

Crystallographic Approaches for the Investigation of Molecular Materials: Structure Property Relationships and Reverse Crystal Engineering

Piero Macchi*

Abstract: This article discusses the connection between crystallography and material science. It sheds light on some of the research opportunities that are currently available and it critically reviews the directions taken by the scientific community in the field of crystal engineering. The focus is on materials formed by the assembly of organic and organometallic molecular building blocks.

Keywords: Crystal engineering · Material science

1. Introduction

Historically chemistry (alchemy)^[1] has been the science searching for new materials and tuning their properties for desired applications. In the last century a somewhat new perception of the *science of materials* emerged, which is multidisciplinary and at the crossroads of basic sciences and engineering. During this transformation, it is sometime overlooked that a ‘narrower’ science, namely crystallography, has produced some time ago a substantial amount of the theoretical basis (as well as the corresponding scientific language) necessary for the development of this new material science. In fact, crystallography is itself at the crossroads of chemistry, physics, mathematics and biology and – transgressing the definition of a crystal^[2] – crystallographers often investigate amorphous samples, material surfaces and fibers as well.

Originally born as a purely *natural* science, crystallography relies since the 19th century also on *formal* sciences, especially mathematics, which provided the group theory basis of crystallography.

In addition, what is nowadays called the fabrication of materials has always been within the realm of crystallography; it includes the studies of the kinetics and thermodynamics of crystal growth, of phase transformations and of material processing. Furthermore, the inherent connection between crystallography and engineering is often overlooked, especially by chemists. Metallurgy, the ancestor of material science, could be considered as a discipline quite entangled with engineering. Metallurgists are the ‘crystallographers of metals’, they use crystallographic concepts to analyze and describe the structures of metals and alloys, their mechanical, electrical, optical and magnetic properties as well as the phase transitions and the reactions occurring during metal processing. Surprisingly, however, metallurgists are not interacting routinely with the rest of the crystallographic community (and *vice versa*), neither at meetings, in the national and international associations, nor in the scientific journals traditional dealing with crystallographic topics. This lack of interaction is probably due to the now widespread and erroneous perception of crystallography as a subfield of (molecular) structural chemistry or biology. A comprehensive discussion of the position of crystallography within the sciences is beyond the scope of this paper. The interested reader is referred to a series of recent review papers in which the author has tried to address this problem.^[3] Additional interesting reading material on this subject is found in the ‘white paper’ on Crystal and Materials Technology for Energy Savings, Renewable Energy, Health and Education recently edited by Bruni and Scheel.^[4]

This article focuses on molecular-based

materials with the aim of highlighting the importance of crystallography in the design of new materials and investigations of their properties. Moreover, a critical discussion is presented of the field and scope of crystal engineering.

2. Molecular Materials and the Role of Crystallography

In general, organic and metal organic materials are based on the aggregation of a single type of molecules, or on the self-assembly of different neutral or ionic molecules. These so-called *building blocks* form multi-dimensional architectures, typically in the solid state.

Although the crystalline phase of an organic or organo-metallic molecular compound is not necessarily an interesting material itself, the stereo-electronic flexibility of such molecules can be the basis for property control obtained through the periodically homogeneous organization of atoms and molecules in space, as it occurs in a crystal or in a partially crystalline phase. Amino acids for example, well-known building blocks of life, have been proposed for use as optical device materials,^[5] which exploit the above mentioned property amplification obtained through the homogeneous assembly of molecules. Two features in particular are making these compounds quite attractive: i) α -amino acids are chiral (with the exception of glycine) and naturally available in enantiopure form and their homo-chiral crystals show high non-linear optical efficiency;^[6] ii) mono-crystals of large size and good quality are easily grown, a prerequisite for their use as devices.

*Correspondence: PD Dr. P. Macchi
University of Bern
Department of Chemistry and Biochemistry
Freiestrasse 3
CH-3012 Bern
E-mail: piero.macchi@dcb.unibe.ch

This simple example shows that engineering molecular materials implies the *selection* of adequate molecular carriers of specific functionalities, and their optimal *arrangement* in an ideally periodic system. Given that large-size crystals are necessary for real-world devices, controlling the crystal growth is a third important aspect of the engineering process, *i.e.* controlling the production of *real* crystals, as opposed to *ideal* ones.^[7]

The role of crystallography in these studies is obvious, but unfortunately often not fully appreciated and sometime limited to mere X-ray crystal structure determination. In fact, crystallography is still considered a descriptive science whose main contribution is simply the interpretation of the diffraction pattern from single crystals (nowadays a well-established and rapid procedure) or powders, in order to yield information on the nature^[8] and the disposition of atoms and molecules in the solid state, on the type of supra-molecular networks and perhaps on some specific geometric parameters, such as intermolecular distances. It should be pointed out, however, that this viewpoint does not reflect a limitation of crystallography as a science, it rather indicates restricted usage of its potential by scientists.

The great potential of crystallography will be illustrated in more detail in section 4, after having reviewed energetic aspects of molecular materials in section 3.

