

## Mathematical modelling for solvated crystallization

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We present a mathematical model for solvated crystallization of  $\alpha$ -lactose monohydrate based on population, mass and energy balance equations. We prove global existence and uniqueness of solutions under realistic conditions for a system operated in batch or semi-batch mode.

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### 1. Introduction

Crystallization is the unitary operation of formation of solids from a liquid solution. In process engineering crystallization is an important separation technique used in the chemical, pharmaceutical, food, material and semiconductor industries (Mullin *et al.*, 1971; Tavare, 1995). Crystallizers can be operated in batch, semi-batch or continuous mode (Jones, 2002).

The crystallization process is initiated if a solution becomes supersaturated. This may be triggered by cooling, evaporation of solvent, addition of anti-solvent, or by a chemical reaction. The principal processes in crystallization include nucleation or crystal birth, crystal growth, crystal breakage and attrition, agglomeration, but models should also include external processes like heating and cooling, or evaporation. Nucleation is the phase where solute molecules dispersed in the surrounding solvent start to form clusters, which according to the operating conditions are arranged in a defined periodic manner. Crystal growth is the subsequent accretion process of nuclei, driven by supersaturation. Crystal birth and growth cease when the solid-liquid system reaches equilibrium because of the exhaustion of supersaturation (Mersmann, 2001; Jones, 2002).

In the food processing industry there has been growing interest in the crystallization of lactose in (McLeod, 2007; Mimouni, 2007; Mimouni A. *et al.*, 2009). For a number of reasons,  $\alpha$ -lactose monohydrate is the most commonly used form of lactose in making medications. It is affordable, physically and chemically stable, easy to mix, it readily dissolves in but does not absorb water. Lactose monohydrate is available as a powder in different grades, density, and flowability. Here we present a mathematical

model of solvated crystallization of  $\alpha$ -lactose monohydrate.

Two forms of lactose,  $\alpha$ - and  $\beta$ -lactose, exist simultaneously in aqueous solution, the exchange being described by the process of mutarotation with exchange rates  $k_1, k_2$ . For temperatures  $T \leq 90^\circ\text{C}$  only  $\alpha$ -lactose crystallizes, with the specificity that a water molecule is integrated in the crystal. Nucleation and growth of crystals are the basic mechanisms, which may be complemented by modeling attrition, breakage, agglomeration and secondary nucleation effects.

Here we are interested in semi-batch crystallization, where the container is initially only partially filled. The model shown schematically in Figure 1 combines the dynamics of four interacting populations, one of them aging, governed by an energy balance. For a schematic view of the crystallizer, see Figure 2.

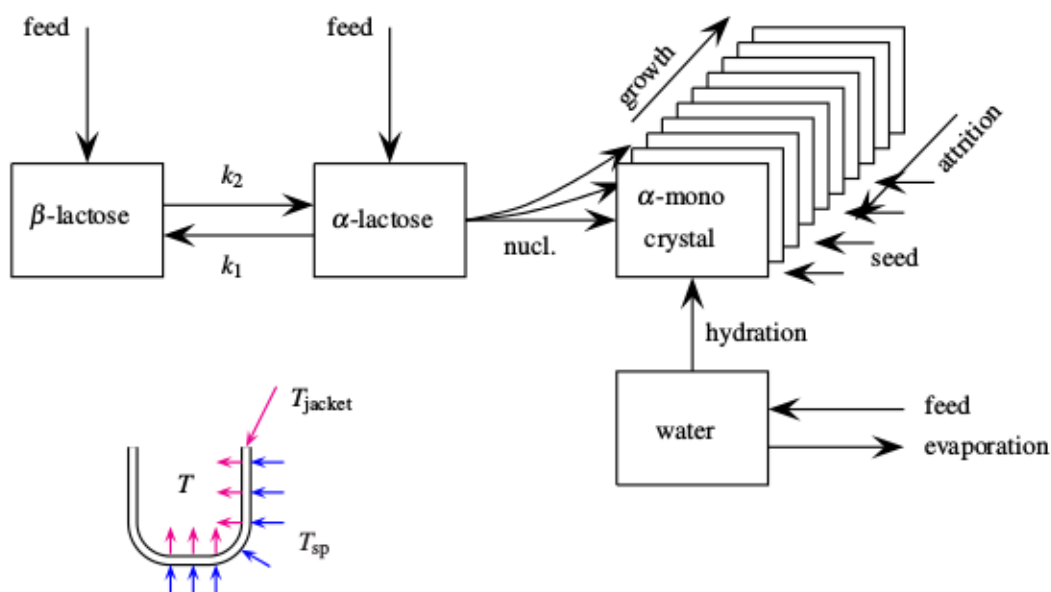


FIG. 1. Crystallization of  $\alpha$ -lactose monohydrate. The model includes four interacting populations:  $\alpha$ -lactose and  $\beta$ -lactose in liquid phase, water, and crystals of  $\alpha$ -lactose monohydrate. The two forms of lactose,  $\alpha$ -lactose and  $\beta$ -lactose, exist simultaneously in aqueous solution, the exchange being governed by mutarotation, with exchange rates  $k_1$  and  $k_2$ , depending on the temperature, governed in turn by the energy balance. The latter includes the internal heat produced by the crystallization reaction, and the heating and cooling system used to trigger and control the process. Altogether this involves the temperature of the slurry (Mersmann, 2001), or suspension,  $T(t)$ , the temperature of the crystallizer jacket,  $T_{\text{jacket}}(t)$  used in cooling the crystallizer, the set-point temperature  $T_{\text{sp}}(t)$  used to control the crystallizer jacket, and the temperature of the feed added during the process.

Mathematical models of crystallization are known for a variety of processes, but solvated crystallization of  $\alpha$ -lactose has not been discussed in the literature within a complete model including population, molar and energy balances. The model we derive here includes breakage and attrition, but does not include agglomeration, as the latter is negligible. We validate the model mathematically by proving global existence of solutions based on physically meaningful hypotheses. Our method of proof expands on Gurtin (see Gurtin *et al.* (1974)) and Calsina (see Calsina *et al.* (1995)), see also Smith (1994); Cushing (1989).

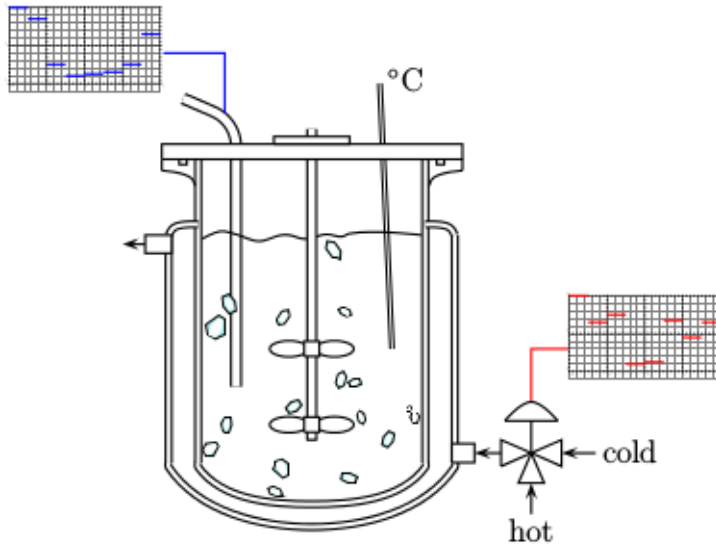


FIG. 2. Schematic view of the crystallizer, the container in which operated the crystallization process. Control inputs are the solute feed, and the set-point temperature.

For more general information on crystallization of lactose we mention Thurlby, Bronlund, Butler and Dincer (Thurlby *et al.*, 1976; Bronlund, 1997; Butler, 1998; Dincer, 2000). In fact, lactose has long been regarded as a mere admixture, but recent research has revealed several new possibilities for its utilization (McSweeney *et al.*, 2009).

The structure of the paper is as follows. In the section 2 we present the mathematical model of semi-batch solvated crystallization of  $\alpha$ -lactose monohydrate. In section 3 we present our main result on global existence and uniqueness of the solution. We conclude the proof of global existence and uniqueness by way of the characteristic curves and moments in discussed in section 4. In section 3 we present realistic hypotheses which we need in the proof of our result. In section 5 we discuss prior estimates. Section 6 discuss the proof of our main result, which uses the method of characteristics with a fixed point argument for an operator, which acts as a contraction with respect to a specific metric. The final section 7 presents conclusions.

## 2. Modelling and dynamics of process

In this section we present the population, mass and energy balance equations which describe the dynamic model of crystallization of  $\alpha$ -lactose monohydrate.

### 2.1 Population balance equation

The population balance equation describes a first interaction between the population of solid crystals, characterized by their length  $L$ , and two ageless populations of solute molecules of the constituent in liquid phase. The population balance equation models birth, growth and death of crystals due to

breakage and is given by

$$\begin{aligned} \frac{\partial (V(t)n(L,t))}{\partial t} + G(c_\alpha(t), c_\beta(t), T(t)) \frac{\partial (V(t)n(L,t))}{\partial L} \\ = -a(L)V(t)n(L,t) + V(t) \int_L^\infty a(L')b(L',L)n(L',t) dL' \end{aligned} \quad (2.1)$$

$$V(0)n(L,0) = V_0n_0(L) \quad (2.2)$$

$$n(0,t) = \frac{B(c_\alpha(t), c_\beta(t), T(t))}{G(c_\alpha(t), c_\beta(t), T(t))} \quad (2.3)$$

Here  $n(L,t)$  is the distribution of  $\alpha$ -lactose crystals, CSD, that is, the number of  $\alpha$ -lactose crystals per unit volume  $1 \text{ m}^3$  and per unit length  $1 \text{ m}$ , expressed as  $number \cdot m^{-3} \cdot m^{-1}$ . The quantities  $c_\alpha(t), c_\beta(t)$  are the dimensionless concentrations of  $\alpha$ - and  $\beta$ -lactose in the liquid phase, that is

$$m_\alpha = c_\alpha m_{\text{H}_2\text{O}}, \quad m_\beta = c_\beta m_{\text{H}_2\text{O}}, \quad (2.4)$$

where  $m_\alpha, m_\beta$  represent the mass of  $\alpha$ - respectively  $\beta$ -lactose in the liquid phase,  $m_{\text{H}_2\text{O}}$  the mass of water not integrated in crystals.

The total volume of slurry  $V(t)$  in the crystallizer is a dependent variable given in (2.19),  $G(c_\alpha, c_\beta, T)$  is the temperature-dependent growth coefficient of  $\alpha$ -crystals, or the *velocity* of crystal growth in  $m \cdot s^{-1}$ , assumed independent of crystal size  $L$ .

The boundary condition  $n(0,t)$  involves the temperature dependent birth coefficient  $B(c_\alpha, c_\beta, T)$ , the velocity of nucleation or crystal birth in  $number \cdot m^{-3} \cdot s^{-1}$ . The initial condition  $n(L,0)$  represents the *crystal seed*  $n_0(L)$ .

The right hand side of (2.1) describes breakage and attrition. The breakage rate  $a(L)$  represents the probability that a particle of size  $L$  and volume  $k_v L^3$  undergoes breakage, where  $k_v$  is a volumic shape factor. The daughter distribution  $b(L, L')$  represents the conditional probability that a particle of size  $L$ , when broken, produces a particle of size  $L' < L$ . Following (Ziff, 1985), assuming that a particle breaks on average into  $N_p$  parts leads to

$$\int_0^L b(L, L') dL' = N_p. \quad (2.5)$$

In the crystallization literature it is customary to assume binary breakage  $N_p = 2$ , as this seems general enough to model practical phenomena. We refer to Ziff (Ziff, 1985), Kostoglou *et al.* (Kostoglou *et al.*, 2002), Hounslow *et al.* (Hounslow *et al.*, 2001), Ramkarishna (Ramkrishna *et al.*, 2000) and Hede (Hede *et al.*, 2006) for more information on fragmentation.

