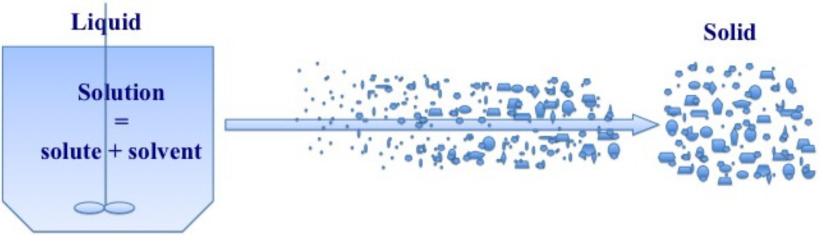
Population balance-based optimal control of a crystallization process

Amira Rachah - Dominikus Noll
Mathématiques pour l'Industrie et la Physique
Institut de Mathématiques de Toulouse

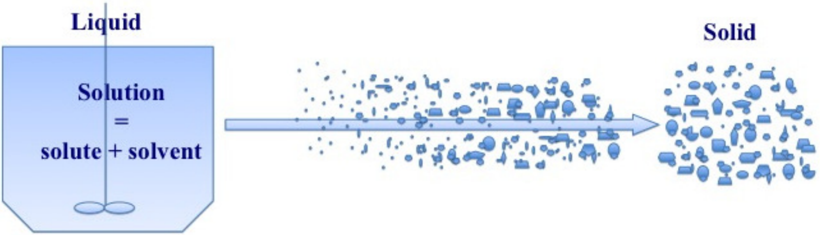
Journées SMAI-MODE 2016

March 25, 2016

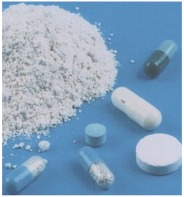
Crystallization process



Crystallization process

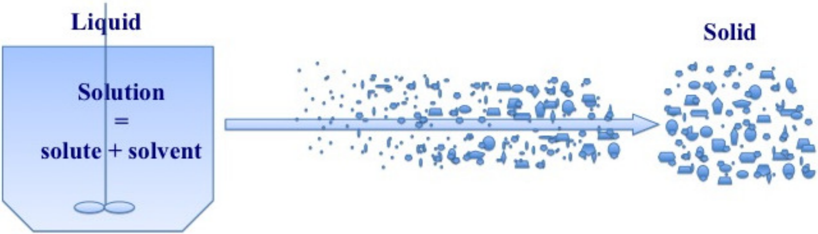


Product meets the set of specifications of the industry

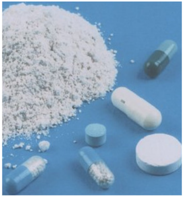


pharmaceutical

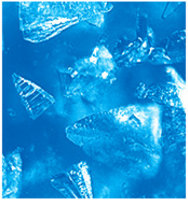
Crystallization process



Product meets the set of specifications of the industry

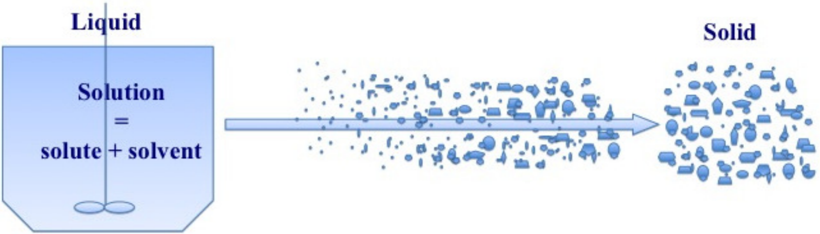


pharmaceutical

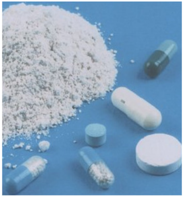


chemical

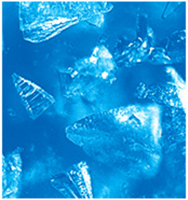
Crystallization process



Product meets the set of specifications of the industry



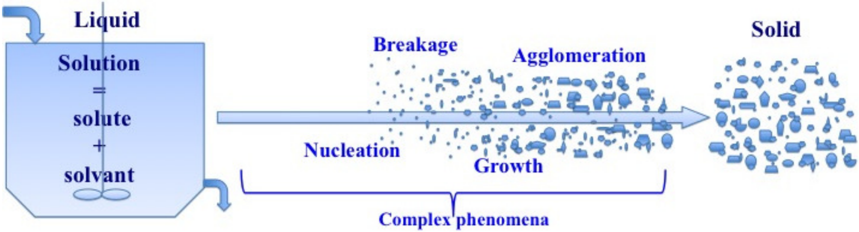
pharmaceutical



chemical

agri-food

Problem



- Complex phenomena during the crystallization
- Complex operating mode
- Difficulty in controlling the process

Aim of process : To meet product specifications

- Desired particle size distribution
- Fabrication of high quality materials
- Maximum yield

Study

Control of crystallization of α-lactose monohydrate most commonly used form of lactose (milk sugar) in seeded semi-batch mode

$\Rightarrow$ Product meets the set of specifications of the industry **LACTALIS**

