
Book Section:

Ramachandran, V, Halfpenny, PJ and Roberts, KJ orcid.org/0000-0002-1070-7435 (2017) Crystal science fundamentals. In: Engineering Crystallography: From Molecule to Crystal to Functional Form. NATO Science for Peace and Security Series A: Chemistry and Biology . Springer , Dordrecht , pp. 3-19. ISBN 978-94-024-1115-7

https://doi.org/10.1007/978-94-024-1117-1_1

Chapter 1

Crystal Science Fundamentals

Vasuki Ramachandran, Peter J. Halfpenny and Kevin J. Roberts

Abstract The fundamentals of crystal science notably crystallography, crystal chemistry, crystal defects, crystal morphology and the surface chemistry of crystals are introduced with particular emphasis on organic crystals.

Keywords: Crystallography, Crystal Lattices and Systems, Crystal Planes and Directions, Crystal Defects, Crystal Chemistry, Crystal Morphology, Surface Chemistry

Introduction

Production of many crystalline products such as pharmaceuticals are underpinned by a science-led quality by design (QbD) approach. This typically involves the need to understand, predict, manipulate and control the core processes involved in drug design, development and manufacture. The latter can be understood through a consideration of an integrated 5F materials transformation pathway developed from the target molecule's molecular structure which links and interrelates:

- Formulae (atomic and molecular structure),
- Formation (crystallisation, precipitation, spray drying, etc.),
- Form (crystal size, morphology, polymorphic form, etc.),
- Formulation (blending, granulation, compaction, etc.),
- Function (product purpose and performance).

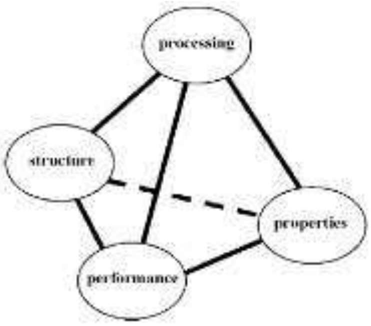


Fig. 1 The material science tetrahedron, after Sun [1], (reproduced with the permission of Journal of Pharmaceutical Science)

This approach enables cross-correlation (see Fig. 1) for a given crystalline material's or formulated drug product's

- molecular and crystal structure,
- physical and chemical properties,
- processing behaviour,
- performance.

The above holistic approach forms the overall aim of this Erice Summer School and in this brief introductory chapter the aim is to provide a short primer to the attendees for those unfamiliar with basic concepts of crystal science. The materials introduced here will underpin further chapters.

Crystals and Crystallography

Crystalline Solids

The principle differences between the three states of matter, solids, liquids and gases, illustrated in Fig. 2, lie in the separation and mobility of the atoms or molecules of which they are composed. In the gaseous state, molecules are highly mobile and separated by large distances. In liquids, molecules are in close proximity but still retain substantial mobility. While in the solid-state, molecular motion is typically limited to vibration and intermolecular distances are at a minimum.

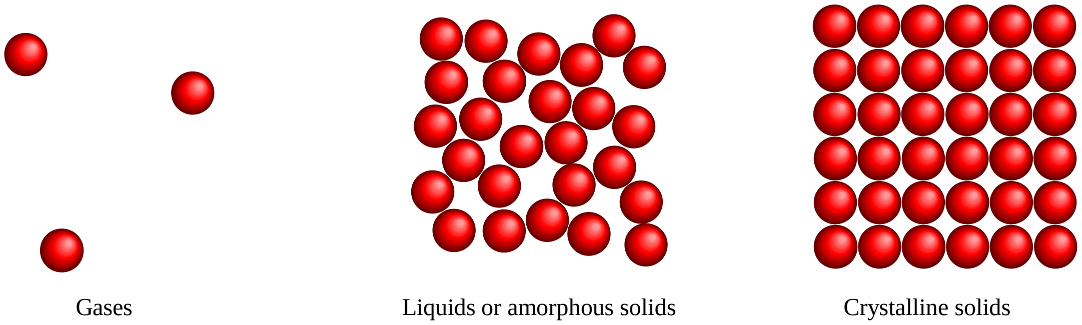


Fig. 2 Schematic diagram highlighting the differences between the gaseous (left), liquid (centre) and solid (right) states of matter