3. Forces between Molecules

Molecules use different forces to aggregate in the crystalline solid state, as summarized in Fig. 1. First there are the covalent bonds. In organic molecules these bonds are very strong and highly directional. In a crystal, three-dimensional crystalline architectures can be formed which are normally rather robust. Molecules may react in solution to form polymers or oligomers that become insoluble and rapidly crystallize. The first synthetic organic polymers were mono-dimensional chains, held together by weaker London type forces (see below). The rapid crystallization, the low dimensionality and the conformational flexibility of the covalent network made these polymers very poorly, if at all, crystalline and this is exactly the source of their – temperature dependent – plastic behavior.^[11]

In the past two decades the coordinative bond between metals and organic ligands has been deployed extensively for synthesizing metal–organic polymers. In this case, the junction between the building blocks is softer: the bond is still partially covalent, *i.e.* associated with the donation and acceptance of electron pairs (from the

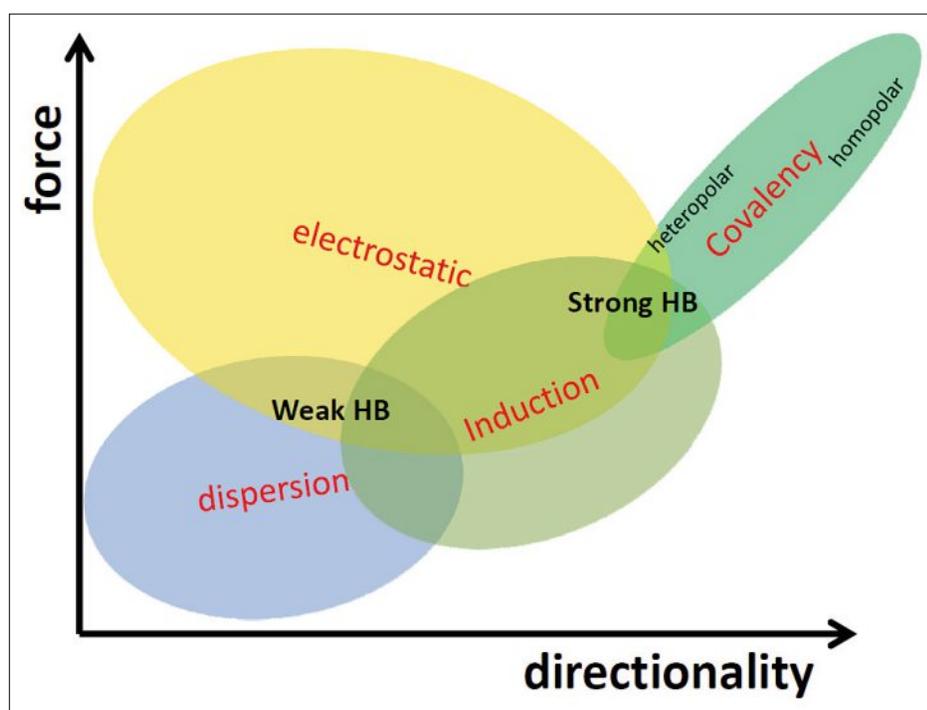


Fig. 1. Schematic representation of the types of bonds used to produce molecular based materials. Definitions are from McWeeny.^[9] Covalent bonding is due to the exchange of electrons between two or more atoms. For such bonds a single wave function for all the electrons can be written. For intermolecular interactions, the total wave function is approximated as the product of the molecular wave functions. Within this approximation, the electrostatic bond is due to the interaction between the ground state *charge* densities (= nuclear - electron probability) of two molecules. This interaction can be seen as involving the permanent electrostatic moments of each fragment/molecule.^[10] The induction (or polarization)^[9] energy is due to the interaction between the permanent electric moments of one molecule and the induced moments of the other (and *vice versa*). In quantum chemical practice the singly excited configurations are involved. London (dispersive) Forces correspond to the interaction between non-permanent multipole moments of the two molecules; they arise from the doubly excited configurations centered on each molecule.

ligand to the metal and *vice versa*),^[12] and somewhat more polar. It remains quite directional, but is usually weaker than homopolar bonds between main group atoms. The dimensionality of the network can be quite high due to the stereochemical flexibility of the metal centers. Therefore, these materials are normally crystalline and sometime quite robust, *i.e.* resistant to thermal, mechanical or chemical stress.^[13] Their properties such as porosity, anisotropic magnetism and conductivity, light emissivity and absorptivity are based on the periodicity and homogeneity of the crystals.

The field of organometallic coordination compounds has impressively grown, thanks primarily to the appeal of porous materials such as the metal–organic framework compounds (MOFs).^[14] They have attracted chemists for a number of reasons: first their preparation is simple and often low-cost, normally based on self-assembly processes in solution; second the structures of MOFs are extremely attractive, with intriguing topologies that have triggered a renewed interest^[15] in mathematical and theoretical crystallography.^[16] The functionalities of MOFs are also potentially in-

teresting and useful, although the majority of the compounds reported so far have not yet found applications.

Despite the widespread research activities, modeling MOFs^[17] and predicting their topologies, structures and properties is still quite difficult. So far most of the approaches used to fabricate these materials are empirical. ‘Material design’ is much less advanced than ‘drug design’. Nevertheless, MOFs have contributed significantly to a renaissance of purely organic polymers, the closely analogous ‘covalent organic frameworks’ (COF) in particular.^[18] These are porous crystals based on organic monomers and strong covalent bonds. Note however, that research on these species, sometime considered as very new, have been proposed already in the 1960s when inclusion compounds of organic polymers have been reported for the first time.^[19]

Crystal engineers make use not only of the strongest, but very often of the weaker interactions as well. In this respect they mimic nature. The best known such interaction is of course the hydrogen bond (HB). The HB is special because of its extremely varied nature ranging from

partially covalent to weakly electrostatic, thereby offering a variety of aggregation modes. In terms of binding energies,^[20] HB energies span the range from a few kJ/mol for weaker to *ca.* 100 kJ/mol for stronger bonds.^[21] The HB can be highly directional, if it contains a large covalent component, but much less so if based on small electrostatic forces and competing with the dispersive forces. In the plot of Fig. 1, the strong HB is located at the cross-over of covalent, electrostatic and induction forces, whereas the weak HB is at the overlap of electrostatic, induction and dispersive regions. Any intermediate situation is also possible depending on the nature of the HB donor and acceptor groups.

