ERT 313
Bioseparation Engineering
CRYSTALLIZATION

Zulkarnain Bin Mohamed Idris
e-mail: zulkarnainidris@unimap.edu.my
COURSE OUTCOME (CO)

Ability to describe the basic principles and applications of crystallization process. Ability to calculate the yields, material and energy balance in crystallization.

OUTLINES

1. Basic principles and applications of crystallization process.
2. Calculation of yields, material and energy balance in crystallization.
CRystallization

- Process of producing crystals from a homogeneous phase which is obtained from a solution.
- Capable of producing bioproducts at very high purity and considered to be a polishing step and a purification step.
- Two different application of crystallization:
  i. Crystallization for polishing and purification
  ii. Crystallization for crystallography
## Comparison of Crystallization and Precipitation

<table>
<thead>
<tr>
<th>Description</th>
<th>Crystallization</th>
<th>Precipitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solubility</td>
<td>Wide range, usually medium to high</td>
<td>Sparingly soluble</td>
</tr>
<tr>
<td>Relative supersaturation</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Product morphology</td>
<td>Well-defined</td>
<td>Ill-defined (not clearly defined)</td>
</tr>
<tr>
<td>Product crystal size</td>
<td>Large</td>
<td>Small</td>
</tr>
<tr>
<td>Nucleation mechanism</td>
<td>Secondary</td>
<td>Primary</td>
</tr>
<tr>
<td>Nucleation rate</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Growth Rate</td>
<td>Wide Range</td>
<td>Low</td>
</tr>
<tr>
<td>Controllability</td>
<td>Controllable</td>
<td>Difficult to control</td>
</tr>
</tbody>
</table>
Saturated and Supersaturated Solutions

There is a limit to the quantity of solute which will dissolve in a given quantity of solvent. For example, if 36 g KCl crystals is shaken with 100 g H₂O at 25°C only 35.5 g of the solid dissolves. If the temperature is raised, all the KCl will dissolve, but on cooling to 25°C again, the extra 0.5 g KC1 will precipitate, leaving exactly 35.5 g of the salt dissolved. A solution of this composition is also described as a saturated solution since it can accommodate no more KCl.

Under some circumstances it is possible to prepare a solution which behaves anomalously and contains more solute than a saturated solution. Such a solution is said to be supersaturated. A good example of supersaturation is provided by Na₂S₂O₃, sodium thiosulfate, whose solubility at 25°C is 50 g Na₂S₂O₃ per 100 g H₂O. If 70 g Na₂S₂O₃ crystals is dissolved in 100 g hot H₂O and the solution cooled to room temperature, the extra 20 g Na₂S₂O₃ usually does not precipitate. The resulting solution is supersaturated; consequently it is also unstable. It can be “seeded” by adding a crystal of Na₂S₂O₃, whereupon the excess salt suddenly crystallizes and heat is given off. After the crystals have settled and the temperature has returned to 25°C, the solution above the crystals is a saturated solution—it contains 50 g Na₂S₂O₃.
Crystallization from Supersaturated Solutions of Sodium Acetate

- **Description:** A supersaturated solution of sodium acetate is crystallized by pouring it onto a seed crystal, forming a stalagmite-like solid. Heat is radiated from the solid.

- **Source:** Shakhshiri, B.Z. Chemical Demonstrations: A Handbook for Teachers of Chemistry
Crystallization Principles

Crystals

• Can appear as polyhedrons, or solids formed by plane faces when allowed to form freely.

• *Angles* made by the corresponding faces of the same material do not vary – can be classified by this characteristics.

• *Relative sizes* of the faces of a crystal in a particular system can vary considerably – resulting in a variety of crystal shapes. This variation is called a *habit*.

• *Crystal habit* is influence by the conditions of crystallization, particularly by the impurities present and by the particular solvent or solvents used.

• Impurities can stunt the growth of a crystal in certain directions.
POLYHEDRONS SHAPE

cube
tetrahedron
dodecahedron
icosahedron
TABULAR
Book-like (tablets) that are thicker than platy but not as longated as bladed. **Wulfenite** forms crystals that are a good example of tabular crystals.