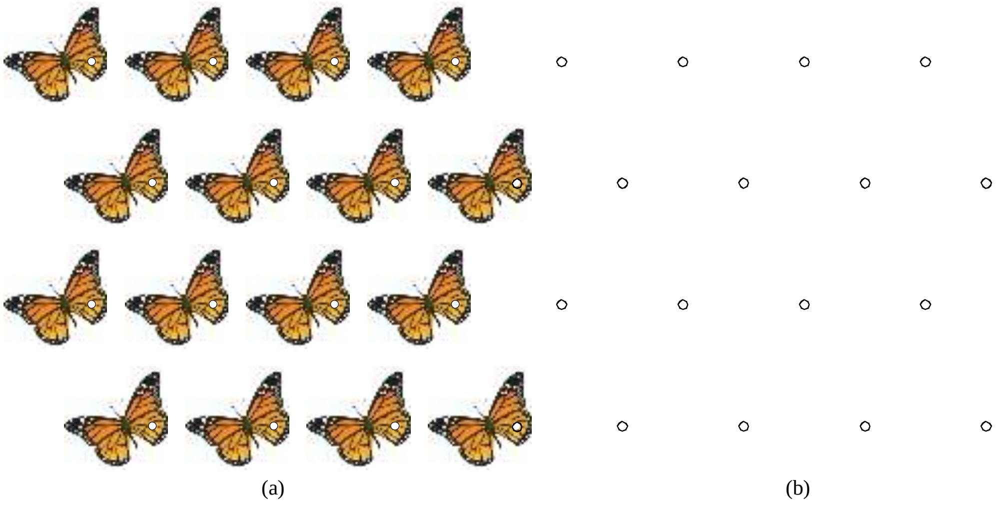
A crystal is a regular array of molecular entities, ordered in 3D where this degree of order extends up to macroscopic dimensions. A single crystal is the one in which this 3D order extends up to the sample's physical size. In contrast, a polycrystalline solid is the one where the crystal size is smaller than the actual sample size. In the latter case the sample could be aggregate of a number of smaller micro-crystalline grains such as an iron bar or a ceramic block, either of which could have a grain size of ca. 1 μm. It should be noted that the atomic level properties of both poly- and mono-crystalline solids are the same as the atomic-scale forces operate on the nm scale size, at which level the difference in nature of the molecular interactions between 1 μm^3 (micro-crystal produced in industrial crystallisation reactors) or 100 cm^3 (for electronic device materials) samples are negligible. Hence, the science underlying the structure and crystallisation behaviour for both of these types of materials, i.e. single crystals and polycrystalline solids is essentially the same.

Solids may be either crystalline or amorphous in nature. Crystalline solids are characterised by long-range 3D order and exhibit a periodic three-dimensional pattern in terms of the arrangement of the component atoms of the solid. The structure of amorphous solids, in contrast, closely resembles that of the liquid state. Although some short-range order may be present in amorphous solids, they are best described as disordered. An amorphous solid is thermodynamically metastable. It may transform to a crystalline structure if the kinetic barriers are not too great. However, many amorphous materials, such as glass, have retained their disordered structure for centuries. Materials with the same molecular structure can also have different crystal structures and this is referred to as polymorphism. For example, carbon forms crystals which can have one of three well known structures: graphite, diamond and buckminsterfullerene.

The structural differences between the different polymorphic forms of crystals and also those of amorphous forms of a given substance can give rise to substantial differences in both their physical and chemical properties. The relationship between structure and properties is a recurring theme which runs throughout this school.

Crystal Lattice

The simplest definition of a crystal is a 3D repeating pattern of atoms. The schematic given in Fig. 3(b) represents a 2D pattern of a single butterfly being repeated in the same orientation (a) which can be simply represented by an array of circles.



(a) (b)

Fig. 3 A simple 2D pattern of a complex object (a butterfly) **(a)** together with its corresponding lattice **(b)** as represented by circles

The 2D pattern (butterfly) is called the **motif** and the points which make up the array are called **lattice points**. One important feature of a lattice is that the environment of each lattice point is identical. In order to describe the scheme of repetition it is not, however, necessary to reproduce the entire lattice, but a small representative part, such as the parallelogram shown more completely in 3D in Fig. 4(a). This still contains all the information necessary to define how the pattern is repeated and can be fully described using only the lengths of the sides (a and b) and the angle (γ) between the sides. This representative part of the lattice is referred to as a **unit cell**, as shown in Fig 4(b),

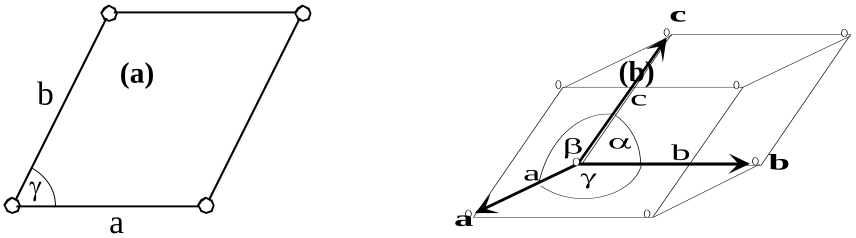


Fig. 4 (a) The unit cell and lattice parameters of the two dimensional pattern and **(b)** a three-dimensional unit cell, crystallographic axes a, b, c and the lattice parameters, a, b, c, α, β, γ.

An entity or motif sitting at the lattice point could be an atom (e.g. for metallic or elemental compounds), group of atoms (for complex atomic solid such as silicon which has 2 atoms/lattice point), collection of ions (e.g. ionic solid such as K_2SO_4 would have 2 K^+ and 1 SO_4^{2-} ions at each lattice point) or a molecule (e.g. organic compound would have complete molecule at each lattice point).

The key crystal science concepts are:

- Crystal = Motif (what is being repeated) + Lattice (where to repeat),
- A more advanced definition of crystal = Asymmetric unit (motif or what to repeat) + Space group (how to repeat about the lattice points) + Wykoff positions (where to repeat in the unit cell),
- Crystal lattice - infinite 3D array of points (lattice points),
- Unit cell - smallest reproducible unit within crystal lattice (Fig. 4),
- Lattice direction [uvw] - line drawn through lattice, where u, v, w are unit vectors along three non- orthogonal directions (Fig. 5),
- Miller plane (hkl) - 2D surface cut through lattice (Fig. 6),

- Asymmetric unit - atom, molecule, ions, groups of molecules.