While the HB is genuinely diverse,^[22] it has become quite popular in recent times to 'discover' new types of HB interactions, assigning *ad hoc* names to them which tend to stress sometime minor and sometime even irrelevant differences. For example, Braga *et al.*^[23] suggested to call the HB occurring between two equally charged molecular ions 'pseudo-hydrogen bond'. These authors claimed that, because they are not stably in isolated species, the HB would not be a true one. After some discussion in the literature,^[24] it was demonstrated that the HB in those cases is strongly localized and actually quite covalent, hence insensitive to the global charges of the donor and acceptor ions. The prefix 'pseudo' was fortunately abandoned soon afterwards.^[25]

From the material crystallography point of view, the main question is how HBs determine material properties. Given the large variety of hydrogen-bonded supramolecular structures a universally valid answer to this question is probably impossible. However, we can identify two main roles for the HB: a) in the absence of stronger covalent interactions, the HB organizes the molecules in space, taking advantage of its directionality; b) the HB polarizes the molecules involved so that their stereo-electronic features are modified. The role of 'organizer' is very often the most important for HBs in molecular materials, because, as mentioned above, many properties depend more on the periodical homogeneity of a crystal, than on the electronic/electrostatic perturbation locally produced by an HB. Note that polarization effects occurring in crystals are mainly due to the sum of many long range interactions that repeat periodically, rather than to the strength of a few short range interactions. Consider, for example the dipole moment enhancement occurring in molecules embedded in polar crystals: after the real extent of these enhancements had been established,^[26] it was found that this effect cannot be attributed to just one or a few HBs within the first coordination

sphere.^[27] It is important to understand that the dipole enhancement is not just due to the molecule being in a polarizing medium, because an enhancement of the same extent is not observed in solution, which is only a statistically but not periodically homogeneous medium. This observation once more demonstrates the unique amplification effect due to the crystal lattice.

Among the many weaker intermolecular interactions the 'halogen bond',^[28] and more recently even the 'chalcogen bond'^[29] has attracted a growing interest. The name 'halogen bond' was chosen by virtue of the structural analogy with the HB. It can be adequately described within the conventional schemes of intermolecular interactions, taking into account induction, exchange-repulsion and dispersion as implemented in semi-classical approaches,^[30] see caption of Fig. 1. In a recent work, Stone^[31] suggested that the real driving force of the halogen bond could be the need to minimize the short range repulsion^[32] rather than an electrostatic attraction. It is also interesting to note that materials based on halogen bonding are often investigated for the same structural features and applications as those based on other intermolecular forces. This analogy renders the distinction questionable.

Counteracting this tendency to differentiate intermolecular interaction from each other, Gilli and collaborators have recently proposed a unifying approach that even includes the HB.^[33] They tend to classify all intermolecular interactions within the well established framework of frontier molecular orbital interactions,^[34] that work so well in explaining chemical bonding and reactions in classical organic and organometallic chemistry. Applying this approach, there would be no discontinuity in the scheme of Fig. 1 between heteropolar (donor-acceptor) covalent interactions and polarization induced ones. Frontier orbitals minimize the role of permanent and field-induced molecular electric moments, because they emphasize 'orbital controlled' (or *soft*) acid-base interactions.^[35] In practice, it should be considered that molecular materials are largely dominated by *soft* interactions, unless hard cations are present which is rarely the case. Moreover, the orbitalistic description of soft interactions inherently includes both a true covalent effect (a dative-type bond) and a polarization effect, due to a configuration interaction producing a substantial redistribution of electron density within the interacting molecules, see caption of Fig. 1.

This unifying theory based on simplified quantum mechanical theory is preferable to the sometime random structural classifications because it allows a more physically oriented description of the interactions occurring in crystals and a more

evident justification of their properties. In fact, an inspection of the binding energies and the anisotropies associated with intermolecular interactions could inform us, for example, on the resistance of a material against mechanical stress (compression, expansion and shear): covalent bonds have high force constants and binding energies, therefore the corresponding materials have a large bulk modulus and a small thermal expansion. Among the non-covalent materials, those based on ionic bonds or HBs are normally harder than those aggregated through dispersive forces. The latter interactions leave the materials extremely compressible, at least in the range of few kbar. At higher pressure, phase transformations or chemical reactions form new covalent bonds thus producing harder materials. This simple consideration is also useful for mixed materials, for example layered structures, where two directions are associated with covalent connections, and are therefore less compressible, whereas the third direction is softer and more compressible. Analysis of chemical bonding also enables the evaluation of hardness.^[36] This property, although associated with some obvious effects such as indentation, lacks a precise definition.

All research on molecular materials takes enormous advantage of crystallographic studies. A fundamental contribution is certainly the crystal structure determination, obtained normally through X-ray, neutron or electron diffraction on single crystals or powders. Also important is the rationalization of the supramolecular architectures in terms of network topology, the prediction of crystal structures, the determination of molecular electrostatic or magnetic moments and their derivatives, the analysis of chemical bonding, the accurate measurement or calculation of crystal properties etc. Moreover, studies of disorder, extended defects, modulation *etc.*, are extremely important because they inform us on the behavior of *real* crystals and not only of the *ideal* ones.^[17]

4. Beyond Crystal Structure Determination

As anticipated above, crystallography is not only the science of 'determining crystal structures'; its contribution to the field of molecular material science is much wider. Some examples of such contributions are briefly discussed in the following paragraphs.

4.1 Crystal Structure Prediction

From the material science point of view, crystal structure prediction is even more important than crystal structure determination.^[37] In contrast to molecular

chemistry, where simple stereo-electronic rules enable scientists to anticipate the product(s) of a synthesis, or at least to formulate a short list of reasonable hypotheses, supramolecular chemistry is much less predictable due to the complex phenomenon of polymorphism, the crystal analog of molecular isomerism. It is produced by the large number of competing intermolecular interactions, with comparable binding energies to stabilize the supra-molecular assemblies.

