THAPAR INSTITUTE
OF ENGINEERING & TECHNOLOGY
(Deemed to be University)

Mass Transfer-I

Crystallization

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Crystallization

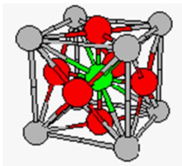
Introduction

- Crystallization refers to the formation of solid crystals from a homogeneous solution.
- It is a solid-liquid separation technique
- Used to produce
  - Sodium chloride
  - Sucrose from a beet solution
  - Desalination of sea water
  - Separating pharmaceutical product from solvents
  - Fruit juices by freeze concentration
- Crystallisation requires much less energy than evaporation
- e.g. water, enthalpy of crystallisation is 334 kJ/kg and enthalpy of vaporisation is 2260 kJ/kg

Crystal

- A crystal is a solid form of substance (ice)
- Some crystals are very regularly shaped and can be classified into one of several shape categories such rhombic, cubic, hexagonal, tetragonal, orthorhombic, etc.
- With pharmaceuticals, crystals normally have very irregular shapes due to dendritic growth which is a spiky type appearance like a snowflake. It can be difficult to characterise the size of such a crystal.
- Crystals are grown to a particular size that is of optimum use to the manufacturer. Typical sizes in pharmaceutical industry are of the order of 50μm.

A crystal is the most highly organised type of non-living matter. It is characterised by the fact that its constituent particles like atoms or molecules or ions are arranged in an orderly three-dimensional arrays called *space lattices*. The angles made by corresponding faces of all crystals of the same material are equal and characteristic of that material, although the size of the faces and edges may vary.



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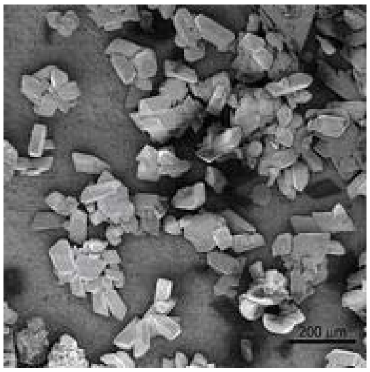
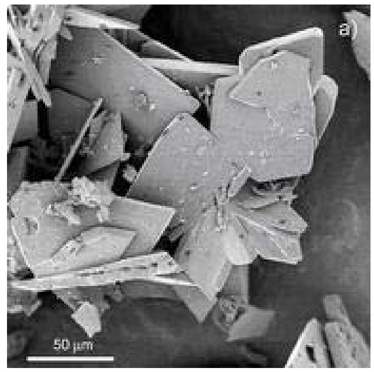
Paracetamol crystals precipitated from acetone solution with compressed CO_2 as anti-solvent using the GAS technique





Source http://www.ipe.ethz.ch/laboratories/spl/research/crystallization/project05

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- In general, crystallisation should be a straight forward procedure. The objective is to grow crystals of a particular size or crystal size distribution (CSD). If this is not successful, problems that can occur are:
  - Inconsistency from batch to batch
  - Difficult to stir and filter
  - Crystals damaged in filtration/agitation
  - Creation of polymorphs
  - Difficult to dry

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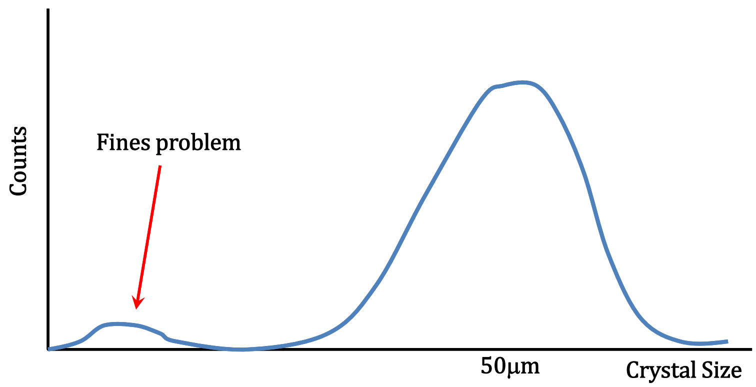
Crystal Size Distribution (CSD)

The following CSD is very common. 50 μm crystals are the desired outcome in this crystallisation. However, some fines are created also.