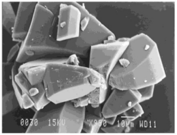
Study

Control of crystallization of α-lactose monohydrate most commonly used form of lactose (milk sugar) in seeded semi-batch mode

$\Rightarrow$ Product meets the set of specifications of the industry **LACTALIS**

Proprieties of α-lactose monohydrate

- Used as carrier and stabilizer of aromas and pharmaceutical products due to its bland flavor



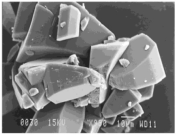
Study

Control of crystallization of α-lactose monohydrate most commonly used form of lactose (milk sugar) in seeded semi-batch mode

$\Rightarrow$ Product meets the set of specifications of the industry **LACTALIS**

Proprieties of α-lactose monohydrate

- Used as carrier and stabilizer of aromas and pharmaceutical products due to its bland flavor



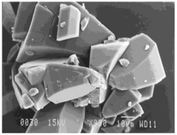
- Added to tablets and capsules as a filler, due to good physical properties and low price

Study

Control of crystallization of α-lactose monohydrate most commonly used form of lactose (milk sugar) in seeded semi-batch mode

$\Rightarrow$ Product meets the set of specifications of the industry **LACTALIS**

Proprieties of α-lactose monohydrate

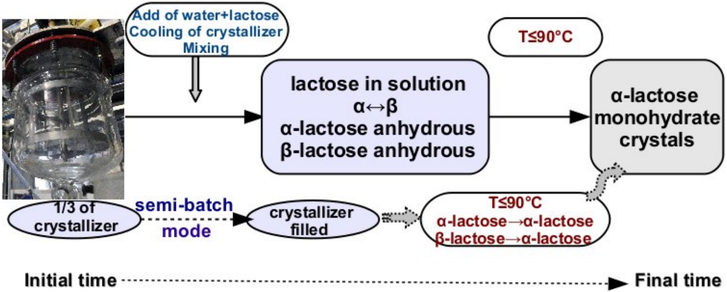


- Used as carrier and stabilizer of aromas and pharmaceutical products due to its bland flavor
- Added to tablets and capsules as a filler, due to good physical properties and low price
- Available as powder in different grades, depending on particle size distribution, density and flowability

