IN-SITU VIAL STRAIN MEASUREMENTS DURING FREEZE/ THAW PROCESSES USING AMORPHOUS EXCIPIENTS

Investigators: *Ian Flynn (Purdue/LyoHUB), Drew Strongrich (Purdue/LyoHUB)*

The effects of mechanical stresses developed between a frozen formulation and glass vial during freezing and thawing operations are not well understood. In many cases, the interfacial forces can become significant, leading to catastrophic failure of the primary packaging (i.e. breakage). To investigate these effects, an experimental campaign using wireless strain gauges was carried out as part of the Purdue's Chemical Engineering Professional Master's Program. The sensors measured strain output using foil gauges and vial wall temperature via a resistance temperature detector (RTD). A 6R vial illustrating the location of the RTD and strain gauge is provided in **Figure 1**. The study focused on freeze/thaw cycles with different concentrations of amorphous excipients, specifically sucrose and trehalose.

The strain response during freezing and thawing for sucrose concentrations between 5% w/v and 80% w/w is provided in **Figure 2**. Results clearly indicate a dependence on excipient concentration and frozen matrix temperature. Additionally, local maxima appear near a product temperature of around -32C for concentrations of 10% and 20% w/v. This behavior was attributed to a glass transition in the freeze-concentrated solute and subsequent stress relaxation within the frozen matrix. Results using trehalose were qualitatively similar but exhibited larger gauge output magnitudes, especially at the end of the freezing step. The ability to quantify strain throughout the freezing and thawing process suggest the strain sensors may have utility as a new process analytical technology for cycle design, especially when operating in conditions that are known to produce breakage. Computational studies were also performed as part of this work to develop a better understanding of the principal stresses and strains during the experiments.

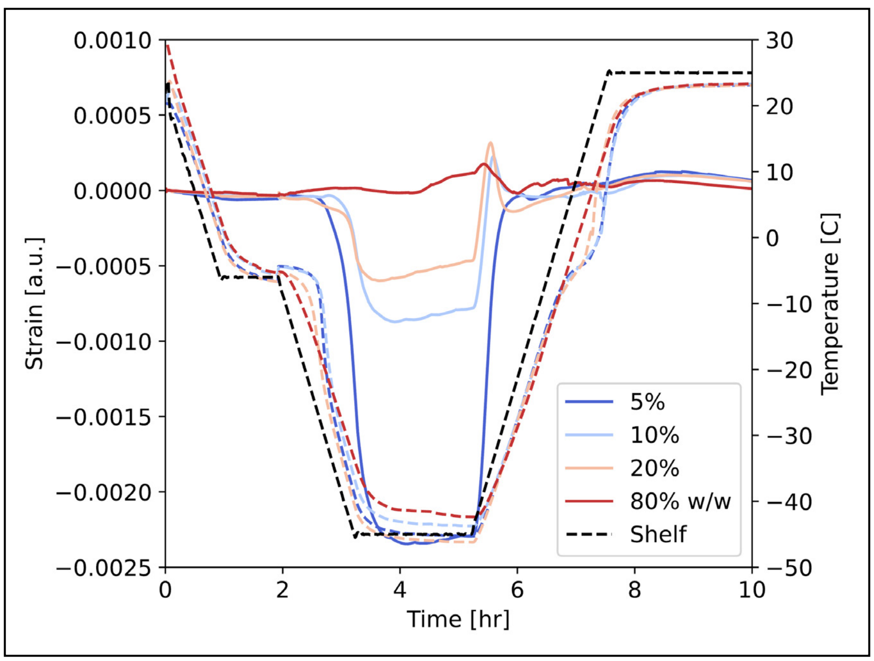

Figure 1: *Image of gauged vial used to characterize thermomechanical response of borosilicate vials during freezing and thawing.*

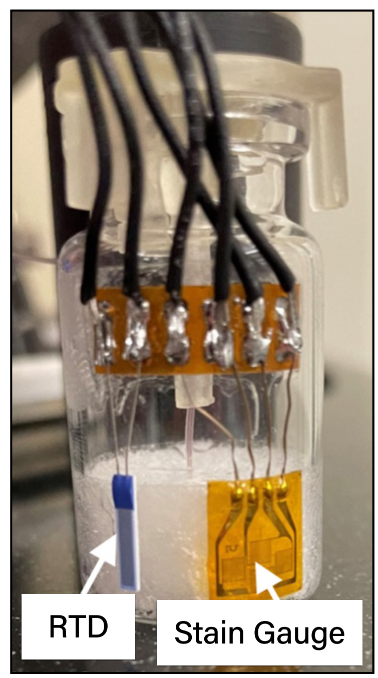

Figure 2: *Measured gauge output during freezing and thawing for different concentrations of sucrose (%w/v unless indicated). The strain response varies with concentration and temperature, response of borosilicate vials during freezing and thawing.*