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Classification of Crystal

Cubic: Three equal rectangular axes.

Tetragonal: Three rectangular axes, two of which are equal and different in length from the third.

Hexagonal: Three equal coplanar axes inclined to 60° to each other and a fourth axis different in length from the other three and perpendicular to them.

Trigonal: Three equal and equally inclined axes.

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Orthorhombic: Three unequal rectangular axes.

Monoclinic: Three unequal axes, two of which are inclined but perpendicular to the third.

Triclinic: Three mutually inclined and unequal axes, all angles unequal and other than 30°, 60° and 90°.

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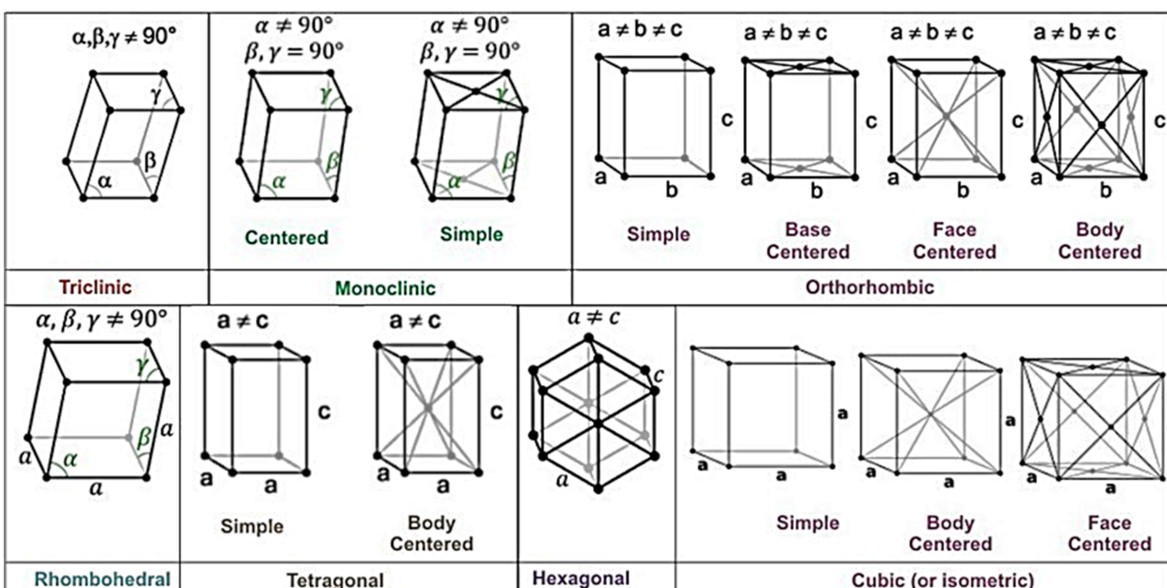