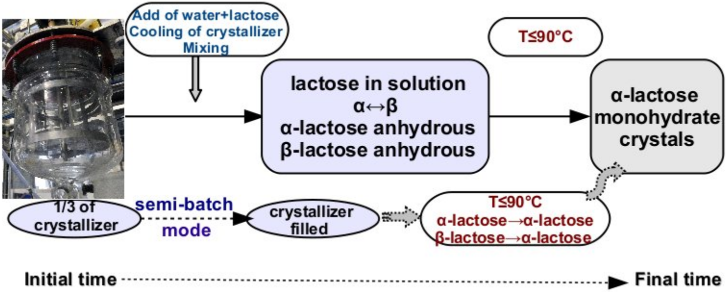
Outline

1. Mathematical modelling and process dynamics
2. Optimal control of the crystalization of α-lactose monohydrate
3. Conclusions

Crystallization of α-lactose monohydrate in semi-batch mode



Crystallization of α-lactose monohydrate in semi-batch mode



Mathematical model

- Mass balances : $m_{H_2O}(t)$, $m_\alpha(t)$, $m_\beta(t)$,
- Energy balances : $T(t)$, $T_{\text{jacket}}(t)$,
- Population balance : $n(L, t)$.

Mass balance of solvent (water)

- Water molecule integrated in α-lactose crystal : Loss due to crystallization
- Feed of solution during semi-batch phase.

$$\frac{dm_{\mathrm{H_2O}}(t)}{dt} = -\underbrace{\left(1-\frac{1}{R}\right)\frac{dm_{\mathrm{cry}}(t)}{dt}}_{\frac{dm_{\mathrm{H_2O\subset cry}}}{dt}} + q_{\mathrm{H_2O}}(t)$$

$$\frac{dm_{\mathrm{cry}}(t)}{dt} = 3k_v\rho_{\mathrm{cry}}G(C_\alpha(t), C_\beta(t), T(t))V(t)\int_0^\infty n(L,t)L^2 dL$$

$$C_\alpha = \frac{m_\alpha}{m_{\mathrm{H_2O}}}, \quad C_\beta = \frac{m_\beta}{m_{\mathrm{H_2O}}}$$

Mass balance of α-lactose in liquid phase

- Loss due to crystallization
- Loss due to mutarotation $\alpha \rightarrow \beta$
- Gain due to mutarotation $\beta \rightarrow \alpha$
- Gain through feed of solution in semi-batch phase
  $\dot{m}_{\alpha}^{+}(t) = q_{\mathrm{H_2O}}(t) C_{\alpha,0}$

$$\frac{dm_{\alpha}(t)}{dt} = -\frac{1}{R}\frac{dm_{\mathrm{cry}}(t)}{dt} + [-k_1(T(t))m_{\alpha}(t) + k_2(T(t))m_{\beta}(t)] + q_{\mathrm{H_2O}}(t) C_{\alpha,0}$$

$$m_{\alpha} = C_{\alpha} m_{\mathrm{H_2O}}, \quad m_{\beta} = C_{\beta} m_{\mathrm{H_2O}}$$

Mass balance of β-lactose

- Loss due to mutarotation $\beta \to \alpha$
- Gain due to mutarotation $\alpha \to \beta$
- Gain due to feed of solution in semi-batch phase $\dot{m}_\beta^+(t) = q_{\mathrm{H_2O}}(t) C_{\beta,0}$

$$\frac{dm_\beta(t)}{dt} = k_1(T(t))m_\alpha(t) - k_2(T(t))m_\beta(t) + q_{\mathrm{H_2O}}(t) C_{\beta,0}$$

Mass balance of β-lactose

- Loss due to mutarotation $\beta \to \alpha$
- Gain due to mutarotation $\alpha \to \beta$
- Gain due to feed of solution in semi-batch phase $\dot{m}_\beta^+(t) = q_{\mathrm{H_2O}}(t) C_{\beta,0}$

$$\frac{dm_\beta(t)}{dt} = k_1(T(t)) m_\alpha(t) - k_2(T(t)) m_\beta(t) + q_{\mathrm{H_2O}}(t) C_{\beta,0}$$

