Batch crystallisation is an essential unit operation in the fine and specialty chemicals manufacturing industry. The process is extremely complex and difficult to control. The modelling of the process is often characterised by highly non-linear mathematical equations, which are difficult to solve. Owing to the complex nature of models and the process itself, most designs are based on heuristic rules. Optimisation of the process model is often extremely difficult. In this presentation, a comprehensive and general modelling and optimisation framework will be presented for batch and semi-batch crystallisation processes. In addition to mathematical programming tools, a graphical method will also be presented to give valuable insights into the process. The framework not only enables a comprehensive multivariable optimisation to be implemented, but also can be used for sensitivity analysis. The framework has been applied in the batch cooling crystallisation of Citric Acid-Water and Potassium Sulphate-Water systems. Results of the optimisation demonstrate the fallibility of using heuristic rules.
Outline

1. Introduction
2. Modelling of Crystallisation
3. Graphical Representation
4. Optimisation of Crystallisation Processes
5. Case study I
6. Case study II
7. Conclusions
8. Future work
1. Introduction
Why Crystallisation?

- Many chemical products are in the form of solid crystals
- Product of high degree of purity can be obtained e.g. Separation of optical isomers in the pharmaceutical industry
- Requires less energy compared with distillation
- Good separation method for systems which are heat sensitive
- Effective for close boiling compounds or/and high boiling point compounds
Modes of crystallisation

Here we shall concentrate on the most common crystallisation problem: **Solution Crystallisation**

Modes of solution crystallisation:

- Cooling crystallisation
- Evaporative crystallisation
- Dilution crystallisation
- Reactive crystallisation

Other less conventional types:

- Pressure crystallisation
- Reverse osmosis crystallisation
In continuous cooling crystallisation, as the temperature decreases, the state of the system changes from the unsaturated state A, through saturated state B, then to C, where spontaneous crystallisation begins and reaches the supersaturated state D. In continuous isothermal evaporative crystallisation, the solute concentration changes from A, through E, F, where spontaneous crystallisation begins and finally G. Operation of crystallisers normally avoids the labile region.
## Continuous vs Batch Crystallisation

<table>
<thead>
<tr>
<th>Continuous</th>
<th>Batch</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Not flexible</td>
<td>• Flexible</td>
</tr>
<tr>
<td>• High capital investment</td>
<td>• Low capital investment</td>
</tr>
<tr>
<td>• Intensive process development</td>
<td>• Less process development</td>
</tr>
<tr>
<td>• Good reproducibility</td>
<td>• Poor reproducibility</td>
</tr>
<tr>
<td>• Low labour cost</td>
<td>• High labour cost</td>
</tr>
</tbody>
</table>
Semi-batch Crystallisation

- Can be beneficial and superior to batch operation
- Can produce better crystal quality and more uniform crystal distribution

<table>
<thead>
<tr>
<th>Mode of crystallisation</th>
<th>Semi-batch operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooling</td>
<td>Continuous addition of solution</td>
</tr>
<tr>
<td>Dilution</td>
<td>Continuous addition of diluent</td>
</tr>
<tr>
<td>Reactive</td>
<td>Continuous addition of reactants</td>
</tr>
<tr>
<td>Evaporative</td>
<td>Continuous addition of solution</td>
</tr>
</tbody>
</table>

There have been few publications regarding semi – batch crystallisation. Semi-batch operation offers an additional control variable for optimisation. In the case of reactive crystallisation, the flow rate of the reactants offers another way of controlling the process. In some cases, semi – batch operation can offer significant advantages. In other cases, it might not.
2. Modelling of Crystallisation

2.1 Crystallisation Kinetics

2.2 Crystal Size Distribution
2.1 Crystallisation Kinetics
When a solvent contains more solids than it is able to dissolve, it is in a **supersaturated** condition