The sink term on the right of (2.1) gathers particles leaving size  $L$  by being broken down to smaller sizes  $L' < L$ ,

$$\mathcal{Q}_{\text{break}}^-(L,t) = \int_0^L a(L)b(L, L')n(L,t)dL'.$$

On the other hand the source term at size  $L$  has the form

$$\mathcal{Q}_{\text{break}}^+(L,t) = \int_L^\infty a(L')b(L', L)n(L',t)dL',$$

representing particles broken down from all possible larger sizes  $L' \geq L$  to size  $L$ . Now conservation of mass is ensured by

$$\int_0^{L'} L^3 b(L', L) dL = L^3. \quad (2.6)$$

| quantity                  | symbol    | unit                               |
|---------------------------|-----------|------------------------------------|
| Crystal size distribution | $n(L,t)$  | $number \cdot m^{-3} \cdot m^{-1}$ |
| Crystal seed              | $n_0(L)$  | $number \cdot m^{-3} \cdot m^{-1}$ |
| Crystal breakage rate     | $a(L)$    | $1/s$                              |
| Breakage type             | $b(L',L)$ | $1/m$                              |

Table 1. Size related quantities

Indeed, the total mass of crystals being broken is

$$m_{\text{break}}^-(t) = \int_0^\infty a(L)n(L,t)L^3 dL.$$

On the other hand, the total mass of new crystals born due to breakage is

$$\begin{aligned} m_{\text{break}}^+(t) &= \int_0^\infty \int_L^\infty a(L')b(L',L)n(L',t)dL'L^3 dL \\ &= \int_0^\infty a(L')n(L',t) \int_0^{L'} L^3 b(L',L)dLdL' \\ &= \int_0^\infty a(L')n(L',t)L'^3 dL' = m_{\text{break}}^-(t), \end{aligned}$$

using (2.6). This confirms that breakage leaves the total crystal mass invariant. In contrast, if we compute the balance of number of individuals being broken, we obtain

$$\begin{aligned} \mathcal{Q}_{\text{break}}^+(t) &= \int_0^\infty \int_L^\infty a(L')b(L',L)n(L',t)dL'dL \\ &= \int_0^\infty a(L')n(L',t) \int_0^{L'} b(L',L)dLdL' \\ &= \int_0^\infty a(L')n(L',t)N_p dL = N_p \mathcal{Q}_{\text{break}}^-(t), \end{aligned}$$

which confirms that breakage multiplies by  $N_p$  the total number of individuals of that part of the population which undergoes breakage.

## 2.2 Crystal mass and solvent mass balance

We consider the mass  $m_{\text{cry}}(t)$  of mono-hydrated  $\alpha$ -lactose crystals as a function of time and relate it to the crystal size distribution  $n(L,t)$  through

$$m_{\text{cry}}(t) = k_v \rho_{\text{cry}} \int_0^\infty V(t)n(L,t)L^3 dL,$$

where  $\rho_{\text{cry}}$  is the crystal density. Therefore, we have

$$\frac{dm_{\text{cry}}(t)}{dt} = \rho_{\text{cry}} k_v \int_0^\infty \frac{\partial (V(t)n(L,t))}{\partial t} L^3 dL, \quad (2.7)$$

the initial condition associated with (2.7) being

$$m_{\text{cry},0} = k_v \rho_{\text{cry}} V_0 \int_0^\infty n_0(L) L^3 dL. \quad (2.8)$$

The particularity of solvated crystallization is that the variations of solvent mass,  $\frac{dm_{\text{H}_2\text{O}}}{dt}$ , and of crystal mass,  $\frac{dm_{\text{cry}}}{dt}$ , are coupled. The fact that  $\alpha$ -lactose crystals integrate a water molecule means that molecular weights of the solid and liquid phase of  $\alpha$ -lactose are related as

$$R = \frac{M_{\text{cry}}}{M_\alpha} = 1.0525 > 1. \quad (2.9)$$

Therefore, if we temporarily define the mass of water inside crystals as  $m_{\text{H}_2\text{O}\subset\text{cry}}$ , we have

$$m_{\text{H}_2\text{O}\subset\text{cry}} = \left(1 - \frac{1}{R}\right) m_{\text{cry}}.$$

In consequence,

$$\frac{dm_{\text{H}_2\text{O}}}{dt} = -\frac{dm_{\text{H}_2\text{O}\subset\text{cry}}}{dt} + \dot{m}_{\text{H}_2\text{O}}^\pm = -\left(1 - \frac{1}{R}\right) \frac{dm_{\text{cry}}}{dt} + \dot{m}_{\text{H}_2\text{O}}^\pm, \quad (2.10)$$

where  $\dot{m}_{\text{H}_2\text{O}}^\pm$  includes external sources and sinks, like the feed of water during the semi-batch mode. The interpretation is that the variation of the free water mass  $m_{\text{H}_2\text{O}}$  is governed by the inclusion of water molecules in crystals where it is bound, and by external sources and sinks.

By using the population balance equation (2.1), and by combining (2.10) and (2.7) allows us now to establish the solvent mass balance

$$\frac{dm_{\text{H}_2\text{O}}(t)}{dt} = (R^{-1} - 1) 3k_v \rho_{\text{cry}} G(c_\alpha(t), c_\beta(t), T(t)) V(t) \int_0^\infty n(L, t) L^2 dL + \dot{m}_{\text{H}_2\text{O}}^\pm(t). \quad (2.11)$$

### 2.3 Mass balance of $\alpha$ -lactose

The next step concerns the mass balance for  $\alpha$ -lactose in the liquid phase. The variation of mass  $m_\alpha$  of  $\alpha$ -lactose in the liquid phase is related to the variation of crystal mass  $m_{\text{cry}}$  and the mass  $m_\beta$  of  $\beta$ -lactose via

$$\begin{aligned} \frac{dm_\alpha(t)}{dt} &= -\frac{1}{R} \frac{dm_{\text{cry}}(t)}{dt} - k_1(T(t)) m_\alpha(t) + k_2(T(t)) m_\beta(t) + \dot{m}_\alpha^\pm(t) \\ &= -\frac{1}{R} \frac{dm_{\text{cry}}(t)}{dt} + m_{\text{H}_2\text{O}}(t) [-k_1(T(t)) c_\alpha(t) + k_2(T(t)) c_\beta(t)] + \dot{m}_\alpha^\pm(t), \end{aligned} \quad (2.12)$$

where  $k_1$  and  $k_2$  are the mutarotation exchange coefficients. Analytic expressions for  $k_1$  and  $k_2$  will be given in the section 2.7.

The factor  $1/R$  in the first term takes (2.9) into account, while the second term models loss and gain of  $\alpha$ -lactose in the liquid phase due to mutarotation. The third term  $\dot{m}_\alpha^\pm$  regroups external sources and sinks for  $\alpha$ -lactose. By definition of the concentrations we have  $m_\alpha = c_\alpha m_{\text{H}_2\text{O}}$ , so that

$$\frac{dm_\alpha}{dt} = m_{\text{H}_2\text{O}} \frac{dc_\alpha}{dt} + c_\alpha \frac{dm_{\text{H}_2\text{O}}}{dt}.$$

This leads to

$$m_{\text{H}_2\text{O}}(t) \frac{dc_\alpha(t)}{dt} + c_\alpha(t) \frac{dm_{\text{H}_2\text{O}}(t)}{dt} = m_{\text{H}_2\text{O}}(t) [-k_1(T(t))c_\alpha(t) + k_2(T(t))c_\beta(t)] - \frac{1}{R} \frac{dm_{\text{cry}}(t)}{dt} + \dot{m}_\alpha^\pm(t).$$

Substituting (2.11) gives

$$m_{\text{H}_2\text{O}} \frac{dc_\alpha}{dt} - c_\alpha \left(1 - \frac{1}{R}\right) \frac{dm_{\text{cry}}}{dt} = -\frac{1}{R} \frac{dm_{\text{cry}}}{dt} + m_{\text{H}_2\text{O}} [-k_1c_\alpha + k_2c_\beta] + \dot{m}_\alpha^\pm - c_\alpha \dot{m}_{\text{H}_2\text{O}}^\pm,$$

which can be simplified to

$$m_{\text{H}_2\text{O}} \frac{dc_\alpha}{dt} + \left[\frac{1}{R} - c_\alpha \left(1 - \frac{1}{R}\right)\right] \frac{dm_{\text{cry}}}{dt} = m_{\text{H}_2\text{O}} [-k_1c_\alpha + k_2c_\beta] + \dot{m}_\alpha^\pm - c_\alpha \dot{m}_{\text{H}_2\text{O}}^\pm.$$

We can interpret the source term  $\dot{m}_\alpha^\pm$  as  $\dot{m}_\alpha^\pm = \dot{c}_\alpha^\pm m_{\text{H}_2\text{O}}^\pm + c_\alpha^\pm \dot{m}_{\text{H}_2\text{O}}^\pm$ . Then we obtain

$$m_{\text{H}_2\text{O}} \frac{dc_\alpha}{dt} + \left[\frac{1}{R} - c_\alpha \left(1 - \frac{1}{R}\right)\right] \frac{dm_{\text{cry}}}{dt} = m_{\text{H}_2\text{O}} [-k_1c_\alpha + k_2c_\beta] + \dot{c}_\alpha^\pm m_{\text{H}_2\text{O}}^\pm + (c_\alpha^\pm - c_\alpha) \dot{m}_{\text{H}_2\text{O}}^\pm.$$

Dividing by  $m_{\text{H}_2\text{O}}$  gives the equation

$$\frac{dc_\alpha}{dt} = -\frac{1}{m_{\text{H}_2\text{O}}} \left[\frac{1}{R} - c_\alpha \left(1 - \frac{1}{R}\right)\right] \frac{dm_{\text{cry}}}{dt} - k_1c_\alpha + k_2c_\beta + \dot{c}_\alpha^\pm \frac{m_{\text{H}_2\text{O}}^\pm}{m_{\text{H}_2\text{O}}} + (c_\alpha^\pm - c_\alpha) \frac{\dot{m}_{\text{H}_2\text{O}}^\pm}{m_{\text{H}_2\text{O}}}. \quad (2.13)$$

Our study uses  $\dot{c}_\alpha^\pm = 0$  and  $c_\alpha^- = 0$ , and  $c_\alpha^+$  constant, which means the fraction of  $\alpha$ -lactose in the feed does *not* change, even though the feed rate  $\dot{m}_{\text{H}_2\text{O}}^+(t)$  is time-varying and may be used to control the process.

#### 2.4 Mass balance of $\beta$ -lactose

Proceeding in analogous fashion for the mass balance of  $\beta$ -lactose, we have

$$\frac{dm_\beta}{dt} = k_1m_\alpha - k_2m_\beta + \dot{m}_\beta^\pm, \quad (2.14)$$

which accounts for mutarotation and feed. Using  $\frac{dm_\beta}{dt} = m_{\text{H}_2\text{O}} \frac{dc_\beta}{dt} + c_\beta \frac{dm_{\text{H}_2\text{O}}}{dt}$  in tandem with (2.11), we obtain

$$m_{\text{H}_2\text{O}} \frac{dc_\beta}{dt} - c_\beta \left(1 - \frac{1}{R}\right) \frac{dm_{\text{cry}}}{dt} = m_{\text{H}_2\text{O}} [k_1c_\alpha - k_2c_\beta] + \dot{m}_\beta^\pm - c_\beta \dot{m}_{\text{H}_2\text{O}}^\pm.$$

Again we interpret  $\dot{m}_\beta^\pm$  as  $\dot{m}_\beta^\pm = \dot{c}_\beta^\pm m_{\text{H}_2\text{O}}^\pm + c_\beta^\pm \dot{m}_{\text{H}_2\text{O}}^\pm$ , then

$$\frac{dc_\beta}{dt} = \frac{c_\beta}{m_{\text{H}_2\text{O}}} \left(1 - \frac{1}{R}\right) \frac{dm_{\text{cry}}}{dt} + k_1c_\alpha - k_2c_\beta + \dot{c}_\beta^\pm \frac{m_{\text{H}_2\text{O}}^\pm}{m_{\text{H}_2\text{O}}} + (c_\beta^\pm - c_\beta) \frac{\dot{m}_{\text{H}_2\text{O}}^\pm}{m_{\text{H}_2\text{O}}}. \quad (2.15)$$

The crucial point about equations (2.13) and (2.15) is that on substituting (2.7), the state  $m_{\text{cry}}$  disappears.

Our study uses  $\dot{c}_\beta^\pm = 0$  and  $c_\beta^- = 0$ . Since in our experiment, we have only a source and no sink, then

$\dot{m}_{\text{H}_2\text{O}}^- = 0$ , so that the source term is  $c_\beta^+ \frac{\dot{m}_{\text{H}_2\text{O}}^+}{m_{\text{H}_2\text{O}}}$ , with  $c_\beta^+$  fixed. For the same reason, we are left with a

source term  $c_\alpha^+ \frac{\dot{m}_{\text{H}_2\text{O}}^+}{m_{\text{H}_2\text{O}}}$  on the mass balance of  $\beta$ -lactose. We shall switch to the notation  $q_{\text{H}_2\text{O}} := \dot{m}_{\text{H}_2\text{O}}^+$ ,

then the source term will given by  $c_\beta^+ \frac{q_{\text{H}_2\text{O}}}{m_{\text{H}_2\text{O}}}$ .

