Industrial crystallization in practice

From process to product

Scope of the book

Crystallization refers to the phase transformation of a compound from a fluid or an amorphous solid state to a crystalline solid state. However, a crystallization process is not just a separation process; it is also a production process and a purification technique, as well as a branch of particle technology. It thus encompasses key areas of chemical and process engineering (Davey and Garside, 2000).

Crystallization is an extremely old unit operation, but is still used to produce highly specified speciality chemicals, and pharmaceuticals. In fact, there are few branches of the chemical and process industries that do not, at some stage, employ crystallization or precipitation for production or separation purposes (Mullin, 2003). Crystalline products include bulk chemicals such as sodium chloride and sucrose, fertilizer chemicals such as ammonium nitrate, potassium chloride, ammonium phosphates and urea; valuable products such as pharmaceuticals, platinum group metal salts and organic fine chemicals; products from the new and rapidly expanding field of engineered nanoparticles and crystals for the electronics industry, as well as biotechnology products such as protein crystals.

Although crystallization is an increasingly important industrial process, one that is governed by thermodynamics of phase separation, mass and heat transfer, fluid flow and reaction kinetics, it is not usually explicitly covered in any of the existing core chemical engineering material.

A large percentage of final or intermediate industrial products consist of a product of a crystallization process, i.e. tiny crystals or particles that have to conform to product specifications with respect to crystal size and shape, crystal size distribution, degree of agglomeration and uptake of either liquid or solid impurities. These product properties relate to the selected type of crystallization process as well as to the specific crystallization mode and type of hardware used for production. Crystallization is therefore much more than just a simple separation process. Unfortunately, the technology to design, operate and optimize crystallization processes is usually covered only very briefly as part of a broader overview on separations or particle technology, such as the chapter on Crystallization and Precipitation by Mullin in *Ullmann's Encyclopaedia of Industrial Chemistry* (Mullin, 2003) or other, similar, volumes (Richardson *et al.*, 2002 and Ruthven, 1997). The few textbooks that do focus on

industrial crystallization are mostly more than nine years old (Hurle, 1993, Jones, 2002, Mersmann, 2001, Mullin, 2001, Myerson, 2001, Nývlt, 1992, Söhnel and Garside, 1992, Ulrich and Glade, 2003) and do not cover the latest developments in what has recently been a rapidly changing field. A recent contribution to the field is the volume edited by Beckmann (2013).

In a crystallization process, many factors inter-relate, and thus it is not easy to operate the process unless there is an awareness of how all of these factors are connected. So the choices that are made have many interactive consequences. For example, the stirring in a crystallizer affects the interaction among particles in the suspension, and growth, agglomeration and attrition. In organic crystallization, for example, the solvent choice can have a significant influence on the nucleation of a certain polymorph, but also on the growth kinetics. In addition, there are many examples of how early choices in the design of a process or crystallizer can have a negative impact on the process. This is crucial and typical for crystallization – unlike other fields, like distillation. The interaction between the different aspects of the crystallization process and the crystallizer equipment is also why this book cannot be read as a collection of single separate chapters, and also why all the chapters refer to each other.

This book covers the field of crystallization as both a separation and a particle synthesis process. The main focus is on crystallization as a production process and how the product specifications introduce complexities into crystallization process and equipment. It is an attempt to collect the most relevant information from the currently scattered and disparate material in order to learn how to develop, operate and optimize industrial crystallization processes and their equipment. In addition, this book intends to provide new and industrially relevant information that has not been published before.[1]

It is aimed at undergraduate and postgraduate students, as well as industrial practitioners, and therefore, there is a balance between theoretical underpinnings (equations) and conceptual approaches to the various aspects of crystallization processes.

The book has three main objectives:

- to update the current information on industrial crystallization in line with recent advances in the field;
- to provide a core teaching text for undergraduate and postgraduate students studying separation processes, particle synthesis, particle technology and industrial crystallization at university level;
- to provide a text that is accessible to industrial practitioners – engineers and chemists involved in the development, operation and optimization of industrial crystallization processes in the pharmaceutical, fine chemicals, metallurgical, food, bioprocessing, pigments and dye production industries.

---

[1] "Industrial" in this case means that the text deals only with a suspension of small crystals or particles (mass crystallization) and not with large single crystals for electronic devices. Books about single large crystals are mostly called crystal growth.

