Mesocrystals and Nonclassical Crystallization

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Preface

Crystallization is certainly among the most studied processes in science and also of great practical importance. This is because the properties of many solid bodies and materials depend on their crystal structure, the crystal shape and their mutual texture. In addition, crystallization is an elemental separation technique, one of the most simple self-assembly processes to create order from the atomic to the macroscopic scale. Finally, it creates beautiful objects of esthetical value, which fascinate humankind already for centuries.

It is not astonishing that crystallization processes are already studied for a long time, beginning with alchemy (where crystallization was one of the ''elemental operations''), and in a systematic, scientific fashion since the end of the 18^{th} century. One might think that a process of such scientific and technological importance is well known down to the finest details after such intense studies for more than a century, but this is not true. It is true that a ''classical'' picture of crystallization has been established, supported by a pleiora of experimental work. It describes crystallization as a layer-wise deposition of atom/ion/molecules on the surfaces of a crystal nucleus, amplifying it within the constraints dictated by the crystal unit cell. Nevertheless, it is also well known that this classical model does not apply for many ''real-life'' crystallization processes (i.e. beyond conditions chosen which are especially good to observe the ''classical'' growth). It is still mostly not possible to quantitatively predict crystallization processes as well as the formed intermediates. Application of crystallization theories fails often even for most simple systems, and thus the modelling of crystallization processes. After 200 years of systematic scientific work, one might also state that the understanding of crystallization beginning from the atomar level is still rather restricted, as well as it is for the interface of a crystal with solvent and the other dissolved compounds.

Apart and apparently separated from synthetic crystallization processes, crystalline biominerals have been analyzed, which have nothing in common with the conception of a single crystal, anymore. Despite physical single crystal properties, they exhibit curvature as a common feature, e.g. as sea urchin spines. Up to now, their precise formation is often still unknown. Such structures are a true challenge for the classical crystallization model, which simply by no means can explain the formation of such structures. Amorphous precursor phases as well as nanoparticle based crystallization pathways were recently identified to contribute to the formation processes of Biominerals, and this knowledge could be folded back to the growth of synthetic crystals. Reanalyzing the literature, this

turns out to be a ''rediscovery'', as it seems that many important original observations are meanwhile forgotten and hidden in the past literature, as they simply did not comply with the classical crystallization model.

It is interesting to guess how crystallization processes were perceived in the early days. Natural scientists were quite universally trained and did not differentiate between biological and inorganic matter to an extent which is common nowadays. It was therefore ''clear'' to observe their scientific objects with an interdisciplinary view – a skill which is weak nowadays and indeed is worth to be rediscovered. As a tutorial exercise, we will start this book with the early descriptions of Biominerals and other crystals, which do not agree with the classical view on crystallization. These old papers already contain the keys towards a deeper understanding of crystal complexity – even if the analytical techniques to probe the assumptions made were often not yet developed. For example the philosopher and biologist Ernst Haeckel carefully observed the complexity of crystallization in the presence and absence of biomolecules and coined notations as ''living crystal field'' and ''diseased crystals''. These words do not sound as exact science in todays language, but in fact already indicate the importance of long-ranged physical fields or additives for crystallization processes. It was presumably the biggest challenge of this book that we seriously tried to gather all available information from historical colloid studies together, which are often only available in german language, and to refresh them for modern use.

The early observations of crystallization pathways well beyond the classical crystallization model (which is much younger) were followed by experimental evidence from the last decade for nanoparticle based formation mechanisms of single crystals, and nowadays this evidence is literally exploding. An increasing number of densified concepts like ''Oriented Attachment'' or ''Mesocrystal formation'' as well as elucidation of the role of amorphous precursor particles, also in Biominerals, was following. This explosion of knowledge can certainly be attributed to the increasing interest in nanotechnology and colloid science, but is to our opinion mainly due to the improved analytical possibilities as compared to those available only 20 years ago. For example, tactoids, which are oriented nanoparticle assemblies, were described as early as 1925 by Zocher but could only be analyzed by light microscopy. A detailed analysis with modern methods would certainly have changed crystallization models as such.

It is also the intention of this book to present the whole wealth of experimental observations available meanwhile, and to formulate mechanisms of non classical crystallization in an attempt to extend the classical textbook knowledge on crystallization. This is especially important in view of the fact that all more general textbooks, e.g. for physical chemistry, still only consider the classical atom/ion/molecule mediated crystallization pathway. In this book, we will try to summarize the classical and non classical crystallization pathways not only by experimental evidence but also with a comprehensive discussion of possible formation mechanisms and features of the various crystallization pathways as well as the necessary analytics. It is a go for a comprehensive treatment of modern crystallization science, and we know well that it is impossible at the present stage of knowledge to provide detailed and well backed up mechanisms for all non classical crystallization pathways which are discussed in this book. We nevertheless hope to provide the necessary toolbox for all scientists who work in the many areas related to modern crystallization to gain a better understanding of their systems; the book

hopefully gives some guidelines how to deal with these often highly complex crystal systems.

The emerging crystallization picture is a more open one where the borderlines between crystallization schemes leading to single crystals and polycrystalline aggregates as well as those between liquid crystalline systems and solid crystals vanish. There appears to be a unifying crystallization picture, which combines all well known observations of the past so far attributed to different mechanisms. A comprehensive treatment of classical and non classical crystallization will catalyze future progress in the field since it helps to identify mechanisms on the base of their typical features and by suitable analytical techniques.

It is a special wish that also students and young researchers can confront themselves with the ''self-organization'' view of crystallization since up to now, there is no equivalent densified treatment of non classical crystallization. The expectations for the future are high: The gain of basic knowledge in the field of organized crystalline arrays will lead to highly sophisticated crystalline materials of the future, covering topics such as hierarchical organic-inorganic hybrid structures, better understanding of biomineralization processes, enhanced predictive tools of crystallization events, new morphosynthesis strategies, new hybrid materials combining the physical properties of different nanoparticles in a single crystalline material, and many more.

