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Exergy analysis of freeze drying of pharmaceuticals in vials on trays

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Abstract

The expressions for determining the exergy inputs and exergy losses due to heat and mass transfer in the primary and secondary drying stages as well as in the water vapor condenser and vacuum pump of the lyophilization process involving freeze drying of pharmaceuticals in vials on trays, are constructed and presented in this work. The structures of the exergy expressions indicate the importance of the magnitude of the duration times of the primary and secondary drying stages as well as those of the gradient of temperature and of the pressure gradients of water vapor and inerts in the material being dried, on the magnitude of the exergy inputs and exergy losses. This information is then used to indicate policies for the control variables of the lyophilization process that can result in reductions in the exergy losses in the primary and secondary drying stages, as well as in the water vapor condenser and in the vacuum pump system for heat-transfer and mass-transfer controlled freeze drying processes. The distribution of the exergy inputs and exergy losses for a lyophilization system are presented and the results show that most of the exergy input is consumed and most of the exergy losses result by the primary drying stage, the water vapor condenser, and vacuum pump in that order. By using the exergy expressions presented in this work operational control policies can be constructed that minimize the irreversibilities occurring in the operations of a freeze drying system of a given design, thus enhancing the efficiency of energy utilization in lyophilization.

Keywords: Freeze drying; Lyophilization; Exergy inputs; Exergy losses; Exergy analysis; Exergy distribution

1. Introduction

Freeze drying is a very important separation process and the use of lyophilization is widespread in the fine chemicals, food, biotechnology and pharmaceutical industries [1–11]. As a rule, freeze drying produces the highest quality dried product obtained by any drying method [4,11]. However, lyophilization is an expensive form of dehydration because of the slow drying rate and the use of vacuum.

While the fundamental heat and mass transfer mechanisms that characterize the dynamic behavior of the primary and secondary drying stages of the freeze drying process have both been studied, reasonably well modeled, and employed in the construction of optimal control policies [3,4,7,11–14] with respect to heat input, total pressure in the drying chamber, and the temperature of the condenser to minimize the operational times of the primary and secondary drying stages of lyophilization and provide a product of high quality at the end of the secondary drying stage, it is still considered necessary [6,11,14] to improve the economic efficiency of the freeze drying process by (a) understanding and evaluating the distributions of the exergy [6,15,16] inputs and exergy losses during the primary and secondary drying stages of lyophilization, (b) studying the effect of system parameters on exergy losses, and (c) examining whether the time optimal control policies [3,4,7,11–14,17] represent operational policies that minimize the exergy losses during the primary and secondary

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Nomenclature

AEL	accrued exergy losses (kJ)
c_p	heat capacity (kJ/kg)
$c_{p,\text{ice}}$	heat capacity of ice (kJ/kg)
c_{sw}	concentration of bound (sorbed) water (kg water/kg solid)
E	exergy flux (kJ/m^2 s)
$\text{EA}_{\text{pd,w,in}}$	accrued exergy of water vapor and inerts (Eq. (16)) in any ring-shaped volume element in the dried layer I (kJ)
EI	exergy input (kJ)
EL	exergy losses (kJ)
$\text{EL}_{\text{pd,mt}}$	exergy losses (Eq. (20)) in any ring-shaped volume element in the dried layer I per unit time and unit volume due to mass transfer during the primary drying stage (kJ/m^3 s)
$\text{EL}_{\text{sd,mt}}$	exergy losses (Eq. (28)) in any ring-shaped volume element in the dried layer I per unit time and unit volume due to mass transfer during the secondary drying stage (kJ/m^{3}s)
$H(t,r)$	geometric shape (as per Fig. 1a) of the moving interface, a function of time and radial distance (m)
k	thermal conductivity (kW/m K)
L	length of sample in vial (m)
M_{in}	molecular weight of inerts (kg/kmol)
M_{mm}	mass of moist material in the vial (kg)
M_{sd}	mass of moisture in the material during the secondary drying stage (kg)
M_{w}	molecular weight of water (kg/kmol)
N	molar flux (kmol/m^{2}s)
n	moles (kmol)
P	total pressure (Pa)
P_Z	total pressure at surface of moving interface, $P_Z = P(t, z = Z = H(t,r), r)$ (Pa)
p	partial pressure (Pa)
$p_{\text{in,pd}}$	partial pressure of inerts in any ring-shaped volume element (Eq. (19)) in the dried layer I (Pa)
$p_{\text{in,vp}}$	inlet pressure of the vacuum pump system (Pa)
$p_{\text{out,vp}}$	exhaust pressure of the vacuum pump system (Pa)
$p_{\text{w,pd}}$	partial pressure of water vapor in any ring-shaped volume element (Eq. (18)) in the dried layer I (Pa)
q_{I}	heat flux (as per Fig. 1a) in the dried layer I at $z = 0$ (kW/m^2)
q_{II}	heat flux (as per Fig. 1a) in the frozen layer II at $z = L$ (kW/m^2)
q_{III}	heat flux (as per Fig. 1a) in the side of the vial (kW/m^2)
$Q_{\text{c,cond}}$	cooling capacity of water vapor condenser (kJ)
R	radius of vial (m)
R_{g}	ideal gas constant (kJ/kmol K)
r	space coordinate of radial distance (m)
S_{vp}	theoretical pumping speed of vacuum pump system (m^3/s)
t	time (s)
t_{a}	time when $H(t,r) = L$, as per Fig. 1a (s)
$t_{T_{\text{I,aver,sd}}}$	time in the secondary drying stage at which $T_{\text{I,aver,sd}} = T_0$ (s)
T	temperature (K)
$T_{\text{c,cond}}$	temperature of the cooling source of the condenser (K)
T_{init}	initial temperature of the material in the vial at the beginning ($t = 0$) of the primary drying stage (K)
$T_{\text{in,cond}}$	inlet temperature of gas (water vapor and inerts) to the condenser (K)
$T_{\text{in,vp}}$	gas inlet temperature to the vacuum pump system (K)
$T_{\ell,\text{cond}}$	lowest temperature of ice cooled down by the condenser (K)
$T_{\ell,\text{in,cond}}$	lowest temperature of inerts cooled down by the condenser (K)
T_{solid}	solidification temperature of water vapor (K)
T_Z	temperature at surface of moving interface, $T_Z = T_{\text{I}}(t, z = Z = H(t,r), r)$ (K)
$T_{\text{I,aver,sd}}$	average temperature in the dried layer at any time t (Eq. (35)) during the secondary drying stage (K)
$T_{\text{I,pd}}$	temperature in any ring-shaped volume element (Eq. (17)) in the dried layer I during the primary drying stage (K)
W_{air}	mass of air pumped out of the system (Eq. (46)) during a drying cycle (kg)
W_{in}	mass of inerts through the vacuum pump during a drying cycle (kg)
W_{init}	initial mass of moisture in the material at the beginning of the primary drying stage (kg)
$W_{Z=L,\ 0\leqslant r\leqslant R}$	mass of moisture in the material at the end of the primary drying stage (kg)
W_{sd}	mass of moisture in the material at the end of the secondary drying stage (kg)
z	space coordinate of distance along the length of the vial (m)
$z_{T_{\text{I}}(t=t_{\text{pd}},z,r)=T_0}$	value of z measured from the surface ($z = 0$) of the dried layer I where the temperature at the end of the primary drying stage is equal to T_0 (m)
Z	value of z at the moving interface (m)

Greek symbols

α_j	represents the ratio of the exergy losses for operation j ($j = 1$ denotes the primary drying stage, $j = 2$ represents the secondary drying stage, $j = 3$ is the water vapor condenser, and $j = 4$ denotes the vacuum pump) to the exergy input of

	operation j multiplied by one hundred ($\alpha_j = ((\text{exergy losses (kJ/kg)})_j/(\text{exergy input (kJ/kg)})_j) \times 100$)
β_j	represents the ratio of the exergy input for operation j to the total exergy input multiplied by one hundred ($\beta_j = ((\text{exergy input (kJ/kg)})_j/(\text{total exergy input (kJ/kg)})) \times 100$)
γ_j	denotes the ratio of the exergy losses for operation j to the total exergy losses multiplied by one hundred
ΔE_{vp}	variation of exergy (Eq. (49)) due to the compression of a perfect gas (kJ)
ΔH_{s}	heat of sublimation of ice (kJ/kg)
ΔH_{solid}	heat of solidification of water vapor into solid ice (kJ/kg)
ΔH_{v}	heat of vaporization of bound (sorbed) water (kJ/kg)
Δt	time interval (s)
Δr	radial increment in the ring-shaped volume element (as per Fig. 1a) (m)
$\Delta S_{\text{pd,I}}$	irreversible entropy change due to heat transfer in a ring-shaped volume element (as per Fig. 1a) per unit time (kJ/K s)
Δz	increment along the axial direction in the ring-shaped volume element (as per Fig. 1a) (m)
Λ	polytropic exponential (Eq. (47)) of compression
Ω	power input for the vacuum pump (power of compressor) (kW)

Subscripts

ab	above the reference temperature
bel	below the reference temperature
cond	water vapor condenser
dcham	drying chamber of freeze dryer
e	effective value of a parameter
ht	heat transfer
in	Inerts
mt	mass transfer
pd	primary drying stage
sd	secondary drying stage
vp	vacuum pump system
w	water vapor
0	reference value of a variable
I	dried layer
II	frozen layer

drying stages of the lyophilization process, otherwise it will be necessary to develop new operational control policies that would actually minimize the exergy losses for a given freeze drying system. Of course, it is apparent that in order to perform the research studies indicated in items (a)–(c) above, one would first have to construct the expressions that could be used to evaluate quantitatively the exergy inputs and exergy losses for the primary and secondary drying stages of the lyophilization process.