PRISMATIC
One of the most common of crystal habits. Prismatic crystals are "pencil-like", elongated crystals that are thicker than needles (see acicular). **Indicolite** (a variety of **elbaite**) forms good examples of prismatic crystals.

ACICULAR
Long and needle-like, thinner than prismatic but thicker than fibrous. **Natrolite** crystals can be good examples of acicular crystals.
Crystals grow in 2 steps:

2. Growth.
   - Thermodynamically distinct
   - Want a few nuclei to grow big
   - Use thermodynamics to understand the required conditions
Nucleation

• The generation of ultramicroscopic particles in the process of nucleation is the sum of contributions by primary nucleation and second nucleation.

• Primary nucleation: occurs in the absence of crystals, secondary nucleation: attributed to the influence of existing crystals

• Primary nucleation can be either homogeneous (no foreign particles are present) or heterogeneous (foreign particles present during heterogeneous nucleation)

• Rate of primary nucleation has been modeled by the following power law expression:

\[ B = \frac{dN}{dt} = k_n (c - c^*)^n \]

\[ B: \text{number of nuclei formed per unit volume per unit time; } \]
\[ N: \text{number of nuclei per unit volume; } k_n: \text{rate constant; } \]
\[ c: \text{instantaneous solute concentration; } c^*: \text{solute concentration at saturation. } (c-c^*) \text{ term: supersaturation, the exponent of } n \text{ can range up to 10 but typically is in the range of 3 to 4.} \]
Crystallization Principles

• Two types of secondary nucleation: shear nucleation (occurs as a result of fluid shear on growing crystal faces), contact nucleation (happens because of crystals colliding with each other and with the impeller and other vessel internal surfaces).

• Rate of secondary nucleation in crystallization is the following:

\[
B = \frac{dN}{dt} = k_1 M_T^j (c - c^*)^b
\]  

(2)

- \(k_1\): rate constant;
- \(M_T\): suspension density;
- \(b\): can range up to 5 but has a most probable value of 2;
- \(j\): ranges up to 1.5 with 1 being the most probable value.
- The **supersaturation** must be above a certain value before nucleation will begin.

- **Metastable region**: the supersaturation is low that nucleation will not start.

- Once the supersaturation has been raised enough to be in the labile region, nucleation can begin.

- **At this point**, crystals begin to grow, and the supersaturation decreases.

- If the supersaturation becomes too high, the nucleation rate will be too great, and amorphous precipitate will result.

**Figure 1**: Typical phase diagram. The components in solution consist of the product (ordinate) and the precipitating reagent (abscissa). The lines with arrows out line one possible way of performing the crystallization.
1. The precipitation zone is where the excess of protein molecules immediately separates from the solution to form amorphous aggregates.

2. The nucleation zone is where the excess of protein molecules aggregates in a crystalline form. Near the precipitation zone, crystallisation may occur as a shower of microcrystals, which can be confused with precipitate.

3. A metastable zone; a supersaturated solution may not nucleate for a long period, unless the solution is mechanically shocked or a seed crystal introduced. To grow well-ordered crystals of large size, the optimal conditions would have to begin with the formation of a preferably single nucleus in the nucleation zone just beyond the metastable zone. As the crystals grow, the solution would return to the metastable region and no more nuclei could occur. The remaining nuclei would grow, at a decreasing rate that would help to avoid defect formation, until equilibrium is reached.
Crystal Growth

- Post nucleation process in which molecules in solution are added to the surface of existing crystals.
- The rate of mass deposition $R$ during crystal growth is:

$$R = \frac{1}{A} \frac{dW}{dt} = k_G(c - c^*)^g$$  \hspace{1cm} (3)

- Overall linear growth rate can also be expressed as:

$$G \equiv \frac{dL}{dt} \approx k_G(c - c^*)^g$$  \hspace{1cm} (4)

$W$: mass of crystals per volume of solvent;
$A$: the surface area of crystals per volume of solvent;
$k_G$: overall mass transfer coefficient (depends on temperature, crystal size, hydrodynamic conditions, the presence of impurities);
$g$: usually 0 and 2.5