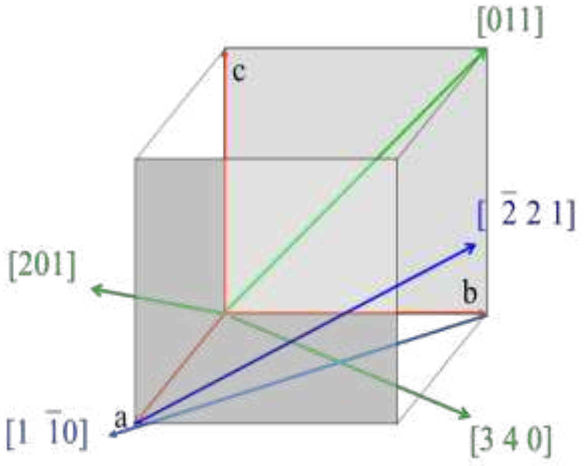


Fig. 5 Crystallographic directions shown by coloured arrows. A direction is denoted by the smallest coordinates of a point through which the line passes and usually the smallest integer are used

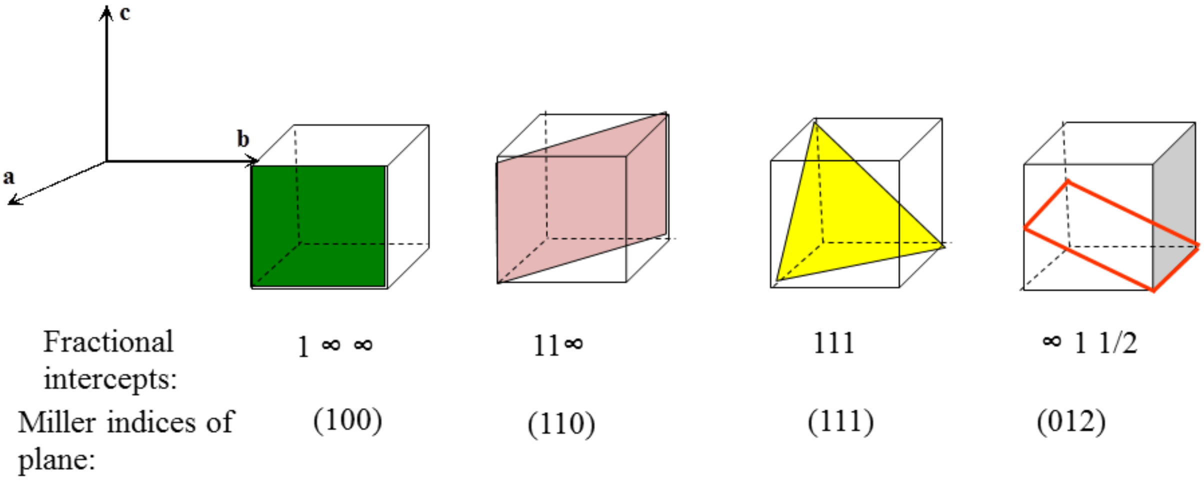


Fig. 6 Crystallographic planes or Miller planes are denoted by the reciprocal of the fractional coordinates of intercept of the plane with crystallographic axes

Crystal Systems

A vector r_{uvw} in lattice with respect to the three (integer) vectors u, v, w is defined as:

$$r_{uvw} = ua + vb + wc \tag{1}$$

a, b and c are lattice parameters defining the size and shape of the unit cell but are not necessarily orthogonal. Hence, this is why we additionally need three angles to define the unit cell. α - angle between b and c; β - angle between a and c, γ – angle between a and b.

The inter-relationship between a, b, c, α, β and γ gives rise to a total of 7 crystal systems as shown in Table 1. Examples of unit cells, Ibuprofen and D-mannitol, are illustrated in Fig. 7.

Table 1 Seven crystal systems and examples

System	**Axial lengths and angles**	**Example**
Cubic	$a = b = c$, $\alpha = \beta = \gamma = 90^o$	NaCl
Tetragonal	$a = b \neq c$, $\alpha = \beta = \gamma = 90^o$	TiO_2 , Urea
Orthorhombic	$a \neq b \neq c$, $\alpha = \beta = \gamma = 90^o$	$(NH_4)2SO_4$
Rhombohedral or trigonal	$a = b = c$, $\alpha = \beta = \gamma \neq 90^o$	$CaCO_3$, α-Quartz
Hexagonal	$a = b \neq c$, $\alpha = \beta = 90^o, \gamma = 120^o$	Zn

Monoclinic	$a \neq b \neq c$, $\alpha = \gamma = 90^o \neq \beta$	Paraffin, sucrose
Triclinic	$a \neq b \neq c$, $\alpha \neq \beta \neq \gamma \neq 90^o$	$CuSO_4\,5(H_2O)$

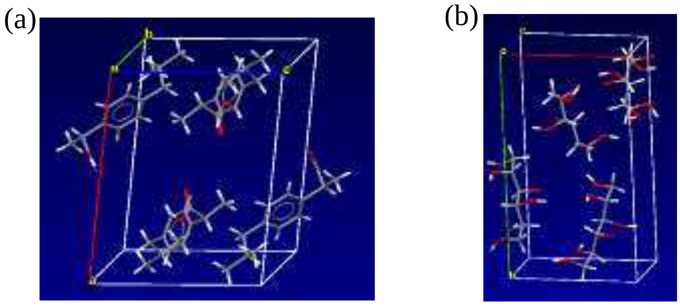


Fig. 7 Examples of unit cells: **(a)** Ibuprofen [2] belonging to monoclinic structure with: a = 14.67, b = 7.89, c = 10.73, β = 99.36; **(b)** D-mannitol [3] belonging to orthorhombic structure with: a = 8.67, b = 16.88, c = 5.56