**Main driving force - supersaturation**

Three definitions:

i. $\Delta c = c - c^*$

ii. $S = c / c^*$

iii. $S' = (c - c^*) / c^*$

$c = \text{concentration of solute} \quad ; c^* = \text{solubility}$

There are three definitions for supersaturation. Here we shall use the first.
Primary homogeneous nucleation refers to the spontaneous nucleation in a homogeneous solution that is free of impurities and foreign particles. Primary heterogeneous nucleation is the primary nucleation that occurs in the presence of foreign particles and impurities in the solution. Secondary nucleation occurs when there are crystals of the same material present in the solution. This type of nucleation predominates in industrial applications. Crystal growth refers to the deposition of solid crystals on the existing crystal surface.
Primary Nucleation

\[ B_p = k_p \left( c - c^* \right)^p \]

- \( B_p \) = primary nucleation rate, no./(kg s)
- \( k_p \) = rate constant dependent on system properties, temperature, presence of impurities and hydrodynamics, no./(kg s (kg/kg)^p)
- \( p \) = constant, dependent on the mechanism of primary nucleation

There have been numerous attempts to describe the primary nucleation process on theoretical and thermodynamic grounds. Nevertheless, theoretical expressions for primary nucleation are complex and inconvenient to use in the industrial context. An empirical equation that is simpler has been used instead. For heterogeneous primary nucleation, the value of \( p \) is smaller than that for homogeneous primary nucleation.
Secondary Nucleation

\[ B_s = k_s \ N^k \ M_T^i \ (c - c^*)^s \]

- \( B_s \) = secondary nucleation rate, no./\((\text{kg s})\)
- \( k_s \) = rate constant, function of temperature, no./\((\text{kg s Hz}^k (\text{kg/kg})^{s+i})\)
- \( N \) = impeller / stirrer speed, Hz
- \( M_T \) = crystals concentration in suspension, kg/kg
- \( k, i, s \) = constants determined experimentally

This form of equation is a semi-empirical one. The exponent to which the supersaturation is raised is much smaller than that in primary nucleation. The presence of \( N \) and \( M_T \) in the expression is because the onset of secondary nucleation is associated with the collision between crystals, between crystals and the impeller, between crystals and the crystalliser wall. It is also associated with the fluid shear.
Crystal Growth

Can be measured as **Overall Linear Crystal Growth Rate, G**

\[ G = k_{gl} (c - c^*)^g \]

- \( k_{gl} \) = rate constant, function of temperature, crystal size and hydrodynamics, \( \text{m/(s (kg/kg)^g)} \)
- \( g \) = constant

The unit for \( G \) is length per unit time, e.g. \( \text{m/s, cm/min} \)

There have been numerous attempts to derive theoretical expression for crystal growth. Nevertheless, the derived equations are complex and tedious to be used for engineering design. For engineering purposes in crystalliser design, the simple empirical power-law relationships expressing the linear crystal growth rate has been used widely.
Seeding

• The addition of large amount of small crystals into a solution prior to the crystallisation process is called SEEDING

• Seeding can improve crystal quality

• It can be used to trigger nucleation initially

• The amount of seeds added and the seed size are normally determined through experience and trial and error
2.2 Crystal Size Distribution
Before the crystal size distribution in a batch crystalliser can be modelled, two essential assumptions have to be made. A well-mixed tank means the spatial variation of the crystal properties can be eliminated. This enables a time-variation only treatment to be applied on the model. If the distribution of the crystals can be adequately described by one property, this will reduce the complexity of the model.
The population balance equation is derived from the number balance of crystals. The derivation involves complex mathematical transformations and manipulations. Nevertheless, this equation has been regarded as the classical approach to model the crystal size distribution. The solution of the equation yields information regarding the crystal distribution with respect to both time and size.
Partial differential equations - Difficult to solve
Moment method is introduced

Moment of \( j \) with respect to \( L \):

\[
m_j = \int_{0}^{\infty} L^j n(L) dL
\]

In many systems of engineering interest, knowledge of the complete particle distribution is unnecessary. Rather, some average or total quantities are sufficient to represent the particle distribution. The moment measures the average properties of the crystal size distribution. The multivariable partial differential nature of the Population Balance Equation can be converted into a set of ordinary non-linear differential equations through the use of Moment Transformation.