Exergy is a measure of energy quality and can be associated with the irreversibilities occurring during the lyophilization process. It is important to minimize the exergy losses in freeze drying because this approach would improve the economic efficiency of lyophilization by increasing the efficiency of energy utilization in the freeze drying system, and, thus, conservation of the higher quality energy could be realized. Since in a given process exergy is consumed or destroyed due to process irreversibilities, exergy analysis can show [6,19–21] whether or not as well as by how much it is possible to design and operate the given process more efficiently by reducing the sources of existing inefficiencies. Therefore, in a world where there are limitations in the supply and use of energy and where also environmentally acceptable processes have to be employed, exergy analysis represents one of the most powerful methods for providing appropriate quantitative information for optimum design and operation of systems and processes. Thus, in recent years various studies have been undertaken by several investigators [19–24] to examine thermodynamic aspects of conventional drying processes by employing exergy analysis. In lyophilization, Bruttini et al. [6] constructed the expressions that allowed the quantitative exergy analysis of the freezing [11,14] stage of the lyophilization process and showed that very substantial reductions in the magnitudes of the total exergy input and total exergy losses due to the heat that must be removed during the freezing stage, can be obtained when the freezing stage is operated through the use of a rational distribution in the magnitude of the temperature of the cooling source. Furthermore, the rational distribution in the magnitude of the temperature of the cooling source while it provides significant savings in the utilization of energy during the freezing stage of the lyophilization process, it can also provide satisfactory freezing rates that form ice crystals that are continuous and highly connected [11,18] and their shape and size could be such that the pore structure of the porous matrix of the dried layer generated by sublimation during the primary drying stage, allows high rates for mass and heat transfer during the primary and secondary drying stages of the freeze drying process.

In this work, we present (1) the expressions that could be used to evaluate quantitatively the exergy inputs and exergy losses for (a) the primary and secondary drying stages of the lyophilization of pharmaceuticals in vials on trays and (b) the water vapor condenser and the vacuum pump of the freeze dryer, and (2) simulation results indicating the distribution of exergy inputs and exergy losses in the primary and secondary drying stages, as well as in the water vapor condenser and vacuum pump of a lyophilization system.

2. Exergy analysis

The geometry considered for the lyophilization in a vial is represented in Fig. 1a. Prior to the start-up of drying, the solution to be dried is first frozen [3,4,6,7]. At the start of drying, the vial contains frozen solution of depth L and radius R. Fig. 1a depicts the vial after a period of time has progressed during the primary drying stage; there exist two distinct regions, a dried layer (region I), from which water has been mostly removed by sublimation [3,4] to leave behind a porous solid matrix, and a frozen layer (region II) consisting of frozen solution (of solute and solvent) as yet unsublimed. The locus of the moving boundary between these two regions is described by the function $H(t,r)$, measured down from the plane $z = 0$; thus, this is a moving boundary or Stefan problem [3,25] and the interface is receding due to sublimation of the frozen ice layer. Other mechanisms at work here are the removal of water vapor arising from sublimation (by diffusion and convection through the free space of the porous structure of the dried layer) and desorption of bound water [26] from the solid matrix phase of the porous structure. Secondary drying describes the water removal which occurs after the frozen layer has been completely removed. Thus, during the secondary drying stage there is no longer any moving interface; the dried layer represents the whole geometry and $H(t,r)$ may be considered uniformly equal to L for the duration of secondary drying. The mechanisms of water removal here are the desorption of bound water and the transport of water vapor through the void space of the porous structure.

During drying, the energy for sublimation of ice and desorption of bound water is supplied by heat transfer from the heating plates above and below the vial and also from the chamber environment to the vial sides [3,4,7,11]. These heat fluxes are quantified q_{I}, q_{II} and q_{III}, as shown in Fig. 1a. This heat is conducted to the moving interface through the dried and frozen layers. The curvature of the interface and indeed all radial effects are brought about by the heat transfer to the vial sides, which accelerates the sublimation close to the vial wall (relative to the sublimation rate obtained at the vial center).

The theoretical model for the primary and secondary drying stages of lyophilization in vials constructed and solved by Sheehan and Liapis [3] has been shown to describe properly the dynamic behavior of the freeze drying process [3,7,11,13,17,27] and is employed in this work in order to obtain the quantitative dynamic behavior and distribution of (i) the temperature of the dried layer, $T_{\mathrm{I}}(t,r,z)$, (ii) the temperature of the frozen layer, $T_{\mathrm{II}}(t,r,z)$, (iii) the partial first and second-order derivatives $\partial T_{\mathrm{I}}/\partial z$, $\partial T_{\mathrm{I}}/\partial r$, $\partial T_{\mathrm{II}}/\partial z$, $\partial T_{\mathrm{II}}/\partial r$, $\partial^2 T_{\mathrm{I}}/\partial z^2$, $\partial^2 T_{\mathrm{I}}/\partial r^2$, $\partial^2 T_{\mathrm{II}}/\partial z^2$, and $\partial^2 T_{\mathrm{II}}/\partial r^2$, (iv) the partial pressures of water vapor and inert gas in the free space of the porous structure of the dried layer, $p_{\mathrm{w}}(t,r,z)$ and $p_{\mathrm{in}}(t,r,z)$, respectively, (v) the partial first and

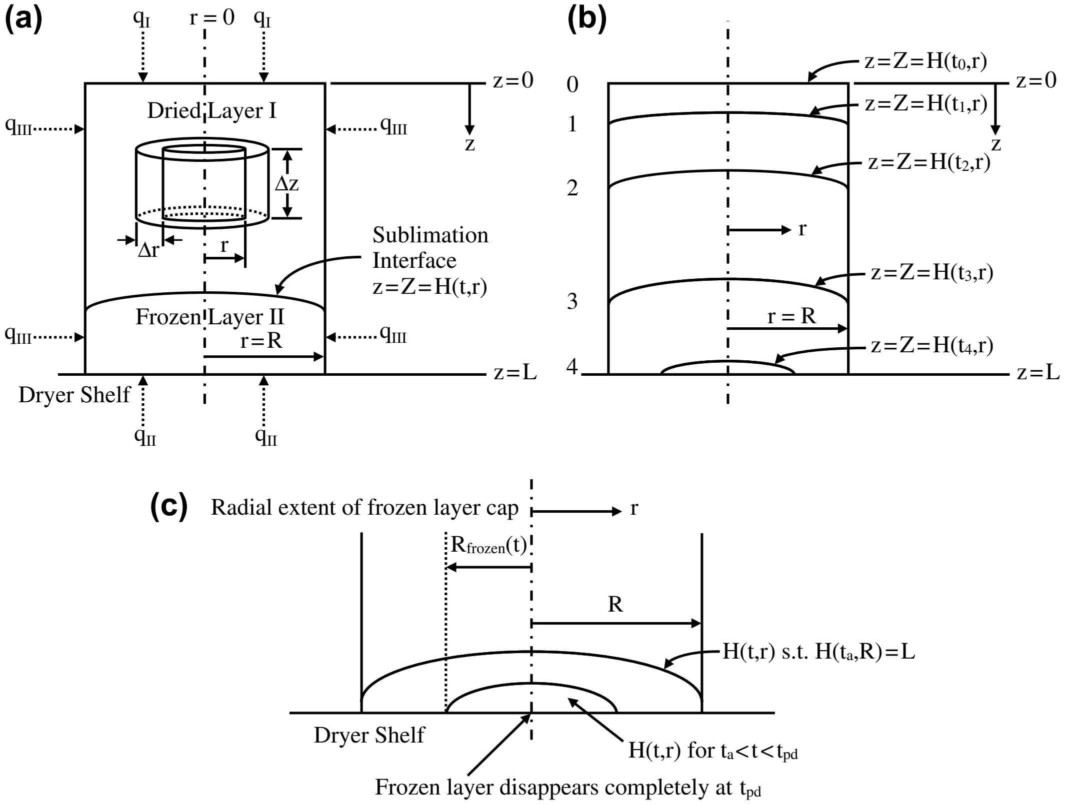

Fig. 1. (a) Diagram of a material being freeze dried in a vial; (b) depiction of the observed movement of the moving sublimation interface in a lyophilization vial; (c) radially distributed disappearance of frozen layer.

second-order derivatives $\partial p_w/\partial z$, $\partial p_w/\partial r$, $\partial p_{in}/\partial z$, $\partial p_{in}/\partial r$, $\partial^2 p_w/\partial z^2$, $\partial^2 p_w/\partial r^2$, $\partial^2 p_{in}/\partial z^2$, and $\partial^2 p_{in}/\partial r^2$, (vi) the total pressure $P(t,z,r)$ in the free space of the porous structure of the dried layer ($P = p_w + p_{in}$), as well as the partial first and second-order derivatives $\partial P/\partial z$, $\partial P/\partial r$, $\partial^2 P/\partial z^2$, and $\partial^2 P/\partial r^2$, (vii) the water vapor and inert gas molar fluxes in the free space of the porous structure of the dried layer, $N_w(t,z,r)$ and $N_{in}(t,z,r)$, respectively, as well as the partial first-order derivatives $\partial N_w/\partial z$, $\partial N_w/\partial r$, $\partial N_{in}/\partial z$, and $\partial N_{in}/\partial r$, (viii) the concentration, $c_{sw}(t,z,r)$, of bound water (unfrozen water) contained in the solid matrix (i.e., the solute being dried), as well as the accumulation term, $\partial c_{sw}/\partial t$, (ix) the position, geometric shape, and velocity of the moving interface $H(t,r)$, and (x) the effective thermal conductivity of the dried layer, k_{Ie}, which is a function of the total pressure, P, in the porous dried layer [3,7,11,26]. The quantitative information in items (i)–(x) above can then be used to determine from the exergy expressions that are presented in the following subsections of Section 2, the exergy inputs and exergy losses during the primary and secondary drying stages of lyophilization.

2.1. Exergy expressions for the primary drying stage

The exergy losses per unit volume and unit time, $EL_{pd,I}$, due to conductive heat transfer in the dried layer in a ring-shaped element whose volume could be approximated by $2\pi r\Delta r\Delta z$ (Fig. 1a) is given by

$$EL_{pd,I} = \frac{T_0 \Delta S_{pd,I}}{2\pi r \Delta r \Delta z} \tag{1}$$

where T_0 represents the reference temperature, $\Delta S_{pd,I}$ denotes the irreversible entropy change due to conductive heat transfer in the volume element ($2\pi r\Delta r\Delta z$) per unit time, and Δr and Δz represent finite size increments along the positive r and z directions. By considering the components of the heat flux vector in the dried layer along the r and z directions and that heat conduction in the dried layer is described by Fourier's constitutive equation, one can show that

$$\Delta S_{pd,I} \cong \left[\frac{(2\pi r\Delta r\Delta z)k_{Ie}}{T_I^2}\right]\left[\left(\frac{\partial T_I}{\partial z}\right)^2 - T_I\left(\frac{\partial^2 T_I}{\partial z^2}\right) + \left(\frac{\partial T_I}{\partial r}\right)^2 - \left(\frac{1}{r}\right)T_I\left(\frac{\partial T_I}{\partial r}\right) - T_I\left(\frac{\partial^2 T_I}{\partial r^2}\right)\right] \tag{2}$$

where k_{Ie} represents the effective thermal conductivity of the dried layer I.

