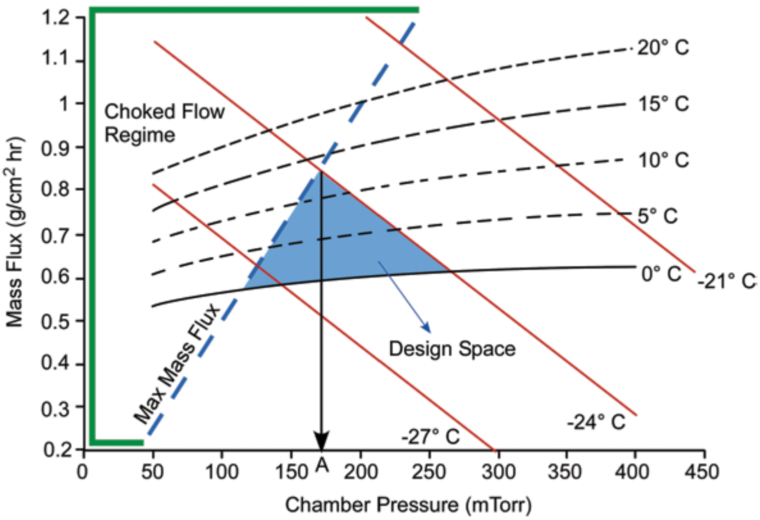

Fig. 3 Design space graph for primary drying stage of lyophilization with design space, control space, and set point

where $\dot{Q}$ is the heat transfer rate (cal/s), A_v is the outer cross-sectional area of the vial (cm^2), K_v is the vial heat transfer coefficient ($cal/s.cm^2.K$), T_s is the shelf surface temperature (°C), and T_p is the product temperature at the sublimation interface (°C).

Mass transfer of water vapor through the dried product layer (ignoring the small resistance of the stopper) can be represented using [25]:

$$\frac{dm}{dt} = A_p \cdot \frac{p_{ice} - p_c}{\widehat{R}p} \tag{2}$$

where dm/dt is the sublimation rate per vial (g/h/vial), A_p is the internal cross-sectional area of the vial (cm^2), P_{ice} is the vapor pressure of ice (Torr), P_c is the chamber pressure (Torr), and $\dot{Q}$ is the area-normalized dry layer resistance ($cm^2.Torr.h.g^{-1}$) of the product in the vial. P_{ice} (the vapor pressure of water above ice at temperature T_{ice}) can be expressed as [26]:

$$p_{ice} = 2.69 \times 10^{13} \times e^{-6144.96/T_{ice}} \tag{3}$$

where T_{ice} (or T_p) is the temperature of the ice (or product) at the sublimation interface (K) which can be expressed as [26]:

$$T_p = T_b \frac{(\dot{Q}) \cdot L'}{A_v \cdot K} \tag{4}$$