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Chemical Crystallography before X-ray Diffraction**

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chirality · crystallography · history of science · optical activity · solid state

Written on the centennial of the first crystal structure determination (Bragg 1913)
and dedicated to Prof. Biserka Kojić-Prodić on the occasion of her 75th birthday
and to Prof. Branko Kaitner on the occasion of his 70th birthday

The crystal structure determination of sodium chloride in 1913,[1] which was a consequence of Max von Laue's diffraction of X-rays from single crystals of copper sulfate[2] as well as of the postulation of Bragg's law[3] the previous year, marks the beginning of a new era in solid-state chemistry and the science of crystallography.[4] During the century following these discoveries, the importance of X-ray diffraction in the study of the crystalline state has become so overwhelming that the terms "crystallography" and "X-ray crystallography" (i.e. the study of crystal structures by means of X-ray diffraction) are today regarded by many as synonymous. It is, however, important to remember that crystallography is a much broader discipline and includes many other methods besides diffraction (although this probably is the most important method). Crystallography is also much older than X-ray diffraction, with its roots reaching not only to the beginnings of modern science, but also, in a way, to the ancient world.

Over the course of the last century, crystallography has transcended from mineralogy to physics and into all branches of chemistry—indeed, it is hard to imagine structural chemistry or simply a molecular structure without thinking about X-ray diffraction—and (over the last couple of decades) to biology. However, crystallography has also been an integral part of chemistry since the beginnings of science. One of the main traits of modern chemistry is its ability to connect the macroscopic (bulk) properties of a substance with its microscopic (atomic, molecular) constitution.

This Essay is not intended as a history of pre-1912 crystallography (several accounts on this subject have been published recently[5] and the seminal textbook of "classical" chemical crystallography was written at the beginning of 20th century by P. Groth)[6] but rather as a review of various aspects in which early crystallography has aided the development of chemistry. In this Essay we describe the evolution of some key concepts in chemistry that have their roots in crystals and macroscopic crystallography.

Proto-Crystallography

> "*Let us examine a crystal. We are at once interested by an equality between the sides and between the angles of one of its faces: the equality of the sides pleases us; that of the angles doubles the pleasure. On bringing to view a second face in all respects similar to the first, this pleasure seems to be squared; on bringing to view a third it appears to be cubed, and so on. I have no doubt indeed, that the delight experienced, if measurable, would be found to have exact mathematical relations such as I suggest; that is to say, as far as a certain point, beyond which there would be a decrease in similar relations.*"
> Edgar Allen Poe (1809–1849), *Rationale of Verse*, **1843**.

Our fascination with crystals is much older than science. In fact, it appears to be older than mankind itself! The first "crystallographers" were probably of the species *Homo erectus*, who collected quartz crystals for making tools, which were found among 250000–700000 year old bones, stone tools, and fragments of stone unearthed in the Zhoukoudian cave system in China.[7] However, some of these crystals do not show any signs of use and may have had some other function, possibly ceremonial or decorational. Similarly, quartz crystals were also found in the Singi Talav cave in India (300000–150000 years old).[8] The beauty of various crystalline minerals attracted the attention of prehistoric men and women, and for this reason they were collected as precious stones. They became an important part of everyday life, so that one may find references to crystals in many early texts, and even holy books.[9]

The word crystal is derived from Ancient Greek word κρύσταλλος (meaning ice or "rock crystal", that is, quartz; the term was often used for any transparent solid),[10] which is itself derived from κρύος (frost).[10] Ancient Greeks believed rock crystal to be ice frozen very hard. This belief was retained throughout the ancient times, and stubbornly persisted during the Middle Ages and the Renaissance; even a spurious proof of it was believed to exist—little drops of water were supposed to be found inside pieces of rock crystal.

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This was known to be a fact to such an extent that it became a common artistic symbol in poetry. The Roman poet Claudius Claudianus (died ca. 404 AD) wrote as many as six poems on the subject of water contained in crystals.[11,12]

The concept of crystals and minerals was rather vague in ancient times and the available ancient sources mentioning crystals are rather scarce. In the masterpiece of classical-age natural science *De rerum natura*,[13,14] Titus Lucretius Carus listed some solids in order of their hardness: diamond, quartz (corundum), iron, and brass, and linked their properties to their atomic compositions. Pliny the Elder offered some glimpses into proto-mineralogy and proto-crystallography in his capital work *Naturalis historia*.[15,16] Pliny was fascinated by perfectly flat smooth faces of quartz and described habits of four gemstones whose single crystals are regularly found in nature: quartz ("crystallus"), "rainbow-stone" ("iris", probably quartz colored by impurities), diamond ("adamas"), and beryl ("smaragdus"). The crystals are described as "hexagonal" and "hexahedral" ("sexangula figura", "sexangulus laterbius" etc.); however, note that no general word for crystal existed.