Size independent growth:
\[ \frac{dm_j}{dt} = jGm_{j-1} + B^0L_0^j \]

Size dependent growth:
\[ \frac{dm_j}{dt} = jG_o(m_{j-1} + am_j) + B^0L_0^j \]

\[ m_i = j \text{ moment with respect to the size, no.m}/kg \]
\[ B^0 = \text{nucleation rate, no.}/(kg s) \]
\[ L_0 = \text{the size of the nuclei, m} \]
\[ a = \text{constant, m}^{-1} \]
Moments of crystal distribution

The first four moments* are associated with properties of the crystals

<table>
<thead>
<tr>
<th>Moment</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$m_0$</td>
<td>Total specific number of crystals, no./kg</td>
</tr>
<tr>
<td>$m_1$</td>
<td>Total specific length of crystals, no. m/kg</td>
</tr>
<tr>
<td>$\beta m_2$</td>
<td>Total specific surface area of crystals, no. m²/kg</td>
</tr>
<tr>
<td>$\alpha m_3$</td>
<td>Total specific volume of crystals, no. m³/kg</td>
</tr>
</tbody>
</table>

$\alpha, \beta$ = Shape factors of crystal

These moments can be used to measure:

1. Average crystal size
2. Coefficient of variation

---

* The moments are defined as:

$$m_0 = \langle N \rangle$$

$$m_1 = \langle L \rangle$$

$$m_2 = \langle S \rangle$$

$$m_3 = \langle V \rangle$$

Where $N$, $L$, $S$, and $V$ are the number of crystals, total length, total surface area, and total volume, respectively.
Modelling of crystallisation processes

- Kinetics
- Physical parameters

Integrate with respect to time:
1. Mass balance of solute
2. Moment equations

Moments

Average crystal size, coefficient of variation etc

Performance of crystalliser

The energy balance equation is not taken into account as the thermal effect due to the heat of crystallisation is usually negligible for normal solution crystallisation. In the event when the heat of crystallisation is significant, the energy balance can be incorporated into the model.
Objectives

- Maximising the mean crystal size
- Maximising the mean crystal size subject to specified coefficient of variation
- Minimising the coefficient of variation of the crystal size distribution
- Minimising the coefficient of variation of the crystal size distribution subject to specified mean crystal size
- Maximising the yield of crystal mass

This means:

Maximising the crystal growth rate, minimising the nucleation

Nucleation produces abundant amounts of small and irregular crystals. Those small crystals will increase the coefficient of variation and decrease the average crystal size. Small crystals provide more surface area for the adsorption of impurities onto the crystals. This in turn will reduce the purity of the crystals. Fine and small crystals also complicate the downstream separation processes such as filtration and drying.
3. Graphical Representation
Case study: Isothermal Reactive Crystallisation

Data extracted from Tavare and Garside (1990)
Objective: Minimising nucleated crystal number

Reaction kinetics

A + B → C  \[ r = k_i C_A C_B \]
C is the product of crystallisation

Crystallisation kinetics

Nucleation rate, \( B = k_b(c - c^*)^b \) (Primary Nucleation)
Crystal growth rate, \( G = k_g(c - c^*)^g \)

In reactive precipitation, the crystals that are produced are usually small. It is difficult for small crystals to cross the streamlines of the flow. This reduces the crystal collisions. Furthermore, secondary nucleation is thought to be insignificant in crystallisation of sparingly soluble substances. Most of the reactive precipitation studies tend to neglect secondary nucleation.
The batch trajectory is obtained by integrating the set of non-linear ordinary differential equations that include the mass balance of solute and the moments from $t = 0$ to $t = \text{batch time}$. The continuous trajectory is obtained by solving a set of non-linear algebraic equations for different values of residence times. The corresponding values of $N$ and $c$ are then plotted on the same graph.
Objective: Minimising nucleated number of crystals