Crystal Chemistry

We now need to add the chemical nature of the material into our concept of the crystal lattice. For a given molecule there are two dominant factors (Fig. 8) which influence what crystal structure a given material might adopt:

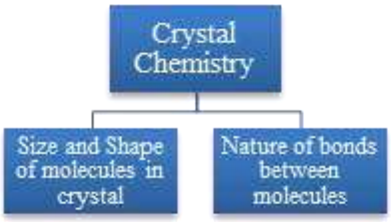


Fig. 8 Schematic explaining crystal chemistry with the key factors that affect the crystal structure.

These factors affect physical and crystallographic properties. We can subdivide types of solid into 5 main groups of materials (see Fig. 9).

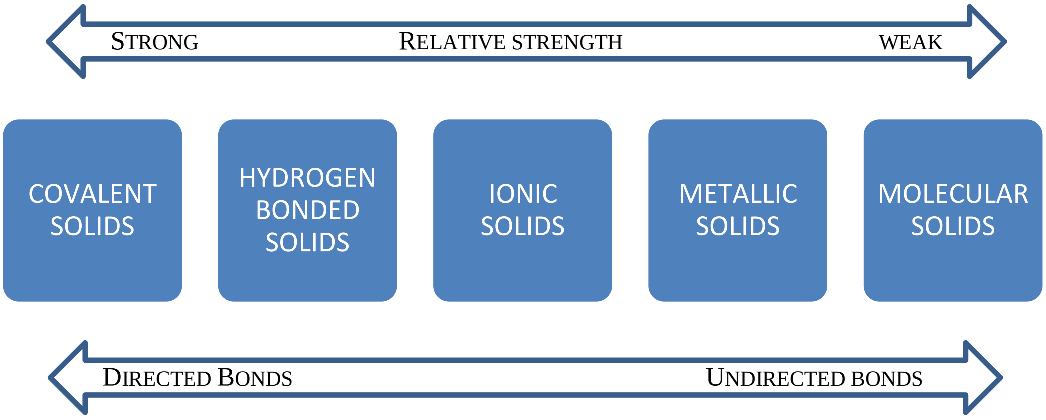


Fig. 9 Schematic showing the major types of inter-molecular bonding expected in the solid-state in relation to their relative strengths and their directional nature

Directed bonds tend to stop or restrict close packing which, in turn, makes for a lower density solid when compared with similar materials which have undirected bonds. The size of a molecule is reflected on the magnitude of the unit cell lattice parameters; e.g. the molecular solid benzophenone [4] ($(C_6H_5C=O)_2$) has lattice parameters of a = 10.28, b = 12.12, c = 7.99 A (orthorhombic) whilst much smaller atomic materials such as metal copper has a = 3 Å (cubic). The shape of a molecule reflects on the crystal system:

- Elemental compounds, such as metals and semiconductors, crystallising in high symmetry crystal classes such as cubic and hexagonal.
- Irregularly shaped molecules, such as organic molecules and inorganic complexes, crystallising in the lower symmetry triclinic, monoclinic classes.

The nature of bonding in any solid is of considerable importance since it influences, either directly or indirectly, a wide range of properties, notably melting point, crystal structure and mechanical properties. Most organic solids are molecular in nature. While the atoms within a molecule are held together by strong covalent bonds, the interatomic interactions are saturated and hence only weak intermolecular forces exist between molecules. Many pharmaceutical compounds are utilised in the form of salts and therefore exist as ionic species. In such cases, the role of strong ionic interactions must also be considered.

Three factors are of particular importance in assessing the influence of intermolecular bonding on the properties of organic solids:

- Strength of the interaction,
- Distance over which the interaction exerts an influence,
- Extent to which the bonding is directional.

Table 2 summarises the principle types of intermolecular bonding in organic solids.

Table 2 Types of bonding in organic solids

Type	**Occurrence**	**Strength of Interactions**	**Range**	**Directed Interactions?**
van der Waals	All atoms and molecules	Weak (1 - 10 kJ/mol)	short	No
Dipole-dipole	Between polar molecules only	Weak (3 - 4 kJ/mol)	long	No
Hydrogen bonding	Molecules containing O, N or F and a hydrogen bonded to one of these electronegative atoms	Strong (10 – 40 kJ/mol)	short	Yes
Ionic	Monatomic and molecular ions	Strong (10 – 50 kJ/mol)	short	No
Covalent	Intramolecular interactions between atoms	Strong	short	Yes

In organic compounds bond strengths are characterised by:

- Strong intra-molecular bonds - robust molecules,
- Weak and isotropic inter-molecular bonds - soft solids with low melting point.

The bonding directionality is un-directed except for covalent crystals and where there are H-bonds.

In summary, the main features that influence the organic solids are:

- Size of Molecules – large unit cells,
- Shape of Molecules – non-spherical shape,
- Nature of intermolecular forces – weak undirected,
- van der Waals bonds – close packed structures.

As a result, the organic crystalline solids have:

- Low melting point solids,
- Low symmetry crystallography,

- Polymorphic nature,
- Anisotropic deformation.