Total volume of slurry :

$$V(t) = \frac{m_\alpha(t)}{\rho_{\mathrm{lac},\alpha}} + \frac{m_\beta(t)}{\rho_{\mathrm{lac},\beta}} + \frac{m_{\mathrm{cry}}(t)}{\rho_{\mathrm{cry}}} + \frac{m_{\mathrm{H_2O}}(t)}{\rho_{\mathrm{H_2O}}}$$

Mass balance of β-lactose

- Loss due to mutarotation $\beta \to \alpha$
- Gain due to mutarotation $\alpha \to \beta$
- Gain due to feed of solution in semi-batch phase $\dot{m}_\beta^+(t) = q_{\mathrm{H_2O}}(t) C_{\beta,0}$

$$\frac{dm_\beta(t)}{dt} = k_1(T(t))m_\alpha(t) - k_2(T(t))m_\beta(t) + q_{\mathrm{H_2O}}(t)C_{\beta,0}$$

Total volume of slurry :

$$V(t) = \frac{m_\alpha(t)}{\rho_{\mathrm{lac},\alpha}} + \frac{m_\beta(t)}{\rho_{\mathrm{lac},\beta}} + \frac{m_{\mathrm{cry}}(t)}{\rho_{\mathrm{cry}}} + \frac{m_{\mathrm{H_2O}}(t)}{\rho_{\mathrm{H_2O}}}$$

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

Thermodynamic balance equation

- Heating and cooling : $T_{\mathrm{sp}}(t) \rightarrow T_{\mathrm{jacket}}(t) \rightarrow T(t)$ (identified from experimental data)
- Heat created by chemical reaction
- Heating or cooling due to temperature difference with feed

$$\frac{dT(t)}{dt} = P_1 \Big\{ - P_2(T(t) - T_{ref}) + UA(t)\,(T_{\mathrm{jacket}}(t) - T(t)) + q_{\mathrm{H_2O}}(t)\,(Cp_{\mathrm{H_2O}} + Cp_\alpha c_{\alpha,0} + Cp_\beta c_{\beta,0})\,(T_{\mathrm{H_2O}} - T_{\mathrm{ref}}) - \Delta H(T_{ref}) \frac{dm_{\mathrm{cry}}(t)}{dt} \Big\}$$

$$P_1 = \frac{1}{(m_{\mathrm{H_2O}}(t) Cp_{\mathrm{H_2O}} + m_\alpha(t) Cp_\alpha + m_\beta(t) Cp_\beta + m_{\mathrm{cry}}(t) Cp_{\mathrm{cry}})}$$

$$P_2 = \frac{dm_{\mathrm{H_2O}}(t)}{dt} Cp_{\mathrm{H_2O}} + \frac{dm_\alpha(t)}{dt} Cp_\alpha + \frac{dm_\beta(t)}{dt} Cp_\beta + \frac{dm_{\mathrm{cry}}(t)}{dt} Cp_{\mathrm{cry}}$$

Population balance equation

$$\underbrace{\frac{\partial\left(V(t)n(L,t)\right)}{\partial t}}_{\textit{accumulation}} + \underbrace{G\left(C_\alpha(t), C_\beta(t), T(t)\right)\frac{\partial\left(V(t)n(L,t)\right)}{\partial L}}_{\textit{growth}}$$

$$= \underbrace{-a(L)\,V(t)n(L,t) + \int_L^\infty a(L')b(L' \to L)\,V(t)n(L',t)\,dL'}_{\textit{breakage}}$$

$$n(L=0,t) = \frac{B\left(C_\alpha(t), C_\beta(t), T(t)\right)}{G\left(C_\alpha(t), C_\beta(t), T(t)\right)} \quad \text{Boundary condition}$$

$$n(L,t=0) = n_0(L) \quad \text{Initial condition (seed)}$$

$n(L,t)$ = crystal size distribution

$T(t)$ = crystallizer temperature

a, b = rates of breakage

$c_{\alpha/\beta}$ = concentration of α/β-lactose in solution

$V(t)$ = volume of slurry

G = growth rate

B = birth rate

$n_0(L)$ = *seed*

Moments

Moment μ_i of the crystal size distribution $n(L, t)$:

$$\mu_i(t) = \int_0^\infty n(L, t) L^i dL$$

For $i = 0$, $\mu_0 \sim$ number of crystals

Moments

Moment μ_i of the crystal size distribution $n(L, t)$:

$$\mu_i(t) = \int_0^\infty n(L, t) L^i dL$$

For $i = 0$, $\mu_0 \sim$ number of crystals

For $i = 1$, $\mu_1 \sim$ length of crystals

Moments

Moment μ_i of the crystal size distribution $n(L,t)$:

$$\mu_i(t) = \int_0^\infty n(L,t) L^i dL$$

For $i = 0$, $\mu_0 \sim$ number of crystals

For $i = 1$, $\mu_1 \sim$ length of crystals

For $i = 2$, $\mu_2 \sim$ surface of crystals

Moments

Moment μ_i of the crystal size distribution $n(L,t)$:

$$\mu_i(t) = \int_0^\infty n(L,t) L^i dL$$

For $i = 0$, $\mu_0 \sim$ number of crystals

For $i = 1$, $\mu_1 \sim$ length of crystals

For $i = 2$, $\mu_2 \sim$ surface of crystals

For $i = 3$, $\mu_3 \sim$ volume of crystals

Mathematical model

- Mass balances : $m_{\mathrm{H_2O}}(t)$, $m_\alpha(t)$, $m_\beta(t)$

$\hookrightarrow$ 3 ODE + integral = Integro-differential equations

Mathematical model

- Mass balances : $m_{\mathrm{H_2O}}(t)$, $m_\alpha(t)$, $m_\beta(t)$

$\hookrightarrow$ 3 ODE + integral = Integro-differential equations

- Energy balances : $T(t)$, $T_{\mathrm{jacket}}(t)$

$\hookrightarrow$ 2 ODE + integral = Integro-differential equations

Mathematical model

- Mass balances : $m_{\mathrm{H_2O}}(t)$, $m_\alpha(t)$, $m_\beta(t)$

$\hookrightarrow$ 3 ODE + integral = Integro-differential equations

- Energy balances : $T(t)$, $T_{\mathrm{jacket}}(t)$

$\hookrightarrow$ 2 ODE + integral = Integro-differential equations

- Population balance : $n(L, t)$ of particles of size L

$\hookrightarrow$ 1 PDE

Mathematical model

- Mass balances : $m_{\mathrm{H_2O}}(t)$, $m_\alpha(t)$, $m_\beta(t)$

$\hookrightarrow$ 3 ODE + integral = Integro-differential equations

- Energy balances : $T(t)$, $T_{\mathrm{jacket}}(t)$

$\hookrightarrow$ 2 ODE + integral = Integro-differential equations

- Population balance : $n(L, t)$ of particles of size L

$\hookrightarrow$ 1 PDE

Problem

Set of Integro-differential equations coupled + PDE + nonlinearity

Optimal control problem

By acting on the feed rate of solution $q_{\mathrm{H_2O}}(t)$, on the set-point temperature $T_{\mathrm{sp}}(t)$ and on the crystal seed $n_0(L)$ we wish to

1. **Specific criterion**
   steer the process in such a way that the growth of particles within the size range $130\mu m \leq L \leq 330\mu m$ is maximized.