Objective: Minimising nucleated number of crystals

Concentration of C, mol/kg solvent

<table>
<thead>
<tr>
<th>Concentration of C, mol/kg solvent</th>
<th>Crystals number, no/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td>0.2</td>
<td>2E+10</td>
</tr>
<tr>
<td>0.3</td>
<td>4E+10</td>
</tr>
<tr>
<td>0.4</td>
<td>6E+10</td>
</tr>
<tr>
<td>0.5</td>
<td>8E+10</td>
</tr>
<tr>
<td>0.6</td>
<td>1E+11</td>
</tr>
</tbody>
</table>

Solubility of C = 0.1 mol/kg solvent

Semi-batch operation region

Continuous

Batch

- Semi-batch and continuous modes reduce the crystal number
- Continuous mode seems best, but there are other issues to consider

Although continuous mode emerges the best mode for reducing the number of nucleated crystals in this case, there are other crucial factors to consider before deciding the appropriate mode of operation. If the production rate is small, batch mode is inevitably the suitable mode of operation. Corrosivity and toxicity of the products and operation also necessitate a batch treatment.
There are various types of semi-batch operation. Shown in the diagram is the mode of operation considered in this case study. A and B are added continuously according to various profiles for a fixed period of time after which the addition stops and the system will remain in the batch mode until the batch time is reached. Various semi-batch trajectories with different reactant feeding profiles should remain in the region bounded by batch and continuous trajectories.
Results by Tavare and Garside (1990) verify the approach:
- It is beneficial to operate in semi-batch mode (relative to batch)
- The semi-batch trajectories are confined between those of batch and continuous

In the simulations carried out by Tavare and Garside (1990), the total batch time for each semi-batch trajectory is fixed to be 10000s whereas the reactant addition time is fixed to be 6000s. The main motive of having a time span between the addition time and the final batch time is to let the reaction and crystallisation processes reach a satisfactory yield and conversion.
Advantages of Graphical Approach

- Graphical presentation
- Provides conceptual insights

Limitations of Graphical Approach

- Due to the graphical nature, insights are limited to two variables
- In our example, more than two variables are needed for analysis if the system:
  - is non-isothermal
  - has significant secondary nucleation occurring

A more general tool is needed!
4. Optimisation of Crystallisation Processes
Modelling of crystallisation

The moment equations are modelled as series of reactions

\[
\frac{d m_j}{dt} = jGm_{j-1} + B^0L_0^j
\]

A $\rightarrow$ m$_j$

A is a hypothetical reactant, m$_j$ is the product

The rate of reaction, \( r_{mj} = \frac{d m_j}{dt} = jGm_{j-1} + B^0L_0^j \)

The main motive of modelling the crystallisation process as a reactive process is to exploit the optimisation framework designed for reaction superstructures. In fact, over the past decades, considerable effort has been expended to employ chemical reaction engineering concepts in modelling complex crystallisation processes.
The crystallisation process can be modelled as competitive/series reactions.

The order of $r_1$ is higher than that of $r_2$ with respect to supersaturation. This means that when the supersaturation is increased, $r_1$ increases much faster than $r_2$. Consequently, more new crystals are produced. Therefore, by controlling the supersaturation level, crystal growth can be maximised and nucleation can be minimised.
REMARKS

- The crystallisation models are general across all solute/solvent systems
- No need to build a new model for each system
- Only the equation parameters change from system to system
  need to be fitted to experimental data
The batch crystallisation is converted into batch reaction

- The batch time is divided into smaller time intervals
- Each time interval is a steady state

The total batch time is divided into a few equal sub-steady states. By doing this, the set of ordinary differential equations are converted into algebraic equations. The accuracy of the representation increases as the number of sub-steady states increases. In fact, it can be said that the batch process consists of infinite sub-steady states.
Example: Batch cooling crystallisation

In batch cooling crystallisation,

- The main supersaturation generation method is temperature

- Initial temperature is high, and reduce gradually to lower final temperature

- Two main objective functions:
  - Maximising average crystal size
  - Minimising coefficient of variation of crystal size