Summary of the chapters

Chapter 1: Thermodynamics, crystallization methods and supersaturation

The choice of which crystallization method to use depends on the solubility of the final product. This chapter covers how the thermodynamics of crystallization, in the form of either phase diagrams or mathematical solubility models, provides the information required to select a crystallization method. Thermodynamics also defines the maximum yield and the energy consumption associated with the process. The supersaturation, the driving force for the crystallization process, is also defined and it is discussed how this can be expressed in terms of concentrations, undercooling or activities. For precipitation and anti-solvent crystallization, the supersaturation is generally high. It is also necessary to take into account the speciation of the different components in the system.

Chapter 2: Characterization of a crystalline product

Particulate products have to meet increasingly stringent demands on quality. The product specifications are generally related to properties such as the crystal size distribution of the product, the shape of the crystals, the mother liquor inclusions in the crystals, the uptake of impurities in the crystal lattice, the degree of agglomeration and the surface roughness of the crystals. This chapter deals with each of these features, outlining the characteristics of each, as well as how they are characterized through measurement.

Chapter 3: Basic process design for crystallization

This chapter discusses the basic design of industrial crystallizers. The major design tasks are the selection of the crystallization method, the crystallizer equipment and the mode of operation, the calculation of the flow sheet of the process and of the dimensions of the equipment, the area for heat transfer and evaporation, and the power requirement for the circulation devices. With the help of a costing model, the basic design also yields a first cost estimate of the process, in terms of both capital and operational costs.

The method described in this chapter has been developed and tested for evaporative and cooling crystallization processes, but can be adapted relatively easily for melt crystallization processes from suspensions. Examples are given for evaporative and cooling processes, for a DTB evaporative crystallizer, including mother liquor recycling, and for an Oslo evaporative crystallizer.

Chapter 4: Nucleation

Crystallization starts with the formation of a new crystalline phase. This nucleation of crystals is only possible if the liquid is supersaturated or undercooled. There are two mechanisms by which nucleation occurs: primary and secondary nucleation. This chapter deals with classical approaches to primary and secondary nucleation, but also covers new research on the latest thinking around two-step nucleation processes.

Chapter 5: Crystal growth

Whilst nucleation concerns the formation of the smallest possible sized particles that do not redissolve under the given conditions, the next step is crystal growth. This chapter covers the basic concepts of crystal growth and the different growth mechanisms, as well as equations to model the growth rate. The influence of the growth mechanism on surface roughness and crystal shape is also addressed.

Chapter 6: Agglomeration

Agglomeration is the process by which particles collide and adhere, and are eventually cemented together with crystalline material to form a stable particle or agglomerate. Particle agglomeration plays an important (but not always desirable) role in the formation of larger particles in precipitation and crystallization processes. This chapter discusses the physicochemical steps that lead to the formation of these agglomerates. In addition, mathematical models are discussed that are capable of describing the agglomeration process. Some basic modelling approaches are also included.

Chapter 7: The population balance equation

In crystallization processes, the size distribution of the produced crystals is essential because it determines not only the efficiency of the subsequent solid–liquid separation and drying steps, but also the final quality of the crystalline product. In this chapter, the concept of the population balance is introduced in order to describe the evolution of the crystal size distribution (CSD) in the crystallizer. This population balance describes the evolution of the number of crystals as a function of the crystal size, as a result of the crystallization kinetics and convection (mixing and in- and output flows). Modeling this CSD also requires the mass and enthalpy balances, as they describe the process conditions for the crystallization processes in the crystallizer. In addition, equations for the kinetic phenomena in the crystallizer, like nucleation, growth and agglomeration, are needed to connect the mass and energy balances to the population balance.

Solution methods for PBE-based crystallizer models are discussed, and it is shown how this information can be used in the design phase to select the appropriate crystallizer equipment, including specific features to manipulate the CSD. Multi-compartment models that describe the effects of profiles in the process conditions on the performance of an industrial crystallizer are also introduced. Profiles in conditions are unavoidable for crystallizers with large volumes or complex geometries. Multi-compartment models are therefore important to predict the CSD in scaling up.

Chapter 8: Batch crystallization

Although crystallization during batch operation is dictated by the same kinetic phenomena as the continuous crystallization process, and thus, in principle, can be described by the same models, there are a number of aspects of a batch-operated crystallization process that require special attention and are discussed in this chapter. These include the dynamic nature of the batch process, the changing suspension volume, the dominating

influence of the start-up phase (i.e. the initial population of crystals) on the product quality and the additional degree of freedom that the batch mode offers in the operation of the process. In batch crystallization, seeding is preferred over unseeded operation for better control of the product quality. However, the addition of seeds brings its own complications. This chapter covers these and other aspects of batch crystallization, such as the impact of supersaturation control during batch operation.