In the past decades more and more efforts were spent on developing theoretical tools for predicting the solid-state forms of organic and organometallic molecules. A unifying approach is missing as yet. However, depending on the class of compounds, semi-empirical or *ab initio* calculations have had at least partial success.^[38] Nevertheless, the crystal structure prediction of molecular materials remains a rather complex, time consuming business, certainly not doable on the back of an envelope. Currently there are two main limitations: the accuracy in the evaluation of the interaction energies and the completeness of the inspection of the energy landscape associated with the multidimensional conformational/configurational space of supramolecular arrangements. In fact, it is quite difficult to identify the stable structure (that of lowest free energy) from a collection of phases with very similar enthalpies. Moreover, the conformational space is sometime so complex that the structure of the stable phase cannot be identified. What one can realistically expect, even from semi-empirical calculations, is a reasonable idea of the stability of a given crystal phase, in other words being able to exclude the phases that are highly unlikely to occur, even as metastable ones.

4.2 Topology

The physical properties of crystals are usually represented by tensors whose forms are determined by the *crystal class*, *i.e.* the point group symmetry of the crystal.^[39] However, the symmetry alone does not predict the magnitude of a property and thus the efficiency of a given material; it simply determines whether or not a macroscopic property is theoretically allowed (*necessary condition*).

The functionality of a given phase, *e.g.* conductivity, magnetism, elasticity, toughness, ductility, often depends on a particular net of bonds. Therefore, the topology of the crystal net is an important additional descriptor. It could be regarded as a *sufficient condition* for a property, if the definition of the topological object 'bond' is correctly chosen.

So far, topological research has been oriented mainly toward the classification of networks, rather than towards their impli-

cation for material properties. Exceptions are the properties purely related to structure, such as porosity and interpenetration. Network classification has been extensively studied by Blatov *et al.*^[40] following earlier ideas by O'Keefe.^[41] Note that the topological classification of networks represents the basis for the modern and popular *reticular chemistry*, proposed by O'Keefe and Yaghi.^[42] The concept of reticular chemistry is probably the only attempt so far to formulate a paradigm of supramolecular synthesis somehow comparable with synthesis design and retrosynthetic approaches commonly adopted in organic chemistry.

Of course, the topological classification of three-dimensional periodic networks is a pure mathematical analysis, but if applied in combination with the physical origin of a given property, it may become an important tool for material design.

4.3 Reverse Crystal Engineering and Material Design

The term 'Crystal Engineering' first appeared in the 1970s.^[43] It started being used frequently during the 1990s and today it is common practice to associate 'engineering' concepts with much of the traditional crystallographic work. A provocative discussion was initiated a few years ago by Jack Dunitz who in a short article^[44] reported on the same crystal structure determinations that he had carried out more than 50 years earlier for his PhD thesis, and had already published in the 1940s.^[45] He vividly illustrated the difference in discussing the very same compounds then and now. While somewhat bizarre, the article implicitly criticizes the use of the word 'crystal engineering': new words do not necessarily bring new insight.

While this criticism is still valid, it is also true that the combination of a basic science and engineering could have contributed to a more application-oriented molecular crystallography. This would have required more attention to the design of materials and a better understanding of the machinery beneath their functionalities, rather than the more traditional 'description & classification' approach of a natural science. However, the 'crystal engineering' language has mainly generated new, sometime exotic, descriptions of the struc-

tures and has only marginally increased the application-oriented nature of this science. An important aspect of engineering has so far been neglected: *reverse engineering*. This concept is somewhat similar to 'retro-synthesis' in organic chemistry, which enables the prediction of the fastest and/or the cheapest routes to synthesize a target molecule. In material science, reverse engineering implies in first instance an understanding of which component is important (and why) in order to generate the desired functionality and secondly ideas on how to improve the component and its functionality. In crystal engineering, the purpose of a reverse analysis is finding the suitable functional groups and their arrangement, hence the *ideal* crystal structure that would produce a desired microscopic^[46] or macroscopic property.

As a matter of fact, the products obtained during a 'crystal engineering' research project are very rarely *engineered*: even the most interesting materials are often obtained from some kind of 'trial & error' combination of building blocks, at best selected to design new *structural* – but more rarely *functional* – features.

Admittedly this criticism is severe though necessary. However, it frees the way to developing a serious reverse crystal engineering approach, therefore filling the gap between the current crystal engineering and a more rigorous applied discipline.

Fig. 2 summarizes the important steps of the process, which include the selection of a suitable arrangement of functional molecules or groups, the design of the corresponding stable or metastable crystal structure and eventually its preparation.

The first step involves pure modeling and requires a rapid, though sufficiently accurate, estimation of material properties from a given assembly of molecules. The approach needs to be applied systematically to a large number of *ideal* candidate crystal structures. In order to efficiently explore the associated immense conformational search spaces, the evaluation of a property must be rapid, *i.e.* necessarily based on a large number of approximations. Once the potentially interesting arrangements of building blocks have been recognized, the stability of the corresponding crystal structure must be tested. As mentioned above, crystal structure prediction is now

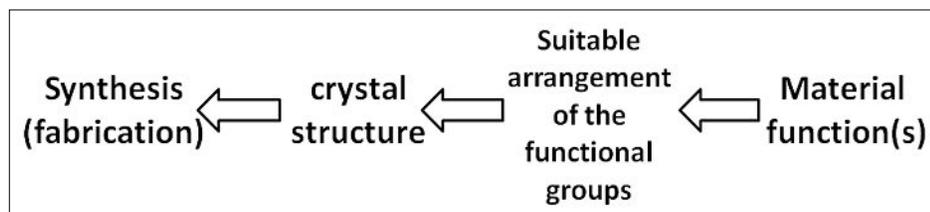


Fig. 2. A schematic summary of the principal steps of an ideal reverse crystal engineering procedure.

sufficiently advanced to rapidly scrutinize candidate structures. The identification of the stable phase at given thermodynamic conditions, is difficult, but not at all a problem for reverse crystal engineering. In fact, metastable phases with potentially interesting properties should not be screened out and treated like the stable phase of a material. Metastable phases can often be synthesized anyway and put to practical use. One notable example is diamond. If we were asked to predict whether a hard material can be produced from elemental carbon, we would make an obvious mistake if we would first scrutinize the phase most stable at ambient condition (graphite) rather than the metastable ones (including diamond). Of course, the fact that the interesting phase is only metastable at ambient conditions makes its synthesis more difficult, but – at least in this case – still feasible.