### 2.5 Relating volume of slurry to masses

The total volume of slurry  $V(t)$  in the crystallizer is a dependent variable, which we now express as a function of the states  $m_\alpha$ ,  $m_\beta$ , and  $m_{\text{H}_2\text{O}}$ . Observe that we have the relations

$$V_\alpha = m_\alpha \rho_{\text{lac},\alpha}^{-1}, \quad V_\beta = m_\beta \rho_{\text{lac},\beta}^{-1}, \quad V_{\text{cry}} = m_{\text{cry}} \rho_{\text{cry}}^{-1}, \quad V_{\text{H}_2\text{O}} = m_{\text{H}_2\text{O}} \rho_{\text{H}_2\text{O}}^{-1}, \quad (2.16)$$

with the obvious meanings, so that the total volume is

$$V(t) = V_\alpha(t) + V_\beta(t) + V_{\text{H}_2\text{O}}(t) + V_{\text{cry}}(t). \quad (2.17)$$

Substituting the expressions from the previous sections,

$$V_\alpha = c_\alpha m_{\text{H}_2\text{O}} \rho_{\text{lac},\alpha}^{-1}, \quad V_\beta = c_\beta m_{\text{H}_2\text{O}} \rho_{\text{lac},\beta}^{-1}, \quad V_{\text{H}_2\text{O}} = m_{\text{H}_2\text{O}} \rho_{\text{H}_2\text{O}}^{-1},$$

and using

$$V_{\text{cry}}(t) = \left( k_v \rho_{\text{cry}} V(t) \int_0^\infty n(L,t) L^3 dL \right) \rho_{\text{cry}}^{-1} = k_v V(t) \int_0^\infty n(L,t) L^3 dL,$$

we obtain

$$V(t) \left( 1 - k_v \int_0^\infty n(L,t) L^3 dL \right) = m_{\text{H}_2\text{O}}(t) \left[ c_\alpha(t) \rho_{\text{lac},\alpha}^{-1} + c_\beta(t) \rho_{\text{lac},\beta}^{-1} + \rho_{\text{H}_2\text{O}}^{-1} \right]. \quad (2.18)$$

This may be written as

$$V(t) = \frac{m_{\text{H}_2\text{O}}(t)}{1 - k_v \int_0^\infty n(L,t) L^3 dL} \left[ \rho_{\text{lac},\alpha}^{-1} c_\alpha(t) + \rho_{\text{lac},\beta}^{-1} c_\beta(t) + \rho_{\text{H}_2\text{O}}^{-1} \right]. \quad (2.19)$$

This expression will have to be substituted for  $V(t)$  in the formulae below and above. The initial condition  $V(0) = V_0$  now leads to

$$\frac{m_{\text{H}_2\text{O}}(0)}{1 - k_v \int_0^\infty n_0(L) L^3 dL} \left[ \rho_{\text{lac},\alpha}^{-1} c_\alpha(0) + \rho_{\text{lac},\beta}^{-1} c_\beta(0) + \rho_{\text{H}_2\text{O}}^{-1} \right] = V_0, \quad (2.20)$$

where

$$m_{\text{H}_2\text{O}}(0) = m_{\text{H}_2\text{O},0}, \quad (2.21)$$

which when substituted into (2.20) gives the initial condition

$$V_0 = m_{\text{cry},0} \rho_{\text{cry}}^{-1} + m_{\text{H}_2\text{O},0} \left[ \rho_{\text{lac},\alpha}^{-1} c_{\alpha,0} + \rho_{\text{lac},\beta}^{-1} c_{\beta,0} + \rho_{\text{H}_2\text{O}}^{-1} \right]. \quad (2.22)$$

Using  $m_\alpha = m_{\text{H}_2\text{O}} c_\alpha$  and  $m_\beta = m_{\text{H}_2\text{O}} c_\beta$ , we obtain

$$m_{\alpha,0} = m_{\text{H}_2\text{O}}(0) c_\alpha(0), \quad (2.23)$$

and

$$m_{\beta,0} = m_{\text{H}_2\text{O}}(0) c_\beta(0). \quad (2.24)$$



In addition, if we assume that  $\alpha$ - and  $\beta$ -lactose are initially at an equilibrium of mutarotation, we have to add the initial condition

$$c_{\beta,0} = k_m(T_0)c_{\alpha,0}, \quad (2.25)$$

where

$$T_0 = T(0) \quad (2.26)$$

is the initial temperature of the slurry. Clearly if  $m_{\text{H}_2\text{O},0}$  and  $c_{\alpha,0}$ ,  $c_{\beta,0}$  are known, we also know  $V_0$ . Conversely, if  $V_0$  and  $c_{\alpha,0}$ ,  $c_{\beta,0}$  are known, we can determine  $m_{\text{H}_2\text{O},0}$ . Likewise, since we assume that  $\alpha$  and  $\beta$  are initially at equilibrium of mutarotation, it suffices to know  $V_0$  and  $c_{\alpha,0} + c_{\beta,0}$  to reconstruct  $m_{\text{H}_2\text{O},0}$ . Quantities depending on temperature and initial values are given in Table 4 and Table 5.

## 2.6 Energy balance

The energy balance includes the internal heat produced by the crystallization reaction, and the heating and cooling system used to trigger and control the process. Altogether this involves the state  $T(t)$  representing the temperature of the slurry, assumed homogeneous due to stirring, the temperature of the crystallizer jacket  $T_{\text{jacket}}(t)$ , and the set-point temperature  $T_{\text{sp}}(t)$ , which is used as control input. We also need  $T_{\text{feed}}$ , the temperature of the feed, which we assume constant, and a reference temperature  $T_{\text{ref}} = 25 \text{ }^\circ\text{C}$ , needed to quantify the heating respectively cooling effect of the feed on the crystallizer temperature  $T$ ; see Mersmann (2001). This leads to the equation

$$\begin{aligned} \frac{dT(t)}{dt} = P_1(t) \left[ -P_2(t)(T(t) - T_{\text{ref}}) - \Delta H \frac{dm_{\text{cry}}(t)}{dt} + UA(t)(T_{\text{jacket}}(t) - T(t)) \right. \\ \left. + q_{\text{H}_2\text{O}}(t) \left( C_{\text{H}_2\text{O}}^p + C_{\alpha}^p c_{\alpha}(0) + C_{\beta}^p c_{\beta}(0) \right) (T_{\text{feed}} - T_{\text{ref}}) \right], \end{aligned} \quad (2.27)$$

where

$$\frac{dT_{\text{jacket}}(t)}{dt} = -a(T_{\text{jacket}}(t) - T_{\text{sp}}(t)) \quad (2.28)$$

was obtained through identification of the system where  $a$  is determined experimentally in the laboratory. Note that  $T_{\text{sp}}(t)$  is used as a control input to regulate  $T_{\text{jacket}}(t)$ , and therefore indirectly  $T(t)$ , via the heat exchange between the jacket and the crystallizer through the contact surface  $A(t)$ , which is a dependent function of  $V(t)$ . The constants  $C_{\text{H}_2\text{O}}^p$ ,  $C_{\alpha}^p$ ,  $C_{\beta}^p$  are the specific heat capacities, and  $\Delta H$  is the heat of crystallization in  $\text{kJ/kg}$ , see McSweeney *et al.* (2009). We have used the abbreviations

$$P_1(t)^{-1} = m_{\text{H}_2\text{O}}(t)C_{\text{H}_2\text{O}}^p + m_{\alpha}(t)C_{\alpha}^p + m_{\beta}(t)C_{\beta}^p + m_{\text{cry}}(t)C_{\text{cry}}^p, \quad (2.29)$$

and

$$P_2(t) = \frac{dm_{\text{H}_2\text{O}}(t)}{dt}C_{\text{H}_2\text{O}}^p + \frac{dm_{\alpha}(t)}{dt}C_{\alpha}^p + \frac{dm_{\beta}(t)}{dt}C_{\beta}^p + \frac{dm_{\text{cry}}(t)}{dt}C_{\text{cry}}^p, \quad (2.30)$$

with  $m_{\alpha} = c_{\alpha}m_{\text{H}_2\text{O}}$ ,  $m_{\beta} = c_{\beta}m_{\text{H}_2\text{O}}$  as before.

### 2.7 Mutarotation and saturation

The mutarotation exchange coefficients  $k_1, k_2$  depend on temperature via the Arrhenius law

$$k_2(T) = k_0 \exp\left(-\frac{E_a}{R_g(T+273.15)}\right), \quad k_1(T) = k_2(T)k_m(T),$$

where  $k_0, E_a$  are constants,  $R_g$  is the gas constant, and where according to Mcleod (2007)  $k_m$  follows the affine law

$$k_m(T) = 1.64 - 0.0027 \cdot T.$$

The equilibrium of mutarotation therefore occurs at

$$c_{\alpha,\text{sat,eq}}(T) = \frac{\theta_1 \exp(\theta_2 T)}{100(1 + k_m(T))},$$

where  $\theta_1 = 10.9109$  and  $\theta_2 = 0.02804$  are determined experimentally according to Mcleod (2007), so that the saturation level for the formation of  $\alpha$ -crystals is also temperature dependent and expressed as

$$c_{\alpha,\text{sat}}(c_\beta, T) = c_{\alpha,\text{sat,eq}}(T) - F(T)(c_\beta - k_m(T)c_{\alpha,\text{sat,eq}}(T)),$$

with  $F(T) = 0.0187 \cdot \exp(0.0236 \cdot T)$  a correction factor for  $\alpha$ -lactose solubility following a Visser type law according to Mcleod (2007). Note that the saturation concentration varies in time as  $c_{\alpha,\text{sat}}(c_\beta(t), T(t))$ , because  $c_\beta(t)$  and  $T(t)$  vary in time.

### 2.8 Nucleation and growth rates

The nucleation and growth rates are based on phenomenological laws which are usually determined experimentally. Following Mcleod (2007), we used the birth rate

$$B(c_\alpha, c_\beta, T) = k_b \exp\left(-\frac{B_0}{(T+273.15)^3 \ln^2\left(\frac{c_\alpha}{c_{\alpha,\text{sat}}(c_\beta, T)}\right)}\right) \quad (2.31)$$

for  $c_\alpha > c_{\alpha,\text{sat}}$ , while  $B(c_\alpha, c_\beta, T) = 0$  for  $c_\alpha \leq c_{\alpha,\text{sat}}(c_\beta, T)$ . Constant  $k_b$  given in Table 3 determines the unit of  $B$ , while the unit of  $B_0$  is  $^\circ\text{C}$  (Mimouni, 2007; Mimouni A. *et al.*, 2009).

Similarly, the growth rate was based on Mcleod (2007) and chosen as

$$G(c_\alpha, c_\beta, T) = k_g (c_\alpha - c_{\alpha,\text{sat}}(c_\beta, T)),$$

with unit determined by the unit of the growth coefficient  $k_g$  in  $m \cdot s^{-1}$ . As we can see,  $c_\alpha > c_{\alpha,\text{sat}}$  leads to  $G > 0$ , in which case crystals grow, while  $c_\alpha < c_{\alpha,\text{sat}}$  means crystals shrink.

## 3. Main result

In this section we present our main result, the global existence and uniqueness theorem. The complete model for which this will be proved includes the population balance equation (2.1), coupled with the mass balances equations (2.7), (2.11), (2.12), (2.14), and the energy balance (2.27). The initial condition for the population balance is  $n(L, 0) = n_0(L)$ , while the initial conditions of the mass balances (2.7),

|               |                             |                                       |
|---------------|-----------------------------|---------------------------------------|
| $n(L, t)$     | number / m · m <sup>3</sup> | particle size distribution            |
| $m_\alpha(t)$ | kg                          | mass of $\alpha$ -lactose in solution |
| $m_\beta(t)$  | kg                          | mass of $\beta$ -lactose in solution  |
| $V(t)$        | m <sup>3</sup>              | volume of slurry                      |
| $A(t)$        | m <sup>2</sup>              | contact surface                       |

Table 2. Units of dynamic quantities

(2.11), (2.12), (2.14), and the energy balance (2.27) are given by the expressions (2.8), (2.21), (2.23), (2.24) and (2.26).

Let us next present the hypotheses under which global existence of a solution will be shown. These are motivated by the physics of the process, leading to prior bounds on mass, volume, and temperature. A detailed discussion of these hypotheses will be given in the prior estimate section 5.