Chapter 9: Measurement techniques

The major process variables in a crystallization process are the level of supersaturation of the solute in the solution, the crystal size distribution and their distribution over the crystallizer. These variables determine the processes of nucleation, growth and agglomeration, which dominate the crystallization process. This chapter reviews and explains the latest available techniques for measuring these process variables.

Chapter 10: Industrial crystallizers

This chapter focuses on two aspects: firstly, the selection of an appropriate crystallizer and secondly, the optimization of an existing crystallizer to achieve the desired outcome. Several different types of industrial crystallizers are discussed, with a view to highlighting their distinguishing features, as well as how to optimize their operation in an industrial environment.

Chapter 11: Precipitation and anti-solvent crystallization

Although there is not a well-defined distinction between crystallization and precipitation, its definition is often based on the speed of the process, with precipitation usually being defined as a fast process that results in rapid formation of (extremely) small crystals. However, a more scientific definition of precipitation is the fact that the product is formed by a chemical reaction. Thus, precipitation is often referred to as "reactive crystallization."

Another important distinction is that the solubility of precipitates is low, typically in the range 10^{-3} to 1 kg m^{-3}, in comparison to products formed by crystallization, where solubilities are in the range 10 to 300 kg m^{-3}. A direct consequence of this low solubility that requires the mixing of reactants to achieve a sufficiently high yield is that the precipitation process is often mixing dominated. This has profound implications for both control and product quality in precipitation processes.

This is also the reason why anti-solvent crystallization is covered in the same chapter, since anti-solvent crystallization is the process of crystallizing out a solute by adding a solvent in which it is relatively insoluble. Thus, the anti-solvent process also forms products that can have a very low final solubility and is also usually mixing dominated.

Chapter 12: Melt crystallization

From a practical point of view, melt crystallization is an important method of crystallization that has a number of specialized applications. In essence, it is a method of producing

www.cambridge.org

ultra-pure chemicals on a large scale with low energy consumption and without using solvents.

Although the distinction between solution crystallization and melt crystallization has no theoretical basis, the very different industrial techniques used for melt crystallization have historically justified the categorization. This chapter discusses both the theoretical and the practical aspects of melt crystallization. It also discusses eutectic freeze crystallization, which is a combination of melt and cooling crystallization.

Chapter 13: Additives and impurities

Although additives and impurities are often present in relatively small concentrations, even trace amounts can have a significant effect on the crystallization process as a whole. Thus, when working in "real" crystallization processes, understanding the influence of additives and impurities is very important. This chapter discusses the mechanisms by which additives and impurities act on crystals in solution.

Chapter 14: Polymorphism

Polymorphism is the ability of a compound to form more than one crystal structure. The reason that this is important is that the physical properties of a crystal (such as solubility and dissolution rate), melting temperature, density, morphology, stability, optical properties, conductivity and color are all dependent on the polymorph.

References

Beckmann, W. 2013. *Crystallization: Basic Concepts and Industrial Applications*, Wiley.

Davey, R. and Garside, J. 2000. *From Molecules to Crystallizers*, Oxford University Press.

Hurle, D. T. J. 1993. *Handbook of Crystal Growth*, North-Holland.

Jones, A. G. 2002. *Crystallization Process Systems*, Butterworth-Heinemann.

Mersmann, A. 2001. *Crystallization Technology Handbook*, Marcel Dekker.

Mullin, J. W. 2001. *Crystallization*, Butterworth-Heinemann.

Mullin, J. W. 2003. Crystallization and precipitation. In Ullmann, F. and Gerhartz, W. (eds.) *Ullmann's Encyclopedia of Industrial Chemistry.* VCH.

Myerson, A. S. 2001. *Handbook of Industrial Crystallization*, Butterworth-Heinemann.

Nývlt, J. 1992. *Design of Crystallizers*, CRC Press.

Richardson, J. F., Coulson, J. M., Harker, J. H. and Backhurst, J. R. 2002. *Coulson and Richardson's Chemical Engineering: Particle Technology and Separation Processes*, Butterworth-Heinemann.

Ruthven, D. M. 1997. *Encyclopaedia of Separation Technology*, Wiley.

Söhnel, O. and Garside, J. 1992. *Precipitation: Basic Principles and Industrial Application*, Butterworth-Heinemann.

Ulrich, J. and Glade, H. 2003. *Melt Crystallization: Fundamentals, Equipment and Applications*, Shaker.