The idea of optimizing material properties, instead of minimizing lattice energy or enthalpy of a crystal, has been proposed by Oganov and co-workers for elemental solids and binary inorganic compounds.^[47] His approach takes advantage of his previous research in the field of crystal structure prediction, which uses evolutionary algorithms^[48] to explore the complicated energy landscape associated with the structures of minerals, inorganic phases and (more recently) molecular crystals.^[49] The evolutionary algorithm locates the relevant minima even in a very complicated energy landscape. However, it is important to stress that the energy landscape itself depends on the type of calculations; it may well differ for semi-empirical and first principle calculations, the latter being typically limited to density functional theory^[50] (DFT). For inorganic materials, the property optimization can also be carried out at a DFT level. For molecular materials an analogous calculation would be much more intricate because of the large number of atoms per unit cell.

In recent work, Krawchuk *et al.*^[51,52] proposed a way to simplify the calculation of optical properties in organic materials by using atomic (hyper)polarizabilities that are easily and rapidly calculated for the building blocks in isolation (Fig. 3). This approach simplifies the estimation of optical properties enormously and it is easily combined with the generation of ideal crystal structures through evolutionary algorithms as proposed by Oganov.^[47b] Thus the methods of crystal property calculations developed for binary phases may easily be applied to molecular materials as well.

As mentioned in section 4.1, current modeling methods cannot at present evaluate the synthesis conditions necessary to obtain a given material, *e.g.* temperature

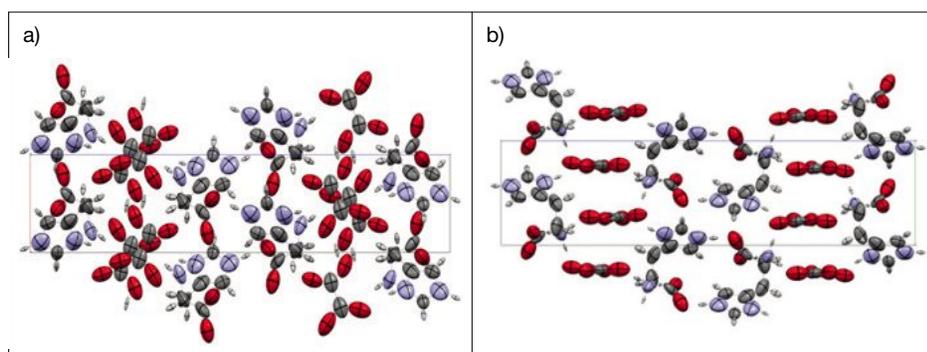


Fig. 3. A plot of the atomic polarizabilities in L-histidinium hydrogen-oxalate, an orthorhombic P2₁2₁2₁ phase containing oxalic acid and L-histidine in a 1:1 mixture. The atomic polarizabilities have been calculated for the isolated ions and used to evaluate the refractive indexes of the crystal.^[52]

and pressure. This is in keeping with analogous limitations of computational chemistry which is also still quite far from the calculation of the best solvent, temperature and concentrations necessary to carry out a given chemical reaction.

4.4 Material Response

The material crystallography approach can be made even more powerful, if the response of a material to an external perturbation is experimentally investigated. Such experiments provide empirical access to some of the information obtained from modeling. If the latter uses crucial approximations it requires experimental validation.

Among the many possible studies of crystalline materials, those that attract the largest interest nowadays are the *in situ* experiments, where the response of a material to a given stimulus is recorded together with the structural data. Such stimuli range from those that are easy to measure, such as thermal or mechanical stress, to more complex and perhaps combined ones, such as a temperature or pressure gradient combined with an electric,^[53] magnetic or light induced excitation.^[54] In the past few decades, the technological improvement has been enormous so that today a combined diffraction and/or spectroscopic experiment can be performed under many environmental conditions. This often requires access to large scale facilities, in particular synchrotron stations, because the response of materials may be very weak and therefore the largest possible sources may be necessary to detect it. In the future, free electron lasers^[55] will make this kind of studies even more informative.

4.5 Electron Distribution and Material Properties

One of the most appealing applications of X-ray diffraction in the past 4–5 decades has been the accurate determination of the electron density distribution in crystalline materials. While research in this direction

had been already anticipated by Debye in 1915,^[56] it did not become possible until X-ray diffracted intensities could be measured with sufficient accuracy and the amplitude of atomic motions in crystal could be significantly reduced by lowering the temperature of the experiment.^[3b,57]

In principle, chemical and physical properties can be understood once the distribution of electrons is known with precision.^[58] For example, the electrostatic forces produced by a molecule and acting on another molecule reveal the potential sites of hard nucleophilic–electrophilic interactions.^[59] The direction of the largest electron density accumulations in a crystal inform us on some potential properties of a species, for example its compressibility, which is associated with the amount of kinetic energy density.^[60] In this respect, the quantum theory of atoms in molecules^[61] has proven to be a very useful tool for characterizing the nature of the chemical bonds in molecules and solids.^[62] It provides a basis for the above discussion on networks of bonds and their correlation with material functionality.

