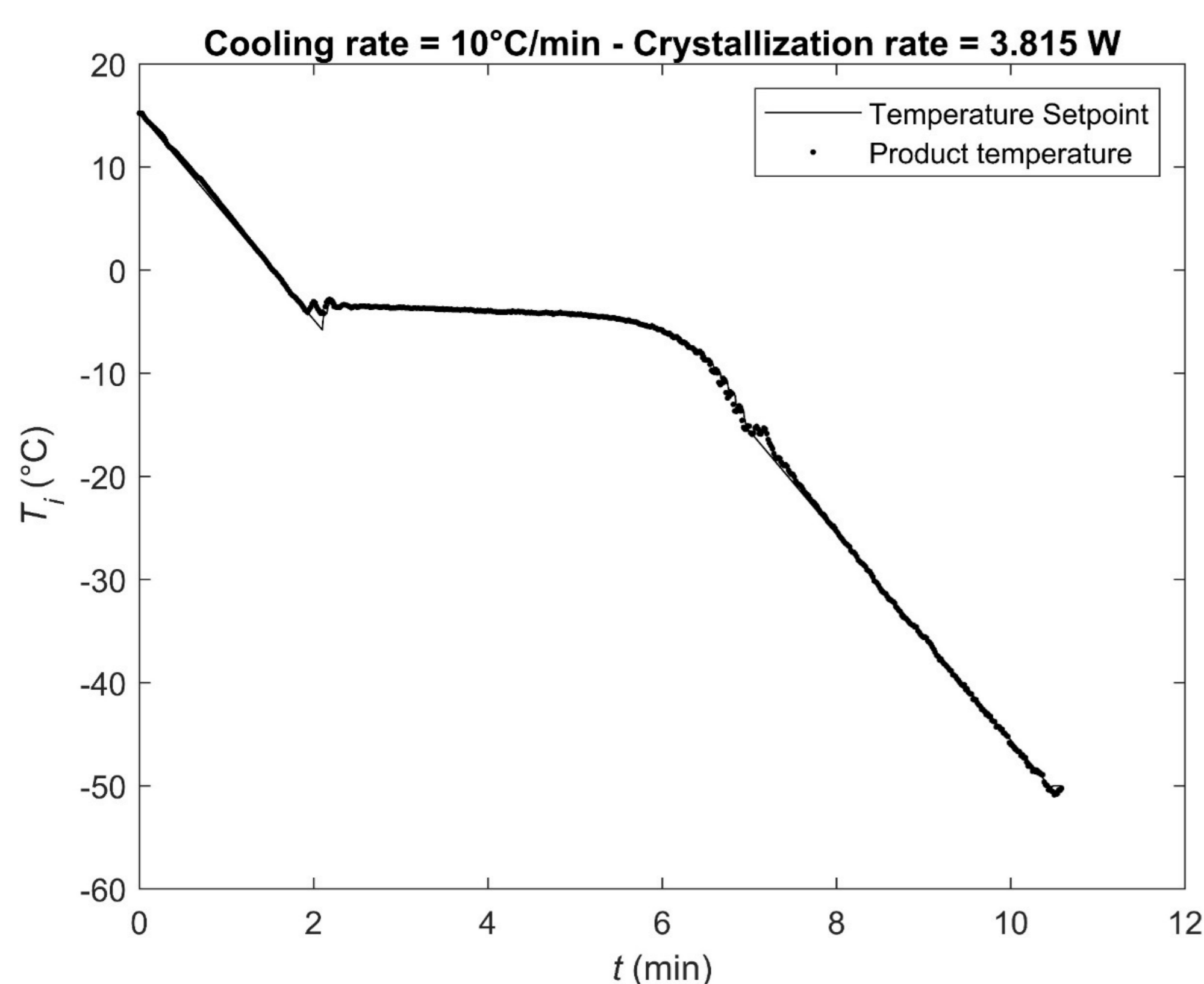


Figure 4: Illustration of controlled spin freezing

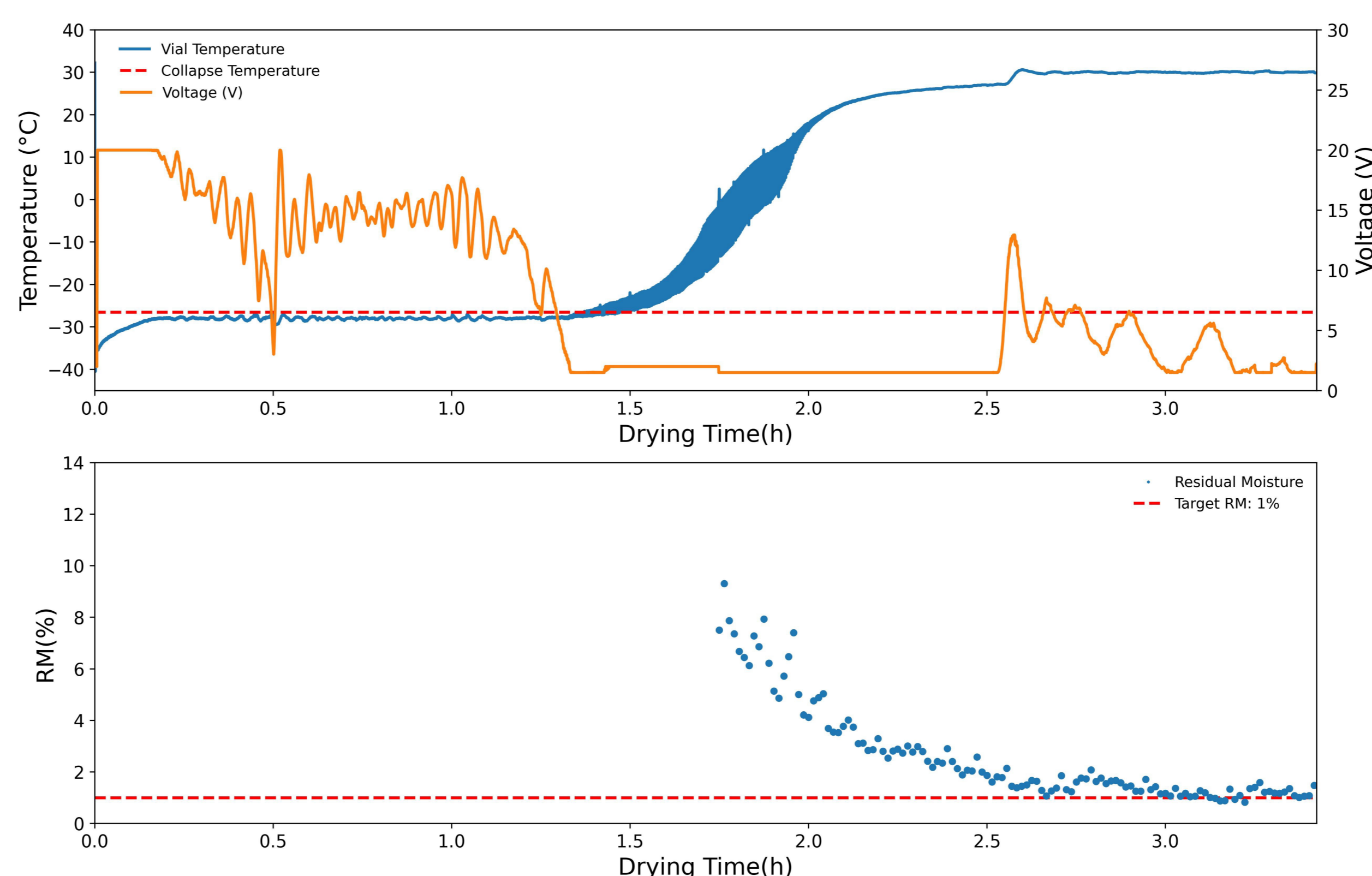


Figure 5: Illustration of controlled drying: Temperature and residual moisture profile



Figure 6: Spin freeze-dried end product

Continuous freeze-drying of unit doses allows 100% real-time product temperature measurement and control at the individual vial level

Questions?