We have structured our book into 12 chapters. After the introduction, we introduce the existing crystallization theory (Chapter 2), opposed by the presentation of crystals challenging this classical textbook view on crystallization (Chapter 3). Some non classical particle mediated crystallization pathways are presented afterwards. (Chapter 4). Their foundations are discussed with a treatment of self organization (Chapter 5), colloidal crystals (Chapter 6) as well as the mesocrystal concept and properties (Chapter 7). Formation mechanisms of mesocrystals are discussed in chapter 8, as well as the analytical tools to study such mesocrystals (Chapter 9). Possibilities for the tuning of mesocrystal properties are delineated in (Chapter 10). Finally, a unifying crystallization scenario combining classical and non-classical crystallization will be presented (Chapter 11), and the analogy between hierarchically structured crystals and biopolymers as well as oriented Aggregation and polymers will be discussed (Chapter 12). An outlook to the future with a short glance of what might be possible with an extended toolbox of crystallization will be given. We are deeply indebted to Annette Pape for her enduring assistance during the writing process of this book. We also thank Profs. Lennart Bergström, Stockholm and Shu Hong Yu, Hefei for the useful discussions on the content of this book.

Finally we would like to acknowledge our families who have supported us through all the years of doing science, but especially during the two years of writing this book. It is clear that an active scientist has no time to write such book predominantly at the normal working hours, and many weekends and nights were sacrificed for the writing process. We are therefore extremely grateful to our wives Steffi and Sigrun as well as to our children for their patience to accept passionate science as it is.

Potsdam March 2008

1

Mesocrystals and Nonclassical Crystallization

1.1 Introduction

This chapter presents a history of observations that crystallization can go well beyond the simple 'expected' behaviour found in the salt cellar or when you buy a chemical. Biomorphs, crystal gardens, 'crystal souls', but also the remarkable pattern and structures of biominerals made researchers think that there is something beyond the concept of the bare three-dimensional regularity of molecules. This chapter introduces the beauty and diversity of 'old knowledge'.

Crystallization is the most elementary step in the handling of solid compounds. Crystallization is used for purification or isolation, but crystallization also creates order and beauty. It is presumably no exaggeration that the beauty of crystals has brought humankind to think in categories of substances and molecules. Although crystallization is well known, it is astonishing how little we know about this most elemental process between molecules, and their self-organization.

Of course, there is a classical view on crystallization, presented in textbooks [1] and a plethora of scientific articles. But how much do we really know, and how many original observations have been forgotten in the effort to arrange and compact our knowledge, creating the classical crystallization theory?

In the early days of chemistry, people were quite open in their views and differentiated little between biology and inorganic chemistry, and indeed many similarities have been observed. The first work on a chemical approach to address the morphological complexity of biominerals that we are aware of is the 1873 work of Peter Harting on the morphological complexity of calcium carbonate crystals synthesized in oyster marrow. His schematic drawings are shown in Figure 1.1, highlighting the absence of clear faces

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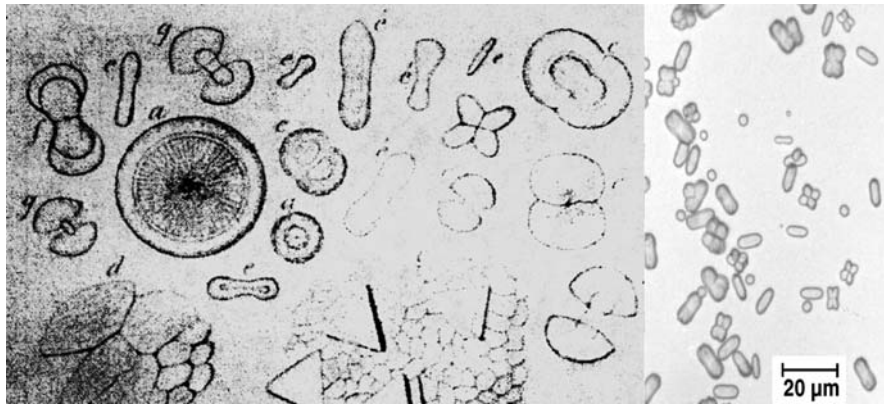

Figure 1.1 *Left: $CaCO_3$ crystals obtained via a double diffusion experiment in Oyster marrow [2]. (P. Harting,* Recherches de morphologie synthetique sur la production artificielle de quelques formations calcaire organiques*, van der Post, Amsterdam, 1872). Right: $CaCO_3$ synthesized in a double jet reactor in presence of 1 g/l (PEG-b-PEI-$COC_{17}H_{35}$ $(CH_2\text{-}COOH)_n$) [3]. (M. Sedlak and H. Cölfen,* Macromolecular Chemistry and Physics, 2001, ***202***, 587).

and the appearance of curvature, properties that are classically not attributed to crystalline matter. We parallel this traditional drawing with an actual photograph, which depicts many of the described morphologies mimicked by synthetic processes, as they will be described later in the book. It is clear that the observation of such structures made people suspect that there were no clear borderlines between biology and dead inorganic matter.

In his book *Kristallseelen – Studien über das anorganische Leben* [4], the philosopher and biologist Ernst Haeckel tried to approach the interplay between crystallography and biological structure formation. He carefully observed the complexity of crystallization with and without biomolecules and coined such notations as 'living crystal field' and 'diseased crystals', which (also from a modern view) hit the effects to be described in the very heart, but sound 'nonscientific' in today's language. Haeckel was presumably the first to compile the evidence that the amazing complexity of biominerals can be, to some extent, mimicked *in vitro* with rather simple ingredients.

The colloid chemist Herbert Freundlich devoted in his book [5] no less than two chapters on crystallization and its dependence on additives. Freundlich described nucleation agents and nucleation inhibitors, binodal crystallization and spinodal processes (the latter being long forgotten afterwards), as well as 'little facts' such as that dyes which are able to stain an inorganic crystal can also inhibit its crystallization. In the book, the first full synthetic experiments for synthesis of morphology (morphosynthesis) found entry, where the shapes of AgCl crystals were modified by adsorption of methylene blue [6].

The actual versions of all these experiments will be discussed in more detail later in this book; it is just amazing how similar the thinking and experimental approaches were in those days. The main improvement is not the mindset, but only the existence of much

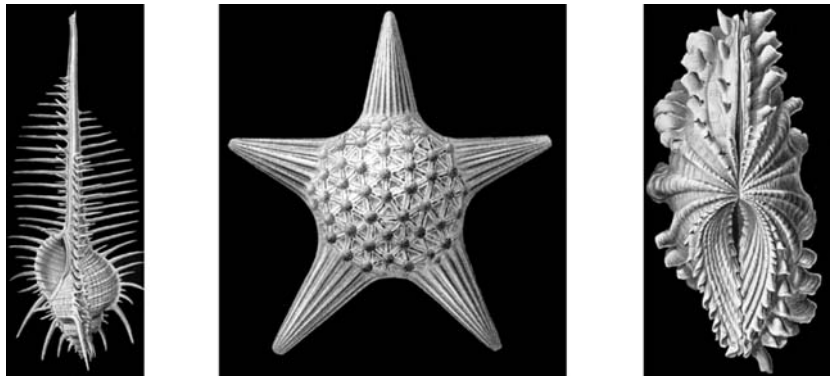

Figure 1.2 *Various biominerals with complex forms. Left: Prosobranchia, center: Thalamophora, right: Acephala. (From Ernst Haeckel, Kunstformen der Natur, 1899 – 1904. http://www.zum.de/stueber/haeckel/kunstformen/natur.html. Copyright 1999, Kurt Stueber and Max-Planck-Institut für Züchtungsforschung).*

better analytical tools, which have enabled us to grab the details of these unconventional crystallization processes.