Defects in Crystals

So far we have assumed that the crystal lattice is perfect with no variations in crystal structure taking place on a dimensional range spanning atomic to macro-scale. Given that all molecules have thermal motion and that crystal growth is not an equilibrium process, this is an unrealistic prospect. In reality, a crystal during its formation and subsequent processing is likely to develop a range of lattice imperfections. Hence, all crystals are imperfect and can have atoms missing or in the wrong crystal lattice positions. In many respects the properties of a crystalline material are determined as much by the imperfections in the arrangement of its component atoms as by the crystal structure itself. The following discussion serves to illustrate the nature of these defects together with their importance in terms of controlling the properties and behaviour of crystalline solids.

Defects and their Dimensionality with Respect to the Crystal Lattice

These collections of displaced atoms may also extend through the crystal in one, two or three dimensions. Thus the dimensionality of crystal defects beyond the atomic scale is a useful way of categorising the different types of imperfections which may exist.

Point Defects (0D). These are the most localised form of lattice defects and comprise:

- Vacancies (atoms missing from the crystal structure),
- Interstitials (atoms located in the, normally empty, voids within the structure),
- Impurities which can be foreign atoms incorporated into the crystal latter either, substitutionally, at a normal lattice site, or at an interstitial site.

Line Defects (1D). One dimensional line defects known as dislocations consist of atomic displacements and structural distortions which are confined to lie along a line through the crystal structure.

Planar Defects (2D). A variety of planar defects are known to exist within crystals. One of the most common of these is a stacking fault. These are regions of a crystal which contain either an extra layer of atoms or a missing layer of atoms. Within such regions there is a disruption to the normal stacking sequence of atoms in the structure.

Volume Defects (3D). Finally, three dimensional defects such as precipitates or inclusions are common in most crystals. Precipitates arise from the aggregation of impurity atoms whose concentration in the crystal exceeds the solubility limit due, for example, to a decrease in temperature. Inclusions, on the other hand are macro/microscopic particles or volumes of solvent trapped inside the crystal as the growth front advances.

Point Defects and their Role in Facilitating Solid State Diffusion

Point defects are equilibrium defects, i.e. due to Boltzmann statistics some atoms will always have sufficient kinetic energy to escape from their crystal lattice sites moving into interstitial sites or creating a vacancy. Without these defects we would not have any chemical reactivity in the solid state. Point defects influence almost all properties of crystalline solids, from electronic and optical properties through to mechanical behaviour. The process of solid-state diffusion, i.e. the movement of atoms through a solid is central to many physical properties and processes. It is involved in, for example, the mechanical behaviour of solids under deformation or their chemical degradation. Consider an idealised perfect crystal as shown on the left of Fig. 10. Because of the close packing of the atoms it would be extremely difficult for an atom of any type to move through the crystalline solid. If, however, the crystal contains vacancies (which all crystals do), atoms are able to change their positions by moving into the vacancy as shown in 4 diagrams to the right hand side of Fig. 10. The resulting movement of the vacancies also allows foreign atoms to move, albeit slowly, through the crystal.

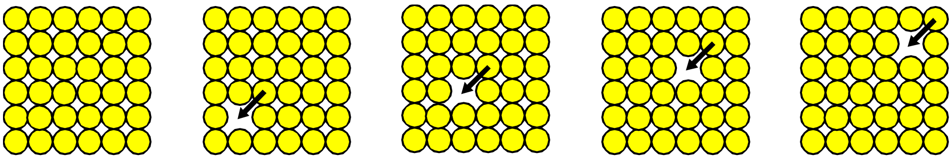


Fig. 10 Schematic atomistic view of a close packed crystal lattice showing how solid state diffusion processes though the movement of lattice vacancies

Dislocations and their Character

The edge dislocation is perhaps the simplest type of dislocation to visualise. The geometry of an edge dislocation can be understood by considering an extra half plane of atoms inserted into an otherwise perfect crystal structure as shown in Fig. 11.

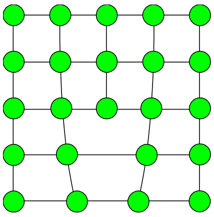


Fig. 11 Schematic atomistic representation showing the insertion of an extra half plane associated with the formation of an edge dislocation within the crystal lattice

The edge of the extra half plane of atoms is the dislocation line. Close to the line the structure is highly distorted with significant displacement of the atoms. The direction of this distortion is called the Burgers vector and its magnitude decreases rapidly with distance from the line leaving the surrounding crystal essentially perfect. Since the chemical bonds close to the dislocation line are strained, the activation energies for chemical reactions or dissolution can be expected to be different from the surrounding crystal. Hence, the fact that dislocations can influence on reactivity and dissolution. Note that the region below the extra half plane is in tension. This may allow the accumulation of impurities along the dislocation line which can further modify the chemical, electrical and other properties of the dislocation.

The nature and properties of a dislocation are determined by two vectors:

- Line direction (**l**)
- Burgers vector (**b**)

together with their orientation with respect to each other.

The edge dislocation, where l is perpendicular to b, is not the only type of line defect. Fig. 12 shows a second type of line defect, the screw dislocation so-called because the atomic planes around the dislocation line are helical in form. The geometry of the screw dislocation can be understood in the following hypothetical manner. A cut is made part-way through a block of crystal. The two sides are then displaced by one lattice translation with respect to each other. The dislocation line lies at the bottom of the cut. Thus, for a screw dislocation the Burgers vector and line direction are parallel. A feature of the screw dislocation, which is highly relevant to e.g. crystallisation, is the fact that it produces a partial step on the crystal surface.