$L$: characteristic dimension of the crystal, such as length.
**Crystallization Principles**

- **Crystal growth** is a process that consists of two steps in series – diffusion and surface integration.

\[
\text{Diffusion: } R = k_d (c - c_i)^d \quad (5)
\]
\[
\text{Surface integration: } R = k_r (c_i - c^*)^r \quad (6)
\]

\[c_i: \text{ concentration at the interface between the liquid and solid phase; } k_d \text{ and } k_r: \text{ mass transfer coefficients}\]

When the exponents are unity, combining Equation 3, 5, 6 gives

\[
\frac{1}{k_G} = \frac{1}{k_d} + \frac{1}{k_r} \quad (7)
\]

Thus, if surface integration is very fast compared with bulk diffusion, then \(k_r >> k_d\), and \(k_G, k_d\).
Yields and Heat and Material Balances in Crystallization

• Yields and material balance in crystallization
• The solution (mother liquor) and the solid crystals are in contact for enough time to reach equilibrium. Hence, the mother liquor is saturated at the final temperature of the process, and the final concentration of the solute in the solution can be obtained from the solubility curve.
• The yield can be calculated knowing the initial concentration of solute, the final temperature, and the solubility at this temperature.
• In making the material balances, the calculations are straightforward when the solute crystals are anhydrous. Simple water and solute material balances are made. When the crystallizations are hydrated, some of the water in solution is removed with the crystals as a hydrate.
Example 1

Yield of a Crystallization Process

A salt solution weighing 10000 kg with 30 wt % Na$_2$CO$_3$ is cooled to 293 K (20 °C). The salt crystallizes as the decahydrate. What will be the yield of Na$_2$CO$_3$$\cdot$10H$_2$O crystals if the solubility is 21.5 kg anhydrous Na$_2$CO$_3$/100 kg of total water? Do this for the following cases:

(a) Assume that no water is evaporated.
(b) Assume that 3% of the total weight of the solution is lost by evaporation of water in cooling.

FIGURE 3. Process flow for crystallization
Example 1

Solution
The molecular weights are 106.0 for Na$_2$CO$_3$, 180.2 for 10H$_2$O, and 286.2 for Na$_2$CO$_3$ • 10H$_2$O. The process flow diagram is shown in Fig. 3, with W being kg H$_2$O evaporated, S kg solution (mother liquor), and C kg crystals of Na$_2$CO$_3$ • 10H$_2$O. Making a material balance around the dashed line box for water for part (a), where W = 0.

\[
0.70(10000) = \frac{100}{100 + 21.5}(S) + \frac{180.2}{286.2}(C) + 0 \tag{13}
\]

where (180.2)/(286.2) is wt fraction of water in the crystals.
Example 1

Making a balance for Na$_2$CO$_3$,

\[
0.30(10000) = \frac{21.5}{100 + 21.5}(S) + \frac{106.0}{286.2}(C) + 0
\]  \hspace{1cm} (14)

Solving the two equations simultaneously, \( C = 6370 \) kg of Na$_2$CO$_3$ •10H$_2$O crystals and \( S = 3630 \) kg solution.

For part (b), \( W = 0.03(10000) = 300 \) kg H$_2$O. Equation (13) becomes

\[
0.70(10000) = \frac{100}{100 + 21.5}(S) + \frac{180.2}{286.2}(C) + 300
\]  \hspace{1cm} (15)

Equation (14) does not change, since no salt is in the W stream. Solving Eqs. (14) and (15) simultaneously, \( C = 6630 \) kg of Na$_2$CO$_3$ •10H$_2$O crystals and \( S = 3070 \) kg solution.
Heat effects and heat balances in crystallization

• When a compound whose solubility increases as temperature increases dissolves, there is an absorption of heat, called the heat of solution – occurs when the solubility decreases as the temperature increases.

• At equilibrium the heat of crystallization is equal to the negative of the heat of solution at the same concentration in solution.