By inserting the RHS of Eq. (2) for $\Delta S_{pd,I}$ in Eq. (1), the following expression for $EL_{pd,I}$ is obtained:

$$EL_{pd,I} \cong \left[\frac{T_0 k_{Ie}}{T_I^2}\right]\left[\left(\frac{\partial T_I}{\partial z}\right)^2 - T_I\left(\frac{\partial^2 T_I}{\partial z^2}\right) + \left(\frac{\partial T_I}{\partial r}\right)^2 - \left(\frac{1}{r}\right)T_I\left(\frac{\partial T_I}{\partial r}\right) - T_I\left(\frac{\partial^2 T_I}{\partial r^2}\right)\right] \tag{3}$$

Therefore, the accrued exergy losses, $AEL_{pd,I}$, due to conductive heat transfer in the dried layer can be obtained by integrating $EL_{pd,I}$ with respect to time and volume as follows:

$$AEL_{pd,I} = 2\pi T_0 \int_0^t \int_0^R \int_0^{H(t,r)} \left[\frac{k_{Ie}}{T_I^2}\right]\left[\left(\frac{\partial T_I}{\partial z}\right)^2 - T_I\left(\frac{\partial^2 T_I}{\partial z^2}\right) + \left(\frac{\partial T_I}{\partial r}\right)^2 - \left(\frac{1}{r}\right)T_I\left(\frac{\partial T_I}{\partial r}\right) - T_I\left(\frac{\partial^2 T_I}{\partial r^2}\right)\right] r\,dz\,dr\,dt \tag{4}$$

It can be shown that the accrued exergy losses, $AEL_{pd,II}$, in the frozen layer, by adopting the procedure used for the dried layer, can be determined from the following expression:

$$AEL_{pd,II} = 2\pi T_0 \int_0^t \int_0^R \int_{H(t,r)}^L \left[\frac{k_{II}}{T_{II}^2}\right] \times \left[\left(\frac{\partial T_{II}}{\partial z}\right)^2 - T_{II}\left(\frac{\partial^2 T_{II}}{\partial z^2}\right) + \left(\frac{\partial T_{II}}{\partial r}\right)^2 - \left(\frac{1}{r}\right)T_{II}\left(\frac{\partial T_{II}}{\partial r}\right) - T_{II}\left(\frac{\partial^2 T_{II}}{\partial r^2}\right)\right] r\,dz\,dr\,dt \tag{5}$$

where k_{II} denotes the thermal conductivity of the frozen layer. Thus, at any operational time, t, during primary drying, the accrued exergy losses, $AEL_{pd,ht}$, due to conductive heat transfer in the vial could be determined by Eq. (6)

$$AEL_{pd,ht} = AEL_{pd,I} + AEL_{pd,II} \tag{6}$$

It is important to note here that the value of the thermal conductivity of the frozen layer is much larger than that of the dried layer ($k_{II} \gg k_{Ie}$), and also the enthalpy changes that occur in the frozen layer are negligible compared with the enthalpy changes that occur in the dried layer due to the sublimation of the frozen water [3,4,7,11]. Thus, the magnitude of the temperature gradient in the frozen layer is much smaller that the magnitude of the temperature gradient in the dried layer. Therefore, it is expected that the exergy losses during the primary drying stage are resulting mainly by heat and mass transfer in the dried layer. Furthermore, it should be noted that when in Eq. (4) t is set equal to t_{pd} that denotes the total time of the duration of the primary drying stage which is determined when $H(t,r) = L$ for all values of r in $0 \leqslant r \leqslant R$, then Eq. (4) would provide the value of $AEL_{pd,I}$ for the whole primary drying stage; this item of discussion also indicates that in Eq. (5) values of $AEL_{pd,II}$ should be obtained up to a time t^* very close to t_{pd} but less than the value of t_{pd} so that the value of $H(t,r)$ is very close to L but less than the value of L for $0 \leqslant r < R$ [3]. For this latter case, Sheehan and Liapis [3] have shown that nonplanar arrival of a concave interface gives rise to an instance when first $H(t,R) = L$ at some time $t = t_a$; henceforth the frozen layer no longer touches the vial walls, and the radial extent of the frozen layer, R_{frozen}, gradually decreases, starting from $R_{frozen} = R$ at $t = t_a$, as shown in Fig. 1c, the first time when $H(t_a,R) = L$, passing through curve 4 in Fig. 1b, until the radial extent becomes zero ($R_{\text{frozen}} = 0$) at t_{pd}, when the frozen layer no longer exists and the secondary drying stage takes over. In many practical systems [3,4,7,11,14], the duration ($t_{\text{pd}} - t_{\text{a}}$) takes a value of 0.9–1.8% of the time t_{pd} that represents the time at which the primary drying stage ends, and, therefore, if one would set $t = t^* = t_{\text{a}}$ and consider the values of $H(t_{\text{a}}, r)$ that are less than the value of L for $0 \leqslant r < R$, then a physically reasonable approximate value for the integrand between the limits $H(t_{\text{a}}, r)$ and L could be obtained. Of course, if $t = t_{\text{pd}}$ and $H(t, r) = L$ for all values of r in $0 \leqslant r \leqslant R$ in Eq. (5), then there is no more frozen layer since at the end of the primary drying stage there is only one layer and this is the dried layer.

During the primary drying stage, heat transfer occurs at temperatures below T_0 but also above T_0 [3,4,11,14]. At the beginning of the primary drying stage, the temperature of the material in the vial is usually below the reference temperature, T_0. The sublimation temperature T_Z ($T_Z = T_{\text{I}}(t, z = Z = H(t,r), r)$) is also below T_0 and it is well known [3,4,7,11,14] that the value of T_Z depends on the value of the total pressure, P_Z ($P_Z = P(t, z = Z = H(t,r), r)$) at the moving interface. As the thickness of the dried layer increases (Fig. 1b), there are temperatures in the dried layer that are above the value of T_0. Therefore, the exergy input, $\text{EI}_{\text{pd,ht,}}$ resulting from conductive heat transfer would have two parts; the exergy input, $\text{EI}_{\text{pd,ht,bel}}$, resulting from conductive heat transfer below T_0 and the exergy input, $\text{EI}_{\text{pd,ht,ab}}$, resulting from conductive heat transfer above T_0. The value of $\text{EI}_{\text{pd,ht,ab}}$ can be determined from Eq. (7)

$$\text{EI}_{\text{pd,ht,ab}} = 2\pi \int_0^{t_{\text{pd}}} \int_0^R \left[-k_{\text{Ie}} \left.\frac{\partial T_{\text{I}}}{\partial z}\right|_{z=0} \left(1 - \frac{T_0}{T_{\text{I}}(t, z=0, r)}\right) - k_{\text{II}} \left.\frac{\partial T_{\text{II}}}{\partial z}\right|_{z=L} \left(1 - \frac{T_0}{T_{\text{II}}(t, z=L, r)}\right) \right] r \, \mathrm{d}r \, \mathrm{d}t \tag{7}$$

The determination of $\text{EI}_{\text{pd,ht,bel}}$ requires the following two cases to be taken under account:

Case (A): At the start of the primary drying stage ($t = 0$) the temperature, T_{init}, of the material in the vial is below T_0, while the sublimation temperature, T_Z, is determined by the total pressure P_Z at the moving interface, $Z = H(t, r)$. If $T_{\text{init}} < T_Z < T_0$, the temperature change and phase change below T_0 involve (1) the increase in the value of the temperature from T_{init} to T_Z, (2) the frozen water sublimes at T_Z, and (3) the temperature of the material in the vial keeps on increasing. As a result, the exergy input, $\text{EI}_{\text{pd,ht,bel}}$, from heat transfer below the reference temperature T_0 is made up of three contributions

$$\text{EI}_{\text{pd,ht,bel}} = \text{EI}_{\text{pd,ht,bel,1}} + \text{EI}_{\text{pd,ht,bel,2}} + \text{EI}_{\text{pd,ht,bel,3}} \tag{8}$$

where

$$\text{EI}_{\text{pd,ht,bel,1}} = T_0 M_{\text{mm}} c_{p\text{II}} \ln\left[\frac{T_Z}{T_{\text{init}}}\right] - M_{\text{mm}} c_{p\text{II}} (T_Z - T_{\text{init}}) \tag{9}$$

$$\text{EI}_{\text{pd,ht,bel,2}} = (W_{\text{init}} - W_{Z=L, 0\leqslant r\leqslant R}) \Delta H_{\text{s}} \left[\frac{T_0}{T_Z} - 1\right] \tag{10}$$

$$\text{EI}_{\text{pd,ht,bel,3}} = T_0 [M_{\text{mm}} - (W_{\text{init}} - W_{Z=L, 0\leqslant r\leqslant R})] c_{p\text{Ie}} \ln\left[\frac{T_0}{T_Z}\right] - [M_{\text{mm}} - (W_{\text{init}} - W_{Z=L, 0\leqslant r\leqslant R})] c_{p\text{Ie}} (T_0 - T_Z) \tag{11}$$

Case (B): If $T_{\text{init}} < T_0 < T_Z$, then the temperature in the material in the vial changes from T_{init} to T_0 and then continues increasing to the sublimation temperature T_Z. In this case $\text{EI}_{\text{pd,ht,bel}}$ is determined from the following expression:

$$\text{EI}_{\text{pd,ht,bel}} = T_0 M_{\text{mm}} c_{p\text{II}} \ln\left[\frac{T_0}{T_{\text{init}}}\right] - M_{\text{mm}} c_{p\text{II}} (T_0 - T_{\text{init}}) \tag{12}$$

In Eqs. (9)–(12), M_{mm} represents the mass of the moist material in the vial, c_{pIe} and c_{pII} denote the heat capacities of the dried and frozen layers, respectively, ΔH_{s} is the heat of sublimation of ice, W_{init} denotes the initial mass of moisture in the material, $W_{Z=L,\ 0\leqslant r\leqslant R}$ represents the mass of moisture in the material at the end of the primary drying stage where $Z = H(t_{\text{pd}}, r) = L$ for all values of r in $0 \leqslant r \leqslant R$. Thus, the exergy input, $\text{EI}_{\text{pd,ht}}$, resulting from conductive heat transfer during the primary drying stage would be given by Eq. (13)

$$\text{EI}_{\text{pd,ht}} = \text{EI}_{\text{pd,ht,bel}} + \text{EI}_{\text{pd,ht,ab}} \tag{13}$$

where $\text{EI}_{\text{pd,ht,ab}}$ is given by Eq. (7) and $\text{EI}_{\text{pd,ht,bel}}$ is determined from Eq. (8) when Case (A) occurs, while for Case (B) $\text{EI}_{\text{pd,ht,bel}}$ is obtained from Eq. (12).