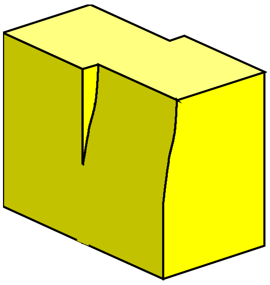


Fig. 12 Schematic representation of a screw dislocation highlighting that this defect generates a step on the crystal surface

The final type of dislocation is the mixed dislocation. The Burgers vector and line direction of a mixed dislocation lie at some arbitrary angle other than 0° or 90°. Visualisation of the geometry of a mixed dislocation is much more difficult than for the other two types. Their most important feature, with respect to crystal growth, is that they may also produce a surface step depending on the relative orientations of the Burgers vector with respect to the crystal face.

Dislocations and Mechanical Properties

The mechanical strength of pure metals is up to five orders of magnitude lower than that predicted theoretically on the basis of the strength of bonds. This is due to the presence of dislocations which allow deformation of the metal crystals without the need for simultaneous breaking of all bonds across a deformation plane. Fig. 13 shows this process on the atomic scale highlighting the motion of an edge dislocation through a crystal resulting in relative displacement of the two regions of the crystal above and below the dislocation line. This process of deformation via dislocation motion is known as slip. The motion of the dislocation itself in this manner is called dislocation glide. Thus, deformation of a crystalline solid can occur by the movement of dislocations through the crystal, requiring much lower stresses to initiate than would be necessary if all bonds across the plane were broken simultaneously.

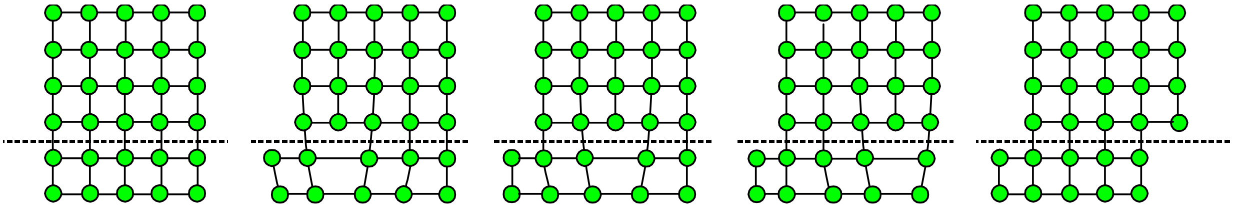


Fig. 13 Schematic atomistic representation of the mechanical deformation of the crystal lattice facilitated through the motion of an edge dislocation along a (close packed) slip plane

In simple terms the Burgers vector can be thought of as the direction in which slip has occurred. A dislocation can only move by glide in a plane which contains both its line direction and its Burgers vector. Such a plane is known as the slip plane (hkl). Thus the edge dislocation in Fig. 13 is confined to glide in a single slip plane indicated by the dotted line. During the mechanical deformation process layers of crystal lattice slip over each other and give rise to plastic deformation with the direction [uvw] of slip being along the Burgers vector.

The energy of a dislocation involved in this process can be approximated to:

$$E \sim G\,|\mathbf{b}|^2 \qquad (2)$$

where G is the modulus of elasticity. From this we can see that, to minimise the dislocation energy, Burgers vectors with the shortest lengths are preferred. Fig. 14 illustrates this for the case of a cubic face centred lattice where the shortest distance between two equivalent atom sites will be from the corner to the face centre site, i.e. a Burgers vector **b** = ½ a [-110] being the most likely with the likely slip plane being (1 1 1).

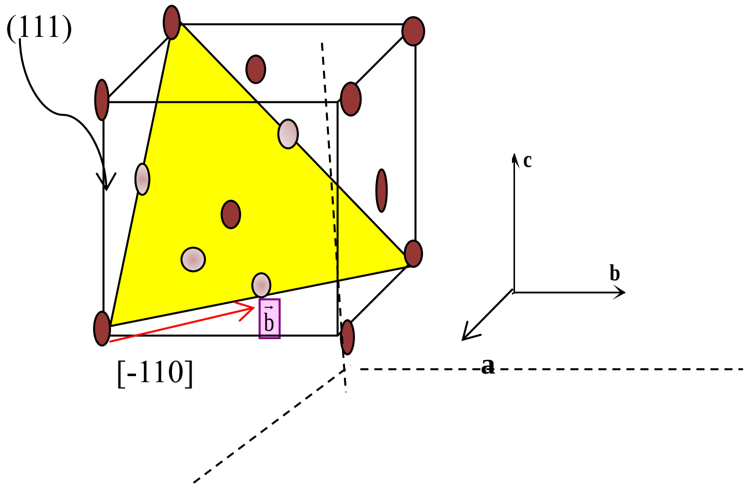


Fig. 14 An example of a dislocation slip system for a face centred cubic crystal structure with the likely slip plane being the most closed packed (111) plane with the dislocation Burgers vector being along the shortest inter-atomic contact, i.e. along the [-110] direction.