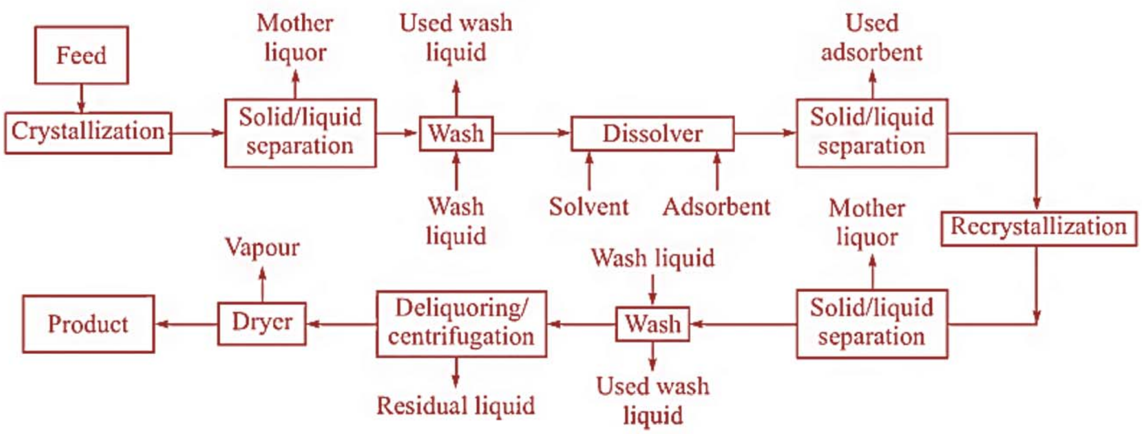
https://www.toppr.com/guides/chemistry/the-solid-state/space-lattice-or-crystal-lattice-and-unit-cell/

Crystallisation

Crystallization is a process in which the solid particles are formed from a homogeneous phase. During the crystallization process, the crystals form from a saturated solution. The mixture of crystals and the associated mother liquor is known as *magma*. The advantages of crystals are given below:

(i) uniform size and shape
(ii) ease in filtering and washing
(iii) caking tendency is minimised
(iv) high purity
(v) they do not crumble easily

Major steps in crystallisation process



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Solutions, Solubility and Solvent

- A solid substance (solute) is termed soluble if it can dissolve in a liquid (the solvent) to create a **solution**
- The **solution** is a homogenous mixture of two or more components
- **Solubility** is normally (but not always) a function of temperature
- **Solubility** can change if the composition of the solvent is changed (e.g. if another solvent is added)
- **Solubility** is usually measured as how many grams of **solvent** can be dissolved in 100 grams of solute

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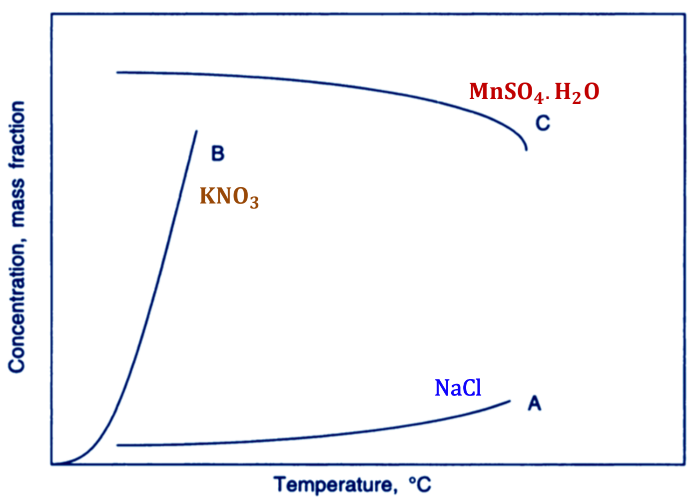
Solubility curve



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Saturation

- An Unsaturated or Undersaturated solution can dissolve more solute
- A saturated solution is one which contains as much solute as the solvent can hold
- A Supersaturated solution contains more dissolved solute than a saturated solution, i.e. more dissolved solute then can ordinarily be accommodated at that temperature
- Two forms of supersaturation
  - Metastable – just beyond saturation
  - Labile – very supersaturated
- Crystallisation is normally operated in the metastable region

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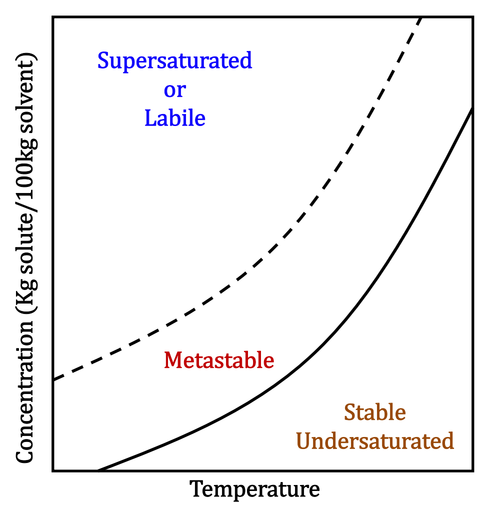
Solubility curve - Saturation diagram