Maybe better known in the English speaking world, the Scottish zoologist D'Arcy Thompson published his historic book, *On Growth and Form* [7], in 1917, referring actually to the extensive work of Haeckel. Thompson used his classical and mathematical training for an integrative approach to describe biological structural motifs, including biominerals. A point that influenced his book very seriously is that he was able to show that most biological complexity still follows very strict physico-chemical rules, partly given by the growth process, and partly driven by mechanical demands on the biomaterials that underlie evolutionary optimization pressure.

It is the topic of this book to clarify how such complex crystallization processes can be controlled. Collected evidence will be presented that – beside classical crystallization treated in former textbooks – there is a second 'reaction channel' that works via parallel crystallization towards amorphous intermediates and then crystalline nanostructures, which act as material deposits or intermediates for arrangement and densification towards the final structure. This way, crystallization gains the freedom and possibilities to generate complex forms, but also mineral heterostructures, gradient materials, and organic/inorganic nanohybrids are brought to the hands of humankind.

Due to the importance of organized self-assembly and the many formal similarities to the formation of organized mesophases, we will call these structures *mesocrystals*, as an abbreviation of *mesoscopically structured crystal*, and the process of parallel crystallization, colloidal assembly, and controlled structure formation, mesocrystallization.

In this analysis, much has been and still can be learned from the processes of biomineralization, leading to those well-defined organic–inorganic hybrid materials with superior material properties, complex morphologies and hierarchical order [8–10]. Biominerals are often iso-oriented crystal structures with amazingly complex morphologies, like the hammer-shaped building units of coccoliths [11] or the skeletal plates of sea urchins [12]. Although it is known that organic templates, as in the case for

coccoliths, play an important role [11], the actual crystallization mechanism of the inorganic phase in many biominerals remained largely unexplored.

Recently, increasing evidence was found that biomineralization also takes place via the colloidal pathways of meso-crystallization. Amorphous precursor particles, for instance, as reported for sea urchin spines [13], allow the storage of large amounts of materials in metastable precursor particles, which are readily available to a crystallization event in a confined reaction environment. Advantages of this crystallization pathway are highly efficient mass fluxes independent of ion products, the coupled high crystallization speeds, and crystallization without changes in the pH and the osmotic pressure, key features for mineralization, especially in biological systems. This is set in strong contrast to the possibilities of classical crystallization, which postulates an ion-by-ion or single molecule attachment to a critical crystal nucleus and is therefore bound to solubility products and diffusion limitations.

These particle mediated crystallization pathways are thus a nonclassical crystallization process involving mesoscopic transformation of self-assembled, metastable or amorphous precursor particles into nanoparticulate superstructures [14,15], as recently reviewed [16]. By mesoscale transformation, not only single oriented crystals with complex morphologies, but also superstructures of nanoparticles interspaced by organic additives can be formed. Their fusion leads to apparently single crystalline, isooriented structures with included organic additives as defects and sometimes also the leftovers of the prior amorphous phases. Support for this view comes from biomineral examples, which –although apparently single crystalline – often contain minor amounts of included biopolymers. This inclusion cannot be understood from the viewpoint of an ion-mediated crystallization process, as additives in this mechanism are generally considered to adsorb at edges and kinks in the developing crystal surface, stopping it from further growth [17]. (see also Figure 2.7).

Mesocrystal formation and the process of mesoscale transformation are, however, not restricted to biominerals, thus motivating this book. It looks like Nature makes use of an advantageous physico-chemical construction principle, gaining speed and flexibility of construction. In synthetic systems, similar inclusions of additives up to 30 wt.% were observed in as-grown crystals, too [18–20]. Revisiting the older literature shows that comparable observations were made in synthetic inorganic chemistry much earlier, even in the absence of additives [21–24], and the relevant question arises as to which role precursor particles and their superstructures play – at least as intermediates – in crystallization in general.

We also want to note that the term ''mesocrystal'' has been used before in the literature, but in the less restricted sense of a mutual three-dimensional translational ordering of various nanocrystals. As templates, pore systems of the MCM 41 type were used for the deposition of quantum sized $BaTiO_3$ [25–27] or $SrBi_2Ta_2O_9$. [26,28] Our definition is more restricted as it also involves, besides translational three-dimensional order, orientational order (vectorial alignment), and spontaneous self-assembly towards normally facetted microstructures.

Besides the interesting scientific question of formation mechanisms and the superior properties of the resulting materials, it is admittedly also a big bonus for this field that mesocrystals are simply beautiful and esthetically appealing. The fascination for objects with complex shapes has always been an integral part of the cultural heritage of

humankind and constitutes inspiration as well as a driving force in architecture, art and also science. The morphological diversity and complexity of naturally occurring forms and patterns has been a motivation for humans to copy Nature to achieve functional, esthetic, and societal value. [29] Although natural materials are often characterized by a finely carved appearance of remarkable aesthetical form, their formation is mostly directed by stringent selection processes, in order to provide efficiency and superior function [30].