Dislocations and Chemical Reactivity

Dislocations also influence chemical reactivity. The points of emergence of dislocations on a crystal surface can be revealed by removing atoms or molecules from the surface with a suitable reagent or solvent. Enhanced reactivity and dissolution at the dislocation can result in a pit or similar feature. As we will see in later chapters, dislocations are also closely involved in the growth of crystals by providing surface steps to which atoms or molecules can more readily bind during growth.

Crystal Morphology and Surface Chemistry

The Nature of Crystal Surfaces

Crystals grown from solution typically exhibit regular, planar facets. Although appearing flat to the naked eye, these crystalline surfaces are rarely so at the molecular level. The various features which make up the nanoscale surface topography of the crystal face are intimately involved in the mechanisms by which crystals grow. Fig. 15 is a schematic representation of crystal surface in which the molecules, or growth units, are represented by cubes. The principal features of interest are:

- Steps,
- Terraces between steps,
- Kink sites on the steps,
- Adsorption of molecules.

It is important to consider at what point a molecule from solution becomes truly part of the crystal. In this simplified model of a crystal surface, each cube can form a maximum of six bonds with surrounding cubes - one per face of the cube.

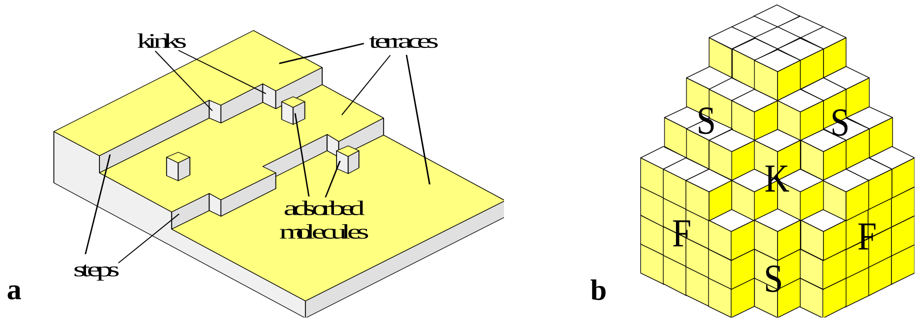
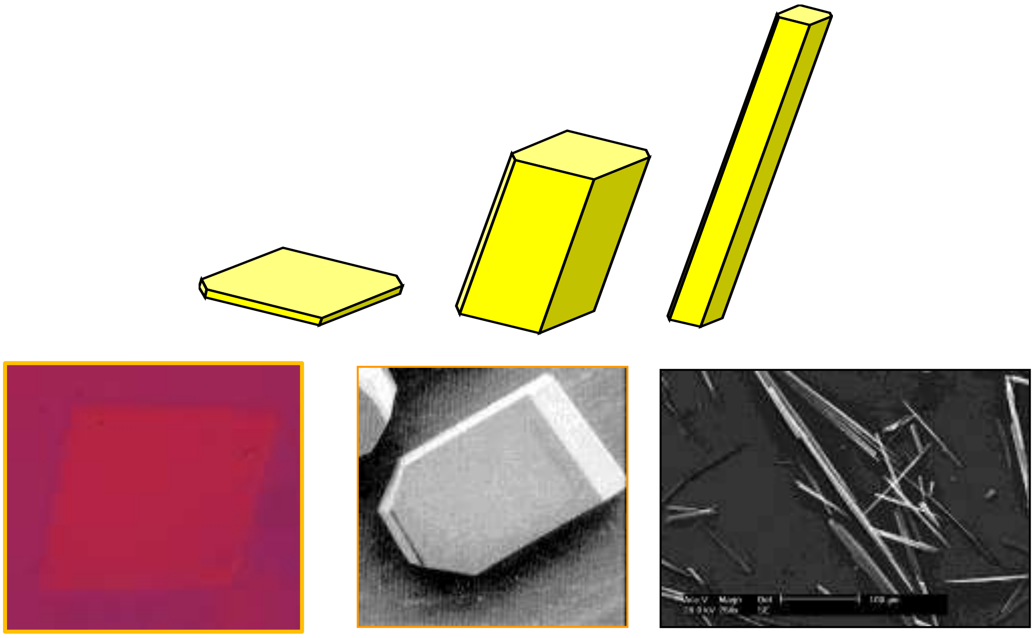


Fig. 15 (a) Steps, terraces, adsorbed molecules and kink sites on a crystal surface; **(b)** flat (F), stepped (S) and kink (K) faces

Examining the various sites on the schematic crystal surface, we can see that each is capable of forming a different number of bonds with an incoming molecule from the solution. A molecule adsorbed onto a terrace can form only one bond with the crystal surface. A molecule in contact with a step can form two bonds while a molecule incorporated at a kink site can form three bonds. The kink site is of particular importance since a molecule placed in such a site does not increase the surface area or, therefore, the surface energy of the crystal. A molecule can, thus, be considered to be truly part of the crystal once it has reached a kink site. Though the nature of bonding for real molecules will be substantially more complex, this simple model reproduces the key differences between the various surface sites. When the cubes of Fig. 15(a) are assembled to form a crystal, we find that three different types of crystal face occur: flat or F faces, stepped or S faces and kink or K faces as shown in Fig. 15(b).

Crystal Morphology

The external shape of a crystal is referred to as the crystal habit. The faceted crystals are bounded by the slowest growing faces and it follows that the crystal habit is determined by the relative growth rates of the possible faces for that crystal structure. Crystal habit is described using a variety of qualitative terms together with the Miller indices of the faces present. Fig. 16 shows examples of (a) plate-like, (b) prismatic and (c) needle-like crystal habits.