The connection between many crystal properties and electron density remains somewhat empirical.^[63] In fact, it is often the changes of the electron density distribution, with respect to time or in response to an applied field, that determine the properties, such as the electric or magnetic susceptibility of a crystal (depending on the polarizability of the electron density under an electric or a magnetic field). The current density is another fundamental property^[58a] that is correlated with many physical quantities. Traditional X-ray diffraction experiments on crystals, maintained in their ground state, are unable to detect material response. However, many recent developments^[64] allow scientists to anticipate at least approximately the changes of the ground state electron density as a function of an applied field, thus opening new opportunities. Moreover, femtosecond X-ray diffraction enables nowadays the deter-

mination of at least approximate time resolved electron density maps.^[65]

5. Conclusions

It is the disposition of atoms in the structure and their linkage that determines the properties of any material. While this concept is easily understood, its usage in scientific research is quite complicated for many reasons: the structure of a material is not easily predicted, the role and the nature of the chemical bonding are sometime ambiguous, the precise connection between the structure and the property is not always clear.

In this review article, it was shown that crystallographic modeling has been and still remains essential for the complete understanding of modern material chemistry and engineering. Crystallography provides the main background for material science and engineering. However, this is not sufficiently recognized, and crystallography is often considered (and used) just as an analytical tool. In the author's view, this is one of the reasons why the design of molecular materials, at variance with that of inorganic materials or metals and alloys, is often only empirical (if not absent).

However, a sensible application of crystallographic concepts and approaches is vital for a successful progress of molecular material science.

Acknowledgment

The Swiss National Science Foundation is thanked for financial support (Projects 141271 and 144534). Prof. H. B. Bürgi is thanked for critically reading this manuscript.