Often, the non-classical nature of crystalline assemblies is not recognized, especially when they scatter X-rays and electrons like single crystals, which makes it difficult to assign mesocrystallization experiments described in the literature unequivocally. It is therefore the main task of this book to close this knowledge gap, to go beyond classical crystallization and to show that both crystallization pathways, particle-mediated and molecule-mediated, are in fact part of a common unifying crystallization scenario. Therefore, our book is structured into main chapters describing the classical crystallization theories and possibilities for crystal morphogenesis (Chapter 2), crystals challenging the classical textbook view on crystallization (Chapter 3), and nonclassical particle-mediated crystallization pathways (Chapter 4). Afterwards, we will give the foundations for the understanding of particle-mediated crystallization processes and mesocrystal formation. These include a treatment of self-organization processes (Chapter 5), colloidal crystals (Chapter 6), and the mesocrystal concept and properties (Chapter 7), including a description of the mesocrystals described so far sorted by their preparation and main occurrence. We will then try to capture the current existing knowledge about the formation mechanisms of mesocrystals (Chapter 8), as well as the analytical tools used to study mesocrystals (Chapter 9) and discuss the possibilities for the tuning of mesocrystal properties (Chapter 10). This will be summarized with the description of a unifying crystallization scenario combining classical and nonclassical crystallization (Chapter 11). This unifying crystallization scenario will allow, at least, for a phenomenological understanding of the crystallization phenomena described in this book. We will finally point out the analogy between hierarchically structured crystals and biopolymers, as well as oriented aggregation and polymers (Chapter 12) to show that a clear distinction between the living organic world and nonliving inorganic world cannot be made, which goes back to the initial views on this subject of people like Haeckel. Finally, we will end with a summary and outlook of possible future research directions (Chapter 13).

We have structured each of the main chapters in such a way that a short summarizing introduction for the general reader is given at the beginning of each chapter. This will enable the fast pick up of the main ideas discussed in the specific chapter, although each chapter also contains detailed material for the specialist or those readers who want to obtain extended knowledge in the described area. The chapters will also give relevant primary literature for more in-depth study of the subjects. Although our book, in view of the rapid development of this research area, has obviously no chance to be really comprehensive, it has at least been tried to capture the most recent developments and current knowledge. It is therefore hoped that this book will further stimulate research in this new and very exiting area, especially in view of the huge scientific and industrial relevance of crystallization processes and their control.

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2

Physico-Chemical Principles of Crystallization

Defining notations first is an enabling step for a scientific discussion of a distinct topic. This chapter introduces the physico-chemical background of crystallization processes and defines notations such as 'supersaturation', 'crystal growth','nucleation' and 'surface properties'. The expert reader may prefer to leave this chapter for later clarifications.

2.1 Classical Crystallization

Before mesocrystal formation and nonclassical crystallization processes are discussed, it is necessary to introduce the picture of classical crystallization itself at a very basic level. Crystallization starts from dissolved atoms or molecules, or in case of salts from different ions. The thermodynamic driving force for crystallization is the supersaturation of the solution. The relative supersaturation S is defined as a dimensionless ratio of the actual concentration of the species c, divided by its equilibrium molecular solubility product k_{sp} under the given set of conditions:

$$S = \frac{c}{k_{sp}} \tag{2.1}$$

In the case of multiple species involved in crystallization as, for example, in ionic crystals, c is the product of the concentrations of the individual components (or more correctly the activity product).

Further, it is important to note that the definition of supersaturation preassumes a structure of the final precipitate. If a species, e.g. calcium carbonate, exists in five different polymorphs and at least one amorphous species, the same concentration can mean different supersaturations depending on which species is precipitated, as a result of the different solubilities of amorphous matter and different crystalline polymorphs. These

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differences in supersaturation can be, in selected cases, rather large, which will turn into an important tool for polymorph control. It must be also mentioned that the magnitude of supersaturation is not the only driving force in crystallization control. On the contrary, the Ostwald rule of stages teaches that it is usually the least dense species and therefore the most soluble species which precipitates first (see also Section 2.5, Thermodynamic and Kinetic Crystallization Pathways). Supersaturation is therefore only a first approach in handling the complex problem of crystallization from a thermodynamic viewpoint, as the supersaturation can be related to the change in the chemical potential and thus the free enthalpy (Equation 2.2) of the crystallization reaction by:

$$\Delta\mu = -kT \ln S \tag{2.2}$$

where $\Delta\mu$ is the change in the chemical potential, k is the Boltzmann constant and T is the thermodynamic temperature.

Supersaturated solutions can be easily prepared by a temperature or pressure jump, by reactions generating the respective species, by adding nonsolvents under mixed solvent conditions, or – in the case of acids and bases – very conveniently by a pH jump.

Figure 2.1 presents the classical 1950 La-Mer curve for the crystallization behavior of sulfur in ethanol [1]. Here a reaction is linearly increasing the amount of sulfur, until a critical supersaturation is reached, and particles spontaneously form thereafter. Due to that, the sulfur concentration decreases again, until finally $S = 1$ or the equilibrium solubility is reached. If the time of the nucleation burst is short, crystal nuclei of uniform size can be obtained, which is often desired in colloid synthesis.

Once supersaturated (i.e. $S > 1$), crystals can, in principle, grow in solution, but need a nucleus to grow from. In *heterogeneous nucleation*, surfaces or dispersed components, such as dust particles or crystal seeds, provide the starting point for the crystallization event. Heterogeneous nucleation is least demanding and becomes relevant when the other

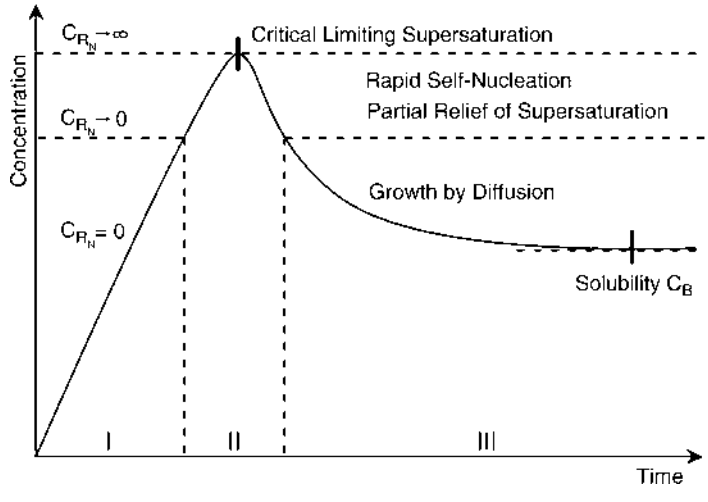

Figure 2.1 *Schematic representation of the concentration of molecularly dissolved sulfur before and after nucleation as a function of time. (Taken from V.K. LaMer, R.H. Dinegar, J. Am. Chem. Soc.* ***1950****, 72, 4847. With permission of the American Chemical Society.)*

options are kinetically excluded. In *homogenous nucleation*, the nucleus forms spontaneously from the solution itself when a critical supersaturation is reached, however it is in a crystal-by-crystal fashion. The nucleation sites in this model can be treated independently. In addition, we will also introduce the concept of *spinodal* (homogeneous) *nucleation*, in which all crystals start to nucleate practically at the same time, i.e. the single nucleation events cannot be treated as thermodynamically independent, but are coupled via a joint concentration field.