The exergy fluxes of water vapor, $E_{\text{pd,w}}$, and inerts, $E_{\text{pd,in}}$, are given by the following expressions:

$$E_{\text{pd,w}} = |N_{\text{w}}| M_{\text{w}} T_0 \left[c_{p\text{w}} \left(\frac{T_{\text{I}}}{T_0} - 1 - \ln\left(\frac{T_{\text{I}}}{T_0}\right) \right) + \frac{R_{\text{g}}}{M_{\text{w}}} \ln\left(\frac{p_{\text{w}}}{P_0}\right) \right] \tag{14}$$

$$E_{\text{pd,in}} = |N_{\text{in}}| M_{\text{in}} T_0 \left[c_{p\text{in}} \left(\frac{T_{\text{I}}}{T_0} - 1 - \ln\left(\frac{T_{\text{I}}}{T_0}\right) \right) + \frac{R_{\text{g}}}{M_{\text{in}}} \ln\left(\frac{p_{\text{in}}}{P_0}\right) \right] \tag{15}$$

In Eqs. (14) and (15), $|N_{\text{w}}|$ and $|N_{\text{in}}|$ denote the magnitudes of the molar fluxes of water vapor and inerts in the porous dried layer, respectively, and are determined from the solution of the mathematical model of Sheehan and Liapis [3], $c_{p\text{w}}$ and $c_{p\text{in}}$ represent the heat capacity of water vapor and inerts, respectively, M_{w} and M_{in} denote the molecular weight of water vapor and inerts, respectively, R_{g} is the ideal gas constant, and P_0 represents the reference pressure. Furthermore, the exergy of gases (water vapor and inerts) accumulated in the ring-shaped volume element of dried layer shown in Fig. 1a having axial and radial thicknesses Δz and Δr, respectively, is given by Eq. (16)

$$\text{EA}_{\text{pd,w,in}} = n_{\text{w}} M_{\text{w}} T_0 \left[c_{p\text{w}} \left(\frac{T_{\text{I,pd}}}{T_0} - 1 - \ln\left(\frac{T_{\text{I,pd}}}{T_0}\right) \right) + \frac{R_{\text{g}}}{M_{\text{w}}} \ln\left(\frac{p_{\text{w,pd}}}{P_0}\right) \right] + n_{\text{in}} M_{\text{in}} T_0 \left[c_{p\text{in}} \left(\frac{T_{\text{I,pd}}}{T_0} - 1 - \ln\left(\frac{T_{\text{I,pd}}}{T_0}\right) \right) + \frac{R_{\text{g}}}{M_{\text{in}}} \ln\left(\frac{p_{\text{in,pd}}}{P_0}\right) \right] \tag{16}$$

where n_{w} and n_{in} are the moles of water vapor and inerts within the ring-shaped volume element, respectively, and can be determined from the values of $|N_{\mathrm{w}}|$ and $|N_{\mathrm{in}}|$ by knowing also the values of the cross-sectional area of the material in the vial and the time interval Δt. In Eq. (16), $T_{\mathrm{I,pd}}$, $p_{\mathrm{w,pd}}$, and $p_{\mathrm{in,pd}}$, represent the temperature, partial pressure of water vapor, and partial pressure of inerts, respectively, in the ring-shaped volume element in the dried layer during primary drying, and their values could be estimated from the following approximate expressions:

$$T_{\mathrm{I,pd}} \cong \frac{1}{2}\left[\left(\frac{T_{\mathrm{I}}(t,z,r)+T_{\mathrm{I}}(t,z+\Delta z,r)}{2}\right) + \left(\frac{T_{\mathrm{I}}(t,z,r)+T_{\mathrm{I}}(t,z,r+\Delta r)}{2}\right)\right] \tag{17}$$

$$p_{\mathrm{w,pd}} \cong \frac{1}{2}\left[\left(\frac{p_{\mathrm{w}}(t,z,r)+p_{\mathrm{w}}(t,z+\Delta z,r)}{2}\right) + \left(\frac{p_{\mathrm{w}}(t,z,r)+p_{\mathrm{w}}(t,z,r+\Delta r)}{2}\right)\right] \tag{18}$$

$$p_{\mathrm{in,pd}} \cong \frac{1}{2}\left[\left(\frac{p_{\mathrm{in}}(t,z,r)+p_{\mathrm{in}}(t,z+\Delta z,r)}{2}\right) + \left(\frac{p_{\mathrm{in}}(t,z,r)+p_{\mathrm{in}}(t,z,r+\Delta r)}{2}\right)\right] \tag{19}$$

Thus, the exergy losses, $\mathrm{EL}_{\mathrm{pd,mt}}$, of the ring-shaped volume element per unit time and unit volume due to mass transfer, could be determined by the following expression:

$$\begin{aligned}\mathrm{EL}_{\mathrm{pd,mt}} = \left(\frac{1}{2\pi r\Delta r\Delta z}\right)\Big[&2\pi r\Delta r((E_{\mathrm{pd,w}}(t,z,r)+E_{\mathrm{pd,in}}(t,z,r)) \\ &-(E_{\mathrm{pd,w}}(t,z+\Delta z,r)+E_{\mathrm{pd,in}}(t,z+\Delta z,r))) \\ &+2\pi r\Delta z((E_{\mathrm{pd,w}}(t,z,r)+E_{\mathrm{pd,in}}(t,z,r)) \\ &-(E_{\mathrm{pd,w}}(t,z,r+\Delta r)+E_{\mathrm{pd,in}}(t,z,r+\Delta r))) \\ &-\left(\frac{\partial(\mathrm{EA}_{\mathrm{pd,w,in}})}{\partial t}\bigg|_{t}\right)\Big]\end{aligned} \tag{20}$$

The accrued exergy losses, $\mathrm{AEL}_{\mathrm{pd,mt}}$, caused by mass transfer during the primary drying stage can be determined by integrating Eq. (20) with respect to space and time as follows:

$$\mathrm{AEL}_{\mathrm{pd,mt}} = 2\pi\int_0^{t_{\mathrm{pd}}}\int_0^{R}\int_0^{H(t,r)}(\mathrm{EL}_{\mathrm{pd,mt}})r\,\mathrm{d}z\,\mathrm{d}r\,\mathrm{d}t \tag{21}$$

Therefore, the accrued exergy losses, $\mathrm{AEL}_{\mathrm{pd}}$, due to heat transfer and mass transfer at the end of the primary drying stage, can be determined from Eq. (22)

$$\mathrm{AEL}_{\mathrm{pd}} = \mathrm{AEL}_{\mathrm{pd,ht}} + \mathrm{AEL}_{\mathrm{pd,mt}} \tag{22}$$

where the terms $\mathrm{AEL}_{\mathrm{pd,ht}}$ and $\mathrm{AEL}_{\mathrm{pd,mt}}$ are determined from Eqs. (6) and (21), respectively. It should be mentioned here that the terms in Eq. (6) should be determined at $t = t_{\mathrm{pd}}$.

The exergy input, $\mathrm{EI}_{\mathrm{pd,mt,w}}$, due to mass transfer of water vapor during primary drying is obtained from Eq. (23)

$$\begin{aligned}\mathrm{EI}_{\mathrm{pd,mt,w}} &= \int_0^{t_{\mathrm{pd}}}\int_0^{2\pi}\int_0^{R}E_{\mathrm{pd,w}}(t,H(t,r),r)\cdot r\left|\frac{\partial H(t,r)}{\partial r}\right|\mathrm{d}r\,\mathrm{d}\theta\,\mathrm{d}t \\ &= 2\pi\int_0^{t_{\mathrm{pd}}}\int_0^{R}E_{\mathrm{pd,w}}(t,H(t,r),r)\cdot r\left|\frac{\partial H(t,r)}{\partial r}\right|\mathrm{d}r\,\mathrm{d}t\end{aligned} \tag{23}$$

where the values of $|\partial H(t,r)/\partial r|$ are evaluated from the solution of the mathematical model of Sheehan and Liapis [3]. The exergy input, $\mathrm{EI}_{\mathrm{pd,mt,in}}$, due to mass transfer of inerts during primary drying could be determined from Eq. (24)

$$\mathrm{EI}_{\mathrm{pd,mt,in}} = \int_0^{t_{\mathrm{pd}}}\int_0^{2\pi}\int_0^{R}E_{\mathrm{pd,in}}(t,z=0,r)r\,\mathrm{d}r\,\mathrm{d}\theta\,\mathrm{d}t \tag{24}$$

Eq. (24) indicates that the gradient of the pressure of inerts in the dried layer is considered to be negligible, as has been found to be the case in practice [3,4,7,11,14,27]. Then the exergy input, $\mathrm{EI}_{\mathrm{pd,mt}}$, resulting from the mass transfer of water vapor and inerts during primary drying is determined from Eq. (25)

$$\mathrm{EI}_{\mathrm{pd,mt}} = \mathrm{EI}_{\mathrm{pd,mt,w}} + \mathrm{EI}_{\mathrm{pd,mt,in}} \tag{25}$$

where the terms $\mathrm{EI}_{\mathrm{pd,mt,w}}$ and $\mathrm{EI}_{\mathrm{pd,mt,in}}$ are obtained from Eqs. (23) and (24), respectively.

The exergy input, $\mathrm{EI}_{\mathrm{pd}}$, due to heat and mass transfer during primary drying is then given by Eq. (26)

$$\mathrm{EI}_{\mathrm{pd}} = \mathrm{EI}_{\mathrm{pd,ht}} + \mathrm{EI}_{\mathrm{pd,mt}} \tag{26}$$

where the terms $\mathrm{EI}_{\mathrm{pd,ht}}$ and $\mathrm{EI}_{\mathrm{pd,mt}}$ are determined from Eqs. (13) and (25), respectively.

2.2. Exergy expressions for the secondary drying stage

In the secondary drying stage there is no moving interface and, thus, there is no frozen layer. During the secondary drying stage, the bound (sorbed) water is being desorbed and the water vapor is transported through the dried layer to the surface at $z = 0$ of the material in the vial. Both heat and mass transfer lead to exergy losses.