- **Stable zone** – crystallisation not possible
- **Metastable zone (MSZ)** – crystallisation possible but not spontaneous
- **Supersaturated or Labile** – crystallisation possible and spontaneous

We need a supersaturated solution for crystallisation



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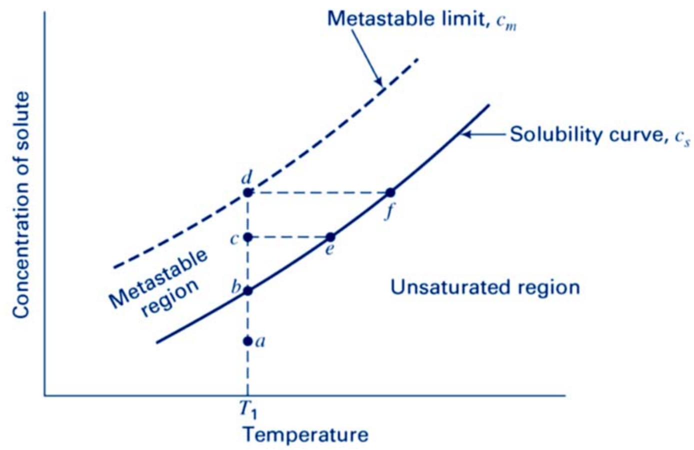
Point a: The solution is undersaturated; crystals of all sizes dissolve

Point b: Equilibrium between a saturated solution and crystals that can be seen by naked eyes

Point c: Metastable region; crystals can grow but cannot nucleate

Point d: Spontaneous nucleation of very small crystals, that are invisible to the naked eyes, occurs



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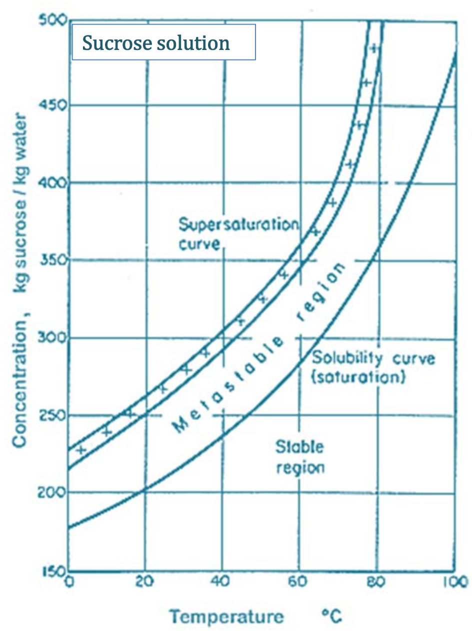

Source: http://www.nzifst.org.nz/unitoperations/conteqseparation10.htm

Supersaturation, ΔC

- Supersaturation is the driving force for
  - Nucleation
  - Crystal Growth
- Creation and control of supersaturation is the key to successful crystallisation

High ΔC ⇒ High Crystal Growth + High Nucleation

- High nucleation means a lot of fines (filtration problems)
- High crystal growth means inclusion of impurities
- ΔC is usually maintained at a low level in the pharmaceutical industry so the right CSD is achieved

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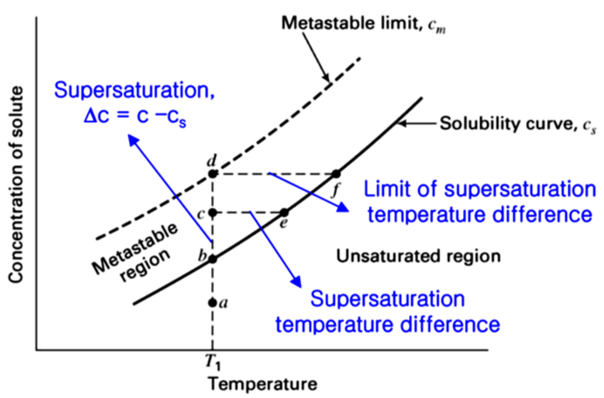