2.2 Definition of a Crystal and Crystal Growth

According to Wikipedia free encyclopedia (http://en.wikipedia.org/wiki/single_crystal, definition taken on 23.7.07), 'a single crystal, also called monocrystal, is a crystalline solid in which the crystal lattice of the entire sample is continuous and unbroken to the edges of the sample, with no grain boundaries. The alternative to the presence of a single crystal sample is a *polycrystalline* sample, which is made up of a number of smaller crystals known as *crystallites*. Because of a variety of entropic effects on the microstructure of solids, including the distorting effects of impurities and the mobility of crystallographic defects and dislocations, single crystals of meaningful size are exceedingly rare in nature, and can also be difficult to produce in the laboratory under controlled conditions.'

In the classical view, a crystal is therefore a solid body with a rigid lattice of molecules, atoms or ions in a characteristic location for the crystal [2]. The smallest repeat unit of the crystal is its unit cell. Due to the regularity of its internal structure, a crystal has a characteristic shape with smooth surfaces parallel to atomic planes in the lattice. Therefore, defined angles exist between the external faces. This is expressed in the law of constant interfacial angles, stating that the angles between corresponding faces of all crystals of a given substance and polymorph are constant. A typical single crystal is displayed in Figure 2.2.

This definition of a crystal expresses single crystals as solid bodies with a defined geometrical outer shape characterized by smooth surfaces. This definition excludes any curvature in the morphology of a single crystal. The flat surfaces of a crystal growing via layer-by-layer adsorption of solute atoms or molecules onto an existing crystal face was suggested by Volmer [3]. When an atom/molecule arrives at the crystal surface from solution, it is not immediately integrated into the crystal lattice, but is able to migrate on the crystal surface in two dimensions. These units form the so-called adsorption layer with a typical thickness of about 1 nm [2]. The migrating units on the crystal surface will get integrated into the crystal lattice at 'active centres' where the attraction of the moving units to the lattice is greatest. These are steps and kinks on the growth surface (Figure 2.3a). The attachment of a growth unit to a kink is the most favoured scenario, so that the kink moves along the step until it is completed and a new step is started.

The nucleation of a new layer starts from surface nucleation of an island on the plane face (Figure 2.3c), which grows further by attachment of further atoms/ions to the steps and kinks of the new layer until the surface is completed (Figure 2.3b). This layer-by-layer growth mode of a crystal surface is expressed in the model of Kossel [4].

However, the growth of a surface is rarely perfect, and a number of imperfections exist in form of vacancies (Figure 2.4 E,F) and dislocations, screw dislocations being a

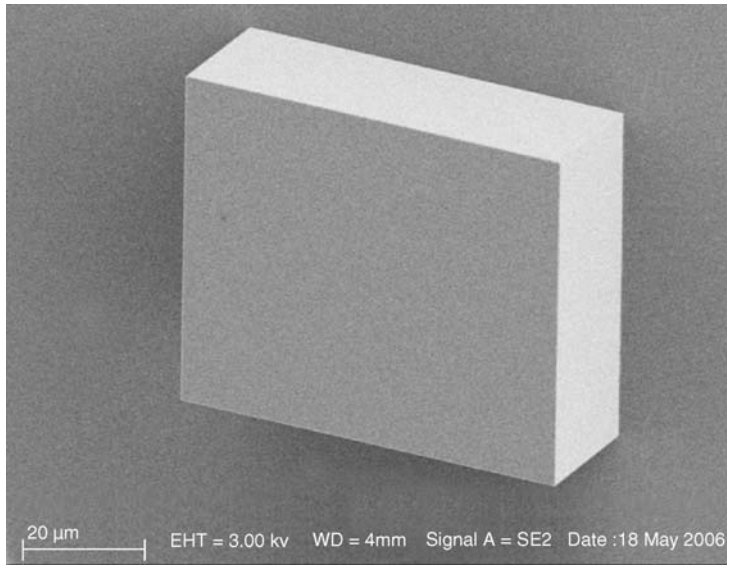

Figure 2.2 *Single crystal of calcite ($CaCO_3$) with the typical rhombohedral morphology.*

particularly important example. In addition, even at equilibrium, the steps have kinks due to thermally activated detachment of molecules from the steps onto either the step edges or the terraces or even back into solution [5–7]. Consequently the step edges are not static; molecules are constantly attaching and detaching, even at equilibrium [8,9]. As a consequence, growth steps are not as ideal, as implied by the Kossel model, but fuzzy (Figure 2.5). Growing crystal surfaces can nowadays be very favourably imaged by scanning force microscopy (SFM), while the growing layers can be depicted with high resolution (Figure 2.6).

In a similar manner, the surface nucleation in form of islands (Figure 2.6c) can be imaged using SFM, and some typical scenarios are shown in Figure 2.7.

The layer-by-layer growth of crystals has important consequences for the effect of impurities on the growth of a crystal face. Potential impurities are all substances other than

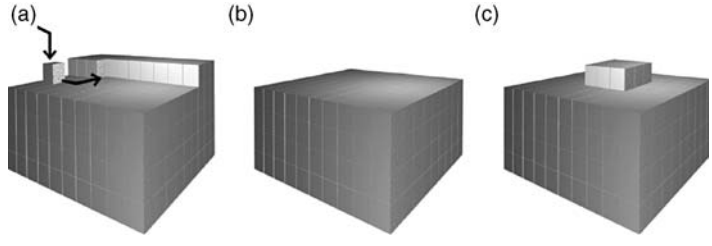

Figure 2.3 *Ideal layer-by-layer crystal growth: (a) migration of a unit towards a kink on the surface; (b) completed layer; and (c) surface nucleation. (Reproduced from J.W. Mullin, Crystallization, 4th edn., Butterworth-Heinemann, Oxford, 2001, with permission of Butterworth-Heinemann).*

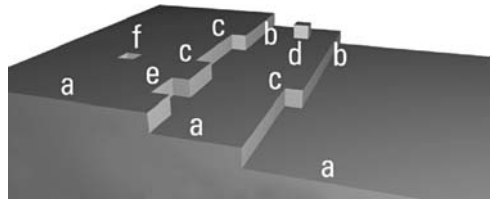

Figure 2.4 *Kossel's model of a growing crystal surface showing: (a) flat surfaces; (b) steps; (c) kinks; (d) surface adsorbed growth units; (e) edge vacancies; and (f) surface vacancies. (Reproduced from J.W. Mullin, Crystallization, 4th edn., Butterworth-Heinemann, Oxford, 2001, with permission of Butterworth-Heinemann).*