It can be shown by following the procedure presented in Section 2.1 that for the secondary drying stage the accrued exergy losses, $\mathrm{AEL}_{\mathrm{sd,ht}}$, in the dried layer due to conductive heat transfer, could be determined from the following expression:

$$\begin{aligned}\mathrm{AEL}_{\mathrm{sd,ht}} = 2\pi T_0\int_0^{t_{\mathrm{sd}}}\int_0^{R}\int_0^{L}\left[\frac{k_{\mathrm{Ie}}}{T_{\mathrm{I}}^2}\right]\Bigg[&\left(\frac{\partial T_{\mathrm{I}}}{\partial z}\right)^2 - T_{\mathrm{I}}\left(\frac{\partial^2 T_{\mathrm{I}}}{\partial z^2}\right) \\ &+\left(\frac{\partial T_{\mathrm{I}}}{\partial r}\right)^2 - \left(\frac{1}{r}\right)T_{\mathrm{I}}\left(\frac{\partial T_{\mathrm{I}}}{\partial r}\right) - T_{\mathrm{I}}\left(\frac{\partial^2 T_{\mathrm{I}}}{\partial r^2}\right)\Bigg]r\,\mathrm{d}z\,\mathrm{d}r\,\mathrm{d}t\end{aligned} \tag{27}$$

In Eq. (27), $t = 0$ represents the start of the secondary drying stage and t_{sd} denotes the time at which the secondary drying stage ends.

The accrued exergy losses, $\mathrm{AEL}_{sd,mt}$, due to mass transfer during the secondary drying stage can be determined from the expression

$$\mathrm{AEL}_{sd,mt} = 2\pi \int_0^{t_{sd}} \int_0^R \int_0^L \mathrm{EL}_{sd,mt} r \, dz \, dr \, dt \tag{28}$$

where $\mathrm{EL}_{sd,mt}$ in Eq. (28) is determined from Eq. (20) with the understanding that the values of the variables and parameters involved in Eqs. (14)–(20), are determined from the solution of the mathematical model [3] that describes the dynamic behavior of the freeze drying process during the secondary drying stage. After the values of $\mathrm{AEL}_{sd,ht}$ and $\mathrm{AEL}_{sd,mt}$ have been determined from Eqs. (27) and (28), respectively, then the total accrued exergy losses, AEL_{sd}, due to heat and mass transfer during the secondary drying stage, can be obtained from the following expression:

$$\mathrm{AEL}_{sd} = \mathrm{AEL}_{sd,ht} + \mathrm{AEL}_{sd,mt} \tag{29}$$

During the secondary drying stage, some of the sorbed water is desorbed at temperatures whose values are below the value of the reference temperature, T_0, and heat transfer at temperatures below T_0 could last for a period of time. Therefore, the exergy input, $\mathrm{EI}_{sd,ht}$, due to conductive heat transfer during the secondary drying stage, has two contributing parts; one is involving exergy input at temperatures above T_0 and another involves exergy input at temperatures below T_0. The exergy input due to conductive heat transfer, $\mathrm{EI}_{sd,ht,ab}$, at temperatures above T_0 during the secondary drying stage, could be determined from the following expression:

$$\begin{aligned}\mathrm{EI}_{sd,ht,ab} = 2\pi \int_0^{t_{sd}} \int_0^R \Bigg[&\left(-k_{Ie} \frac{\partial T_I}{\partial z}\bigg|_{z=0} \right) \left(1 - \frac{T_0}{T_I(t, z=0, r)} \right) \\ &+ \left(-k_{Ie} \frac{\partial T_I}{\partial z}\bigg|_{z=L} \right) \left(1 - \frac{T_0}{T_I(t, z=L, r)} \right) \Bigg] r \, dr \, dt\end{aligned} \tag{30}$$

It is worth noting here that during the secondary drying stage heat is supplied to the dried layer at the top ($z = 0$, $0 \leqslant r \leqslant R$, and $0 \leqslant t \leqslant t_{sd}$) and bottom ($z = L$, $0 \leqslant r \leqslant R$, and $0 \leqslant t \leqslant t_{sd}$) of the dried layer, and the values of the temperatures $T_I(t, z = 0, r)$ and $T_I(t, z = L, r)$ could be above the value of the reference temperature for a large period of time.

The exergy input, $\mathrm{EL}_{sd,ht,bel}$, resulting from conductive heat transfer at temperatures whose values are below T_0, can be determined as follows: At the beginning of the secondary drying stage, the initial distribution of the temperature, T_I, in the dried layer is the same distribution as that obtained at the end of the primary drying stage. Thus if $T_I(t = t_{pd},\ z = L,\ 0 \leqslant r \leqslant R) < T_0$, conductive heat transfer occurs below T_0 and some of the sorbed water is desorbed below the reference temperature, T_0. However, the desorption temperature of the bound water during the secondary drying stage varies, and, therefore, the value of $\mathrm{EI}_{sd,ht,bel}$ can be determined from Eq. (31)

$$\mathrm{EI}_{sd,ht,bel} = \mathrm{EI}_{sd,ht,bel,1} + \mathrm{EI}_{sd,ht,bel,2} \tag{31}$$

where

$$\begin{aligned}\mathrm{EI}_{sd,ht,bel,1} = 2\pi \int_0^R \int_{z_{T_I(t=t_{pd},z,r)=T_0}}^L &\times \left[T_0 c_{pIe} \rho_{Ie} \ln \left(\frac{T_0}{T_I(t = t_{pd}, z, r)} \right) \right. \\ &\left. - c_{pIe} \rho_{Ie} (T_0 - T_I(t = t_{pd}, z, r)) \right] r \, dz \, dr\end{aligned} \tag{32}$$

and

$$\mathrm{EI}_{sd,ht,bel,2} = \int_{M_{sd}|_{t=0}}^{M_{sd}|_{t=t_{T_{I,aver,sd}=T_0}}} \Delta H_v \left(\left(\frac{T_0}{T_{I,aver,sd}} \right) - 1 \right) dM_{sd} \tag{33}$$

In Eqs. (32) and (33), c_{pIe} and ρ_{Ie} denote the effective heat capacity and density of the dried layer, respectively, $z_{T_{I(t=t_{pd},z,r)=T_0}}$ represents the position measured from the surface ($z = 0$) of the dried layer to a fixed point which has a temperature at the end of the primary drying stage whose value is equal to the value of T_0, ΔH_v denotes the heat of vaporization (desorption) of bound (sorbed) water, $T_{I,aver,sd}$ represents the average temperature of desorption in the dried material during the secondary drying stage, $t_{T_{I,aver,sd}=T_0}$ is the time in the secondary drying stage at which $T_{I,aver,sd} = T_0$, M_{sd} represents the mass of moisture in the material during the secondary drying stage, and dM_{sd} denotes the differential of M_{sd}. The value of M_{sd} at any time t during the secondary drying stage, is determined from the integration of the concentration of bound water, $c_{sw}(t, z, r)$, over the volume of the dried layer and the result obtained from this integration is then multiplied by the density of the solid phase, and this product provides the value of M_{sd} at time t. The values of $c_{sw}(t, z, r)$ in the dried layer at any time t are obtained from the solution of the mathematical model of Sheehan and Liapis [3] and the units of c_{sw} are (kg water/kg solid). Thus, the exergy input, $\mathrm{EI}_{sd,ht}$ due to conductive heat transfer during the secondary drying stage, is given by

$$\mathrm{EI}_{sd,ht} = \mathrm{EI}_{sd,ht,ab} + \mathrm{EI}_{sd,ht,bel,1} + \mathrm{EI}_{sd,ht,bel,2} \tag{34}$$

where $\mathrm{EI}_{sd,ht,ab}$, $\mathrm{EI}_{sd,ht,bel,1}$, and $\mathrm{EI}_{sd,ht,bel,2}$, could be determined from Eqs. (30), (32) and (33), respectively.

The exergy input, $\mathrm{EI}_{sd,mt}$, resulting from mass transfer in the dried layer during the secondary drying stage can be determined by expressions similar to those developed for the dried layer during the primary drying stage (Section 2.1) by considering, of course, that there is no moving interface during the secondary drying stage and the size of the dried layer along the axial direction z is always equal to L, and that the upper limit in the time integral should be replaced by t_{sd}. Numerous simulations [3,11–14,26,27] of the primary and secondary drying stages of the freeze drying process have indicated that in the secondary drying stage (i) the water vapor pressure gradient as well as that of the inerts are significantly much smaller than their corresponding gradients during the primary drying stage, (ii) a negligible amount of water vapor accumulates in the pores of the dried layer, (iii) water vapor is mainly transported through the dried layer, and (iv) the temperature of the water vapor within the material could be approximately represented by the temperature $T_{\mathrm{I,aver,sd}}$ (see Eq. (33)) whose value at any time t during the secondary drying stage, could be estimated from the following expression:

$$\begin{aligned} T_{\mathrm{I,aver,sd}} &= \frac{2\pi}{\pi R^2 L}\int_0^R \int_0^L T_{\mathrm{I}}(t,z,r)r\,\mathrm{d}z\,\mathrm{d}r \\ &= \frac{2}{R^2 L}\int_0^R \int_0^L T_{\mathrm{I}}(t,z,r)r\,\mathrm{d}z\,\mathrm{d}r \end{aligned} \tag{35}$$

The implication of items (i)–(iv) presented above, is that the value of $\mathrm{EL}_{\mathrm{sd,mt}}$ could be determined from the following approximate expression:

$$\begin{aligned} \mathrm{EI}_{\mathrm{sd,mt}} = \int_0^{t_{\mathrm{sd}}} \Bigg[c_{p\mathrm{w}}\left(\frac{T_{\mathrm{I,aver,sd}}}{T_0} - 1 - \ln\left(\frac{T_{\mathrm{I,aver,sd}}}{T_0}\right)\right) \\ + \frac{R_{\mathrm{g}}}{M_{\mathrm{w}}}\ln\left(\frac{P_{\mathrm{dcham}}}{P_0}\right)\Bigg]\left(\frac{\partial M_{\mathrm{sd}}}{\partial t}\right)\mathrm{d}t \end{aligned} \tag{36}$$

where P_{dcham} denotes the pressure of the drying chamber of the freeze dryer.

Thus, the exergy input, $\mathrm{EI}_{\mathrm{sd}}$, due to heat and mass transfer during the secondary drying stage could be determined from Eq. (37)

$$\mathrm{EI}_{\mathrm{sd}} = \mathrm{EI}_{\mathrm{sd,ht}} + \mathrm{EI}_{\mathrm{sd,mt}} \tag{37}$$

where $\mathrm{EI}_{\mathrm{sd,ht}}$ and $\mathrm{EI}_{\mathrm{sd,mt}}$ are obtained from Eqs. (34) and (36), respectively.