- Restriction of the total volume of slurry by way of a control constraint limiting the cumulative feed rate via

$$(H_1) \quad \int_0^t q_{\text{H}_2\text{O}}(\tau) d\tau \leq \frac{1}{(c_{\alpha,0} + c_{\beta,0} + 1)} \left[ \frac{V_{\max} - V_0}{\rho_\alpha^{-1} + \rho_\beta^{-1} + \rho_{\text{H}_2\text{O}}^{-1} + \rho_{\text{cry}}^{-1}} \right];$$

- An allowed range for the set-point temperature, corresponding to a control constraint

$$(H_2) \quad \underline{T} \leq T_{\text{sp}}(t) \leq \bar{T} \quad \text{for } t \geq 0;$$

- An assumption about the initial mixture of water and lactose in the crystallizer

$$(H_3) \quad 0 < m_\alpha(0) + m_\beta(0) < \left( \frac{M_{\text{cry}}}{M_\alpha} - 1 \right)^{-1} m_{\text{H}_2\text{O}}(0);$$

- Moreover, mathematically motivated hypotheses on the breakage terms  $a$  and  $b$ :

$$(H_4) \quad \|a\|_\infty := \max_{0 \leq L < \infty} a(L) < +\infty, \quad \|a\|_L = \sup_{0 \leq L < L'} \left| \frac{a(L) - a(L')}{L - L'} \right| < \infty,$$

$$(H_5) \quad \|b\|_\infty := \max_{0 \leq L \leq L'} b(L', L) < +\infty, \quad \|b\|_L := \sup_{L \geq 0} \sup_{L \leq L' < L''} \left| \frac{b(L, L') - b(L, L'')}{L' - L''} \right| < \infty,$$

$$(H_6) \quad \int_0^{L'} \beta(L', L) L^3 dL \leq c L'^3 \quad \text{for some } c > 0.$$

A typical example of  $a$  and  $b$  satisfying these hypotheses are for instance

$$a(L) = 1, \quad b(L, L') = \begin{cases} \frac{6L^2}{L'^3} & \text{if } L \geq L' \\ 0 & \text{else} \end{cases}$$

proposed in Marchisio *et al.*. Other typical breakage rate and daughter distributions based on experiments may for instance be found in Marchisio *et al.* (Marchisio *et al.*, 2002), Reynolds *et al.* (Reynolds *et al.*, 2005), or Ziff and McGrady (Ziff, 1985).

| quantity                              | symbol                      | value                | unit                         |
|---------------------------------------|-----------------------------|----------------------|------------------------------|
| maximum volume                        | $V_{\max}$                  | 0.01                 | $m^3$                        |
| initial volume                        | $V_0$                       | 0.0015               | $m^3$                        |
| crystal density                       | $\rho_{\text{cry}}$         | 1545                 | $kg \cdot m^{-3}$            |
| $\alpha$ -lactose density             | $\rho_{\text{lac},\alpha}$  | 1545                 | $kg \cdot m^{-3}$            |
| $\beta$ -lactose density              | $\rho_{\text{lac},\beta}$   | 1590                 | $kg \cdot m^{-3}$            |
| water density                         | $\rho_{\text{H}_2\text{O}}$ | 1000                 | $kg \cdot m^{-3}$            |
| volumic shape factor                  | $k_v$                       | 0.523598             | –                            |
| ratio of molar masses                 | $R$                         | 1.0525               | –                            |
| universal gas constant                | $R_g$                       | 8.314                | $J/K/mol$                    |
| birth rate coefficient                | $k_b$                       | $10^{10}$            | $number \cdot m^{-3} s^{-1}$ |
| nucleation constant                   | $B_0$                       | $1.4687^8$           | –                            |
| nucleation exponent                   | $b$                         | 2                    | –                            |
| growth rate coefficient               | $k_g$                       | $1.18 \cdot 10^{-7}$ | $m \cdot s^{-1}$             |
| growth exponent                       | $g$                         | 1                    | –                            |
| activation energy                     | $E_a$                       | $7.4 \cdot 10^4$     | $J$                          |
| kinetic mutarotation constant         | $k_0$                       | $2.25 \cdot 10^8$    | $s^{-1}$                     |
| heat of crystallization               | $\Delta H$                  | -43.1                | $kJ/kg$                      |
| heat transfer coefficient             | $U$                         | 300                  | $W/m^2/K$                    |
| heat capacity of water                | $C_{\text{H}_2\text{O}}^p$  | 4180.5               | $J/kg/K$                     |
| heat capacity of $\alpha$ -crystal    | $C_{\text{cry}}^p$          | 1251                 | $J/kg/K$                     |
| heat capacity of $\alpha$ -lactose    | $C_{\alpha}^p$              | 1193                 | $J/kg/K$                     |
| heat capacity of $\beta$ -lactose     | $C_{\beta}^p$               | 1193                 | $J/kg/K$                     |
| fraction of $\alpha$ -lactose in feed | $c_{\alpha}^+$              | 0.521                | $kg/kg$ water                |
| fraction of $\beta$ -lactose in feed  | $c_{\beta}^+$               | 0.359                | $kg/kg$ water                |
| mass of seed                          | $m_{\text{cry},0}$          | 0.1                  | $kg$                         |
| reference temperature                 | $T_{\text{ref}}$            | 25                   | $^{\circ}C$                  |
| feed temperature                      | $T_{\text{feed}}$           | 20                   | $^{\circ}C$                  |
| identified jacket heat coefficient    | $a$                         | 0.0019               | –                            |

Table 3. Numerical constants of industrial crystallizer

Let us now outline the idea of proof of our main result, which uses the method of characteristics with a fixed point argument for an operator  $\mathcal{Q}$ , which will act as a contraction with respect to a specific metric. This operator  $\mathcal{Q}$  is defined by:

$$\mathcal{Q}\mathbf{x} = \tilde{\mathbf{x}} = (\tilde{m}_{\alpha}, \tilde{m}_{\beta}, \tilde{m}_{\text{H}_2\text{O}}, \tilde{m}_{\text{cry}}, \tilde{T}, \tilde{\mu}_2, \tilde{\mu}_1, \tilde{\mu}_0, \tilde{w}).$$

where  $\mathbf{x} = (m_{\alpha}, m_{\beta}, m_{\text{H}_2\text{O}}, T, m_{\text{cry}}, \mu_2, \mu_1, \mu_0, w)$  is an element of the space

$$\mathbf{F} = C[0, t_f]^8 \times C(\mathbb{R}^+ \times [0, t_f]) \cap \mathcal{L}_u^1(\mathbb{R}^+ \times [0, t_f], h(L)dL),$$

where the elements of  $\tilde{\mathbf{x}}$  are defined by way of the characteristics which will be detailed in the section introducing characteristics. The space  $\mathbf{F}$  and the operator  $\mathcal{Q}$  will be detailed in the section global existence and uniqueness. The expressions of the elements of  $\mathbf{x}$  and  $\tilde{\mathbf{x}}$  will be given in section 6. Now our main result, whose proof we will be completed in section 6, is the following

| quantity  | symbol                              | unit                         |
|---|-------------------------------------|------------------------------|
| mutarotation exchange fraction                          | $k_m(T)$                            | –                            |
| mutarotation $\alpha \rightarrow \beta$ exchange rate   | $k_1(T)$                            | $s^{-1}$                     |
| mutarotation $\beta \rightarrow \alpha$ exchange rate   | $k_2(T)$                            | $s^{-1}$                     |
| saturation concentration at equilibrium of mutarotation | $c_{\alpha,\text{sat,eq}}(T)$       | –                            |
| saturation concentration                                | $c_{\alpha,\text{sat}}(c_\beta, T)$ | –                            |
| crystal growth rate                                     | $G(c_\alpha, c_\beta, T)$           | $ms^{-1}$                    |
| crystal birth rate                                      | $B(c_\alpha, c_\beta, T)$           | $number \cdot m^{-3} s^{-1}$ |

Table 4. Quantities depending on temperature

**THEOREM 3.1** Let hypotheses  $(H_1)$ - $(H_3)$  be satisfied, and suppose the initial condition of the crystallizer respects the global volume bound  $V_{\max}$ . Assume further that the breakage kernel satisfies the hypotheses  $(H_4)$ - $(H_6)$ . Then the crystallizer system (2.1), (2.11), (2.13), (2.15), (2.27) has a unique global solution on  $[0, \infty)$ .

#### 4. Introducing characteristics

In this chapter we present a transformation of the formulation of the model by introducing the moments and the characteristic curves.

##### 4.1 Moments

We consider the population balance equation

$$\frac{\partial (V(t)n(L,t))}{\partial t} = -G(c_\alpha(t), c_\beta(t), T(t)) \frac{\partial V(t)n(L,t)}{\partial L} - a(L)V(t)n(L,t) + w(L,t) \quad (4.1)$$

where

$$w(L,t) = \int_L^\infty a(L')b(L',L)V(t)n(L',t) dL' \quad (4.2)$$

is the source term due to breakage and attrition. The boundary condition is

$$n(0,t) = \frac{B(c_\alpha(t), c_\beta(t), T(t))}{G(c_\alpha(t), c_\beta(t), T(t))}, \quad t \geq 0 \quad (4.3)$$

and the initial condition is

$$n(L,0) = n_0(L), \quad L \in [0, \infty). \quad (4.4)$$

Then we can define

$$w_0 = w(L,0) = \int_L^\infty a(L')b(L',L)V(0)n_0(L') dL'. \quad (4.5)$$

Now, we consider the 3rd moment of  $w(\cdot, t)$ , for which we obtain the estimate

$$\begin{aligned} \int_0^\infty w(L,t)L^3 dL &= V(t) \int_0^\infty L^3 \int_L^\infty a(L')b(L',L)n(L',t) dL' dL \\ &= V(t) \int_0^\infty a(L')n(L',t) \left( \int_0^{L'} L^3 b(L',L) dL \right) dL'. \end{aligned}$$

Under (2.6), and with  $a(\cdot) \in L^\infty$ , we now derive the estimate

$$\int_0^\infty w(L,t)L^3 dL \leq \|a\|_\infty \rho^{-1} k_v^{-1} m_{\text{cry}}(t),$$

where  $m_{\text{cry}}(t) = \rho k_v \int_0^\infty V(t)n(L,t)L^3 dL$  is the total crystal mass.

The population balance is coupled with the mass balance of  $\alpha$ -lactose, the mass balance of  $\beta$ -lactose and the energy balance equations.

We start by solving (2.11) with respect to  $m_{\text{H}_2\text{O}}(t)$ , (2.13) with respect to  $c_\alpha(t)$ , (2.15) with respect to  $c_\beta(t)$  and (2.27) with respect to  $T(t)$ , knowing that  $m_{\text{cry}}(t) = k_v \rho_{\text{cry}} \int_0^\infty V(t)n(L,t)L^3 dL$ . For the concentration  $c_\alpha$  the mass balance of  $\alpha$ -lactose gives

$$\begin{aligned} c_\alpha(t) = & \left[ c_{\alpha,0} + \int_0^t \left( k_2(T(\tau))c_\beta(\tau) + \frac{q_{\text{H}_2\text{O}}(\tau)c_{\alpha,0}}{m_{\text{H}_2\text{O}}(\tau)} - \frac{m'_{\text{cry}}(\tau)}{Rm_{\text{H}_2\text{O}}(\tau)} \right) e^{-\int_0^\tau \left( -k_1(T(s)) - \frac{q_{\text{H}_2\text{O}}(s)}{m_{\text{H}_2\text{O}}(s)} + \frac{(1-\frac{1}{R})m'_{\text{cry}}(s)}{m_{\text{H}_2\text{O}}(s)} \right) ds} d\tau \right] \\ & \times e^{\int_0^t \left( -k_1(T(\tau)) - \frac{q_{\text{H}_2\text{O}}(\tau)}{m_{\text{H}_2\text{O}}(\tau)} + \frac{(1-\frac{1}{R})m'_{\text{cry}}(\tau)}{m_{\text{H}_2\text{O}}(\tau)} \right) d\tau} \end{aligned} \quad (4.6)$$

using  $c_{\alpha,0} = c_\alpha(0)$ . Similarly, the mass balance of  $\beta$ -lactose in terms of the concentration  $c_\beta$  gives

$$\begin{aligned} c_\beta(t) = & \left[ c_{\beta,0} + \int_0^t \left( k_1(T(\tau))c_\alpha(\tau) + \frac{q_{\text{H}_2\text{O}}(\tau)}{m_{\text{H}_2\text{O}}(\tau)}c_{\beta,0} \right) e^{-\int_0^\tau \left( -k_2(T(s)) - \frac{q_{\text{H}_2\text{O}}(s)}{m_{\text{H}_2\text{O}}(s)} + \frac{(1-\frac{1}{R})m'_{\text{cry}}(s)}{m_{\text{H}_2\text{O}}(s)} \right) ds} d\tau \right] \\ & \times e^{\int_0^t \left( -k_2(T(\tau)) - \frac{q_{\text{H}_2\text{O}}(\tau)}{m_{\text{H}_2\text{O}}(\tau)} + \frac{(1-\frac{1}{R})m'_{\text{cry}}(\tau)}{m_{\text{H}_2\text{O}}(\tau)} \right) d\tau} \end{aligned} \quad (4.7)$$

using  $c_{\beta,0} = c_\beta(0)$ . Equivalently, we may solve directly for the masses to obtain

$$m_\alpha(t) = \left[ \int_0^t \left( k_2(T(\tau))m_\beta(\tau) - \frac{1}{R}m'_{\text{cry}}(\tau) + c_{\alpha,0}q_{\text{H}_2\text{O}}(\tau) \right) e^{\int_0^\tau k_1(T(s))ds} d\tau + m_{\alpha,0} \right] e^{\int_0^t -k_1(T(s))ds} \quad (4.8)$$

using  $m_\alpha = m_{\text{H}_2\text{O}}c_\alpha$  and  $m_\beta = m_{\text{H}_2\text{O}}c_\beta$ . By solving (2.15) with respect to  $m_\beta$  using variation of the constant, we obtain

$$m_\beta(t) = \left[ \int_0^t \left( k_1(T(\tau))m_\alpha(\tau) + c_{\beta,0}q_{\text{H}_2\text{O}}(\tau) \right) e^{\int_0^\tau k_2(T(s))ds} d\tau + m_{\beta,0} \right] e^{\int_0^t -k_2(T(s))ds}. \quad (4.9)$$