Batch cooling crystallisation is suitable for systems where the solute solubility varies greatly or moderately with temperature. This mode of crystallisation is one of the most common types in industrial crystallisation. There are other objectives in crystallisation operation such as maximising the terminal seed size, minimising the ratio of nucleated mass to seed mass, maximising the production of crystals with specific habits and morphology, maximising the crystal yield and other objectives suited for different plants and product requirement.
Shown here is the trajectory of a batch cooling crystallisation. During the process, the temperature is deliberately brought down and the solute concentration depletes. It is always desirable to keep the trajectory within the metastable region so as to avoid spontaneous nucleation and promote crystal growth.
Types of cooling

Natural Cooling
- Uncontrolled
- Poor crystal quality
- Most common

Linear Cooling
- Constant cooling rate
- Better crystal quality

Controlled Cooling
- Controlled cooling rate
- Superior crystal quality
Optimisation variables:

**BATCH**
1. Temperature profile
2. Number of seeds
3. Size of the seeds
4. Initial level of supersaturation
5. Batch time

**SEMI-BATCH**
1. Solute/Feed flow rate
2. Temperature profile
3. Number of seeds
4. Seed addition profile
5. Size of the seeds
6. Initial level of supersaturation
7. Batch time

The variables can be optimised simultaneously
The main objective of manipulating the initial solute concentration at a fixed initial temperature is to obtain an optimal initial level of supersaturation. If the initial solute concentration is fixed instead, the initial temperature can become an optimisation variable in order to achieve the optimal initial supersaturation level. The more convex the cooling profile, the lower the crystal yield. Although some cooling profiles will yield large average crystal size, the crystal yield will be so low that it is hard to justify economically exploiting the cooling profiles.
Optimisation approach allows:

• detailed crystallisation models to be used
• multivariable optimisation
• different modes of operation to be screened

BUT WE LOSE THE PHYSICAL INSIGHTS FROM THE GRAPHICAL APPROACH!
Insights from graphical presentation....

Example: Natural cooling of Citric Acid-Water system

- Insignificant secondary nucleation
- Significant secondary nucleation

- Significant secondary nucleation can reduce the potential benefit of controlled cooling relative to natural cooling
- The graph can demonstrate the intensity of secondary nucleation

When the effect of secondary nucleation is insignificant, the supersaturation level can be controlled throughout the process, such as no nucleation will occur. Nevertheless, when secondary nucleation is significant, the nucleation is inevitable. Towards the end of the operation, supersaturation decreases and the crystal concentration increases. When secondary nucleation is significant, the nucleation increases towards the end since it is dependent on crystal concentration and has a lower exponential dependency on the supersaturation.
5. Case Study I: Batch Cooling Crystallisation of Citric Acid-Water system
Case study 1: Batch cooling crystallisation of Citric Acid-Water system

Data are extracted from Bohlin and Rasmuson (1990)
The solubility of citric acid is modelled by a polynomial equation

\[ c^* = c_0 + c_1T + c_2T^2 + c_3T^3 \]

Primary nucleation, \[ B_p = k_p(c - c^*)^{n_p} \]
Secondary nucleation, \[ B_s = k_s(T) M_T^{b} (c - c^*)^{n_s} \]
Crystal growth rate, \[ G = k_g(T) (1 + aL)^d (c - c^*)^{n_g} \]