2.3. Exergy expressions for the water vapor condenser

The water vapor resulting from the drying of the material during the primary and secondary drying stages, is captured by the cold surface of the water vapor condenser of the freeze dryer. The changes in the temperature as well as in the state of the water vapor and inerts in the vapor condenser are as follows: (1) the temperature of water vapor is cooled down from the inlet temperature, $T_{\mathrm{in,cond}}$, of the gas (water vapor and inerts) to the condenser to the solidification temperature, T_{solid}, of the water vapor where the water vapor becomes solid ice, (2) the water vapor is converted to solid ice at T_{solid}, (3) the temperature T_{solid} of the ice is decreased to the lowest temperature of ice, $T_{\ell,\mathrm{cond}}$, cooled down by the condenser, and (4) the temperature of the inerts (i.e., air) decreases from $T_{\mathrm{in,cond}}$ to the lowest temperature of inerts $T_{\ell,\mathrm{in,cond}}$, cooled down by the condenser. The energy input of the water vapor condenser, $Q_{\mathrm{c,cond}}$, that is required to condense the water vapor produced by drying and to cool down the inerts leaking into the freeze drying system, could be determined by the energy balance

$$\begin{aligned} Q_{\mathrm{c,cond}} = (W_{\mathrm{init}} - W_{\mathrm{sd}})[c_{p\mathrm{w}}(T_{\mathrm{in,cond}} - T_{\mathrm{solid}}) + \Delta H_{\mathrm{solid}} \\ + c_{p,\mathrm{ice}}(T_{\mathrm{solid}} - T_{\ell,\mathrm{cond}})] + W_{\mathrm{in}}c_{p\mathrm{in}}(T_0 - T_{\ell,\mathrm{in,cond}}) \end{aligned} \tag{38}$$

where W_{init} denotes the initial mass of moisture in the material, W_{sd} represents the mass of moisture in the material at the end of the secondary drying stage, $c_{p\mathrm{w}}$ and $c_{p\mathrm{in}}$ denote the heat capacity of water vapor and inerts, respectively, $\Delta H_{\mathrm{solid}}$ represents the heat of solidification of water vapor into solid ice and its magnitude is equal to the heat of sublimation, ΔH_{s}, of ice, $c_{p,\mathrm{ice}}$, is the heat capacity of ice, and W_{in} denotes the mass of inerts through the vacuum pump during a drying cycle (primary and secondary drying stages are considered together). The value of T_{solid} depends on the water vapor pressure in the condenser and can be determined by the following expression [28]:

$$T_{\mathrm{solid}} = \frac{2.19\Delta H_{\mathrm{solid}}}{23.9936 - \ln\left(\frac{P}{133.32}\right)} \tag{39}$$

The exergy losses for the processes (1)–(4) occuring in the condenser and discussed above, are represented by the variables $\mathrm{EL}_{\mathrm{cond,1}}$, $\mathrm{EL}_{\mathrm{cond,2}}$, $\mathrm{EL}_{\mathrm{cond,3}}$, and $\mathrm{El}_{\mathrm{cond,4}}$, respectively. These exergy losses can be determined from the following expressions:

$$\begin{aligned} \mathrm{EL}_{\mathrm{cond,1}} = T_0 c_{p\mathrm{w}}(W_{\mathrm{init}} - W_{\mathrm{sd}})\Bigg[\ln\left(\frac{T_{\mathrm{solid}}}{T_{\mathrm{in,cond}}}\right) \\ -\left(\frac{T_{\mathrm{solid}} - T_{\mathrm{in,cond}}}{T_{\mathrm{c,cond}}}\right)\Bigg] \end{aligned} \tag{40}$$

$$\mathrm{EL}_{\mathrm{cond,2}} = T_0 \Delta H_{\mathrm{solid}}(W_{\mathrm{init}} - W_{\mathrm{sd}})\left[\left(\frac{1}{T_{\mathrm{c,cond}}}\right) - \left(\frac{1}{T_{\mathrm{solid}}}\right)\right] \tag{41}$$

$$\begin{aligned} \mathrm{EL}_{\mathrm{cond,3}} = T_0 c_{p,\mathrm{ice}}(W_{\mathrm{init}} - W_{\mathrm{sd}})\Bigg[\ln\left(\frac{T_{\ell,\mathrm{cond}}}{T_{\mathrm{solid}}}\right) \\ -\left(\frac{T_{\ell,\mathrm{cond}} - T_{\mathrm{solid}}}{T_{\mathrm{c,cond}}}\right)\Bigg] \end{aligned} \tag{42}$$

$$\mathrm{EL}_{\mathrm{cond,4}} = T_0 c_{p,\mathrm{in}} W_{\mathrm{in}}\left[\ln\left(\frac{T_{\ell,\mathrm{in,cond}}}{T_{\mathrm{in,cond}}}\right) - \left(\frac{T_{\ell,\mathrm{in,cond}} - T_{\mathrm{in,cond}}}{T_{\mathrm{c,cond}}}\right)\right] \tag{43}$$

In Eqs. (40)–(43), $T_{\mathrm{c,cond}}$ represents the temperature of the cooling source of the condenser. It is worth mentioning here that the value of $T_{\ell,\mathrm{cond}}$ ($T_{\ell,\mathrm{cond}} \cong 235$–$240$ K) is in practice usually about 5 K above the temperature of the cooling source, $T_{\mathrm{c,cond}}$, and also the value of $T_{\ell,\mathrm{in,cond}}$ is very close to the value of $T_{\ell,\mathrm{cond}}$ ($T_{\ell,\mathrm{in,cond}} \cong T_{\ell,\mathrm{cond}}$). The exergy losses in the water vapor condenser, $\mathrm{EL}_{\mathrm{cond}}$, can then be determined from Eq. (44)

$$\mathrm{EL}_{\mathrm{cond}} = \mathrm{EL}_{\mathrm{cond,1}} + \mathrm{EL}_{\mathrm{cond,2}} + \mathrm{EL}_{\mathrm{cond,3}} + \mathrm{EL}_{\mathrm{cond,4}} \tag{44}$$

The exergy input for the water vapor condenser, $\mathrm{EI}_{\mathrm{cond}}$, is determined from the expression

$$\mathrm{EI}_{\mathrm{cond}} = Q_{\mathrm{c,cond}}\left[\frac{T_0}{T_{\mathrm{c,cond}}} - 1\right] \tag{45}$$

where $Q_{c,cond}$ represents the cooling capacity of the condenser and its value can be obtained from Eq. (38).

2.4. Exergy expressions for the vacuum pump

The main tasks of the vacuum pump are to (i) reduce the pressure of the drying chamber during the start-up phase so that primary drying can start, (ii) evacuate the non-condensable gases resulting from leakage and outgasing of the wall surfaces of the system, and (iii) evacuate the inert gases from the material being dried. In our analysis for the vacuum pump, it is considered that only air (in practice, air is by far the most abundant component of the inert gases as well as of the leaked in the system gases) is evacuated from the vacuum system and, therefore, the mass of air, W_{air}, that is pumped out of the system during a drying cycle (the time of drying cycle is equal to the sum of t_{pd} and t_{sd}) is

$$W_{air} = 10^{-3}(t_{pd} + t_{sd})\left[\frac{M_{air}p_{in,vp}S_{vp}}{R_g T_{in,vp}}\right] \tag{46}$$

where $p_{in,vp}$, S_{vp}, and $T_{in,vp}$ represent the inlet pressure, theoretical pumping speed or capacity, and gas inlet temperature, respectively, of the vacuum pump system. It is worth mentioning here that the pumping speed, S_{vp}, can be considered to be constant when the vacuum pump runs during the drying cycle except for the start-up stage; in practice, the values of S_{vp} may vary between $0.07\ \mathrm{m^3/s}$ and $0.15\ \mathrm{m^3/s}$. The power input for the vacuum pump system, Ω, can be evaluated [29] from Eq. (47)

$$\Omega = \left(10^{-3}(p_{in,vp}S_{vp})\left(\frac{\lambda}{\lambda-1}\right)\right)\left[\left(\frac{p_{out,vp}}{p_{in,vp}}\right)^{\frac{\lambda-1}{\lambda}} - 1\right] \tag{47}$$

where λ represents the polytropic exponential [29] of compression (the values of λ could vary between 1.2 and 1.7), and $p_{out,vp}$ denotes the outlet or exhaust pressure of the vacuum pump system. It is worth mentioning here that the value of $p_{out,vp}$, could be equal to the value of the reference pressure P_0. By knowing the values of the variables t_{pd}, t_{sd}, and Ω, the exergy input, $\mathrm{EI_{vp}}$, of the vacuum pump system can be determined by the following expression:

$$\mathrm{EI_{vp}} = \Omega(t_{pd} + t_{sd}) \tag{48}$$

In order to determine the exergy losses, $\mathrm{EL_{vp}}$, in the vacuum pump system, it is necessary to evaluate first the variation of exergy, ΔE_{vp}, due to the compression of a perfect gas which can be determined [15,16] by Eq. (49)

$$\Delta E_{vp} = W_{air}T_0\left(\frac{R_g}{M_{air}}\right)\ln\left(\frac{p_{out,vp}}{p_{in,vp}}\right) \tag{49}$$

The exergy losses, $\mathrm{EL_{vp}}$, in the vacuum pump system are then obtained by the expression

$$\mathrm{EL_{vp}} = \mathrm{EI_{vp}} - \Delta E_{vp}. \tag{50}$$

3. Analysis and synthesis on how changes in the control variables of the freeze drying process affect the exergy inputs and exergy losses in lyophilization systems

It is instructive and useful to present first here a qualitative analysis and synthesis discussion of the effects that the key operational variables of the freeze drying process, namely (i) the heat inputs q_I and q_{II}, (ii) the drying chamber pressure, P_{dcham}, and (iii) the lowest temperature, $T_{\ell,cond}$, of ice cooled down by the condenser, could have on the exergy inputs and exergy losses. It is also important to note here that during freeze drying, the values of q_I, q_{II}, and P_{dcham} could be varied with time so that the temperatures in the frozen layer do not exceed the melting temperature, T_m, and the temperatures in the dried layer do not exceed the scorch temperature, T_{scor} [3,4,11]; the value of $T_{\ell,cond}$ is usually kept constant during the drying cycle. By constructing rigorous mathematical models of the freeze drying process and employing them in time optimal control studies, researchers have constructed [3,7,11–13,17] control strategies for the time variation of q_I, q_{II} and P_{dcham} so that the duration times t_{pd} and t_{sd} of the primary and secondary drying stages, respectively, are minimized when the freeze drying process is (a) heat-transfer controlled, (b) mass-transfer controlled, and (c) both heat-transfer and mass-transfer controlled. This is important because the values of t_{pd} and t_{sd} play a very important role in the determination of the magnitude of the exergy inputs and exergy losses of the primary and secondary drying stages, the water vapor condenser, and the vacuum pump, as the expressions presented in Sections 2.1–2.4 indicate; it is worth noting again that the smaller the values of t_{pd} and t_{sd} are, the shorter will be the duration of the operation of the water vapor condenser and vacuum pump.