(a) **(b)** **(c)**

Fig. 16 Examples of crystal shapes (a) (top left) plate-like (example: methyl ester stearate [5]); (b) (top centre) prismatic (example: urea [6]); (c) (top right) needle-like (carbamazepine: nicotinamide co-crystal [7])

Surface Chemistry

The external shape of crystals not only has a considerable influence on the properties of the solid but also has important technological consequences, particularly in relation to handling of particulate materials.

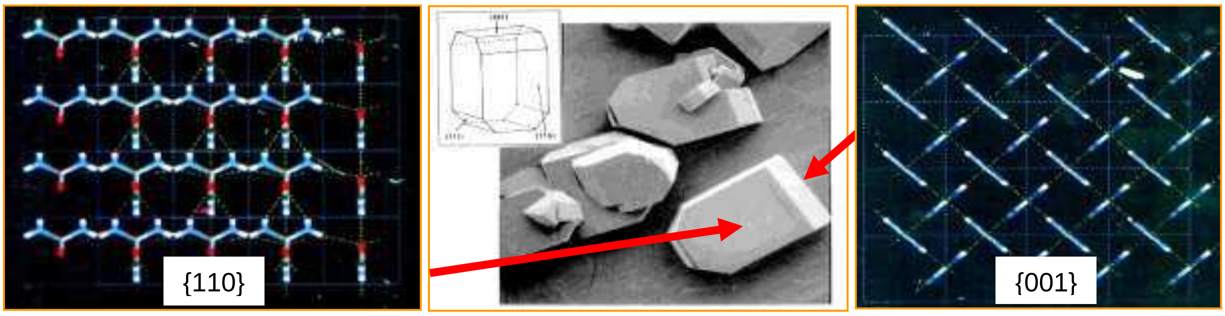


Fig. 17 The different surface chemistry exposed on the {110} facet (left) and the {001} (right) crystal habit faces of urea in relation to the observed crystal morphology (centre), after reference [6]

Such differences are due to the fact that the crystal surfaces represent the termination of the bulk 3D crystal lattice and as such and depending on the crystal structure different crystal surfaces have different surface chemistry and hence interact with other crystals differently due to e.g. differences in surface wetting due to differences in their hydrophobic or hydrophilic nature. It is thus clear that the vertical and horizontal potential faces are each made up from different parts of the molecule and, therefore, contain different functional groups. As a consequence, the surface chemistry of crystals can depend strongly upon the crystal habit. This is demonstrated for the case of urea ($C=O\ NH_2$) shown in Fig. 17 which shows the contrasting surface chemistry exposed on the {110} surfaces which is strongly protic in nature and the {001} surface which comprises an alternative mixture of protic and carbonyl molecular sites.

In addition, the surface area for a given crystal volume depends upon the shape of the crystal. For example, the specific surface area of elongated (needle-like) crystal habit is substantially larger than that of more isometric shapes such as cubes. The combination of differences in both surface chemistry and surface area can result in changes in dissolution rate of crystals as a function of crystal habit. On a technological level, crystal habit can influence a wide range of behaviour including:

- Ease of filtration of a crystal suspension,
- Crystal flow and packing characteristics,
- Crystal compression behaviour.

The latter two are of particular relevance to tabletting. Crystal shape also effects caking behaviour, i.e. the tendency of polycrystalline materials to bind together during storage.

Concluding Remarks

A brief overview of the fundamentals of crystallography and applied crystal science has been provided which will be helpful to those unfamiliar with the basic concepts underpinning the connectivity between molecular structure, the intermolecular interactions that define crystal chemistry and surface properties. The later chapters of this book will illustrate how crystal science concepts provide a useful fundamental understanding regarding how:

- crystal structure links to the physical and chemical properties of crystals,
- structure/property inter-relationship can be controlled by processing,
- structure, properties and processing can impact upon the practical performance of materials.

References

1. Sun CC (2009) Materials science tetrahedron—A useful tool for pharmaceutical research and development, J Pharm Sci 98:1671-1689
2. McConnell JF (1974) 2-(4-Isobuthylphenyl) propionic acid. $C_{13}H_{18}O_2$ ibuprofen or prufen, Cryst Struct Commun 3:73-75
3. Fronczek FR, Kamel HN, Slattery M (2003) Three polymorphs (α, β, and δ) of D-mannitol at 100 K, Acta Crystallogr Sect C:Crystl Struct Commun 59:567-570
4. See e.g. Kutzke H, Klapper H, Hammond RB, Roberts KJ (2000) Meta-stable β-Phase of benzophenone independent structure determinations via X-ray powder diffraction and single crystal studies, Acta Crystallographia B 56:486-496
5. Comacho-Corzo DM, Thomas D, Muller F, Roberts KJ, Lewtas K and More I (2017) Morphology and growth kinetics of methyl stearate as a function of crystallisation environment, Crystal Growth and Design 17:563−575
6. Docherty R, Roberts KJ, Saunders V, Black S, Davey RJ (1993) Theoretical analysis of polar morphology and absolute polarity of crystalline urea. Faraday Discussions 95:11-25
7. Rahim A, Hammond RB, Sheikh AY, Roberts KJ (2013) A comparative assessment of the influence of different crystallisation screening methodologies on the solid forms of carbamazepine co-crystals. CrystEngComm 15:3862-3873