1   Thermodynamics, crystallization methods and supersaturation

1.1   Why this chapter is important

As crystallization is concerned with the phase change in solid–liquid systems, analysis of crystallization processes starts with consideration of *phase diagrams*. In this chapter we will show how phase diagrams help to select a crystallization method, and to determine the yield and the temperature of a crystallization process. The industrially relevant features of the main *crystallization methods* are also presented.

We next consider the state of the liquid phase during crystallization processes. The solution is said to be supersaturated with respect to the crystallizing compound, meaning the solute concentration is higher than the solid–liquid equilibrium value. The *degree of supersaturation* is important because it is the driving force for the elementary rate processes of crystallization, such as nucleation and crystal growth. Therefore, expressions to determine the degree of supersaturation are presented, both rigorous expressions based on thermodynamics and less rigorous expressions commonly found in practice.

In order to calculate the degree of supersaturation, *thermodynamic models* that provide the activity coefficients of the solute are required. The main models available are compared, so that the most suitable model may be chosen, depending on the accuracy, the ease of obtaining model experimental parameters and the types of building units (simple organic molecules, biomolecules, electrolytes, etc.).

1.2   Phase diagrams

Phase diagrams display all the possible thermodynamic states of a system: the proportion and the composition of each coexisting phase. The thermodynamic states are described by a set of independently fixed variables, such as the pressure, the temperature and the mass fractions of all components but one (since the sum of the mass fractions of all components must be unity). For a binary system at constant pressure, the phase diagram may be represented by a two-dimensional T–x plot, where T is the system temperature and x is the mass fraction of one of the components, as exemplified for the silver nitrate–water system at atmospheric pressure in Figure 1.1.
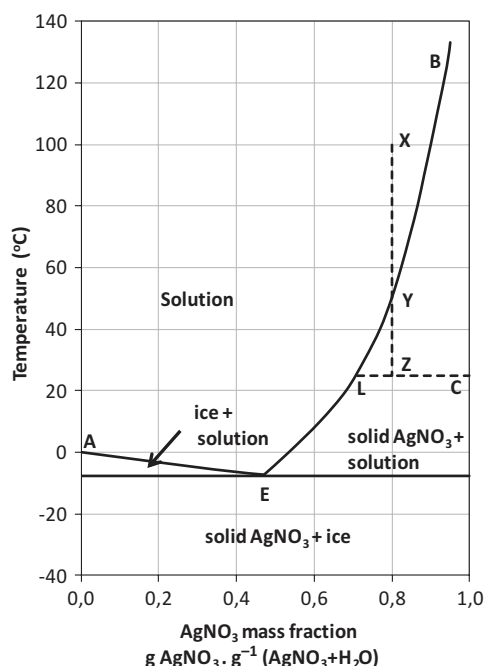
Figure 1.1 Phase diagram of the silver nitrate–water eutectic system at atmospheric pressure (Börnstein and Meyerhoffer, 1905). Reproduced with permission.

Worked example 1

Describe the composition of an $AgNO_3$–H_2O mixture containing 0.8 g $AgNO_3$/g mixture at the following temperatures: (a) 100 °C, (b) 25 °C, (c) −20 °C.

Worked example 1 solution

(a) The thermodynamic state of the system is represented by the point X in the phase diagram, Figure 1.1. The system is a homogeneous solution with a composition equal to the overall composition of the 0.8 g $AgNO_3$/g mixture.

(b) At 25 °C, point Z in the diagram, a solid is in equilibrium with a solution. The left end of the tie line (point L) gives a solution composition of 0.71 g $AgNO_3$/g and the right end (point C) gives as the solid phase pure $AgNO_3$ (there is no water within the solid). The mass fraction of solid phase in the mixture is given by the ratio LZ/LC, $(0.8–0.7)/(1.0–0.7) = 0.33$ g solid/g mixture. This is the so-called lever rule.

(c) For temperatures below the eutectic temperature E, the system is a heterogeneous mixture of pure water (ice) and pure salt (solid silver nitrate).