Operational policies that keep P_{dcham} constant and increase the values of q_I and q_{II} and which result [3,11–13,17] in increases in the values of the temperature of the sample at $z = 0$ and $z = L$ for $0 \leqslant r \leqslant R$, enhance the heat transfer in the sample by increasing the temperature gradient within the material and this leads to higher sublimation rates which increase the water vapor pressure gradient in the dried layer and, thus, mass transfer is enhanced and this results in a shorter duration, t_{pd}, of the primary drying stage. For the secondary drying stage, increases in q_I and q_{II} enhance heat and mass transfer and this results in a shorter value for t_{sd}; but the magnitude of the gradients of temperature and water vapor pressure in the dried layer are smaller than those in the primary drying stage, and this would indicate, from the exergy expressions in Sections 2.1–2.4, that the irreversible losses, and, thus, the exergy losses due to enhancement in heat and mass transfer are larger in the primary drying stage than in the secondary drying stage, when q_I and q_{II} are increased. Furthermore, increased values for $T_I(t, z = 0, 0 \leqslant r \leqslant R)$ and $T_I(t, z = L, 0 \leqslant r \leqslant R)$ imply that the values of the inlet temperature of gas (water vapor and inerts), $T_{in,cond}$, to the condenser will increase and this could result in slightly increased exergy losses, through $\mathrm{EL}_{\mathrm{cond},1}$ (Eq. (40)) and $\mathrm{EL}_{\mathrm{cond},4}$ (Eq. (43)), for the water vapor condenser. Therefore, since increases in q_{I} and q_{II} mainly increase the magnitude of the exergy losses in the primary and secondary drying stages by increasing the gradients of temperature and water vapor pressure in the dried layer, but reduce the duration times (t_{pd} and t_{sd}) of the primary and secondary stages, and this latter result implies from the expressions in Sections 2.1–2.4 that the exergy losses for the two drying stages, the water vapor condenser, and the vacuum pump would decrease, then one would expect that there exist values of q_{I} and q_{II} that would minimize the total exergy losses during the lyophilization and such values for q_{I} and q_{II} could be determined by employing the results obtained from the dynamic freeze drying model of Sheehan and Liapis [3] in the exergy expressions presented in Sections 2.1–2.4.

If during lyophilization the heat inputs q_{I} and q_{II} are kept constant and the value of the drying chamber pressure, P_{dcham}, is increased, then the value of the effective thermal conductivity, k_{Ie}, in the dried layer is increased [3,7,11] and this heat transfer enhancement leads to a decrease of the temperature gradient during the primary and secondary drying stages, and, therefore, the exergy losses due to conductive heat transfer could decrease as the value of P_{dcham} would increase. But the increased value of P_{dcham} reduces the mass transfer rate of water vapor in the dried layer and leads to an increase in the value of the gradient of the total pressure, P ($P = p_{\mathrm{w}} + p_{\mathrm{in}}$), in the dried layer [3,7,11], and, thus, the exergy losses due to mass transfer in the dried layer could increase. For a heat-transfer controlled process during the primary and secondary drying stages, the heat transfer enhancement in the dried layer due to the increase of P_{dcham} would play a more significant role, by reducing the temperature gradient in the dried layer and the drying times t_{pd} and t_{sd} [3,7,11], in the magnitude of exergy losses during the primary and secondary drying stages than the reduced mass transfer, and, thus, the exergy losses in the primary and secondary drying stages could be slightly decreased as P_{dcham} is increased. For a mass-transfer controlled process during the primary drying stage, the decrease in the mass transfer rate of water vapor due to the increase of P_{dcham} could play a more important role, by increasing the gradient of the total pressure and the drying time t_{pd} [3,7,11–13,17,26], in the magnitude of exergy losses during the primary drying stage than the enhanced heat transfer, and, thus, exergy losses in the primary drying stage could be slightly increased as P_{dcham} is increased. Of course, the secondary drying stage of freeze drying is always a heat-transfer controlled process, and, thus, as in the case of a heat-transfer controlled process during the primary and secondary drying stages discussed above, the exergy losses in the secondary drying stage of a lyophilization process that is mass-transfer controlled during the primary drying stage, could be slightly decreased as P_{dcham} is increased. But since the duration time of the primary drying stage, t_{pd}, is most often larger than the duration time of the secondary drying stage, t_{sd} [3,4,7,11–14,17,26,27], one could expect that for a mass-transfer controlled system during the primary stage, the sum of the exergy losses in the primary and secondary drying stages could slightly increase as P_{dcham} is increased. Most importantly, the exergy losses of condensing the water vapor in the condenser and vacuum pumping the inerts (air) from the drying chamber of the freeze dryer, increase substantially as the drying chamber pressure, P_{dcham}, is increased. As the value of P_{dcham} increases, the value of the solidification temperature, T_{solid}, of water vapor increases (Eq. (39)), and this rise in the value of T_{solid} increases the value of $\mathrm{EL}_{\mathrm{cond},2}$ (Eq. (41)) significantly and, thus, since the value of $\mathrm{EL}_{\mathrm{cond},2}$ plays a dominant role in the exergy losses of the condenser, it is apparent that the magnitude of the exergy losses, E_{cond} (Eq. (44)), in the condenser would increase as the value of the drying chamber pressure, P_{dcham}, is increased. Furthermore, when the value of P_{dcham} increases, the value of the mass, W_{air}, of inerts (air) pumped out from the drying chamber of the freeze dryer during the drying cycle increases (Eq. (46)) because the value of $p_{\mathrm{in,vp}}$ in Eq. (46) increases, and, also the value of the power input for the vacuum system, Ω (Eq. (47)), would increase; thus, the exergy losses of vacuum pumping the inerts from the drying chamber increase as the value of P_{dcham} increases. From the above presentation, one could conclude that the sum of the exergy losses occuring in the condenser, vacuum pump, and the primary and secondary drying stages (the total exergy losses) increase as the drying chamber pressure, P_{dcham}, increases. Time optimal control analysis of the lyophilization process [12,13,17] has shown that in order to minimize the duration times t_{pd} and t_{sd} of the primary and secondary drying stages, respectively, the value of the drying chamber pressure, P_{dcham}, should not be constant during drying and its time variation should be such that the heat and mass transfer rates in the dried layer remain always high; furthermore, by minimizing the times t_{pd} and t_{sd} through time optimal control policies on q_{I}, q_{II} and P_{dcham} [12,13,17], the exergy inputs and exergy losses in the primary and secondary drying stages as well as those of the vacuum pump system that depend on the values of t_{pd} and t_{sd} could be reduced, and, of course, the operational time for the water vapor condenser will be decreased since the drying cycle time ($t_{\mathrm{pd}} + t_{\mathrm{sd}}$) has been minimized.

The lowest temperature, $T_{\ell,\mathrm{cond}}$, of ice cooled down by the condenser represents the third key operational variable that could affect the exergy losses of the freeze drying process, as was indicated at the beginning of this section; furthermore, the temperature $T_{\ell,\mathrm{cond}}$ is usually about 5 K above the temperature of the cooling source, $T_{\mathrm{c,cond}}$. In practice, $T_{\ell,\mathrm{cond}} \cong$ 235–240 K and the value of $T_{\ell,\mathrm{cond}}$ is usually kept constant during the drying cycle. But if the value of $T_{\ell,\mathrm{cond}}$ is increased by increasing, of course, the value of the temperature, $T_{\mathrm{c,cond}}$, of the cooling source of the condenser, then the exergy losses of the water vapor condenser will be substantially decreased, as can be clearly seen by the expressions in Eqs. (40)–(43). Also, the increased value of $T_{\ell,\text{cond}}$ will decrease the pressure gradients of the water vapor and inerts in the dried layer [3,7,11–13,17,26] and this will result to a decrease in the gradient of the total pressure P ($P = p_{\text{w}} + p_{\text{in}}$) in the dried layer and, thus, a decrease in the exergy losses due to mass transfer in the dried layer could occur. But it is possible that the increase in the value of $T_{\ell,\text{cond}}$ could slightly affect the values of t_{pd} and t_{sd}; the relative effect on the magnitude of t_{pd} and t_{sd} will depend on whether the process is heat-transfer or mass-transfer controlled. From the structure of the expressions for the exergy losses presented in Sections 2.1–2.4, it is thought that an increase in the value of $T_{\ell,\text{cond}}$ would decrease significantly the magnitude of the total exergy losses of the lyophilization process; it should be noted here that the effect of the increase in the value of $T_{\ell,\text{cond}}$ on the exergy losses in the vacuum pump system (Eqs. (46)–(50)) is considered to be slight and not as significant as that on the exergy losses occurring in the water vapor condenser and the primary and secondary drying stages. While increasing the value of $T_{\ell,\text{cond}}$ can provide an effective method for reducing the total exergy losses of the lyophilization process, one should keep clearly in mind that the temperature of $T_{\ell,\text{cond}}$ has to be such that fast mass and heat transfer rates in the dried layer during the primary and secondary drying stages can be realized so that the melting temperature, T_{m}, and scorch temperature, T_{scor}, constraints can be satisfied and the resulting duration times t_{pd} and t_{sd} of the primary and secondary drying stages, respectively, do not become so large that they are affecting aspects of product quality [3,4,7,11,14] and downstream processing flexibility. For a given lyophilization system, the value of $T_{\ell,\text{cond}}$ that could significantly reduce the total exergy losses of the freeze drying system could be determined by employing the results obtained from the dynamic freeze drying model of Sheehan and Liapis [3] in the exergy expressions presented in Sections 2.1–2.4.