Received: December 11, 2013

- [1] A. Djebbar, 'Une histoire de la science arabe', Editions du Seuil, **2001**.
- [2] W. Steurer, *Z. Kristallogr.* **2007**, *222*, 308.
- [3] a) P. Macchi, *Top. Curr. Chem.* **2012**, *315*, 33; b) P. Macchi, *Chimia* **2009**, *63*, 29.
- [4] F. J. Bruni, H. J. Scheel, 'The Technology of Single Crystals and Epitaxial Layers; The Case for Energy, Water, Health, Education and Security', a white paper, **2013**. Available at www.hans-scheel.ch/pdf/Pub_112.pdf
- [5] a) A. M. Petrosyan, R. P. Sukiasyan, H. A. Karapetyan, S. S. Terzyan, R. S. Feigelson, *J. Cryst. Growth* **2000**, *213*, 103; b) A. M. Petrosyan, H. A. Karapetyan, R. P. Sukiasyan, A. E. Aghajanyan, V. G. Morgunov, E. A. Kravchenko, A. A. Bush, *J. Mol. Struct.* **2005**, *752*, 144; c) A. M. Petrosyan, R. P. Sukiasyan, H. A. Karapetyan, M. Y. Antipin, R. A. Apreyan, *J. Cryst. Growth* **2005**, *275*, e1927; d) H. A. Petrosyan, H. A. Karapetyan, M. Y. Antipin, A. M. Petrosyan, *J. Cryst. Growth* **2005**, *275*, e1919; e) K. E. Rieckhoff, W. L. Peticolas, *Science* **1965**, *147*, 610.
- [6] A. M. Petrosyan, *J. Cryst. Phys. Chem.* **2010**, *1*, 33.
- [7] A real crystal is a single-phase material related to an ideal crystal (i.e. a mathematical object with an idealized, infinite crystal structure). The real crystal can be perfect (i.e. in thermodynamic equilibrium with its defects) or imperfect (i.e. not in equilibrium with the defects).
- [8] Whether or not X-ray diffraction can be considered an analytical technique is a matter of debate. In general the X-ray scattering power of light elements is low and the discrimination between neighboring atoms in the periodic table is poor (coloring problem). The combination of diffraction and crystal ordering (the basis of so-called X-ray crystallography) is helpful though, because the scattering of the X-rays is amplified, i.e. concentrated into the Bragg reflections, by the inherent 'purity' and regularity of a crystal. However, the determination of the chemical composition of a molecule by X-ray diffraction is often based on the fact that stereochemical reasoning is almost always able to resolve ambiguities.
- [9] R. McWeeny, 'Methods of Molecular Quantum Mechanics', Second Edition Academic Press, **1992**.
- [10] Note that the interaction of higher multipoles is sometime considered as part of the van der Waals interaction. While any definition and classification is in principle acceptable, it is important to stress the origin of each of these interactions; grouping the permanent higher multipoles together with the induced multipoles seems to be inappropriate from a genealogy point of view. In the plot an interesting observation emerges: electrostatic interaction loses directionality when it is strongest because the interaction between monopolar charges (the longest ranging of such interactions) is non-directional by definition. This contrasts with the covalent interactions which are most directional when they are strongest (double or higher bond order, for example).
- [11] G. Natta, P. Corradini, *Nuovo Cimento Suppl.* **1960**, *15*, 40.
- [12] a) B. N. Figgis, M. A. Hitchman, 'Ligand Field Theory and its Applications', Wiley-VCH, **2000**; b) I. B. Bersuker, 'Electronic Structure and Properties of Transition Metal Compounds', Wiley-VCH, **1995**.
- [13] a) C. Montoro, F. Linares, E. Quartapelle Procopio, I. Senkovska, S. Kaskel, S. Galli, N. Masciocchi, E. Barea, J. A. R. Navarro, *J. Am. Chem. Soc.* **2011**, *133*, 11888; b) T. D. Bennett, P. Simoncic, S. A. Moggach, F. Gozzo, P. Macchi, D. A. Keen, J.-C. Tan, A. K. Cheetham, *Chem. Commun.* **2011**, 7983.
- [14] O. M. Yaghi, G. Li, H. Li, *Nature* **1995**, *378*, 703.
- [15] a) H. Grimmer, *Z. Kristallogr.* **2006**, *221*, III; b) M. Nespolo, *Z. Kristallogr.* **2006**, *221*, IV; c) M. Nespolo, *Acta Cryst.* **2008**, *A64*, 96.
- [16] H. Hilton, 'Mathematical Crystallography and the Theory of Groups of Movements', Clarendon Press, Oxford, **1903**.
- [17] B. Civalieri, F. Napoli, Y. Noel, C. Roetti, R. Dovesi, *CrystEngComm* **2006**, *8*, 364.
- [18] A. P. Coté, A. I. Benin, N. W. Ockwing, M. O'Keefe, A. J. Matzger, O. M. Yaghi, *Science* **2005**, *310*, 1166.
- [19] M. Farina, G. Allegra, G. Natta, *J. Am. Chem. Soc.* **1964**, *86*, 516.
- [20] It should be emphasized that the binding energy is not a force, however in Morse-type potential a large binding energy means that forces acting in the neighborhood of the equilibrium are quite strong.
- [21] G. A. Jeffrey, 'An Introduction to Hydrogen Bonding', Oxford University Press, **1997**.
- [22] P. Gilli, G. Gilli, *J. Mol. Struct.* **2000**, *552*, 1.
- [23] D. Braga, F. Grepioni, J. J. Novoa, *Chem. Commun.* **1998**, 1959.
- [24] a) T. Steiner, *Chem. Commun.* **1999**, 2299; b) M. Mascal, C. E. Marjo, A. J. Blake, *Chem. Commun.* **2000**, 1591; c) P. Macchi, B. B. Iversen, A. Sironi, B. C. Chakoumakos, F. K. Larsen, *Angew. Chem., Int. Ed.* **2000**, *39*, 2719.
- [25] D. Braga, L. Maini, F. Grepioni, F. Mota, C. Rovira, J. J. Novoa, *Chem. Eur. J.* **2000**, *6*, 4536.
- [26] a) S. T. Howard, M. B. Hursthouse, C. W. Lehmann, P. Mallinson, C. S. Frampton, *J. Chem. Phys.* **1992**, *97*, 5616; b) A. E. Whitten, P. Turner, W. T. Klooster, R. O. Piltz, M. A. Spackman, *J. Phys. Chem.* **2006**, *110*, 8763.
- [27] P. G. Cummins, D. A. Dunmur, R. W. Munn, R. J. Newham, *Acta Cryst. A* **1976**, *32*, 847.
- [28] A. C. Legon, *Angew. Chem., Int. Ed.* **1999**, *38*, 2686.
- [29] W. Wang, B. Ji, Y. Zhang, *J. Phys. Chem. A* **2009**, *113*, 8132.
- [30] a) A. Gavezzotti, *J. Phys. Chem. B* **2002**, *106*, 4145; b) A. Gavezzotti, *J. Phys. Chem. B* **2003**, *107*, 2344.
- [31] A. J. Stone, *J. Am. Chem. Soc.* **2013**, *135*, 7005.
- [32] This term arises from the anti-symmetrization of the wave function and it is often, but improperly, called Pauli repulsion. The reason is that the Pauli Exclusion Principle produces a large short range destabilization. When this is fitted with a potential function an apparent repulsive force can result.
- [33] V. Bertolasi, P. Gilli, G. Gilli, *Cryst. Growth & Des.* **2012**, *12*, 4758.
- [34] I. Fleming, 'Frontier Orbitals and Organic Chemical Reactions', Wiley-VCH, **1978**.
- [35] R. G. Pearson, *J. Am. Chem. Soc.* **1963**, *85*, 3533.
- [36] A. R. Oganov, A. O. Lyakhov, *J. Superhard Materials* **2010**, *32*, 143.
- [37] a) J. Maddox, *Nature* **1988**, *335*, 201; b) A. Gavezzotti, *Acc. Chem. Res.* **1994**, *27*, 309.
- [38] G. M. Day, T. G. Cooper, A. J. Cruz-Cabeza, K. E. Hejczyk, H. L. Ammon, S. X. M. Boerrigter, J. S. Tan, R. G. Della Valle, E. Venuti, J. Jose, S. R. Gadre, G. R. Desiraju, T. S. Thakur, B. P. van Eijck, J. C. Facelli, V. E. Bazterra, M. B. Ferraro, D. W. M. Hofmann, M. A. Neumann, F. J. Leusen, J. Kendrick, S. L. Price, A. J. Misquitta, P. G. Karamertzanis, G. W. A. Welch, H. A. Scheraga, Y. A. Arnautova, M. U. Schmidt, J. van de Streek, A. K. Wolf, B. Schweizer, *Acta Cryst.* **2009**, *B65*, 107.
- [39] J. F. Nye, 'Physical Properties of Crystals: Their Representation by Tensors and Matrices', Oxford University Press, **1985**.
- [40] a) V. A. Blatov, G. D. Ilyushin, O. A. Blatova, N. A. Anurova, A. K. Ivanov-Schits, L. N. Demyanets, *Acta Cryst.* **2006**, *B62*, 1010; b) V. A. Blatov, O. A. Blatova, G. D. Ilyushin, L. N. Demyanets, *Eur. J. Min.* **2005**, *17*, 819; c) V. Blatov, *Acta Cryst.* **2007**, *A63*, 329.
- [41] a) M. O'Keeffe, B. G. Hyde, *Struct. Bond.* **1985**, *61*, 77; b) M. O'Keeffe, B. G. Hyde, 'Crystal Structures. I. Patterns and Symmetry', Mineralogical Society of America, Washington, DC, **1996**.
- [42] M. O'Keeffe, M. A. Peskov, S. J. Ramsden, O. M. Yaghi, *Acc. Chem. Res.* **2008**, *41*, 1782.
- [43] G. M. J. Schmidt, *Pure Appl. Chem.* **1971**, *27*, 647.
- [44] J. D. Dunitz, *Chemistry Eur. J.* **1998**, *4*, 745.
- [45] a) J. D. Dunitz, J. M. Robertson, *J. Chem. Soc.* **1947**, 142; b) J. D. Dunitz, J. M. Robertson, *J. Chem. Soc.* **1947**, 148; c) J. D. Dunitz, J. M. Robertson, *J. Chem. Soc.* **1947**, 1145.
- [46] 'Microscopic property' refers to a property of the microstructure. It should not be confused with molecular or atomic properties, although sometimes microscopic is improperly used to describe what chemists consider the smallest possible structural level.
- [47] a) Q. Zhu, A. R. Oganov, M. A. Savado, P. Pertierra, A. O. Lyakhov, *Phys. Rev. B* **2011**, *83*, 193410; b) A. R. Oganov, 'Crystal structure prediction using the USPEX code', CECAM-Workshop Lausanne, 22-26 October, **2012**.
- [48] A. R. Oganov, C. W. Glass, *J. Chem. Phys.* **2006**, *124*, 244704.

