Mechanical Characteristics of Vial Strain During Freezing and Thawing Operations Using Amorphous Excipients

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Wireless strain sensors developed in LyoHUB are being evaluated for their unique ability to detect mechanical stresses and strains in primary packaging during freezing, thawing, and freeze drying. Prior research in the LyoHUB Demonstration Facility has identified key differences in strain response for amorphous excipients such as sucrose and trehalose at different concentrations. For example, the temperature and strain profiles of sucrose at concentrations from 5-80% are shown in **Figure 1**. Recent studies are focused on leveraging computational modeling to understand the implication of these differences in strain behavior.

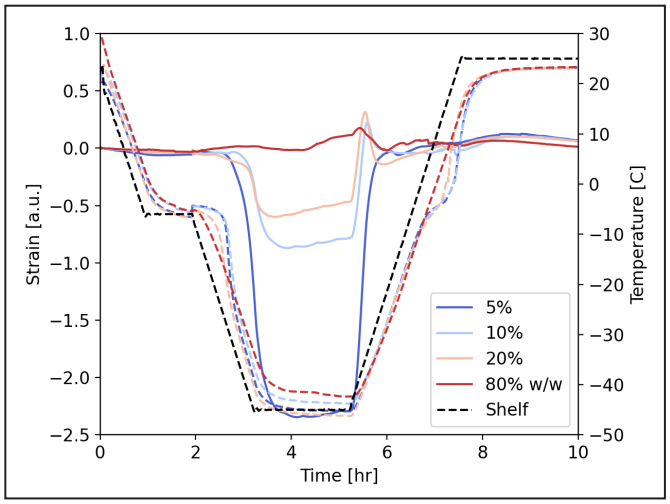

Figure 1: *Measured temperature and strain during freezing and thawing of sucrose at different concentrations.*

A finite element model of the vial was developed to better understand the relationship between principal strain components. The model was verified using an experimental apparatus that allowed the vials to be pressurized (uniformly) with a gas. Model results for a pressure of 50 psig are shown in **Figure 2**. These results were used to understand the vial response to a load as well as identify the appropriate locations for mounting the strain gages.

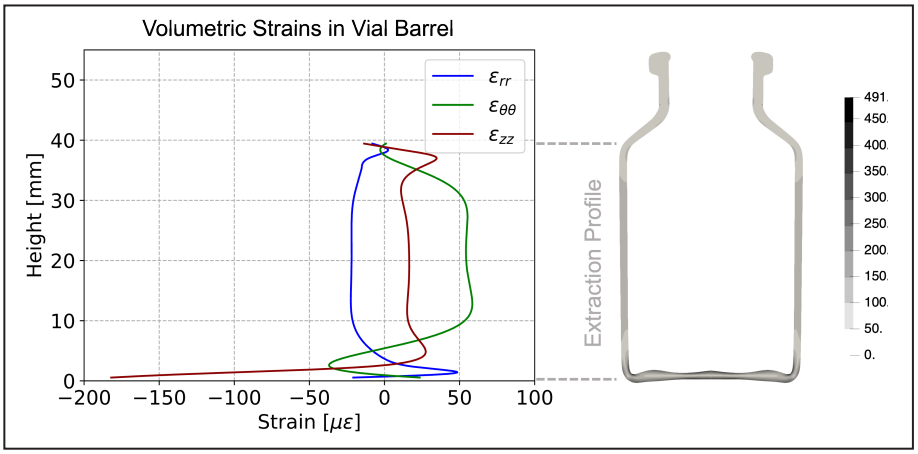

Figure 2: *Computed radial, axial, and hoop strains for a vial under uniform internal pressure.*

One of the key goals of the study is to use the strain sensors and computational modeling to identify the constitutive parameters of the various formulations. To accomplish this, a new experimental setup using a metal pipe with strain and temperature sensors attached to the outer wall has been developed. The apparatus is shown in **Figure 3**.

This approach was selected to reduce the influence of high strain gradients that, due to the configuration of the strain gages, can be difficult to couple to the computation model. In principle, the information collected using the new setup can be used to identify the stress and strain distribution throughout the frozen matrix itself. Future studies will investigate the implications of these mechanical effects on various critical quality attributes.

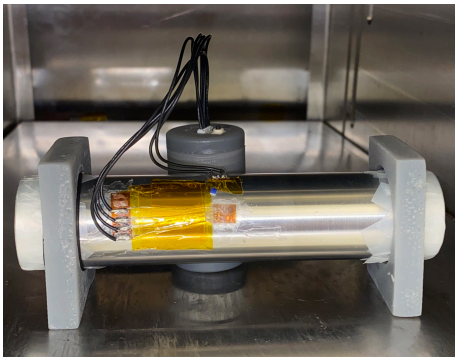

Figure 3: *Image of model metal pipe apparatus used for the identification of a material's constitutive parameters.*