- Limiting supersaturation, $\Delta c_{limit} = c_m - c_s$

- Kelvin equation: a relationship between solubility and crystal size

$$\ln\left(\frac{c}{c_s}\right) = \frac{4v_s\sigma_{s,L}}{vRTD_p}$$

v_s : molar volume of the crystals
$\sigma_{s,L}$: interfacial tension
v : number of ions/molecule of solute
c/c_s : supersaturation ratio (=S)

- Relative supersaturation

$$s = \frac{c - c_s}{c_s} = \frac{c}{c_s} - 1 = S - 1$$

In practice, s is usually less than 2%

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Achieving Supersaturation (Crystallisation Techniques)

For crystallization we need to achieve supersaturated solution

In general supersaturation is achieved by following methods

- **Cooling a solution**
  - If supersaturation is a function of temperature
- **Removal of the solvent by evaporation**
  - Where supersaturation is independent of temperature (e.g. common salt)
- **Addition of another solvent to reduce solubility**
  - When solubility is high and above methods are not desirable, or in combination with above methods
  - The new solvent is called the anti solvent and is chosen such that the solubility is less in this new solution than it was before

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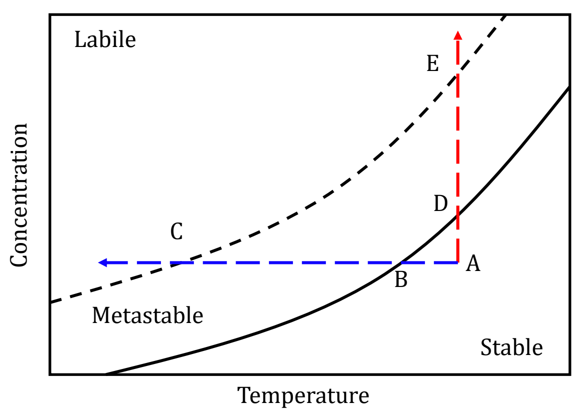

ABC - If A is cooled, spontaneous nucleation not possible until C is reached. No loss of solvent

ADE – If solvent is removed, nucleation occurs at E

Can combine cooling and evaporation

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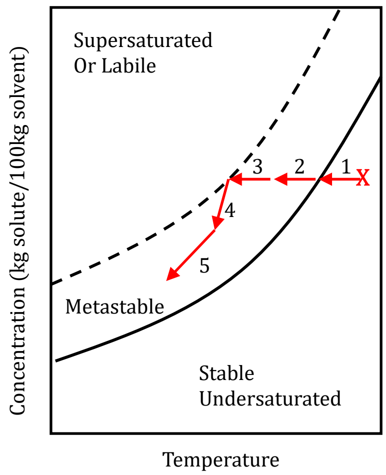