2. **Non-specific criterion**
   minimize the weighted mean size diameter $d_{43} = \frac{\int_0^\infty n(L, t_f) L^4 dL}{\int_0^\infty n(L, t_f) L^3 dL}$

States :

$n(L,t)$, $c_\alpha(t)$, $c_\beta(t)$, $m_{\mathrm{H_2O}}(t)$, $T(t)$, $T_{\mathrm{jacket}}(t)$

Dependent states : $m_{\mathrm{cry}}(t)$, $V(t)$

States :

$n(L,t)$, $c_\alpha(t)$, $c_\beta(t)$, $m_{\mathrm{H_2O}}(t)$, $T(t)$, $T_{\mathrm{jacket}}(t)$

Dependent states : $m_{\mathrm{cry}}(t)$, $V(t)$

Controls :

$u_1(t) = T_{\mathrm{sp}}(t) =$ set-point temperature

$u_2(t) = q_{\mathrm{H_2O}}(t) =$ feed rate of solution

States :

$n(L,t)$, $c_\alpha(t)$, $c_\beta(t)$, $m_{\mathrm{H_2O}}(t)$, $T(t)$, $T_{\mathrm{jacket}}(t)$

Dependent states : $m_{\mathrm{cry}}(t)$, $V(t)$

Controls :

$u_1(t) = T_{\mathrm{sp}}(t) =$ set-point temperature

$u_2(t) = q_{\mathrm{H_2O}}(t) =$ feed rate of solution

Parameters :

$n_0(L) =$ crystals size distribution of seed of given mass

States :

$n(L,t),\ c_\alpha(t),\ c_\beta(t),\ m_{\mathrm{H_2O}}(t),\ T(t),\ T_{\mathrm{jacket}}(t)$

Dependent states : $m_{\mathrm{cry}}(t),\ V(t)$

Controls :

$u_1(t) = T_{\mathrm{sp}}(t) =$ set-point temperature

$u_2(t) = q_{\mathrm{H_2O}}(t) =$ feed rate of solution

Parameters :

$n_0(L) =$ crystals size distribution of seed of given mass

Cost function :

$$k_v \rho_{\mathrm{cry}} V(t_f) \int_{L_1}^{L_2} L^3 n(L,t_f)\,dL = \text{ crystal mass in interval } [L_1, L_2]$$

Use moment approach

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

Use moment approach

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

Population balance splits into

$$\frac{d\mu_i(t)}{dt} + \frac{V'(t)}{V(t)}\mu_i(t) - iG\left(c_\alpha(t), c_\beta(t), T(t)\right)\mu_{i-1}(t)) = 0, \quad i = 1, \dots, N$$

$$\frac{d\mu_0(t)}{dt} = \frac{V'(t)}{V(t)}\mu_0(t) - B\left(c_\alpha(t), c_\beta(t), T(t)\right) = 0$$

Parameters :

$p_i = \mu_i(0), i = 0, \dots, N$ moments of unknown seed

New set of states :
$\mu_0(t), \ldots, \mu_N(t), T(t), T_{\mathrm{jacket}}(t), c_\alpha(t), c_\beta(t), m_{\mathrm{H_2O}}(t)$

New set of states :
$\mu_0(t), \ldots, \mu_N(t), T(t), T_{\mathrm{jacket}}(t), c_\alpha(t), c_\beta(t), m_{\mathrm{H_2O}}(t)$

Controls :
$u_1(t) = T_{\mathrm{sp}}(t) =$ set-point temperature
$u_2(t) = q_{\mathrm{H_2O}}(t) =$ feed rate of solution

New set of states :
$\mu_0(t), \ldots, \mu_N(t)$, $T(t)$, $T_{\mathrm{jacket}}(t)$, $c_\alpha(t)$, $c_\beta(t)$, $m_{\mathrm{H_2O}}(t)$

Controls :
$u_1(t) = T_{\mathrm{sp}}(t) =$ set-point temperature
$u_2(t) = q_{\mathrm{H_2O}}(t) =$ feed rate of solution

Parameters :
Unknown moments of the unknown seed of known mass

New set of states :
$\mu_0(t), \ldots, \mu_N(t)$, $T(t)$, $T_{\mathrm{jacket}}(t)$, $c_\alpha(t)$, $c_\beta(t)$, $m_{\mathrm{H_2O}}(t)$

Controls :
$u_1(t) = T_{\mathrm{sp}}(t) =$ set-point temperature
$u_2(t) = q_{\mathrm{H_2O}}(t) =$ feed rate of solution

Parameters :
Unknown moments of the unknown seed of known mass

Cost function :
? ? ?