For the mass balance of solvent we have

$$m_{\text{H}_2\text{O}}(t) = \int_0^t \left[ -\left(1 - \frac{1}{R}\right)m'_{\text{cry}}(\tau) + q_{\text{H}_2\text{O}}(\tau) \right] d\tau + m_{\text{H}_2\text{O},0}, \quad (4.10)$$

where  $m_{\text{H}_2\text{O},0} = m_{\text{H}_2\text{O}}(0)$ . Finally, the energy balance is

$$\begin{aligned}
 T(t) = e^{\int_0^t (-P_1(\tau)P_2(\tau) - UA(\tau))d\tau} & \left[ T_0 + \int_0^t \left( P_1(\tau)(P_2(\tau)T_{\text{ref}} - \Delta H m'_{\text{cry}}(\tau) \right. \right. \\
 & \left. \left. + UA(\tau)T_{\text{jacket}}(\tau) + q_{\text{H}_2\text{O}}(\tau) \left( C_{\text{H}_2\text{O}}^p + C_{\alpha}^p c_{\alpha,0} + C_{\beta}^p c_{\beta,0} \right) (T_{\text{feed}} - T_{\text{ref}}) \right) \right. \\
 & \left. e^{-\int_0^{\tau} (-P_1(s)P_2(s) - UA(s))ds} d\tau \right], \tag{4.11}
 \end{aligned}$$

where  $T_0 = T(0)$  and  $m_{\alpha} = c_{\alpha} m_{\text{H}_2\text{O}}$ ,  $m_{\beta} = c_{\beta} m_{\text{H}_2\text{O}}$ . By using the third moment  $\mu_3(t) = \int_0^{\infty} V(t)n(L,t)L^3 dL$ , we have  $m_{\text{cry}}(t) = \rho k_v \mu_3(t)$  and  $m'_{\text{cry}}(t) = \rho k_v \mu'_3(t)$ .

#### 4.2 Characteristic curves

Now we are ready to introduce characteristic curves as follows (Evans, 2001). For  $t_0$  and  $L_0$  fixed we let  $\phi_{t_0,L_0}$  be the solution of the initial value problem

$$\phi'(t) = G(c_{\alpha}(t), c_{\beta}(t), T(t)), \quad \phi(t_0) = L_0. \tag{4.12}$$

Since the right hand side does not depend on  $L$ , we have explicitly

$$\phi_{t_0,L_0}(t) = L_0 + \int_{t_0}^t G(c_{\alpha}(\tau), c_{\beta}(\tau), T(\tau)) d\tau. \tag{4.13}$$

We write specifically  $z(t) := \phi_{0,0}(t)$ . Now we introduce a family of functions  $N_{t,L}$  which we use later to define  $V(t)n(L,t)$  via  $N_{t_0,L_0}(t) := V(t)n(\phi_{t_0,L_0}(t), t)$ . We let  $L = \phi_{t_0,L_0}(t)$ , then  $N_{t_0,L_0}$  satisfies

$$\begin{aligned}
 N'_{t_0,L_0}(t) &= \frac{\partial(V(t)n(L,t))}{\partial L} \phi'_{t_0,L_0}(t) + \frac{\partial(V(t)n(L,t))}{\partial t} \\
 &= \frac{\partial(V(t)n(L,t))}{\partial L} G(c_{\alpha}(t), c_{\beta}(t), T(t)) + \frac{\partial(V(t)n(L,t))}{\partial t}. \tag{4.14}
 \end{aligned}$$

Therefore (4.1) transforms into

$$N'_{t_0,L_0}(t) = -a(\phi_{t_0,L_0}(t))N_{t_0,L_0}(t) + w(\phi_{t_0,L_0}(t), t), \tag{4.15}$$

and we consequently use these ODEs to define the functions  $N_{t,L}$ . Integration of (4.15) gives

$$\begin{aligned}
 N_{t_0,L_0}(t) &= \left( N_{t_0,L_0}(t_0) + \int_{t_0}^t w(\phi_{t_0,L_0}(\tau), \tau) \exp \left\{ \int_{t_0}^{\tau} a(\phi_{t_0,L_0}(\sigma)) d\sigma \right\} d\tau \right) \\
 &\quad \times \exp \left\{ - \int_{t_0}^t a(\phi_{t_0,L_0}(\tau)) d\tau \right\}. \tag{4.16}
 \end{aligned}$$

We can exploit this for two possible situations, where  $N_{t_0,L_0}(t_0)$  can be given an appropriate value.

Before putting this to work, we will need two auxiliary functions  $\tau$  and  $\xi$ , which are easily defined using the characteristics. First we define  $\tau = \tau(t, L)$  implicitly by

$$\phi_{\tau,0}(t) = L, \text{ or equivalently, } \phi_{t,L}(\tau) = 0, \tag{4.17}$$

or again,

$$\int_{\tau(t,L)}^t G(c_\alpha(\sigma), c_\beta(\sigma), T(\sigma)) d\sigma = L. \quad (4.18)$$

Then we define  $\xi = \xi(t, L) = \phi_{t,L}(0)$ , which gives  $\xi = L + \int_t^0 G(c_\alpha(\tau), c_\beta(\tau), T(\tau)) d\tau$ . Using  $N_{t,L}$ , respectively (4.16), we can now define

$$V(t_0)n(L_0, t_0) = \begin{cases} \left( V(t_0) \frac{B(c_\alpha(\tau_0), c_\beta(\tau_0), T(\tau_0))}{G(c_\alpha(\tau_0), c_\beta(\tau_0), T(\tau_0))} + \int_{\tau_0}^{t_0} w(\phi_{\tau_0,0}(s), s) \exp \left\{ \int_{\tau_0}^s a(\phi_{\tau_0,0}(\sigma)) d\sigma \right\} ds \right) \\ \quad \times \exp \left( - \int_{\tau_0}^{t_0} a(\phi_{\tau_0,0}(s)) ds \right), \text{ if } L_0 < z(t_0) \\ \\ \left( V(t_0)n_0(\phi_{t_0,L_0}(0)) + \int_0^{t_0} w(\phi_{t_0,L_0}(s), s) \exp \left\{ \int_0^s a(\phi_{t_0,L_0}(\sigma)) d\sigma \right\} ds \right) \\ \quad \times \exp \left( - \int_0^{t_0} a(\phi_{t_0,L_0}(s)) ds \right), \text{ if } L_0 \geq z(t_0) \end{cases} \quad (4.19)$$

where  $\tau_0 = \tau(t_0, L_0)$  and  $t_0 \in [0, t_f]$ . The formula is justified as follows. Let  $t_0, L_0$  be such that  $L_0 < z(t_0) = \phi_{0,0}(t_0)$ . This is the case where  $\tau_0 = \tau(t_0, L_0) > 0$ . Here we consider equation (4.15) for  $N_{\tau_0,0}$  with initial value  $N_{\tau_0,0}(\tau_0) = V(\tau_0)n(\phi_{\tau_0,0}(\tau_0), \tau_0) = V(\tau_0)n(0, \tau_0) = V(\tau_0)B(c(\tau_0))/G(c(\tau_0))$ . This uses the fact that  $\phi_{\tau_0,0}(\tau_0) = 0$  according to the definition of  $\phi_{\tau,0}$ . Integration clearly gives the upper branch of (4.19).

Next consider  $t_0, L_0$  such that  $L_0 \geq z(t_0)$ . Then  $\tau_0 < 0$ , so that we do not want to use it as initial value. We therefore apply (4.15), (4.16) to  $N_{t_0,L_0}$ , now with initial time  $t = 0$ . Then we get

$$N_{t_0,L_0}(t_0) = \left( N_{t_0,L_0}(0) + \int_0^{t_0} w(\phi_{t_0,L_0}(s), s) \exp \left\{ \int_0^s a(\phi_{t_0,L_0}(\sigma)) d\sigma \right\} ds \right) \times \exp \left( - \int_0^{t_0} a(\phi_{t_0,L_0}(s)) ds \right). \quad (4.20)$$

Here  $N_{t_0,L_0}(0) = V(0)n(\phi_{t_0,L_0}(0), 0) = V(0)n_0(\phi_{t_0,L_0}(0))$ , so we get the lower branch of (4.19) all right. This justifies the formula and completes the definition of the characteristic curves and the representation of  $V(t)n(L, t)$  via the characteristics.

## 5. A priori estimates

In this section we discuss two hypotheses on the control inputs  $T_{sp}$  and  $q_{H_2O}$ , which lead to a priori estimates, under which later on global existence of a solution will be shown. These conditions are motivated by the physics of the process and lead to bounds on mass, volume, and temperature. Note that we do not get a priori estimates on surface, length and number of solids, which as we shall see presents a difficulty when proving global existence of solutions.



### 5.1 Hypothesis on total volume using the feed rate

The total mass of slurry  $M$  in the crystallizer is given by

$$M(t) = m_\alpha(t) + m_\beta(t) + m_{\text{H}_2\text{O}}(t) + m_{\text{cry}}(t), \quad (5.1)$$

hence  $M(0) = m_\alpha(0) + m_\beta(0) + m_{\text{H}_2\text{O}}(0) + m_{\text{cry}}(0)$ . The total volume of slurry  $V$  is

$$V(t) = V_\alpha(t) + V_\beta(t) + V_{\text{H}_2\text{O}}(t) + V_{\text{cry}}(t) = \frac{m_\alpha(t)}{\rho_\alpha} + \frac{m_\beta(t)}{\rho_\beta} + \frac{m_{\text{H}_2\text{O}}(t)}{\rho_{\text{H}_2\text{O}}} + \frac{m_{\text{cry}}(t)}{\rho_{\text{cry}}}. \quad (5.2)$$

Since we are only allowed a maximum volume  $V_{\max}$  of slurry in the crystallizer, we have to steer the process such that  $V(t) \leq V_{\max}$  at all times  $t$ . Naturally, this can be arranged by a suitable control of the feed rate, and this is expressed by hypothesis  $(H_1)$ :

LEMMA 5.1 Suppose the feed rate  $q_{\text{H}_2\text{O}}$  satisfies the constraint

$$(H_1) \quad \int_0^t q_{\text{H}_2\text{O}}(\tau) d\tau \leq \frac{1}{(c_{\alpha,0} + c_{\beta,0} + 1)} \left[ \frac{V_{\max} - V_0}{\rho_\alpha^{-1} + \rho_\beta^{-1} + \rho_{\text{H}_2\text{O}}^{-1} + \rho_{\text{cry}}^{-1}} \right] \quad (5.3)$$

at all times  $t \geq 0$ . Then the total volume of slurry  $V(t)$  satisfies  $V(t) \leq V_{\max}$ .

*Proof.* From (5.1) we obviously have

$$M'(t) = m'_\alpha(t) + m'_\beta(t) + m'_{\text{H}_2\text{O}}(t) + m'_{\text{cry}}(t). \quad (5.4)$$

Replacing  $m'_{\text{H}_2\text{O}}$ ,  $m'_\alpha$  and  $m'_\beta$  in (5.4) by their expressions (2.11), (2.12) and (2.14), we obtain

$$M'(t) = (c_{\alpha,0} + c_{\beta,0} + 1) q_{\text{H}_2\text{O}}(t) \quad (5.5)$$

which on integration gives

$$\int_0^t q_{\text{H}_2\text{O}}(\tau) d\tau = \frac{M(t) - M(0)}{c_{\alpha,0} + c_{\beta,0} + 1} \quad (5.6)$$

for every  $t > 0$ . Hence, using the hypothesis  $(H_1)$  and (5.6), we obtain

$$M(t) \leq \frac{V_{\max}}{\rho_\alpha^{-1} + \rho_\beta^{-1} + \rho_{\text{H}_2\text{O}}^{-1} + \rho_{\text{cry}}^{-1}}. \quad (5.7)$$

Using (5.1) and (5.2), this implies  $V(t) \leq V_{\max}$ .  $\square$

In a practical process,  $q_{\text{H}_2\text{O}}$  could be steered by feedback to avoid overflow of the crystallizer.