The Middle Ages did not contribute much to the increase in crystallographic knowledge. The greatest contributions to crystallography since ancient times appeared in the mid-16th century—The *Pirotechnia* by Vannoccio Biringuccio (1540)[17] and *De Re Metallica* by Georg Bauer (1556).[18,19] Biringuccio in his *Pirotechnia* provides quite accurate descriptions of many crystals, also noticing the crystals' perfection. Crystals of alum are thus "thick squares with beautiful corners that look like large diamonds", and those of pyrites are "little cubes (…) so correctly squared that no draftsman could draw their corners more accurately or better with any sort of instrument." Also he gives a detailed description of how crystallization was used to purify some ores such as (green) vitriol and alum. However, even this astute observer of nature and technology, who criticizes the credulity of alchemists and other "philosophers" who write from books rather than from experience, becomes guilty of the same fault when discussing precious stones, and reports some quite fantastic properties.[20] Similarly Agricola, although careful in most technical details, still retains many of the old beliefs, such as the power of garlic to demagnetize magnetite.[16]

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One of the last contributions preceding (although not predating, see the next section) scientific crystallography was the classification of minerals as proposed in *Systema Naturae*, the epochal masterwork of the great systematizer of nature, Carl Nilsson Linnæus, Baron von Linné.[21] Like plants and animals, minerals are divided into classes, orders, families, and genera, with each mineral given a two-word name in analogy to the Linnaean names of plants and animals. In this system there are three classes of minerals: *Petrae*, (rocks), *Minerae* (ores), and *Fossilia* (excavations). The majority of (macro)-crystalline materials were classified as ores, and these were further divided into three orders: *Salia* (salts, including most transparent crystals), *Sulphura* (sulfurs, including amber, oil, and sulfides), and *Mercuralia* (mercurials, metals).[22] Linnaeus' classification was neither in accord with the chemical composition, nor with crystallographic rules, and could be regarded as a mere historical curiosity, had it not been for one significant, albeit probably unintended, consequence. Linnaeus' book sparked an interest in mineralogy in the young French priest René Just Haüy, and the far-reaching results of his interest will be the subject of one of the following sections.

Measuring the Angles—Birth of a Science

> "*An experiment is a question which science poses to Nature, and a measurement is the recording of Nature's answer.*"
> Max Planck, *Scientific Autobiography*, 1949

At the beginning of a modern crystallography textbook one will usually find a statement that "the angles between two corresponding faces on the crystals of any solid chemical or mineral species are constant and are characteristic of the species". This First Law of Crystallography is often considered to be the first scientific statement in crystallography. Today this seems quite obvious, but in reality it took almost two millennia of observing natural crystals to establish this fact. The overall shape of crystals of any given substance was observed not to be constant, so that the angles between faces were also expected to vary. As late as 1564 Conrad Gessner wrote that "one crystal differs from another in its angles and consequently in its figure".[23] It took a keen observer of nature to see the better, and such a man was Nils Stensen.

Stensen (better known by the latinized version of his name, Nicolaus Steno), a son of a Copenhagen goldsmith, instead of continuing in his father's footsteps, studied medicine,[24] and contributed greatly to the study of human anatomy. However, his father's trade had left some mark on him, as he continued to be interested in minerals (precious stones, fossils etc.), alongside his medical pursuits. He left his native Denmark in 1661 and spent some time in the Netherlands and France, settling finally in Italy in 1666. The same year a huge female shark was caught near Livorno, and Stensen had the opportunity to dissect the head of the brute. He noted that the shark's teeth were quite reminiscent of certain objects found in rocks, known at the time as *glossopetrae* (rock-tongues), which he recognized as petrified shark's teeth. This led him to consider different ways in which a solid body (such as a shark tooth but also a crystal) might end up contained in another solid (a rock).[25] As far as crystals were concerned, his attention was focused almost completely on rock crystals. In spite of this somewhat limited approach, his conclusions had tremendous impact. He ascertained that crystals grow by the addition of new layers of minute particles, proved by the existence of fine stria in the crystals. Therefore, crystals were not formed at the beginning, but have subsequently grown, and continue to do so even at the present day. But the most important of his statements was definitely his assertion that, although the number and size of crystal sides may vary from one crystal to another, the angles between corresponding sides are always the same ("*In plano axis laterum et numerum et longitudinem varie mutari, non mutatis angulis*")[26]—the famous First Law of Crystallography.[27]

One would expect that such a general observation of the constancy of angles must be a result of meticulous measurements of a large number of crystals. In fact, Stensen does not mention any sort of measurement performed on the crystals—either he had some apparatus for measurement, but did not find it necessary to mention it, or he simply reached them by observation and philosophical contemplation.[28]

However, at the time an actual measurement of an angle in a crystal had already been reported. In his 1665 masterpiece *Micrographia*, Robert Hooke described numerous observations made with a microscope, along with some observations of quite macroscopic objects. Among those that attracted his attention were the figures of ice that appeared on puddles of urine (Figure 1). As he wrote: "*Where ever there was a center, the branchings from it, (…), were never fewer, or more then six, which usually concurr'd, or met one another very neer in the same point or center; though oftentimes not exactly; and were enclin'd to each other by an angle, of very neer sixty degrees, I say, very neer, because, though having endeavoured to measure them the most acurately I was able, with the largest Compasses I had, I could not find any sensible variation from that measure, yet the whole six-branched Figure seeming to compose a solid angle, they must necessarily be somewhat less.*"[29]