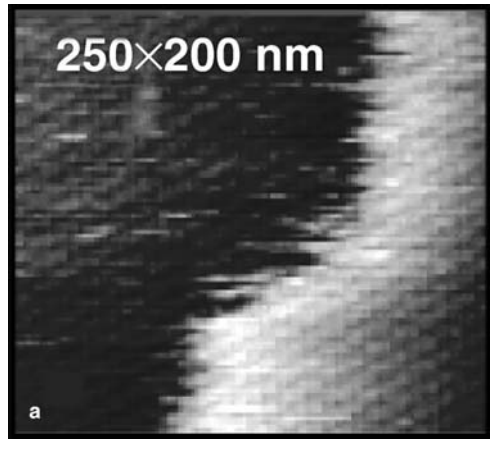

Figure 2.5 *AFM images of a step on a crystal of the protein canavalin showing the fuzziness of the step due to attachment and detachment of molecules. (Image reproduced from [10] with permission of Mineralogical Society of America.)*

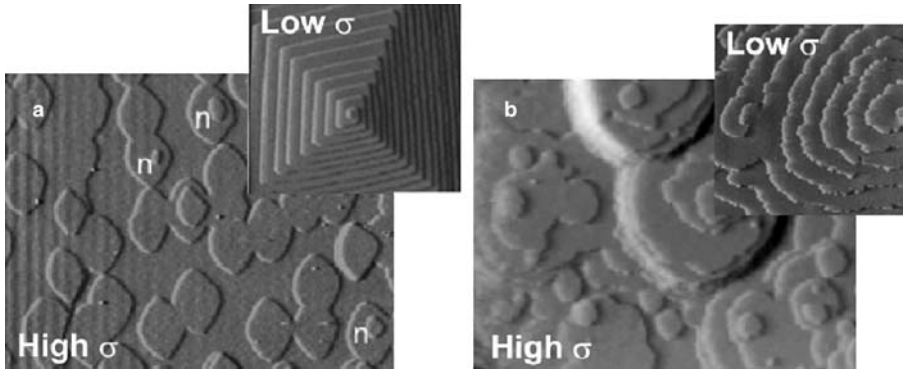

Figure 2.6 *AFM images showing examples of two-dimensional nucleation at high supersaturation for (a) calcite and (b) canavalin. N - locations where islands have nucleated on top of other islands. σ is the supersaturation in this image. (Image reproduced from [10] with permission of Mineralogical Society of America.)*

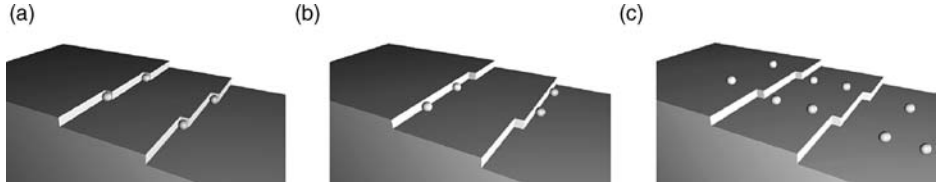

Figure 2.7 *Sites for impurity adsorption on a growing crystal based on the Kossel model. (a) kink, (b) step and (c) surface after impurity adsorption. [11] Reproduced from [2] with permission of Butterworth-Heinemann at Oxford.*

the crystallizing material, including even the solvent. Impurities can adsorb at various sites of the growing crystal as shown in Figure 2.7 and both lower the surface energy of the crystal face as well as inhibit step edges from further growth. The influence of an impurity on crystallization is therefore both thermodynamic and kinetic in character.

The adsorption of impurities onto kinks or steps allows a tiny amount of an impurity to retard or even block the growth of a complete crystal face. The surface is 'poisoned,' which is often a desired effect to selectively block the growth of a certain face if an impurity is found which selectively adsorbs to this specific crystal face. This is further discussed in Section 2.7, Crystal Morphology and the Role of Additives and Selective Adsorption.

One example of proteins adsorbing to the step edges of a growing calcite (104) surface is illustrated in Figure 2.8. It can be seen that the step edges become rounded, which is equivalent to a macroscopic habit modification of a crystal by additive adsorption.

On the other hand, the additives can also nucleate the growth of new layers, as found for the protein perlucin (Figure 2.9) [13]. The nucleation of new layers will also modify the macroscopic crystal morphology.

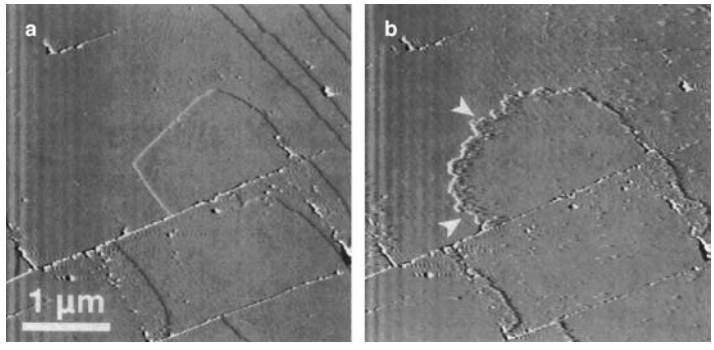

Figure 2.8 *(a) A calcite (104) surface without proteins. Light grey and dark grey lines are obtuse and acute step edges, respectively. Step edges are generally straight and smooth, with sharp corners. Some kinks are visible in the acute step edges in the upper right corner. (b) With proteins. Step edges have become rounded (suggesting an isotropic step edge speed) and more convoluted. The step edge appears highlighted, as by a raised lip of proteins. Strong white-and-black features (that are identical in (a) and (b)) are defects in the crystal that can act as barriers to step edge motion. (Reprinted from [12] with permission of the Biophysical Society.)*

