MEASURING LYOPHILIZED POROUS STRUCTURES WITH MICRO-CT SCANNING

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The mass transfer resistance R_p is an essential parameter in models of the primary drying step of lyophilization. This value quantifies how much dried material obstructs the flow of water vapor, and is known to depend on many factors (including formulation, freezing conditions, and drying conditions). By investigating the porous structure of lyophilized material, we hope to improve estimates and understanding of R_p.

Micro-CT scanning is a technique for imaging the insides of structures (analogous to medical CT scans), using X-ray images of a material captured from many angles (a typical example shown in **Figure 1**). This method yields images which each represent a thin slice of the material (such as the horizontal slice in **Figure 2**), which can be assembled into a full volumetric image of the structure. This method has some limitations, such as poor image contrast when using glass vials, as well as requiring robust image processing procedures. However, it is nondestructive in nature, and can provide 3-dimensional information which 2D imaging techniques like SEM inherently cannot; for example, pore connectivity and pore size cannot be rigorously estimated from only 2D information.

Using plastic vials (manufactured by SiO2) and a Bruker SkyScan 1272 (owned by CP3 at Purdue), micro-CT scans of lyophilized mannitol and sucrose have been captured at varying resolutions. A software tool written in the Julia language is under development for computing features like porosity, surface area, and spatially varying pore size distribution. **Figure 3** shows the average pore size as a function of vertical and radial position for a 0.5mm-tall region (corresponding to the region boxed in red on Figure 1). Porosity and surface area estimates in this region are within 10% of the estimates in the top and bottom regions of the cake, but pore sizes vary significantly. Since pore size is known to relate to R_p, this can yield estimates of how mass transfer resistance varies within a single cake and enable detailed models.

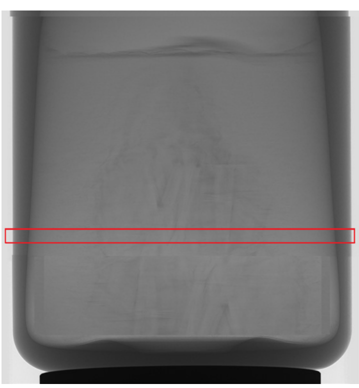

Figure 1: *X-ray image of lyophilized mannitol in a 10mL plastic vial.*

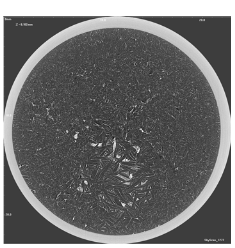

Figure 2: *Reconstructed slice of cake shown in Figure 1, taken from region marked in red.*

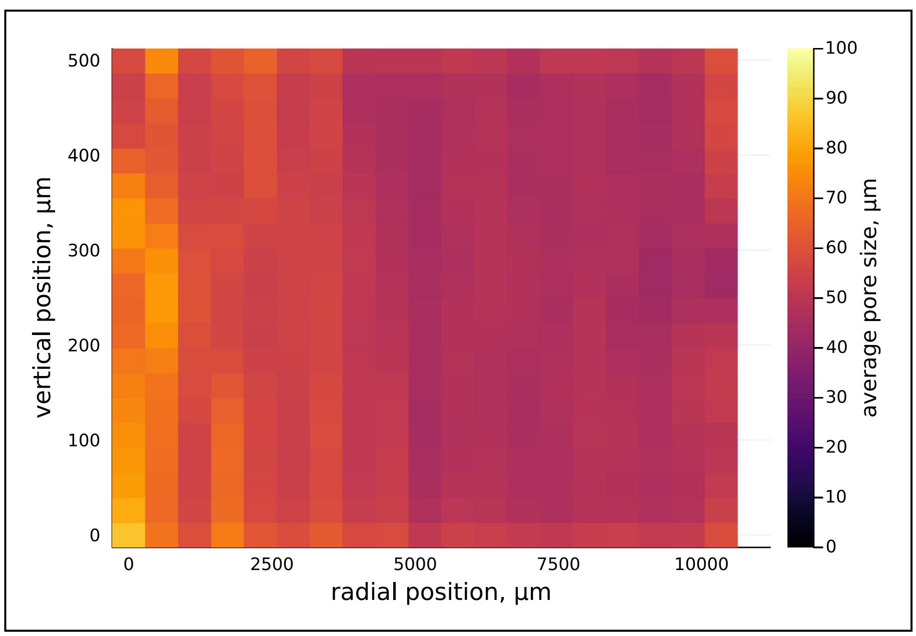

Figure 3: *Average pore size as a function of vertical and radial position for the region of Figure 1 marked in red. Note the distinctly larger pores in the center of the cake (left side of this figure).*