### 5.2 Hypothesis on set-point temperature

As we have seen, bounding the feed rate via  $(H_1)$  gives a bound on the total volume of slurry, and also on the total mass, namely

$$M(t) \leq M_{\max} = \frac{V_{\max}}{\rho_\alpha^{-1} + \rho_\beta^{-1} + \rho_{\text{H}_2\text{O}}^{-1} + \rho_{\text{cry}}^{-1}}. \quad (5.8)$$

Now we also need to propose a hypothesis concerning the regulation of temperature, where we specify a range

$$(H_2) \quad \underline{T} \leq T_{\text{sp}}(t) \leq \bar{T} \quad \text{for } t \geq 0 \quad (5.9)$$

for the set-point temperature. On the one hand this reflects obvious material constraints on the equipment, but more importantly, we have to assure that the regulated temperature of slurry  $T(t)$  stays in the range where  $\alpha$ -lactose crystallizes, i.e.,  $T \leq 90^\circ$ . We start by deducing a bound on the jacket temperature.

LEMMA 5.2 Suppose the set-point temperature satisfies  $(H_2)$ . Then the temperature of the jacket satisfies

$$T_{\text{low}} \leq T_{\text{jacket}}(t) \leq T_{\text{high}} \quad (5.10)$$

at all times  $t$ , where  $T_{\text{low}} = T_{\text{jacket}}(0) + \underline{T}$  and  $T_{\text{high}} = T_{\text{jacket}}(0) + \bar{T}$ .

*Proof.* Solving the energy balance (2.28) with respect to  $T(t)$  using variation of the constant gives

$$T_{\text{jacket}}(t) = \left[ \int_0^t a T_{\text{sp}}(\tau) e^{\int_0^\tau a ds} d\tau + T_{\text{jacket}}(0) \right] e^{-\int_0^t a ds}. \quad (5.11)$$

Hence, using the hypothesis  $(H_2)$  and (5.11), we obtain

$$e^{-at} T_{\text{jacket}}(0) + \underline{T} \leq T_{\text{jacket}}(t) \leq T_{\text{jacket}}(0) + \bar{T}$$

for  $t \geq 0$ , which proves the claim.  $\square$

LEMMA 5.3 Suppose the set-point temperature satisfies  $(H_2)$ , and the feed rate satisfies  $(H_1)$ . Then there exist bounds  $T_l, T_h$  such that the temperature of slurry satisfies  $T_l \leq T(t) \leq T_h$  at all times  $t \geq 0$ . In particular, it can be assured that  $T(t) \leq 90^\circ$ , so that only  $\alpha$ -lactose crystallizes.

*Proof.* Solving the energy balance (2.27) with respect to  $T(t)$  using variation of the constant, we obtain

$$\begin{aligned} T(t) &= \int_0^t P_1(\tau) \left[ (P_2(\tau) - \theta(\tau)) T_{\text{ref}} - \Delta H m'_{\text{cry}}(\tau) + UA(\tau) T_{\text{jacket}}(\tau) + \theta(\tau) T_{\text{feed}} \right] \\ &\quad \times e^{-\int_\tau^t (P_1(\tau) P_2(s) + UA(s)) ds} d\tau + T_0 e^{-\int_0^t (P_1(s) P_2(s) + UA(s)) ds}, \end{aligned} \quad (5.12)$$

where  $\theta(\tau) := q_{\text{H}_2\text{O}}(\tau) \left( C_{\text{H}_2\text{O}}^p + C_\alpha^p c_\alpha(0) + C_\beta^p c_\beta(0) \right)$  and  $P_1(t), P_2(t)$  are given by (2.29), (2.30). Substituting the expressions of  $m'_{\text{H}_2\text{O}}(t), m'_\alpha(t), m'_\beta(t)$  and  $m'_{\text{cry}}(t)$  in (2.30), we obtain

$$P_2(t) = \sigma m'_{\text{cry}}(t) + \theta(t) \quad (5.13)$$

where  $\sigma := C_{\text{cry}}^p - C_{\text{H}_2\text{O}}^p(1 - R^{-1}) - C_\alpha^p R^{-1} < 0$  and  $\theta(t)$  as above.

Since the temperature of the jacket satisfies  $T_{\text{low}} \leq T_{\text{jacket}}(t) \leq T_{\text{high}}$  by Lemma 5.3, we obtain now the bounds  $T_l, T_h$  on the temperature  $T(t)$ . Namely, using (5.1), hypothesis  $(H_1)$  and (5.7), we first obtain  $T_l(t) \leq T(t) \leq T_h(t)$ , where

$$T_l = \left[ (T_{\text{feed}} - T_{\text{ref}})(M_{\text{max}} - M_0) + T(0) + \underline{\xi} \sigma M_{\text{max}} \right] e^{-(M_{\text{max}} - M_0 + tUA_0)} + \underline{\xi} e^{-(M_{\text{max}} - M_0)} (1 - e^{-tUA_0})$$

with  $\underline{\xi} = \min\{T_{\text{ref}}, T_{\text{low}}\}$ , and

$$T_h = \left( \bar{\xi} M_{\text{max}} + T(0) \right) \frac{e^{-tP_0 \sigma M_{\text{max}}}}{UA_0} + \frac{A_{\text{max}}}{A_0}$$

with  $\bar{\xi} = \max\{T_{\text{ref}}, T_{\text{high}}\}$ ,  $P_0 = \left( C_{\text{H}_2\text{O}}^p + C_{\alpha}^p + C_{\beta}^p + C_{\text{cry}}^p \right)^{-1} M_{\text{max}}^{-1}$ . Here  $A_{\text{max}}$  is the maximal surface which corresponds to  $V_{\text{max}}$  and  $A_0$  is the surface which corresponds to  $V_0$ . Now the bounds are  $T_l = \min_{t \geq 0} T_l(t)$  and  $T_h = \max_{t \geq 0} T_h(t)$ . Since all the elements used to compute  $T_h$  can be computed, we can arrange  $T_h \leq 90^\circ$ .  $\square$

**COROLLARY 5.1** From the bounds  $T_l \leq T(t) \leq T_h$  we obtain bounds

$$k_i(T(t)) \leq \kappa \quad \text{for } i \in \{1, 2, m\} \quad \text{and } t \geq 0$$

on the mutarotation exchange rates.

*Proof.* By using the bounds  $T_l \leq T(t) \leq T_h$  and the expressions of mutarotation  $k_2(T) = k_0 \exp\left(-\frac{E_a}{R_g(T+273.15)}\right)$ ,  $k_m(T) = 1.64 - 0.0027T$  and  $k_1(T) = k_2(T)k_m(T)$ , we obtain

$$\begin{aligned} k_2(T) &\leq k_0 \exp\left(-\frac{E_a}{R_g(T_h + 273.15)}\right) := \bar{k}_2 \\ k_m(T) &\leq 1.64 - 0.0027T_l := \bar{k}_m \\ k_1(T) &\leq \bar{k}_2 \bar{k}_m := \bar{k}_1 \end{aligned}$$

Then for  $\kappa = \max\{\bar{k}_2, \bar{k}_m, \bar{k}_1\}$ , we deduce

$$k_i(T(t)) \leq \kappa \quad \text{for } i \in \{1, 2, m\} \quad \text{and } t \geq 0.$$

$\square$

**COROLLARY 5.2** From hypotheses  $(H_1)$  and  $(H_2)$  we obtain a bound  $G(c_\alpha(t), c_\beta(t), T(t)) \leq G_f$ ,  $t \geq 0$  on the growth rate.

*Proof.* By using the hypothesis  $(H_1)$ ,  $(H_2)$  and the relations  $m_\alpha(t) = c_\alpha(t)m_{\text{H}_2\text{O}}(t)$  and  $m_\beta(t) = c_\beta(t)m_{\text{H}_2\text{O}}(t)$ , we obtain  $m_{\text{cry}}(t) \leq M_{\text{max}}$ ,  $c_\alpha(t) \leq \frac{M_{\text{max}}}{m_{\text{H}_2\text{O}}(0)} := c_m$  and  $c_\beta(t) \leq \frac{M_{\text{max}}}{m_{\text{H}_2\text{O}}(0)} := c_m$  for all  $t \geq 0$ . Now using the bound  $T_h$  obtained in lemma 5.3, we can put  $c_s := c_{\alpha, \text{sat, eq}}(T_h) (1 + k_m(T_h)F(T_h))$ . Then  $G(c_\alpha, c_\beta, T) \leq G_f := k_g(c_m - c_s)$ .  $\square$

### 5.3 Hypothesis on mass of water using the feed rate

In this section we discuss a hypothesis which assures that the mass of water does not become too small and stays bounded away from 0. This has also to be assured either by control of the feed, or via the initial values by assuring that a sufficient quantity of water is present at  $t = 0$ . We start by observing that  $(H_3)$  may be written equivalently as

$$(H_3) \quad m_{\text{H}_2\text{O}}(0) > 0 \quad \text{and} \quad \theta := 1 - (R - 1)(c_{\alpha,0} + c_{\beta,0}) > 0,$$

where  $R$  is introduced in (2.9). Now we have the following

LEMMA 5.4 Suppose hypothesis  $(H_3)$  is satisfied. Then the mass of water in the slurry satisfies  $m_{\text{H}_2\text{O}}(t) \geq \theta m_{\text{H}_2\text{O}}(0) > 0$  for all  $t \geq 0$ .

*Proof.* By adding (2.12) and (2.14), we obtain

$$m'_{\text{cry}}(t) = -R \left[ m'_\alpha(t) + m'_\beta(t) \right] + R (c_{\alpha,0} + c_{\beta,0}) q_{\text{H}_2\text{O}}(t). \quad (5.14)$$

By substituting (5.14) in (2.11), we obtain

$$m'_{\text{H}_2\text{O}}(t) = (R-1) \left[ m'_\alpha(t) + m'_\beta(t) \right] + \theta q_{\text{H}_2\text{O}}(t), \quad (5.15)$$

where  $\theta = 1 - (R-1)(c_{\alpha,0} + c_{\beta,0})$ . By integrating (5.15), we obtain

$$\begin{aligned} m_{\text{H}_2\text{O}}(t) &= m_{\text{H}_2\text{O}}(0) - (R-1)(m_\alpha(0) + m_\beta(0)) + (R-1)(m_\alpha(t) + m_\beta(t)) + \theta \int_0^t q_{\text{H}_2\text{O}}(\tau) d\tau \\ &= \theta m_{\text{H}_2\text{O}}(0) + \theta \int_0^t q_{\text{H}_2\text{O}}(\tau) d\tau + (R-1)(m_\alpha(t) + m_\beta(t)) \end{aligned} \quad (5.16)$$

In the worst case all lactose molecules in the liquid phase may crystallize, so that

$$m_{\text{H}_2\text{O}}(t) \geq \theta \int_0^t q_{\text{H}_2\text{O}}(\tau) d\tau + \theta m_{\text{H}_2\text{O}}(0) \geq \theta m_{\text{H}_2\text{O}}(0) > 0. \quad (5.17)$$

□

REMARK 5.1 Hypothesis  $(H_3)$  assures that the water initially present in the crystallizer cannot be completely consumed through crystallization in finite time even in batch mode, where  $q = 0$ . This corresponds to an upper bound on the fraction of lactose:

$$m_{\text{lactose}} \leq \left( \frac{M_{\text{cry}}}{M_\alpha} - 1 \right)^{-1} m_{\text{H}_2\text{O}} = 19.04 m_{\text{H}_2\text{O}},$$

which using (2.25) leads to the temperature-dependent bound

$$m_\alpha \leq \frac{M_\alpha}{(M_{\text{cry}} - M_\alpha)(1 + k_m(T))} m_{\text{H}_2\text{O}} \quad (5.18)$$

at the equilibrium of mutarotation. This should be compared to the lower bound given by the supersaturation constraint, which at the equilibrium of mutarotation according to section 2.7 gives

$$m_\alpha \geq \frac{\theta_1 \exp(\theta_2 T)}{100(1 + k_m(T))} m_{\text{H}_2\text{O}}. \quad (5.19)$$

In (5.19) the solubility concentration ranges from  $c_\alpha = m_\alpha/m_{\text{H}_2\text{O}} = 0.0478$  at  $5^\circ\text{C}$  to  $c_\alpha = 0.5678$  at  $90^\circ\text{C}$ , while the upper bound (5.18) ranges from  $c_\alpha = 7.24$  at  $5^\circ\text{C}$  to  $c_\alpha = 7.9433$  at  $90^\circ\text{C}$ . Since crystallizers are operated in the range between solubility and supersolubility, which in the case of lactose is roughly twice the solubility concentration, cf. (Yee *et al.*, 2011, Fig. 1), concentrations  $c_\alpha > 1$  are highly unrealistic, so that the bound (5.18) is in no way restrictive.

## 6. Global existence and uniqueness of solutions

In this section we will assemble the results from the previous sections and prove global existence and uniqueness of solutions of the crystallizer model. We use the method of characteristics with a fixed-point argument for an operator  $\mathcal{Q}$  which we now define.