Assumption: Total nucleation is the sum of the primary and secondary nucleation

\[ B_T = B_p + B_s \]
Data for citric acid

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_{\text{initial}}$</td>
<td>60°C</td>
</tr>
<tr>
<td>$T_{\text{final}}$</td>
<td>40°C</td>
</tr>
<tr>
<td>$c_0$</td>
<td>0.91176</td>
</tr>
<tr>
<td>$c_1$</td>
<td>0.034857</td>
</tr>
<tr>
<td>$c_2$</td>
<td>$-2.8785 \times 10^{-4}$</td>
</tr>
<tr>
<td>$c_3$</td>
<td>$3.7228 \times 10^{-6}$</td>
</tr>
<tr>
<td>Crystal density, $D_c$</td>
<td>1540 kg/m³</td>
</tr>
<tr>
<td>Volume shape factor, $k_v$</td>
<td>0.52</td>
</tr>
<tr>
<td>$M_T = k_v D_c m_3$</td>
<td></td>
</tr>
<tr>
<td>$k_p$</td>
<td>$1.00 \times 10^7$</td>
</tr>
<tr>
<td>$n_p$</td>
<td>3.54</td>
</tr>
<tr>
<td>$k_s$</td>
<td>$0.88774 \exp\left(\frac{4781}{T}\right)$</td>
</tr>
<tr>
<td>$n_s$</td>
<td>0.543</td>
</tr>
<tr>
<td>$b$</td>
<td>0.84</td>
</tr>
<tr>
<td>$k_g$</td>
<td>$0.02652 \exp\left(-\frac{3584}{T}\right)$</td>
</tr>
<tr>
<td>$n_g$</td>
<td>0.65</td>
</tr>
<tr>
<td>$a$, $d$</td>
<td>0</td>
</tr>
<tr>
<td>Batch time, $t$</td>
<td>3600s</td>
</tr>
</tbody>
</table>
Formulation of the model equations:

Mass balance of solute:
\[ \frac{dc}{dt} = -k_v \rho_c \frac{dm_3}{dt} \]

Moment equations:
\[ \frac{dm_j}{dt} = jGm_{j-1} + (B_s + B_p)L_o^j \]

These are converted into reactions:
\[ r_c = -k_v \rho_c \frac{dm_3}{dt} \]
\[ r_j = jGm_{j-1} + (B_s + B_p)L_o^j \]
Verification of model

Simulation carried out and compared with Runge Kutta Fourth Order Numerical Method

Initial supersaturation = 0.2 kg/kg solvent
Amount of seeds = 5.8 x 10⁷ no/kg solvent
Size of seeds = 80 x 10⁶ m

Cooling profile:

![Cooling profile graph](image-url)
Comparison of simulation results

<table>
<thead>
<tr>
<th>Runge-Kutta Fourth Order solution</th>
<th>20 time intervals</th>
<th>40 time intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>values</td>
<td>error %</td>
</tr>
<tr>
<td>Cc</td>
<td>2.1525</td>
<td>0.0486</td>
</tr>
<tr>
<td>m₀</td>
<td>5.0851 x 10⁸</td>
<td>5.88</td>
</tr>
<tr>
<td>m₁</td>
<td>30135</td>
<td>4.71</td>
</tr>
<tr>
<td>m₂</td>
<td>4.4668</td>
<td>1.08</td>
</tr>
<tr>
<td>m₃</td>
<td>9.270 x 10⁻⁴</td>
<td>0.14</td>
</tr>
<tr>
<td>m₄</td>
<td>2.1878 x 10⁻⁷</td>
<td>2.63</td>
</tr>
<tr>
<td>m₅</td>
<td>5.5506 x 10⁻¹¹</td>
<td>9.48</td>
</tr>
<tr>
<td>R*</td>
<td>0.7185</td>
<td>0.145</td>
</tr>
</tbody>
</table>

* R = crystal yield

The model is verified!

The accuracy of the representation increases as the number of time intervals increases. The accuracy of the higher moments decreases for a fixed number of time intervals. Therefore, a reasonable number of time intervals is determined by the highest order of moment needed in the representation and also the accuracy required in the computation.
Optimisation parameters and constraints

- $T_{\text{initial}}$ and $T_{\text{final}}$ are fixed
- Number of time intervals = 20
- Yield of crystallisation = 0.70 kg/kg solvent

For practical and economic reasons

- The mass of seeds is confined between 0.1% to 3% of total final crystal mass
- The size of seeds is confined between 0.1 and 0.3 of the final crystal size

Base case

Mode of cooling: **Linear cooling**

- Initial supersaturation = 0.0 kg/kg solvent
- Amount of seeds added = 0 no/kg solvent
- Weight mean size of crystal, $L_{wm} = 207 \text{ Fm}$
- Coefficient of variation, $CV_w = 31.9 \%$
- Batch time = 1 hour
**Optimisation Results 1:**

Objective function:
Maximising Weight Mean Crystal Size, \( L_{wm} = \frac{m_4}{m_3} \)

Optimum : 288 \( \text{Fm} \)

Improvement = 39 %

Initial supersaturation = 0.1 kg/kg solvent

The results of the optimisation are in accordance with the following published literature results. The optimal cooling profile is the convex profile which has a slow initial cooling and rapid cooling towards the end.