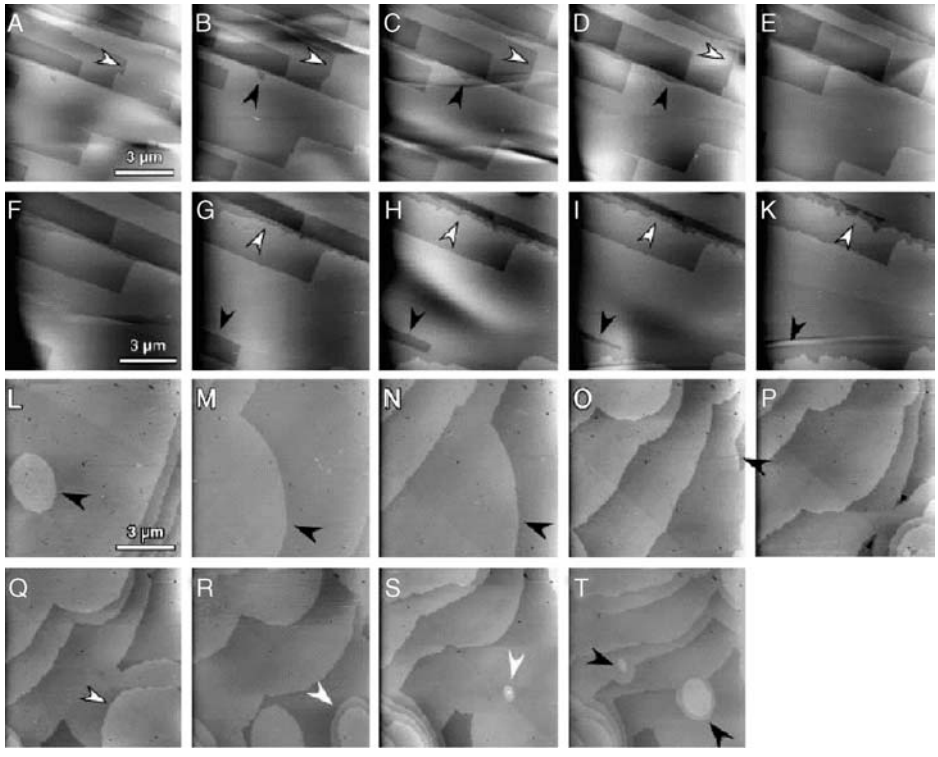

Figure 2.9 *AFM measurements of the interaction of perlucin with geological calcite (3 min interval between two images). (A–E) Consecutive AFM images of a (4-4-1) calcite surface immersed in deionized water. The calcite crystal slowly dissolves layer by layer (white and black arrowheads). (F–K) Consecutive AFM images of the growth of calcite (4-4-1) surface in saturated calcium carbonate solution. Note the growth of the molecular layers (white and black arrowheads). (L–T) Consecutive AFM images show a (4-4-1) calcite surface immersed in saturated calcium carbonate solution with perlucin (0.01 mg/mL). Note that perlucin nucleates small islands (e.g. R, S, light grey arrowheads) for the next molecular layer. As different layers (e.g. L to O, black arrowheads) merge without detectable defects (e.g. small arrowheads in P), it is reasonable to suggest that perlucin induces epitactic growth of new layers in the orientation of the crystal lattice. (Reprinted from [13] with permission of Blackwell Publishing Ltd.)*

If the growth of the face is not completely blocked, the impurities are potentially incorporated into the crystal after they are overgrown by subsequent layers. This can be nicely demonstrated for the case of polymer latexes which are functionalized to adsorb onto certain crystal faces so that they get incorporated into the crystals [14]. Once removed from the crystal by dissolution or calcination, a porous crystal with a 'swiss cheese' morphology is obtained, as shown in Figure 2.10.

The adsorption of additives onto crystal surfaces can be highly selective and even chiral surface textures can be produced with a chiral additive. An example is presented in Figure 2.11, which shows the effect of right-handed and left-handed aspartic acid on the shapes of growth hillocks and the resulting macroscopic crystals [16]. It is obvious that

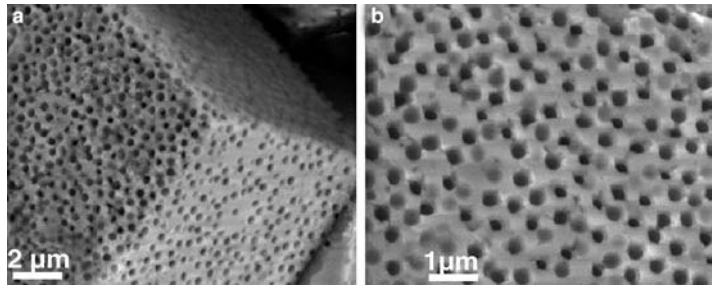

Figure 2.10 *SEM images of $CaCO_3$ particles with porous surface obtained by templating and THF extraction of P(St-MMA-AA) latex particles with a size of 380 nm. (Image reproduced from [15] with permission of the American Chemical Society.)*

the shapes of the growth hillocks are dramatically altered and the symmetry about the calcite glide plane is broken, such that L-aspartic acid gives one chirality, while D-aspartic acid gives the opposite chirality. There are new step directions that can be altered from one side of the glide plane to the other when the amino acid enantiomer is switched from L to D. This observation is explained by changes in the step edge energies caused by the adsorption of the chiral additives.

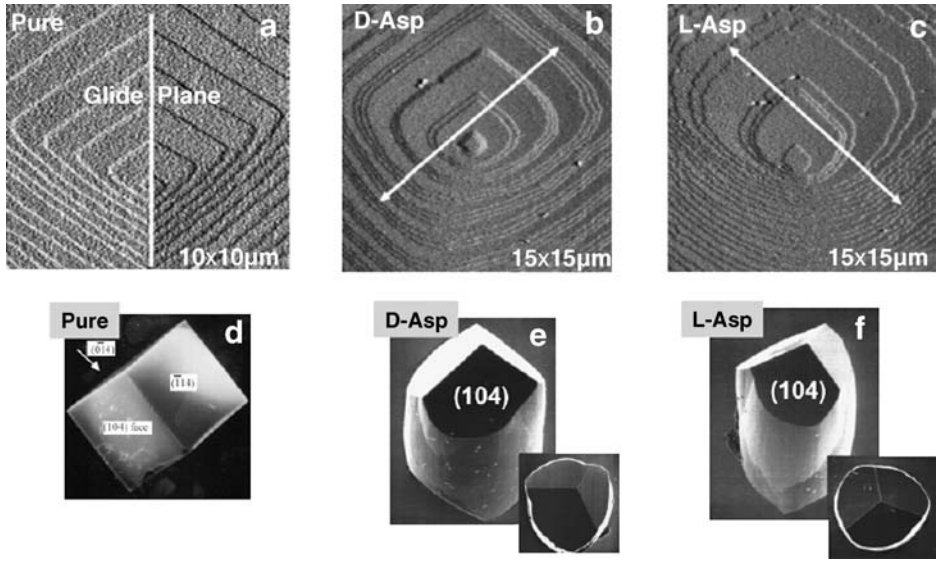

Figure 2.11 *Example of a system that exhibits behavior expected for addition of a growth modifying additive. AFM images of calcite grown in: (a) pure solution; (b) solution containing D-aspartic acid; and (c) solution containing L-aspartic acid. The shape changes dramatically and even shows a left–right shape dependence that corresponds to that of the additive. (d–f) show that the resulting crystal shape reflects these changes. Figure reproduced from [16] with permission from Nature publishing group.*