### 6.1 Setting up the operator

For the function  $w$  defined via (4.2) we introduce the Banach space

$$\mathbf{E} = C(\mathbb{R}^+ \times [0, t_f]) \cap \mathcal{L}_u^1(\mathbb{R}^+ \times [0, t_f], h(L)dL),$$

where we set  $h(L) = \max\{1, L^3\}$ . We introduce the norm on  $\mathbf{E}$  as

$$\|w\| = \|w\|_\infty + \sup_{0 \leq t \leq t_f} \int_0^\infty |w(L, t)| h(L) dL.$$

where the fact that in the second term a supremum over  $t \in [0, t_f]$  is formed is indicated by the index  $u$ , for uniform, in  $\mathcal{L}_u^1$ . Let us introduce the moments of the CSD as

$$\mu_i(t) = \int_0^\infty V(t)n(L, t)L^i dL, i = 0, 1, \dots, \quad (6.1)$$

so that  $m_{\text{cry}} = \rho k_v \mu_3$ . The initial conditions are then

$$\mu_{i,0} = \int_0^\infty V(0)n_0(L)L^i dL, i = 0, 1, \dots \quad (6.2)$$

We consider  $\mathbf{x} = (m_\alpha, m_\beta, m_{\text{H}_2\text{O}}, T, m_{\text{cry}}, \mu_2, \mu_1, \mu_0, w)$  an element of the space

$$\mathbf{F} = C[0, t_f]^8 \times \mathbf{E},$$

where each copy of  $C[0, t_f]$  is equipped with the supremum norm, so that the norm on  $\mathbf{F}$  is

$$\|\mathbf{x}\| = \|m_\alpha\|_\infty + \|m_\beta\|_\infty + \|m_{\text{H}_2\text{O}}\|_\infty + \|T\|_\infty + \|m_{\text{cry}}\|_\infty + \|\mu_2\|_\infty + \|\mu_1\|_\infty + \|\mu_0\|_\infty + \|w\|.$$

We proceed to define the action of the operator  $\mathcal{Q}$  on element  $\mathbf{x} \in \mathbf{F}$ , writing

$$\mathcal{Q}\mathbf{x} = \tilde{\mathbf{x}} = (\tilde{m}_\alpha, \tilde{m}_\beta, \tilde{m}_{\text{H}_2\text{O}}, \tilde{m}_{\text{cry}}, \tilde{T}, \tilde{\mu}_2, \tilde{\mu}_1, \tilde{\mu}_0, \tilde{w}).$$

The initial values at  $t = 0$  are

$$\mathbf{x}_0 = (m_{\alpha,0}, m_{\beta,0}, m_{\text{H}_2\text{O},0}, m_{\text{cry},0}, T_0, \mu_{2,0}, \mu_{1,0}, \mu_{0,0}, w_0),$$

all specified through table (5).

We define  $\tilde{m}_\alpha$  as the left hand side of (4.8), so that it is a function of the old elements  $T, m_{\text{cry}}$  in  $\mathbf{x}$  and the initial values  $\mathbf{x}(0) = \mathbf{x}_0$ . Similarly, we define  $\tilde{m}_\beta$  as the left hand side of formula (4.9). Note that we need the derivative  $m'_{\text{cry}}$  to define these elements, and that can be expressed by the second

| initial value              | expression |
|----------------------------|------------|
| $m_{\alpha,0}$             | (2.23)     |
| $m_{\beta,0}$              | (2.24)     |
| $m_{\text{H}_2\text{O},0}$ | (2.21)     |
| $T_0$                      | (2.26)     |
| $m_{\text{cry},0}$         | (2.8)      |
| $\mu_{i,0}$                | (6.2)      |
| $w_0$                      | (4.5)      |

Table 5. Expression of initial values

moment  $\mu_2$ , which is part of  $\mathbf{x}$ . In fact by substituting the population balance (4.1) in the expression  $m'_{\text{cry}}(t) = \rho k_v \int_0^\infty \frac{\partial(V(t)n(L,t))}{\partial t} L^3 dL$ , we obtain

$$\begin{aligned}
m'_{\text{cry}}(t) &= -\rho k_v \int_0^\infty \left[ G(c_\alpha(t), c_\beta(t), T(t)) \frac{\partial(V(t)n(L,t))}{\partial L} + a(L)V(t)n(L,t) - w(L,t) \right] L^3 dL \\
&= 3\rho k_v G(c_\alpha(t), c_\beta(t), T(t)) \int_0^\infty V(t)n(L,t)L^2 dL - \rho k_v \int_0^\infty a(L)V(t)n(L,t)L^3 dL \\
&\quad + \rho k_v \int_0^\infty w(L,t)L^3 dL \\
&= 3\rho k_v G(c_\alpha(t), c_\beta(t), T(t)) \mu_2(t) - \rho k_v \int_0^\infty a(L)V(t)n(L,t)L^3 dL \\
&\quad + \rho k_v \int_0^\infty w(L,t)L^3 dL.
\end{aligned} \tag{6.3}$$

The third step in the definition of  $\mathcal{Q}$  is to define  $\tilde{m}_{\text{H}_2\text{O}}$  as the left hand side of formula (4.10). The left hand side of (4.11) defines  $\tilde{T}$ , using the elements of  $\mathbf{x}$  and  $\mathbf{x}_0$  on the right. Note that due to the prior estimates we may consider  $T_{\text{jacket}}$  as an input.

In order to define the elements  $\tilde{w}$  and  $\tilde{m}_{\text{cry}}$ , we first have to introduce the characteristics  $\phi_{t,L}$  via formula (4.13), using the old elements  $\mathbf{x}$  on the right. Then we define the functions  $N_{t,L}$  via formula (4.16). We are now ready to define  $\tilde{m}_{\text{cry}}$  as

$$\begin{aligned}
\tilde{m}_{\text{cry}}(t) &= \rho k_v \int_0^\infty V(t)n(L,t)L^3 dL \\
&= \rho k_v \int_0^{z(t)} \left( \frac{V(\tau)B(c_\alpha(\tau), c_\beta(\tau), T(\tau))}{G(c_\alpha(\tau), c_\beta(\tau), T(\tau))} + \int_\tau^t w(\phi_{\tau,0}(s), s) \exp \left\{ \int_\tau^s a(\phi_{\tau,0}(\sigma)) d\sigma \right\} ds \right) \\
&\quad \times \exp \left( - \int_\tau^t a(\phi_{\tau,0}(s)) ds \right) L^3 dL \\
&\quad + \rho k_v \int_{z(t)}^\infty \left( V(0)n_0(\phi_{t,L}(0)) + \int_0^t w(\phi_{t,L}(s), s) \exp \left\{ \int_0^s a(\phi_{t,L}(\sigma)) d\sigma \right\} ds \right) \\
&\quad \times \exp \left( - \int_0^t a(\phi_{t,L}(s)) ds \right) L^3 dL.
\end{aligned} \tag{6.4}$$

In the first integral  $\int_0^{z(t)}$  we use the change of variables  $L \rightarrow \tau = \tau(t, L)$ . Then

$$[0, z(t)] \ni L \mapsto \tau(t, L) \in [0, t], \quad dL = G(c_\alpha(t), c_\beta(t), T(t)) d\tau.$$

In the second integral  $\int_{z(t)}^\infty$  we use the change of variables  $L \rightarrow \xi(t, L) := \phi_{t,L}(0)$ . Then

$$[z(t), \infty) \ni L \mapsto \xi \in [0, \infty), \quad dL = d\xi.$$

The inverse relation is  $L = \xi + \int_0^t G(c_\alpha(\sigma), c_\beta(\sigma), T(\sigma)) d\sigma = \xi + z(t)$ . From (6.4) we therefore obtain

$$\begin{aligned} \tilde{m}_{\text{cry}}(t) &= \rho k_v \int_0^t \left( V(\tau) B(c_\alpha(\tau), c_\beta(\tau), T(\tau)) + \int_\tau^t w(\phi_{\tau,0}(s), s) \exp \left\{ \int_\tau^s a(\phi_{\tau,0}(\sigma)) d\sigma \right\} ds \right) \\ &\quad \times \exp \left( - \int_\tau^t a(\phi_{\tau,0}(s)) ds \right) L(\tau)^3 d\tau \quad (6.5) \\ &+ \rho k_v \int_0^\infty \left( V(0) n_0(\xi) + \int_0^t w(\phi_{0,\xi}(s), s) \exp \left\{ \int_0^s a(\phi_{0,\xi}(\sigma)) d\sigma \right\} ds \right) \\ &\quad \times \exp \left( - \int_0^t a(\phi_{0,\xi}(s)) ds \right) L(\xi)^3 d\xi, \end{aligned}$$

where  $L(\tau) = \int_\tau^t G(c_\alpha(\sigma), c_\beta(\sigma), T(\sigma)) d\sigma$  and  $L(\xi) = \xi + \int_0^t G(c_\alpha(\sigma), c_\beta(\sigma), T(\sigma)) d\sigma$ , and where we use  $\phi_{t,L}(s) = \phi_{0,\xi}(s)$  in the second integral. For fixed  $t$  the functions  $L \mapsto \tau(t, L)$  and  $\tau \mapsto L(\tau)$  are inverses of each other, and similarly,  $L \leftrightarrow \xi$  are in one-to-one correspondence via the formula  $L = \xi + \int_0^t G(c_\alpha(\sigma), c_\beta(\sigma), T(\sigma)) d\sigma$ .

Similarly, continuing to define the operator  $\mathcal{Q}$ , we define the moments  $\tilde{\mu}_i$ ,  $i = 0, 1, 2$  within  $\tilde{\mathbf{x}}$  via

$$\tilde{\mu}_i(t) = \int_0^\infty V(t) n(L, t) L^i dL,$$

where we express the right hand side via characteristics and the elements of  $\mathbf{x}$  in much the same way as done for  $\tilde{m}_{\text{cry}}$ .

We also need to get back to the function  $\tilde{w}(L, t)$ . We introduce

$$\beta(L, L') = \begin{cases} a(L)b(L, L'), & \text{if } L \geq L' \\ 0, & \text{else} \end{cases}$$

then we can write

$$\tilde{w}(L', t) = \int_{L'}^\infty a(L)b(L, L')V(t)n(L, t)dL = \int_0^\infty \beta(L, L')V(t)n(L, t)dL,$$

which is essentially like the moment integral (6.5), the function  $L \mapsto L^i$  being replaced by  $\beta(L, L')$ .

Applying the same technique as in the case of (6.5), we obtain

$$\begin{aligned}
\tilde{w}(L', t) = & \int_0^t \left( V(\tau) \mathbf{B}(c_\alpha(\tau), c_\beta(\tau), T(\tau)) + \int_\tau^t w(\phi_{\tau,0}(s), s) \exp \left\{ \int_\tau^s a(\phi_{\tau,0}(\sigma)) d\sigma \right\} ds \right) \\
& \times \exp \left( - \int_\tau^t a(\phi_{\tau,0}(s)) ds \right) \beta(L(\tau), L') d\tau \quad (6.6) \\
& + \int_0^\infty \left( V(0) n_0(\xi) + \int_0^t w(\phi_{t,L}(s), s) \exp \left\{ \int_0^s a(\phi_{t,L}(\sigma)) d\sigma \right\} ds \right) \\
& \times \exp \left( - \int_0^t a(\phi_{t,L}(s)) ds \right) \beta(L(\xi), L') d\xi,
\end{aligned}$$

which expresses  $\tilde{w}$  in terms of  $w$  and the characteristics, hence by elements of  $\mathbf{x}$ . Here we use  $w \in \mathbf{E}$ , and it is routine to check that  $\tilde{w} \in \mathbf{E}$ , so that  $\tilde{\mathbf{x}} \in \mathbf{F}$ . This completes the definition of  $\mathcal{Q}$ .

We will also need the following hypotheses on the breakage terms  $a$  and  $b$ :

$$(H_4) \quad \|a\|_\infty := \max_{0 \leq L < \infty} a(L) < +\infty, \quad \|a\|_L = \sup_{0 \leq L < L'} \left| \frac{a(L) - a(L')}{L - L'} \right| < \infty,$$

$$(H_5) \quad \|b\|_\infty := \max_{0 \leq L \leq L'} b(L', L) < +\infty, \quad \|b\|_L := \sup_{L \geq 0} \sup_{L \leq L' < L''} \left| \frac{b(L, L') - b(L, L'')}{L' - L''} \right| < \infty,$$

and

$$(H_6) \quad \int_0^{L'} \beta(L', L) L^3 dL \leq c L'^3 \quad \text{for some } c > 0.$$

Note that  $(H_6)$  is in particular true if conservation of mass in breakage (2.6) is satisfied.

## 6.2 Setting up the space

We now have to define a closed subset  $\mathbf{X}$  of  $\mathbf{F}$  on which the operator  $\mathcal{Q}$  acts as a contraction with respect to the metric induced by the norm of  $\mathbf{F}$ . In other words, we need to assure  $\mathcal{Q}(\mathbf{X}) \subset \mathbf{X}$  and

$$|\mathcal{Q}\mathbf{x}^{(1)} - \mathcal{Q}\mathbf{x}^{(2)}| \leq \gamma |\mathbf{x}^{(1)} - \mathbf{x}^{(2)}|$$

for a constant  $0 < \gamma < 1$  and all  $\mathbf{x}^{(1)}, \mathbf{x}^{(2)} \in \mathbf{X}$ . This will be achieved by choosing  $t_f$  *small enough*, as usual, but in order to prove global existence, we will have to make a careful quantification of  $\gamma$  in terms of  $t_f$  and the initial values  $\mathbf{x}_0$ , because we wish to iterate the local existence argument.