At the eutectic (point E), the two pure components as solids and a solution of eutectic composition are all in equilibrium. The curve AEB is called the *liquidus* line and gives all the possible concentrations of solutions in equilibrium with a solid.
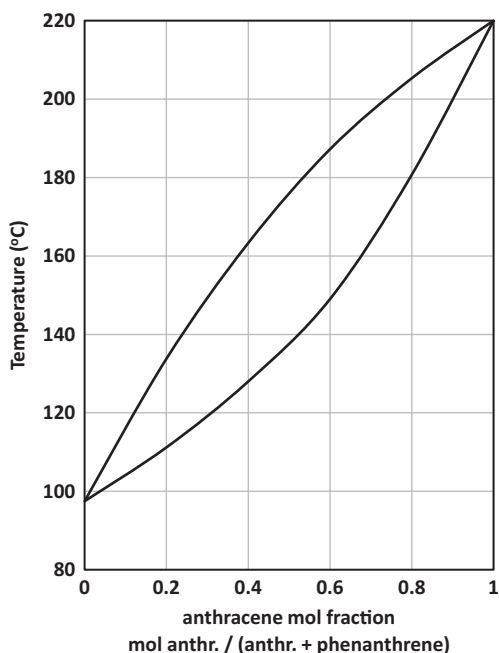
Figure 1.2 Phase diagram of the anthracene–phenanthrene solid–solution system (Schweizer, 1988).
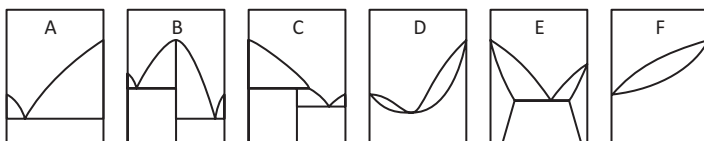

Figure 1.3 Phase diagrams for binary systems. The abscissas give the mass fraction of solute in the mixture, the ordinates represent the temperature.

Systems such as the one just presented, where the only solid phases are the pure components, are called eutectic systems. This behavior is encountered for most inorganic and many organic compounds. However, if the components in the mixture fit into each other's crystalline lattice, solid solutions may form, giving rise to a phase diagram such as the one shown in Figure 1.2. Figure 1.3 shows other common types of phase diagram for binary systems: systems exhibiting a mixed solid phase, i.e. a solid of a fixed composition A_xB_y (diagrams B, C in the figure), a solid solution with a "solid azeotrope" (D) and a combination of eutectic and solid-solution behavior (E). Phase diagrams are also available for multi-component systems and for cases where several solid phases are formed, such as polymorphs, hydrates and double salts.

For crystallization from solution, it is customary to represent the phase equilibrium information in terms of solubility curves, as shown in Figure 1.4. The use of solubility
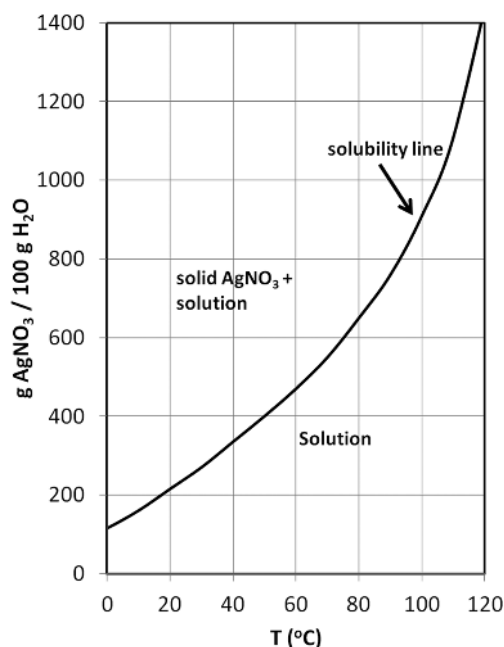
Figure 1.4 Solubility curve for the silver nitrate–water system (Börnstein and Meyerhoffer, 1905) Reproduced with permission.

lines or phase diagrams is equivalent. In a few applications, pressure is used to promote crystallization. In these cases, it is convenient to use a *P–x* phase diagram, such as the one shown in Figure 1.5.

An extensive treatment of thermodynamics for crystallization processes may be found in Nyvlt (1977). A number of excellent textbooks bring useful complimentary information, for instance Beckmann (2013), Mullin (2001) and Myerson (2001).

1.3 Crystallization methods

1.3.1 Modes of operation

Crystallization can be conducted continuously or batchwise. In the first mode, a homogeneous solution or a melt containing the solute to be crystallized is continuously fed to the crystallizer. Here some convenient interaction with the environment is applied (for instance, heat exchange) to promote crystallization. The solid is formed as a dispersed phase, which is kept in suspension by some mixing device. The suspension containing the dispersed solids and a solution leaves the reactor continuously, as exemplified in Figure 1.6. The slurry produced in the crystallizer is generally transported to a centrifuge or filter, where the crystals are separated from the mother liquor (solution or melt) and washed.