- [49] Q. Zhu, A. R. Oganov, C. W. Glass, H. T. Stokes, *Acta Cryst.* **2012**, *B68*, 215.
- [50] P. Hohenberg, W. Kohn, *Phys. Rev.* **1964**, *136*, B864.
- [51] A. Krawczuk-Pantula, D. Perez, K. Stadnicka, P. Macchi, *Trans. Am. Cryst. Soc.* **2011**, 1.
- [52] A. S. Chimpri, M. Gryl, L. H. Rezende Dos Santos, A. Krawczuk, P. Macchi, *Crystal Growth & Design* **2013**, *13*, 2995.
- [53] S. Gorfman, O. Schmidt, M. Ziolkowski, M. von Kozierowski, U. Pietsch, *J. Appl. Phys.* **2010**, *108*, 064911.
- [54] D. Schaniel, M. Nicoul, T. Woike, *Phys. Chem. Chem. Phys.* **2010**, *12*, 9029.
- [55] H. N. Chapman, A. Barty, M. J. Bogan, S. Boutet, M. Frank, S. P. Hau-Riege, S. Marchesini, B. W. Woods, S. Bajt, H. Benner, R. A. London, E. Plonjes, M. Kuhlmann, R. Treusch, S. Dusterer, T. Tschentscher, J. R. Schneider, E. Spiller, T. Moller, C. Bostedt, M. Hoener, D. A. Shapiro, K. O. Hodgson, M. M. van der Seibert, F. R. N. C. Maia, R. W. Lee, A. Szoke, N. Timneanu, J. Hajdu, *Nature Phys.* **2006**, *461*, 839.
- [56] P. Debye, *Ann. Phys.* **1915**, *46*, 809.
- [57] a) P. Coppens, *Science* **1967**, *158*, 1577; b) P. Coppens, 'X-Ray charge densities and chemical bonding', Oxford University Press, Oxford, **1997**.
- [58] a) E. Schrödinger, *Ann. Physik* **1926**, *81*, 109; b) R. F. W. Bader, 'Atoms in Molecules', in 'Encyclopedia of Computational Chem.', Ed. P. V. Schleyer, John Wiley and Sons, Chichester, U.K., **1998**, Vol 1, pp 64.
- [59] a) H. Ott, U. Pieper, D. Leusser, U. Flierler, J. Henn, D. Stalke, *Angew. Chem., Int. Ed.* **2008**, *48*, 2978; b) B. Fournier, E. E. Bendeif, B. Guillot, A. Podjarny, C. Lecomte, C. Jelsch, *J. Am. Chem. Soc.* **2009**, *131*, 10929.
- [60] J. S. Tse, E. V. Boldyreva, 'Electron Density Topology of Crystalline Solids at High Pressure in Modern Charge Density Analysis', Ed. C. Gatti and P. Macchi, Springer, **2012**, p. 573.
- [61] R. F. W. Bader, 'Atoms in Molecules: A Quantum Theory, Oxford University Press', Oxford, UK, **1990**.
- [62] C. Gatti, *Z. Kristallogr.* **2005**, *220*, 399.
- [63] a) W. Scherer, G. Eickerling, C. Hauf, M. Presnitz, E.-W. Scheidt, V. Eyert, R. Pöttgen, 'On the Interplay Between Real and Reciprocal Space Properties in Modern Charge Density Analysis', Ed. C. Gatti, P. Macchi, Springer, **2012**, p. 359; b) J. Overgaard, Y. Grin, M. Takata, B. B. Iversen, 'Charge Density in Materials and Energy Science in Modern Charge Density Analysis', Ed. C. Gatti, P. Macchi, Springer, **2012**, p. 469; c) B. Silvi, C. Gatti, *J. Phys. Chem. A* **2000**, *10*, 947.
- [64] a) A. E. Whitten, D. Jayatilaka, M. A. Spackman, *J. Phys. Chem.* **2006**, *125*, 174505; b) J. E. Barquera-Lozada, A. Obenhuber, C. Hauf, W. Scherer, *J. Phys. Chem. A* **2013**, *117*, 4304.
- [65] T. Elsasser, M. Woerner, 'Transient Charge Density Maps from Femto-second X-Ray Diffraction in Modern Charge Density Analysis', Ed. C. Gatti, P. Macchi, Springer, **2012**, p. 697.