We distinguish between globally bounded states and those for which no prior bound can be put forward. Due to our hypotheses  $(H_1)$ ,  $(H_2)$ ,  $(H_3)$  the masses  $m_\alpha, m_\beta, m_{\text{cry}}, m_{\text{H}_2\text{O}}$  and the temperature  $T$  are globally bounded, the bounds being given by formulas (5.8). We write

$$\mathbf{y} = (m_\alpha, m_\beta, m_{\text{H}_2\text{O}}, m_{\text{cry}}, T)$$

for the globally bounded states. On the other hand, it is not clear whether the moments  $\mu_2, \mu_1, \mu_0$  nor  $w$  are globally bounded, and whether such a bound can be obtained from the physical constraints. This is due to particle breakage, which may lead to an exceedingly large number of small particles, or *finest*. We write

$$\mathbf{z} = (\mu_0, \mu_1, \mu_2) \text{ and } w \in \mathbf{E}$$



for the unbounded state. Altogether

$$\mathbf{x} = (\mathbf{y}, \mathbf{z}, w) \in \mathbf{F}.$$

During the following we therefore assume that the initial data for the bounded states  $\mathbf{y}_0 = (m_{\text{cry},0}, m_{\text{H}_2\text{O},0}, m_{\alpha,0}, m_{\beta,0}, T_0)$  respect these global bounds, that is

$$m_{\alpha,0} + m_{\beta,0} + m_{\text{cry},0} + m_{\text{H}_2\text{O},0} < M_{\text{max}}, \quad (6.7)$$

$m_{\text{H}_2\text{O},0} > 0$ ,  $\theta := 1 - (R - 1)(c_{\alpha,0} + c_{\beta,0}) > 0$  and for the temperature

$$T_l < T(0) < T_h.$$

The hypotheses  $(H_1)$ ,  $(H_2)$ ,  $(H_3)$  on the controls  $q_{\text{H}_2\text{O}}$  and  $T_{\text{sp}}$  will then assure that on every interval of existence of a solution  $\mathbf{x}(t)$ , the bounded states  $\mathbf{y}(t)$  satisfy the same global bounds. We split the initial conditions into  $\mathbf{x}_0 = (\mathbf{y}_0, \mathbf{z}_0, w_0)$ , where  $\mathbf{y}_0$  is the bounded part,  $\mathbf{z}_0$ ,  $w_0$  that part which does not have a prior bound. The state  $\mathbf{x}(t)$  is split accordingly as  $\mathbf{x}(t) = (\mathbf{y}(t), \mathbf{z}(t), w(t))$ . Now define the moments of  $w(L, t)$  as

$$\mu_{w,i}(t) = \int_0^\infty w(L, t) L^i dL$$

and fix  $K > |\mathbf{z}_0| + |\mu_{w,0}(0)| + |\mu_{w,1}(0)| + |\mu_{w,2}(0)| + |\mu_{w,3}(0)|$ . Then we define the space  $\mathbf{X}$  as

$$\mathbf{X} = \left\{ \mathbf{x} \in \mathbf{F} : \mathbf{x}(0) = \mathbf{x}_0, \mathbf{x} = (\mathbf{y}, \mathbf{z}, w), |\mathbf{z}(t)| + \sum_{i=0}^3 |\mu_{w,i}(t)| \leq K \text{ for all } t \in [0, t_f] \right\}.$$

LEMMA 6.1 There exists a constant  $c > 0$  depending only on the global volume bound  $V_{\text{max}}$  such that for every  $\mathbf{y}_0$  satisfying (6.7), every  $\mathbf{z}_0, w_0$ , and every  $K > |\mathbf{z}_0| + \sum_{i=0}^3 |\mu_{w,i}(0)|$  the following is true: Suppose  $t_f > 0$  satisfies

$$0 < t_f < \left( K - |\mathbf{z}_0| - \sum_{i=0}^3 |\mu_{w,i}(0)| \right) / c. \quad (6.8)$$

Then  $\mathcal{Q}(\mathbf{X}) \subset \mathbf{X}$ .

*Proof.* Integrating over an interval  $[0, t_f]$  leads to estimates of the form

$$\tilde{\mathbf{z}}(t) = \mathbf{z}_0 + \int_0^t f(\mathbf{y}(\tau), \mathbf{z}(\tau), w(\tau)) d\tau \leq |\mathbf{z}_0| + (c + K)t_f, \text{ for all } 0 \leq t \leq t_f$$

where a global bound  $c$  for  $\mathbf{y}(t)$  is used on  $[0, t_f]$ , while the bounds  $|\mathbf{z}(t)| \leq K$ ,  $|\mu_{w,i}(t)| \leq K$  are used for the states  $\mathbf{z}, w$ . Then in order to assure  $|\tilde{\mathbf{z}}(t)| \leq K$ , we have but to force the condition

$$|\mathbf{z}_0| + c(1 + K)t_f \leq K,$$

which gives  $t_f \leq \frac{K - |\mathbf{z}_0|}{c(1 + K)} \leq \frac{K - |\mathbf{z}_0|}{c}$ . A similar argument applies to the moments  $\mu_{w,i}$  of  $w$ , and combining the two gives (6.8). For the state  $w$ , hypothesis  $(H_6)$  is used to prove  $|\mu_{w,i}(t)| \leq K$ .  $\square$

### 6.3 Proving $\gamma \in (0, 1)$

For the globally bounded states gathered in  $\mathbf{y}$  we obtain an estimate of the form

$$\|\tilde{\mathbf{y}}^{(1)} - \tilde{\mathbf{y}}^{(2)}\| \leq c_1 (1 + |\mathbf{z}_0| + K) t_f \|\mathbf{x}^{(1)} - \mathbf{x}^{(2)}\|$$

for a global constant  $c_1$  depending only on  $V_{\max}$ . For the state  $\mathbf{z} = (\mu_0, \mu_1, \mu_2)$  on the other hand we obtain an estimation of the form

$$\|\tilde{\mathbf{z}}^{(1)} - \tilde{\mathbf{z}}^{(2)}\| \leq c_2 \left( 1 + |\mathbf{z}_0| + \sum_{i=0}^3 |\mu_{w,i}(0)| + K \right) t_f \|\mathbf{x}^{(1)} - \mathbf{x}^{(2)}\|,$$

where  $c_2$  is another global constant. The Lipschitz constant now depends on the initial condition  $\mathbf{z}_0$ ,  $\mu_{w,i}(0)$ , for which no global bound is available. A similar estimate

$$\|\tilde{\mathbf{w}}^{(1)} - \tilde{\mathbf{w}}^{(2)}\| \leq c_3 \left( 1 + \|\mathbf{z}_0\| + \sum_{i=0}^3 |\mu_{w,i}(0)| + K \right) t_f \|\mathbf{x}^{(1)} - \mathbf{x}^{(2)}\|$$

is obtained for the terms involving  $w$ . Altogether, we have

**LEMMA 6.2** There exists a constant  $c$  depending only on  $V_{\max}$  such that for every initial condition  $\mathbf{y}_0$  satisfying (6.7), every initial  $\mathbf{z}_0, w_0$ , and every  $K$  with  $\|\mathbf{z}_0\| + \sum_{i=0}^3 |\mu_{w,i}(0)| < K$ , the operator  $\mathcal{Q}$  satisfies the following Lipschitz estimate on  $\mathbf{X}$ :

$$\|\mathcal{Q}\mathbf{x}^{(1)} - \mathcal{Q}\mathbf{x}^{(2)}\| \leq c \left( 1 + |\mathbf{z}_0| + \sum_{i=0}^3 |\mu_{w,i}(0)| + K \right) t_f \|\mathbf{x}^{(1)} - \mathbf{x}^{(2)}\|. \quad (6.9)$$

Condition (6.9) in tandem with (6.8) allows us now to apply the Banach contraction theorem to the operator  $\mathcal{Q}$ . Using this, we can prove the theorem 3.1.

### 6.4 Proof of Theorem 3.1

In this section, we present the proof of the theorem 3.1 of existence and uniqueness of solution.

*Proof.* 1) Suppose we choose  $K > |\mathbf{z}_0| + \sum_{i=0}^3 |\mu_{w,i}(0)|$ , then

$$t_f = \min \left\{ \frac{K - |\mathbf{z}_0| - \sum_{i=0}^3 |\mu_{w,i}(0)|}{c + K}, \frac{1}{2c(1 + |\mathbf{z}_0| + \sum_{i=0}^3 |\mu_{w,i}(0)| + K)} \right\} \quad (6.10)$$

assures that  $\mathcal{Q}$  is a self-map and a contraction on  $\mathbf{X}$ , so that a unique solution with the initial condition  $\mathbf{x}_0$  exists on  $[0, t_f]$ .

2) We will now have to iterate the process, and for that we shall change our notation. We write  $\mathbf{w}(t) = |\mathbf{z}(t)| + \sum_{i=0}^3 |\mu_{w,i}(t)|$ . We started the method at  $t_0 = 0$ . Putting  $\mathbf{w}_0 = \mathbf{w}(0)$ , we chose  $K = \mathbf{w}_0 + 1 > \mathbf{w}(0)$  in part 1) above, so that condition (6.10) re-written at  $t_f = t_1$  becomes

$$t_1 = \min \left\{ \frac{1}{c + \mathbf{w}_0 + 1}, \frac{1}{4c(1 + \mathbf{w}_0)} \right\}.$$

This gave a unique solution on  $[0, t_f] = [t_0, t_1]$ .

3) Since by construction of  $\mathbf{X}$  on  $[t_0, t_1] = [0, t_f]$  we have  $\mathbf{w}(t) \leq K$  for every  $t \in [t_0, t_1]$ , we get  $\mathbf{w}_1 \leq K = \mathbf{w}_0 + 1$ . In addition, the initial condition of the bounded states  $\mathbf{y}$  respects (6.7) and therefore the global bound related to  $V_{\max}$ , so that we will be able to continue to use the same global constant  $c$  in the next iteration. We now use  $\mathbf{x}(t_1)$  as the new initial condition at the new initial time  $t_1$  and repeat the same argument to the right of  $t_1$ . That requires choosing a new constant  $K > |\mathbf{z}(t_1)| + \sum_{i=0}^3 |\mu_{w,i}(t_1)| = \mathbf{w}(t_1) = \mathbf{w}_1$ . We choose again  $K = \mathbf{w}_1 + 1$ . Then the final time corresponding to  $t_f$ , which is now called  $t_2 - t_1$ , has to satisfy (6.10), which reads

$$t_2 - t_1 = \min \left\{ \frac{1}{c + \mathbf{w}_1 + 1}, \frac{1}{2c(1 + \mathbf{w}_1 + K)} \right\} \geq \min \left\{ \frac{1}{c + \mathbf{w}_0 + 2}, \frac{1}{4c(2 + \mathbf{w}_0)} \right\}.$$

By recursion we find that

$$t_n - t_{n-1} \geq \min \left\{ \frac{1}{c + \mathbf{w}_0 + n}, \frac{1}{4c(n + \mathbf{w}_0)} \right\},$$

so that for some constant  $c'$  depending only on  $V_{\max}$  and  $\mathbf{w}_0 = |\mathbf{z}_0| + \sum_{i=0}^3 |\mu_{w,i}(0)|$ ,

$$t_N = \sum_{n=1}^N t_n - t_{n-1} \geq c' \sum_{n=1}^N \frac{1}{n} \rightarrow \infty \quad (N \rightarrow \infty).$$

Since the solution can be continued from 0 to any  $t_N$ , this proves global existence and uniqueness.  $\square$

REMARK 6.1 An interesting consequence of the proof is that no global bound for the moments  $\mu_0, \mu_1, \mu_2$  is found from the physically meaningful assumptions of section 5. In particular, it cannot be excluded that despite the bounds on volume and mass a large number of exceedingly small crystals, called fines, may hinder the sustainable growth of larger solids. This phenomenon is really observed in practice. In continuous crystallizers it is therefore mandatory to employ a third control mechanism, the recycling of fines, in order to limit their impact on growth. In Apkarian *et al.* (2011) we have studied feedback control with recycling of fines.

## 7. Conclusion

We have presented and discussed a model of the process of crystallization of  $\alpha$ -lactose monohydrate. The model was validated mathematically by proving existence and uniqueness of global solutions under realistic conditions assuring bounds on mass, volume and temperature of slurry. We observed that no global bounds on crystal surface, length and number can be obtained, but the result shows that none of the states can grow infinitely in finite time.

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