Procedure

- Choose target CSD $n_{\mathrm{target}}(L)$, which has its bulk of crystal mass in the range $[L_1, L_2]$.
- Normalize to unit mass and compute moments of target $\mu_{i,\mathrm{target}}$.

Obtain weighted least squares objective

$$\min \to \sum_{i=0}^{N} w_i \left(\mu_i(t_f) - \mu_{i,\mathrm{target}}\right)^2$$

- Pull moments of unknown $n(L, t_f)$ to moments of target such that third moment matches

$$\begin{aligned}
\text{minimize} \quad & \sum_{i=1}^{N} w_i \left(\mu_i(t_f) - \mu_{i,\text{target}}\right)^2 \\
\text{subject to} \quad & \text{population dynamics (moments)} \\
& \text{mass balances} \\
& \text{energy balance} \\
& \text{initial conditions} \\
& V_0 \leq V(t) \leq V_{\max} \\
& 0 \leq T(t) \leq 70^\circ\mathrm{C} \\
& 0 \leq p \leq P_{\max} \\
& \text{supersaturation}
\end{aligned}$$

Model : PDE+ODEs
Cost function :
$$k_v \rho_{\mathrm{cry}} V(t_f) \int_{L_1}^{L_2} L^3 n(L, t_f) dL$$
Controls : $T_{\mathrm{cnsg}}(t)$, $q_{\mathrm{H_2O}}(t)$
Parameter : $n(L, t = 0)$

Model : PDE+ODEs

cost function :

$$k_v \rho_{\mathrm{cry}} V(t_f) \int_{L_1}^{L_2} L^3 n(L, t_f) dL$$

Controls : $T_{\mathrm{cnsg}}(t)$, $q_{\mathrm{H_2O}}(t)$

Parameters : $n(L, 0)$

Reduce model
(Moment approach)

$\Downarrow$

Model : ODEs

Cost function : min $\rightarrow$

$$\sum_{i=0}^{N} (\mu_i(t_f) - \mu_{i,\mathrm{target}})^2$$

Controls : $T_{\mathrm{cnsg}}(t)$, $q_{\mathrm{H_2O}}(t)$

Parameters : $\mu_i(0)$

Model : PDE+ODEs

Cost function :

$$k_v \rho_{\mathrm{cry}} V(t_f) \int_{L_1}^{L_2} L^3 n(L, t_f) dL$$

Controls : $T_{\mathrm{cnsg}}(t)$, $q_{\mathrm{H_2O}}(t)$

Parameters : $n(L, 0)$

Reduce model

(Moment approach)

$\Downarrow$

Model : ODEs

Cost function : min $\rightarrow$

$$\sum_{i=0}^{N} (\mu_i(t_f) - \mu_{i,\mathrm{target}})^2$$

Controls : $T_{\mathrm{cnsg}}(t)$, $q_{\mathrm{H_2O}}(t)$

Parameter : $\mu_i(0)$

Control

$\Rightarrow$

PSOPT, ACADO

Optimal control :

$T^*_{\mathrm{cnsg}}(t)$, $q^*_{\mathrm{H_2O}}(t)$

Optimal parameters :