Optimisation Results 2:

Objective function:
Maximising Weight Mean Crystal Size, \( L_{wm} = \frac{m_4}{m_3} \)

With seeding

Optimum: 294 Fm
Improvement = 42 %

Seed size = 80 Fm (upper limit)

Amount of seeds = 3.5 x 10^6 no/kg solvent (optimum)

Initial supersaturation = 0.1 kg/kg solvent (optimum)

Besides the results shown on the slide, several other design options that yield objective values close to the optimal value are generated by the optimisation runs. Those design options can be screened for economic criteria and practicality. In addition, those options provide flexibility for design engineers.
Optimisation Results 3:

Objective function:
Minimising weight mean coefficient of variation, \( CV_w = \sqrt{\frac{m_5}{m_3} - \left(\frac{m_4}{m_3}\right)^2} \)

With seeding

\[ m_3 \]

Optimum: 25.7%
Improvement = 19.4%

Seed size = 80 \( \text{mm} \) (upper limit)
Amount of seeds = 5.8 \( \times 10^7 \) no/kg solvent (upper limit)
Initial supersaturation = 0.1 kg/kg solvent (fixed)
Sensitivity studies

Sensitivity studies also carried out on the variables:

1. **For maximising crystal size**:
   - Temperature, number of seeds and initial level of supersaturation are more critical

2. **For minimising coefficient of variation**:
   - Number of seeds and temperature are more critical
### Remarks

<table>
<thead>
<tr>
<th>Cases</th>
<th>Seeding</th>
<th>Crystal Size (nm)</th>
<th>Coefficient of Variation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base case</td>
<td>No</td>
<td>207</td>
<td>31.9</td>
</tr>
<tr>
<td>Results 1</td>
<td>No</td>
<td>288</td>
<td>45.5</td>
</tr>
<tr>
<td>Results 2</td>
<td>Yes</td>
<td>294</td>
<td>44.7</td>
</tr>
<tr>
<td>Results 3</td>
<td>Yes</td>
<td>236</td>
<td>25.7</td>
</tr>
</tbody>
</table>

- Operating conditions to maximise crystal size produce high coefficient of variation and vice-versa
- Choice of objective function is important
- Optimisation produces marked improvement
6. Case Study II: Batch Cooling Crystallisation of Potassium Sulphate-Water system
Case study II: Batch cooling crystallisation of Potassium Sulphate-Water system

The models for nucleation and crystal growth are the same as for citric acid-water system

However,

In this case, the crystal growth is a function of size

\[ G = k_g (1 + aL)(c - c^*)^{n_g} \]