• The enthalpy $H_1$ of the entering solution at the initial temperature is read off the chart, where $H_1$ is kJ for the total feed. The enthalpy $H_2$ of the final mixture of crystals and mother liquor at the final temperature is also read off. If some evaporation occurs, the enthalpy $H_v$ of the water vapor is obtained from the steam tables. Then the total heat absorbed $q$ in kJ is

$$q = (H_2 + H_v) - H_1 \quad (16)$$

• If $q$ is positive, heat must be added to the system. If it is negative, heat is evolved or given off.
Example 2

Heat Balance in Crystallization

A feed solution of 2268 kg at 327.6 K (54.4 °C) containing 48.2 kg MgSO$_4$/100 kg total water is cooled to 293.2 K (20°C), where MgSO$_4$•7H$_2$O crystals are removed. The solubility of the salt is 35.5 kg MgSO$_4$/100 kg total water. The average heat capacity of the feed solution can be assumed as 2.93 kJ/kg• K. The heat of solution at 291.2 K (18 °C) is -13.31 x 10$^3$ kJ/kg mol MgSO$_4$•7H$_2$O. Calculate the yield of crystals and make a heat balance to determine the total heat absorbed, $q$, assuming that no water is vaporized.
Example 2

Solution

Making a water balance and a balance for MgSO4 using equations similar to (13) and (14) in Example 1, C = 616.9 kg MgSO₄•7H₂O crystals and S = 1651.1 kg solution.

To make a heat balance, a datum of 293.2 K (20°C) will be used. The molecular weight of MgSO₄•7H₂O is 246.49. The enthalpy of the feed is $H_1$:

$$H_1 = 2268(327.6 - 293.2)(2.93) = 228600 \text{ kJ}$$
Example 2

The heat of solution is \(-\frac{13.31 \times 10^3}{246.49} = -54.0 \text{ kJ/kg crystals}\). Then the heat of crystallization is \(-(-54.0) = +54.0 \text{ kJ/kg crystals}\), or \(54.0(616.9) = 33312 \text{ kJ}\). This assumes that the value at 291.2 K is the same as at 293.2 K. The total heat absorbed, \(q\), is

\[
q = -228600 - 33312 = -261912 \text{ kJ}
\]

Since \(q\) is negative, heat is given off and must be removed.
### Equipment for Crystallization

#### Tank Crystallization

- Hot saturated solutions are allowed to cool in open tanks.
- After a period of time, the mother liquor is drained and the crystals removed.
- Nucleation and the size of crystals are difficult to control.
- Labor cost are very high.
- Has limited application; used to produce certain fine chemical and pharmaceutical products.
Scraped surface crystallizers

- One type of scraped surface crystallizer is the Swenson-Walker crystallizer, which consists of an open trough 0.6 m wide with a semicircular bottom having a cooling jacket inside.

- Slow-speed spiral agitator rotates and suspends the growing crystals on turning.

- Blades pass close to the wall and break off any deposits of crystals on the cooled wall.

- Used in crystallizing ice cream and plasticizing margarine.
Circulating-liquid evaporated-crystallizer
- **Supersaturation** is generated by evaporation.
- Circulating liquid is drawn by the screw pump down inside the tube side of condensing steam heater
- **Heated liquid** then flows into the vapor space, where flash evaporation occurs, giving some supersaturation.
- The vapor leaving is condensed.
- The supersaturated liquid flow down the downflow tube and then up through the bed fluidized and agitated crystals, which are growing in size.
- The living saturated liquid then goes back as a recycle stream to the heater, where it is joined by the entering feed.
- The larger crystals settle out and a slurry of crystals and mother liquor is withdrawn as product.
- Also called **Oslo crystallizer.**
Circulating-magma vacuum crystallizer

• The magma or suspension of crystals is circulated out the main body through a circulating pipe by a screw pump.
• Magma flows through a heater, where its temperature is raised 2-6 K.
• The heated liquor then mixes with body slurry and boiling occurs at liquid surface.
• This causes supersaturation in the swirling liquid near the surface, which results in deposits on the swirling suspended crystals until they leave again via the circulating pipe.
• The vapors leave through the top.
• A steam-jet ejector provides the vacuum.