2.3 Nucleation Theories

2.3.1 Classical Nucleation Theory

Homogeneous Nucleation. Homogeneous nucleation phenomena have been studied for over 70 years, starting with the pioneering experiments of Wilson and the theoretical studies of Becker and Döring [17] and Volmer [3]. Although spontaneous homogeneous nucleation is well studied, there are still major uncertainties concerning the nucleation mechanisms and their theoretical description. It is well known that the classical nucleation theory (CNT) [17], which is the most commonly found formalism to analyze nucleation phenomena, fails in predicting the temperature dependence and absolute values of the critical supersaturations of a number of substances including water, alcohols and high alkanes [18–23]. A large number of theories [24–28] to test against the experimental data have been reported in the literature in the last two decades, yet a major source of the discrepancies is not clearly identified.

Classical nucleation theory considers the formation of a molecular cluster consisting of $i + 1$ molecules by the attachment of a single vapor molecule (monomer) to an i-mer. The classical homogeneous nucleation (or barrier-crossing) rate J is given by a simple Boltzmann approach:

$$J = K \exp\left(\frac{-\Delta G_i}{kT}\right) \tag{2.3}$$

where k is the Boltzmann constant, ΔG_i is the change in the Gibbs free energy associated with the i-mer formation, and K is the kinetic prefactor. The barrier height or change in the Gibbs free energy is expressed in the CNT as a sum of volume and surface terms:

$$\Delta G_i^{CNT} = \Delta\mu_i + \gamma A(i) \tag{2.4}$$

where ($\Delta\mu_i$ is the change in the chemical potential of the i-mer, *A(i)* is the surface area of the i-mer, and γ is the surface free energy. The volume terms typically drive the reaction, as a new, more stable phase is formed (e.g. by the crystallization enthalpy), whereas the surface terms are usually positive and hinder the formation of a new phase.

As the surface area of each nucleus is proportional to the square of the radius of the spherical cluster r^2, whereas the volume is proportional to r^3, there is a maximum of barrier height for a distinct cluster size r^*, the so-called critical cluster size (see Figure 2.12). Compared to the speed of molecular processes, as described by the Boltzmann probability in Equation (2.3), the clusters rarely reach the size of a so-called critical crystal nucleus. At this point, the change in the free enthalpy of the system becomes negative upon further particle growth, and the gain in lattice energy over-compensates the loss in surface energy. The critical crystal nucleus is the smallest crystalline unit capable of continued further growth. Its existence separates the domain of nucleation from the domain of crystal growth.

It is interesting to note that this critical cluster size was determined in a number of cases. For water, dependent on temperature, critical cluster sizes of 20–35 molecules were reported [20]. For pentanol as a model system, these numbers are between 24–36 [29]. However, the above sizes of the critical crystal nucleus do not only depend on the system, but also on the shape and structure of the nucleus [30]. This is not accounted for

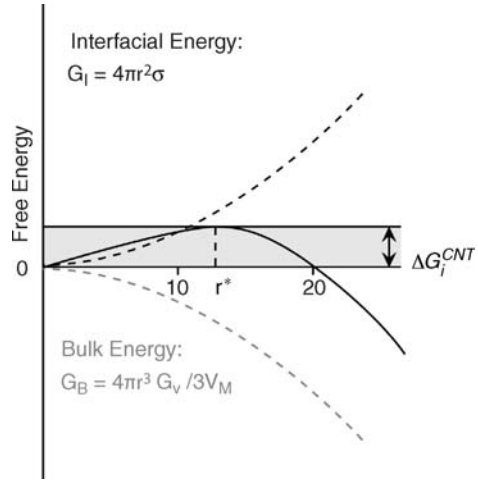

Figure 2.12 *Change of ΔG_i^{CNT} with r. At a distinct particle radius r*, the bulk energy balances the surface energy. ΔG_i^{CNT} at r* is the nucleation barrier. For $r > r^*$, ΔG_i^{CNT} becomes negative, particle growth is favoured.*

in the CNT, which assumes a spherical solid cluster. Indeed, it was possible to follow the crystallization of 12 nm large apoferritin molecules with AFM in a 'movie mode', and a nonspherical, quasi planar shape of this particular critical crystal nucleus was demonstrated, consisting of 20–50 apoferritin units (see Figure 2.13) [31].

The Becker–Döring theory expresses the nucleation rates, i.e. rates of events passing the critical barrier, as:

$$\begin{aligned} J^{BD} &= \upsilon N_i^2 \left[\frac{2\gamma}{\pi M}\right]^{0.5} \exp\left[\frac{-\Delta G_i^{CNT}}{kT}\right] \\ &= K^{BD} \exp\left[\frac{-\Delta G_i^{CNT}}{kT}\right] \end{aligned} \tag{2.5}$$

which gives Equation (2.3), where M is the molecular weight, N_i is the number of i-mers and υ is the molecular volume.

The kinetic prefactor $\upsilon N_i^2 [2\gamma/\pi M]^{0.5}$ was later found to be inconsistent. Two different derivations of the classical nucleation rate performed using both the kinetic theory and constrained equilibrium approach [32,33] showed that the Becker–Döring theory should be corrected by $1/S$. Nevertheless, the Becker–Döring theory, in its original form, remains the most common theory to analyze nucleation processes, probably because the application of the correction $1/S$ to Equation (2.5) makes the agreement with the experimental data even worse. In many contributions, the Becker–Döring theory is even denoted as CNT.

Nucleation rates in the kinetically consistent version of CNT are given by the following equation:

$$J^{CNT} = \upsilon N_1^2 \left[\frac{2\gamma}{\pi M}\right]^{0.5} \frac{1}{S} \exp\left[\frac{-\Delta G_i^{CNT}}{kT}\right] = \frac{1}{S} J^{BD} \tag{2.6}$$