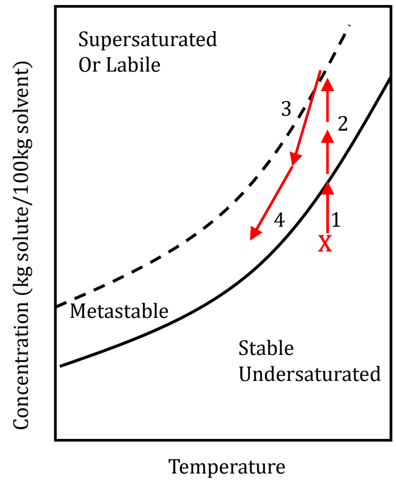

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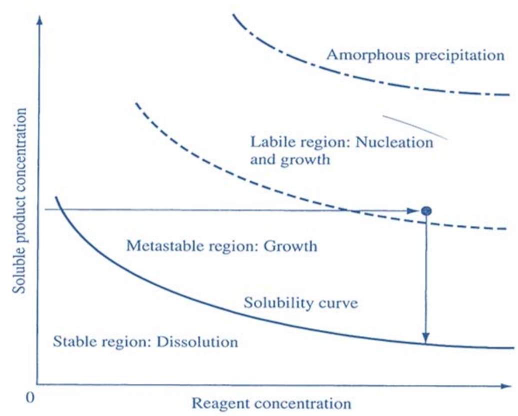
Typical phase diagram: The components in solution consist of the product (ordinate) and the precipitating reagent (abscissa). The lines with arrows out line one possible way of performing the crystallization.

- The supersaturation must be above the 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



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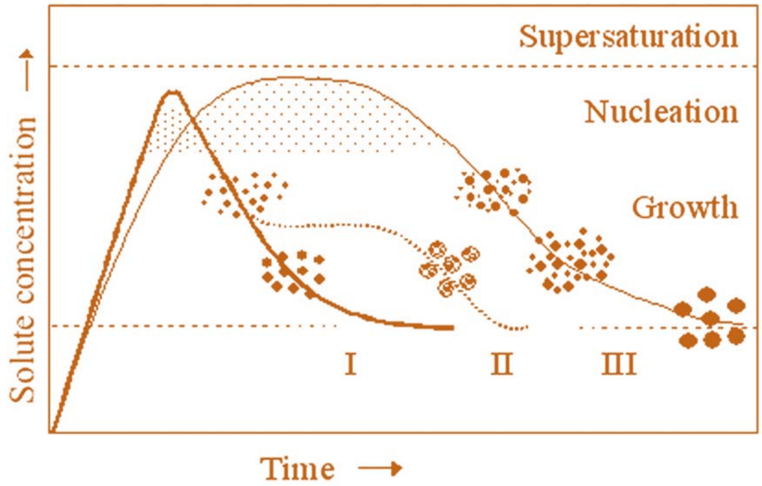
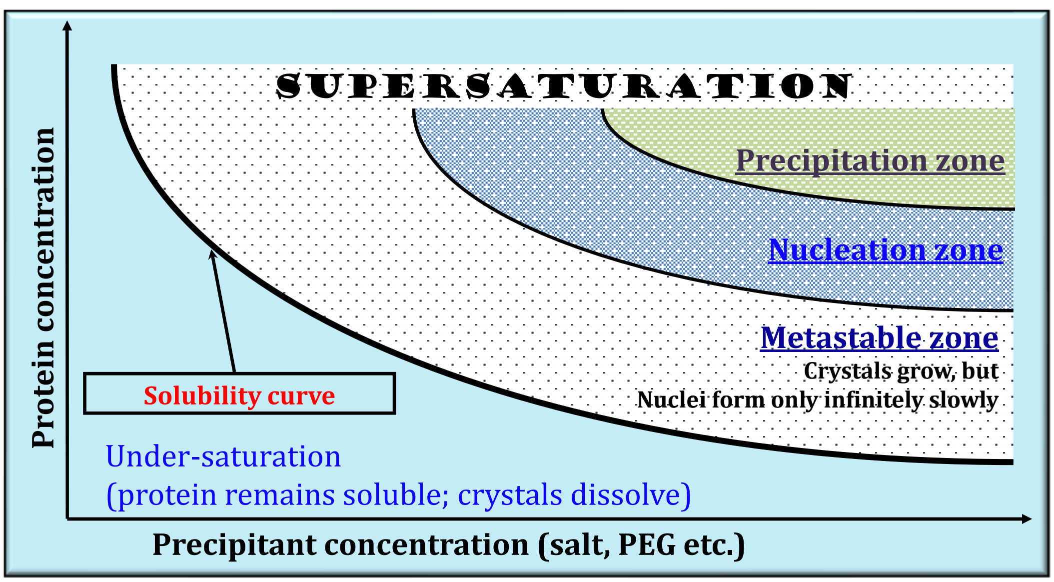
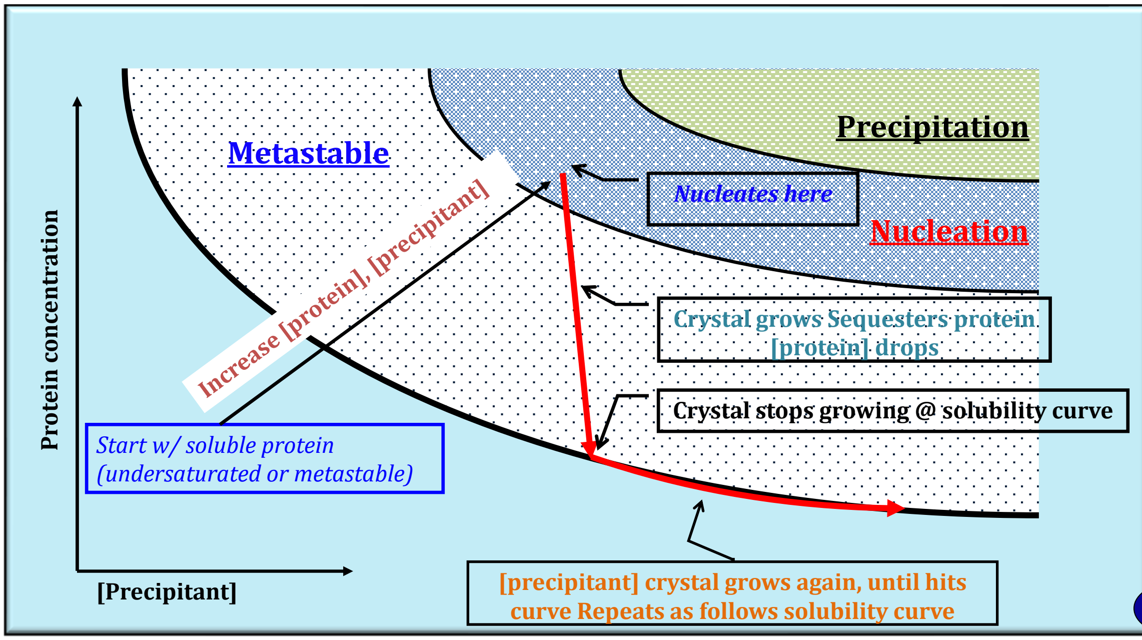