4. Exergy distribution results for a lyophilization system

From the results obtained from the mathematical models that describe the dynamic behavior of the primary and secondary drying stages in bulk solution [11,12,17,26,27] freeze drying in trays as well as freeze drying in vials on trays [3,7,13,17,27], it appears that the contribution in the determination of the exergy losses by the terms involving the gradient of the temperature and the partial pressure gradients of water vapor and inerts, is significantly more important than the contribution of the terms involving second-order spatial partial derivatives of the same variables. Furthermore, from the expressions presented in Sections 2.1–2.4 above, it is apparent that the exergy losses and exergy inputs in the primary and secondary drying stages of lyophilization depend explicitly on the temperature and the water vapor and inerts partial pressure distributions in the material being dried, while the exergy losses and exergy inputs of the water vapor condenser and the vacuum pump system do not explicitly depend on these distributions. But the values of the parameters $T_{\text{in,cond}}$, T_{solid}, W_{in}, $T_{\text{in,vp}}$, $p_{\text{in,vp}}$, and W_{air} in the expressions for determining the exergy losses and exergy inputs in the water vapor condenser and the vacuum pump depend implicitly on the evolution of the temperature and the water vapor and inerts partial pressure distributions in the material being dried. Of course, the magnitude of the exergy losses and exergy inputs for the primary and secondary drying stages as well as for the water vapor condenser and the vacuum pump system depend explicitly and very significantly on the magnitude of the duration times t_{pd} and t_{sd} of the primary and secondary drying stages of the lyohilization process, respectively, as the expressions in Sections 2.1–2.4 and the discussion in Section 3 clearly show.

Case III in the work of Sheehan and Liapis [3] where a vial is placed at the center of the array of vials on the tray is taken to represent here an example for examining the distribution of exergy losses and exergy inputs for the lyophilization of skim milk in vials; skim milk is selected because it could be considered as a complex pharmaceutical product in the sense that it contains enzymes and proteins [3,7,11,27]. In this example, the temperature of the plates during the primary drying stage is adjusted to the highest value which satisfies the constraints imposed by the melting, T_{m}, and scorch, T_{scor}, temperatures; when all of the frozen layer has disappeared, the plates are set to the scorch temperature for the duration of the secondary drying stage [3]. Vial dimensions, tray surface area, values for the properties of skim milk and for other relevant physical parameters, as well as the values of the drying times t_{pd}, and t_{sd}, are given in Tables I and II of Ref. [3]. The values of the reference temperature, T_0, and pressure P_0, were taken to be equal to 293.15 K and 1.01325×10^5 Pa, respectively, while the values of the parameters associated with the water vapor condenser and the vacuum pump system were as follows: $c_{p\text{w}} = 1.857$, $c_{p\text{in}} = 1.013$, and $c_{p,\text{ice}} = 2.104$ kJ/kg K; $T_{\text{c,cond}} = 230$, $T_{\ell,\text{cond}} = 235$, and $T_{\ell,\text{in,cond}} = 239$ K; $p_{\text{in,vp}} = 5.07$ Pa, $p_{\text{out,vp}} = 1.01325 \times 10^5$ Pa, $S_{\text{vp}} = 0.09$ m^3/s, and $\lambda = 1.4$.

In Table 1, the distributions of exergy inputs and exergy losses for the lyophilization system discussed above, are presented. These results were obtained by the following procedure: first, the mathematical model of Sheehan and Liapis [3] was employed and solved numerically in order to obtain the temperature and water vapor and inerts pressure distributions, the values of the molar fluxes of water vapor and inerts, the position of the moving interface, the distribution of sorbed (bound) water in the dried layer, the temperature and water vapor and inerts pressure gradients as well as the second-order spatial partial derivatives of the temperature and water vapor and inerts pressures. Then the required (by the exergy expressions in Sections 2.1–2.4) results from the solution of the mathematical model of Sheehan and Liapis [3] were employed in the exergy expressions presented in Sections 2.1–2.4 in order to obtain the results presented in Table 1; it is worth mentioning here that the differentiations and integrations required in the exergy expressions, were

Table 1
Distribution of exergy inputs and exergy losses per unit mass of moist material for the lyophilization system studied in this work

	Primary drying stage	Secondary drying stage	Water vapor condenser	Vacuum pump	Total exergy input (kJ/kg)	Total exergy losses (kJ/kg)
Exergy input (kJ/kg)	463.27	66.92	407.68	287.64	1225.51	–
Exergy losses (kJ/kg)	284.91	35.46	221.37	127.38	–	669.12
α_j for $j = 1,2,3,4$	61.50%	52.99%	54.30%	44.28%	–	–
β_j for $j = 1,2,3,4$	37.80%	5.46%	33.27%	23.47 %	–	–
γ_j for $j = 1,2,3,4$	42.58%	5.30%	33.08%	19.04 %	–	–

performed numerically. In Table 1, the parameter α_j represents the ratio of the exergy losses for operation j ($j = 1$ denotes the primary drying stage, $j = 2$ represents the secondary drying stage, $j = 3$ is the water vapor condenser, and $j = 4$ denotes the vacuum pump) to the exergy input of operation j multiplied by one hundred ($\alpha_j = ((\text{exergy losses (kJ/kg)})_j/(\text{exergy input (kJ/kg)})_j) \times 100$), β_j represents the ratio of the exergy input for operation j to the total exergy input multiplied by one hundred ($\beta_j = ((\text{exergy input (kJ/kg)})_j/(\text{total exergy input (kJ/kg)})) \times 100$), and γ_j denotes the ratio of the exergy losses for operation j to the total exergy losses multiplied by one hundred. The results in Table 1 clearly show that most of the exergy input is consumed (37.80%) by the primary drying stage followed by the water vapor condenser (33.27%) during the drying cycle of this lyophilization system. Furthermore, the primary drying stage and the water vapor condenser account for 42.58% and 33.08%, respectively, of the total exergy losses, and these results indicate that the primary drying stage and the water vapor condenser have the largest irreversibilities in this freeze drying system. Therefore, in order to reduce the total exergy input and total exergy losses for this lyophilization system, the operating conditions for the primary drying stage and the water vapor condenser should be given higher priority for studies on how to change the operating conditions so that performance improvements can occur. For instance, for this lyophilization system it would be recommended (a) not only to vary the values of q_{I} and q_{II} (and, thus, in effect the values of the temperature of the material at $z = 0$ and $z = L$ for $0 \leqslant r \leqslant R$) with time during the primary drying stage, but also to consider to vary with time the total pressure, P_{dcham}, in the drying chamber, (b) to consider to vary with time the values of $T_{\text{I}}(t, z = 0, 0 \leqslant r \leqslant R)$, $T_{\text{I}}(t, z = L, 0 \leqslant r \leqslant R)$, and P_{dcham} during the secondary drying stage, and (c) to consider to change the value of the temperature, $T_{\text{c,cond}}$, of the cooling source of the condenser which would also affect the values of $T_{\ell,\text{cond}}$ and $T_{\ell,\text{in,cond}}$ and, of course, the actions in items (a) and (b) will affect the inlet temperature, $T_{\text{in,cond}}$, of the gas (water vapor and inerts) to the condenser. Also, the actions in items (a) and (b) could decrease the values of t_{pd} and t_{sd} and this would affect both the exergy inputs and exergy losses in the different operations of the lyophilization process. It should be mentioned here again (it was discussed in detail in Section 3) that if the action in item (c) involves an increase in the value of $T_{\text{c,cond}}$ which, as was discussed in Section 3, would decrease the exergy losses of the water vapor condenser as well as the total exergy losses of the lyophilization process, the increase in the value of $T_{\text{c,cond}}$ has to be such that satisfactory heat and mass transfer rates are realized in the dried layer of the material in the vial. The interesting fact is that whatever may be the selected time control policies for the variables q_{I}, q_{II} and P_{dcham}, and for the value of the temperature $T_{\text{c,cond}}$, of the cooling source of the condenser [3,7,11–14,17,26], the results obtained from the mathematical model in Ref. [3] together with the exergy expressions presented in Sections 2.1–2.4 of this work, could indicate the set of control policies and value of $T_{\text{c,cond}}$ that can decrease the exergy inputs and exergy losses of a given lyophilization process involving freeze drying of a material of interest in vials on trays [3,7].

5. Conclusions

In this work, the expressions for the exergy inputs and exergy losses are constructed and presented for the lyophilization of materials in vials on trays; these expressions are applicable to the primary and secondary drying stages, the condensation of water vapor in the condenser, and the vacuum pumping of inerts by the vacuum pump of the freeze dryer. Furthermore, the exergy expressions for the primary and secondary drying stages incorporate the drying dynamics of the primary and secondary drying stages and, therefore, these exergy expressions can provide information regarding the exergy inputs and exergy losses only after the results on the drying dynamics that have been obtained from the solution of a rigorous dynamic and spatially multidimensional mathematical model [3] that properly describes the drying dynamics of the freeze drying process in vials on trays [3,7], have been introduced in the exergy expressions for the primary and secondary drying stages. It is important to mention that, of course, the drying dynamics also affect the values of the temperature and pressure of the gas streams entering the water vapor condenser and the vacuum pump, and, thus, they affect the exergy inputs and exergy losses associated with the condenser and vacuum pump. The magnitudes of the exergy inputs and exergy losses are shown to depend significantly on the values of t_{pd} and t_{sd} for all operations involved in the course of lyophilization in a freeze dryer, and, therefore, it is important to employ control policies that reduce the duration of the primary and secondary drying stages.

The structure of the exergy expressions is such that a detailed analytical discussion based on physics was presented on how variations in the control variables q_{I}, q_{II}, P_{dcham}, and $T_{\mathrm{c,cond}}$ would affect the values of t_{pd} and t_{sd} as well as the irreversibilities occurring in the material being dried and in the condenser and vacuum pump. This analytical discussion has indicated what could be potentially useful control policies for reducing the exergy inputs and exergy losses for heat-transfer controlled and mass-transfer controlled lyophilization processes. Furthermore, the performance of a given control policy can be evaluated by calculating the values of the exergy inputs and exergy losses and comparing them with the values obtained from other control policies considered for the same freeze drying system. An additional very useful practical result is the fact that from the exergy expressions the distribution of exergy inputs and exergy losses can be obtained for the two drying stages as well as for the condenser and the vacuum pump; the exergy distribution provides a diagnostic tool that indicates the operations in the freeze drying process that require changes in their operating conditions so that their exergy losses can be reduced and improved energy utilization for the freeze drying process can be realized. In effect the exergy expressions presented in this work can be used in the construction of control policies for the operation of a lyophilization system of a given design that minimize the irreversibilities occurring in the given freeze drying system, thus enhancing the efficiency of energy utilization in lyophilization. Finally, values of the distribution of exergy inputs and exergy losses for a lyophilization system were presented and the results showed that most of the exergy input is consumed and most of the exergy losses result (Table 1) by the primary drying stage, the water vapor condenser, and the vacuum pump in that order. Substantial reductions in the exergy losses can be realized by improving the operating conditions of these three operations, and operating policies were recommended that could reduce the exergy losses in the primary drying stage, the water vapor condenser, and the vacuum pump system.

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