\[ \frac{dm_j}{dt} = jG_o (m_{j-1} + am_j) + B^0L^j \]
The data are from Randolph and Sikdar (1976), Jones and Mullin (1974), Mullin (1972), Nyvlt et al. (1985), Sikdar and Randolph (1976) and Tavare and Chivate (1977).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>( T_{\text{initial}} )</td>
<td>60°C</td>
</tr>
<tr>
<td>( T_{\text{final}} )</td>
<td>25°C</td>
</tr>
<tr>
<td>( c_0 )</td>
<td>0.0666</td>
</tr>
<tr>
<td>( c_1 )</td>
<td>0.0023</td>
</tr>
<tr>
<td>( c_2 )</td>
<td>(-6.0 \times 10^{-6})</td>
</tr>
<tr>
<td>( c_3 )</td>
<td>0</td>
</tr>
<tr>
<td>Crystal density, ( D_c )</td>
<td>2662 kg/m³</td>
</tr>
<tr>
<td>Volume shape factor, ( k_v )</td>
<td>0.525</td>
</tr>
<tr>
<td>( M_T = k_v \ D_c \ m_3 )</td>
<td></td>
</tr>
<tr>
<td>( k_p )</td>
<td>( 6.68 \times 10^{17} )</td>
</tr>
<tr>
<td>( n_p )</td>
<td>7.63</td>
</tr>
<tr>
<td>( k_s )</td>
<td>( 4.87 \times 10^8 )</td>
</tr>
<tr>
<td>( n_s )</td>
<td>0.69</td>
</tr>
<tr>
<td>( b )</td>
<td>0.5</td>
</tr>
<tr>
<td>( k_g )</td>
<td>( 9.7497 \times 10^{-7} )</td>
</tr>
<tr>
<td>( n_g )</td>
<td>1.288</td>
</tr>
<tr>
<td>( a )</td>
<td>( 443000 \text{ m}^{-1} )</td>
</tr>
<tr>
<td>Batch time, ( t )</td>
<td>3600s</td>
</tr>
<tr>
<td>Seed size</td>
<td>( 90 \times 10^{-6} \text{ m} )</td>
</tr>
</tbody>
</table>
Objective functions:

1. Maximising average crystal size, $L_{av} = m_3/m_2$

2. Minimising coefficient of variation, $CV = \sqrt{\frac{m_o m_2}{m_1^2} - 1}$

Using the same models as in Case I

Preliminary studies

Critical optimisation variables:

1. Number of seeds
2. Temperature profile

The average crystal size is based on the total surface area of crystals. The coefficient of variation is based on the number of crystals.
Base case

Mode of cooling: **Linear cooling**

Initial supersaturation = 0.008 kg/kg solvent

Amount of seeds added = 0 no/kg solvent

Average crystal size, $L_{av} = 92$ Fm

Coefficient of variation, CV = 3.09

Batch time = 1 hour
The strong size dependence of the crystal growth rate means that the rate is very high in the presence of large seed crystals. The rapid initial cooling accelerates the crystal growth rate much more than that of nucleation. The optimal amount of seeds are the lower boundary value because the increasing amount of seeds will only distribute the crystal mass on an unnecessarily large number of seeds, which results in lower average crystal size.
Optimisation results 2
Objective: Minimising coefficient of variation with seeding

Optimum: 2.02
Improvement = 34.6%

Seed size = 90 Fm

Amount of seeds = 6 \times 10^4 \text{ no/kg solvent (lower limit)}

Initial supersaturation = 0.008 kg/kg solvent

The controlled cooling suppresses nucleation. Large amount of seed crystals will cause increasing number of crystals and intensify the secondary nucleation. Therefore, the above configuration yields the minimum coefficient of variation.
Remarks ..... 

**Optimisation Results 1:**
- The large improvement in crystal size mainly due to a strong size dependent growth rate
- The optimal cooling mode contradicts the heuristic rules

**Optimisation Results 2:**
- Different objectives, different optimal cooling modes
- Optimal amount of seeds same as that of maximising crystal size
- This is in contrast to Case Study 1

Different system, different objective $\rightarrow$ different strategy

Need optimisation, heuristics not satisfactory.......
7. Conclusions
• A comprehensive and general optimisation framework has been proposed for batch and semi-batch crystallisation
  < Size independent and dependent growth rates can be modelled
  < Primary and secondary nucleation can be modelled simultaneously
  < Multivariable optimisation
  < Sensitivity studies
• Complex crystallisation systems are difficult to predict using heuristic rules
• Each system is unique, needs quantitative optimisation
• The model is general to all crystallisation processes, only the parameters change
• Graphical presentation provides insights for complex crystallisation systems
8. Future Work
• Extend to other crystallisation systems: evaporative, reactive and dilution
• Consideration of Ostwald Ripening effect
• Consideration of more complicated seed distribution
• Inclusion of fluid mechanics (agitator speed) into the model