Lyophilization, or vacuum freeze-drying, is a separations process in pharmaceutical manufacturing used to stabilize aqueous drug products by removing nearly all the water at cryogenic temperatures. This process is often applied to final-dose formulations of injectable drugs already dispensed in vials. Despite its benefits, freeze-drying is a slow process, with typical cycle times exceeding two days. To meet demand, lyophilization is applied to large batches of thousands to tens of thousands of vials at time. These large batches are plagued by non-uniformity, non-optimal operating conditions, and slow technology transfer across production scales.

Continuous manufacturing offers a solution to many of these problems, with its demonstrated history in improving efficiency, homogeneity, and control through its inherent parallelization of operations. However, the need to interact directly with vials, as well as modify heat transfer to them, has delayed the development of a continuous lyophilization process.

This work presents the design, control, and implementation of a modular continuous lyophilizer. The continuous lyophilizer is composed of a series of custom aluminum chambers around a magnetic levitation system, which facilitate the heat transfer and motion required. The modular nature ensures that critical geometry is conserved when production rate is scaled between laboratory-, pilot-, and industrial scales. This system demonstrated continuous operation for four days on various solutions in standard 10R vials. In this work, novel continuous freezing and vacuum systems were designed to support the operation. Additionally, an innovative mass sensor was designed to monitor each vial traveling through the system independently. When combined with per-vial temperature data available from thermal imaging, this system enables a more comprehensive understanding of the process dynamics.

This continuous process opens opportunities for expanding the use of lyophilization by simplifying technology transfer during scale-up, improving product uniformity, and increasing process productivity through optimal control.