$\mu_i(0)^*$

Model : PDE+ODEs

Cost function :

$$k_v \rho_{\mathrm{cry}} V(t_f) \int_{L_1}^{L_2} L^3 n(L, t_f) dL$$

Controls : $T_{\mathrm{cnsg}}(t)$, $q_{\mathrm{H_2O}}(t)$

Parameters : $n(L, 0)$

Reduce the model
(Moment approach)
$\Downarrow$

Model : ODEs

Cost function : min $\rightarrow$

$$\sum_{i=0}^{N} (\mu_i(t_f) - \mu_{i,\mathrm{target}})^2$$

Controls : $T_{\mathrm{cnsg}}(t)$, $q_{\mathrm{H_2O}}(t)$

Parameters : $\mu_i(0)$

Control
$\Rightarrow$
PSOPT, ACADO

Optimal controls :
$T^*_{\mathrm{cnsg}}(t)$, $q^*_{\mathrm{H_2O}}(t)$

Optimal parameters :
$\mu_i(0)^*$

Reconstruct
$\Uparrow$
MAXENT

Optimal controls :
$T^*_{\mathrm{cnsg}}(t)$, $q^*_{\mathrm{H_2O}}(t)$

Optimal parameters :
$n(L, 0)^*$

Simulate
$\Leftarrow$

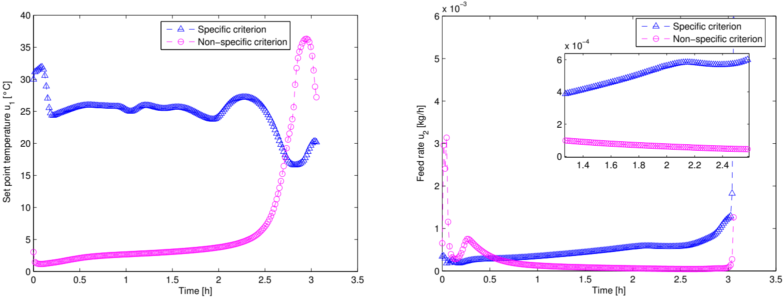
Numerical resolution

- ACADO : software environment and algorithm collection for automatic control and dynamic optimization.
  - http ://www.acadotoolkit.org
- PSOPT :
  - http ://www.psopt.org/Home

Method of reconstruction of distribution : **Maximum entropy**

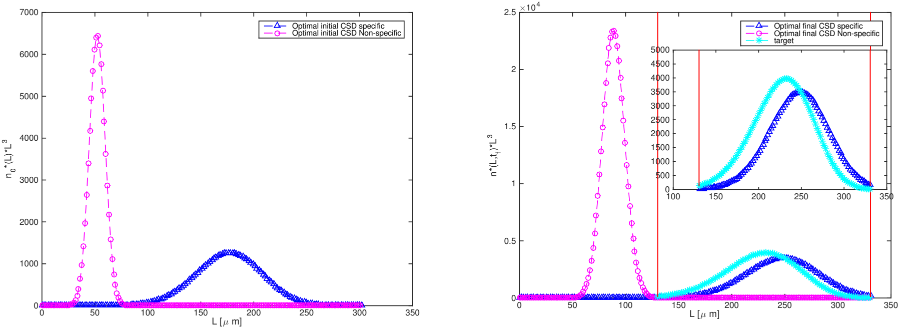
$$(P)\quad \begin{array}{ll} \text{maximize} & S[p] = -\int_0^\infty p(x)\ln p(x)dx \\ \text{subject to} & \int_0^\infty p(x)x^i dx = \mu_i, i = 0, \dots, N \end{array}$$

Results



Optimal regulation of set-point temperature $u_1^*(t) = T_{\mathrm{sp}}^*(t)$ (left) and optimal feed rate $u_2^*(t) = q_{\mathrm{H_2O}}^*(t)$ (right).

Results



Optimal initial seed $n_0^*(L)$ (left) and optimal final CSD $n^*(L, t_f)$ (right)

- Use of the moment approach to obtain a reduced model for control
- Optimal control techniques based on mathematical modelling were used to enhance product quality in solvated crystallization

- Use of the moment approach to obtain a reduced model for control
- Optimal control techniques based on mathematical modelling were used to enhance product quality in solvated crystallization
- The crystal mass of α-lactose monohydrate produced in a specific size range may be substantially increased over standard approaches if optimization is used

THANK you for your attention

:)