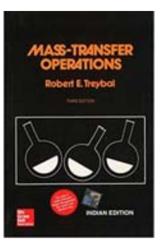
Phase diagrams

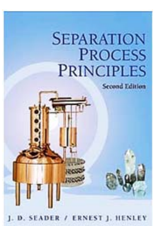


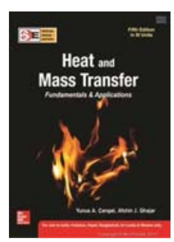
Course of Crystallization Experiment

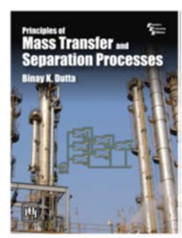


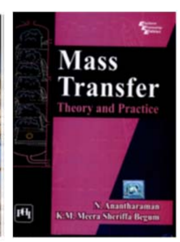
References











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Mass Transfer

Theories for Mass Transfer Coefficients

Lecture 9, 15.11.2017, Dr. K. Wegner

- Lecture notes/ppt of Dr. Yahya Banat (ybanat@qu.edu.qa)

CHEMICAL ENGINEERING AND CHEMICAL PROCESS TECHNOLOGY – Vol. II - *Mass Transfer Operations: Absorption And Extraction* - José Coca, Salvador Ordóñez and Eva Diaz

MASS TRANSFER OPERATIONS: ABSORPTION AND EXTRACTION

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