One might be inclined to deem his observation of the angle being little less than 60° as erroneous, but that would inflict quite an injustice on this careful observer; he also noticed that the center of the figures is always somewhat elevated above the surface (due to the expansion upon freezing), which led him to conclude that the angle between the "branches", which in a two-dimensional projection are at exactly 60° as shown by his "Compasses" are in fact at a somewhat smaller angle.[30]

Hooke's method of measuring angles in crystals using a compass is applicable if the studied crystal is flat and large. However, most crystals are three-dimensional bodies and usually not "above four foot long" like Hooke's puddles. It was necessary therefore to devise a special instrument to measure the angles in crystals; however, the need for such an instrument did not become apparent for almost a whole century.

About 1780 Arnould Carrangeot, an assistant to the French mineralogist Jean-Baptiste Louis Romé de l'Isle, was entrusted with the preparation of clay models of crystals from Romé de l'Isle's collection. To make the models more realistic, Carrangeot devised an instrument for measuring the angles between the crystal faces—a contact goniometer (Figure 2).[31] Using this instrument Romé de l'Isle soon realized that Steno's law is valid for all minerals, not just quartz.

The use of the goniometer soon led to several chemical discoveries. When Rene Just Haüy decided to undertake measurements of a number of crystals labeled "sulphate of

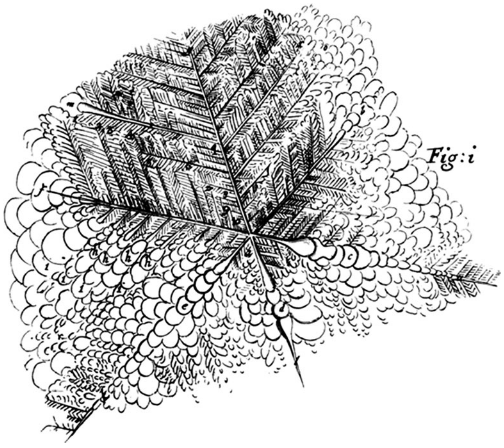

Figure 1. Hexagonal branches of ice crystals on frozen urine, from Hooke's *Micrographia*.[29]

Figure 2. Rene Just Haüy demonstrating use of the contact goniometer on a crystal of (apparently) Icelandic spar. Engraving by R. H. Delvaux.

baryta", he was surprised to see that samples from Sicily had different interfacial angles from those from Derbyshire. The difference was only couple of degrees, but that was enough to convince Haüy that the samples must differ in chemical composition. This was subsequently proven by Louis Nicolas Vaquelin, who showed that the Sicilian samples were in fact strontium sulfate.[32] In another measurement Haüy noticed that the interfacial angles of emerald are identical to those of beryl, and concluded that emerald was only a green variety of beryl. Again Vaquelin was asked to perform an analysis, which yielded the identical sweet-tasting substance from both beryl and emerald. This substance was named "berylia" and shown to be an oxide of a new element—beryllium.[33]

The contact goniometer thus became a standard tool for crystallographers, although it was, in spite of its great usefulness, a rather clumsy and crude device suitable for only rough measurements (with an accuracy no greater than 15′) of quite large crystals. It is therefore not surprising that a more accurate device was soon invented.[28] In 1809 the English chemist William Hyde Wollaston described the reflection, or optical, goniometer, which measures the angle between normals to crystal faces.[34–36] It could be used to measure much smaller crystals—including those (prepared in the laboratory) which rarely exceed a couple of millimetres—with a greater accuracy. During the first half of 19th century the optical goniometer was significantly improved and refined; a telescope for crystal centering was added, and later additions included a telescope for observing reflections (which greatly facilitated measurements), a collimator producing a parallel beam of light, and, eventually, an artificial source of light. Myriad different designs with various geometries were constructed such as those by Mitscherlich and Babinet which greatly improved the accuracy of the instrument, reducing the error to just 30″. The two-circle optical goniometer, which further facilitated crystal measurement, was designed in about 1890 by Yevgraf Stepanovich Fyodorov.[37,38] The two-circle goniometer remained a standard crystallographic tool for the next hundred years, well after attention of chemical crystallography shifted from the external appearance of crystals to their internal structure.[39]

Cannonballs, Snowflakes, and Atoms

> "Atoms are round balls of wood invented by Dr. Dalton."
> Sir Henry Enfield Roscoe (reporting a student's answer), **1887**

Although the idea of the finite divisibility of matter is quite counterintuitive, it has been present in philosophy almost since its beginnings. The first atomist was probably Leucippus,[40] who considered that everything is composed of indivisible atoms which move randomly in a vacuum. His views were elaborated and disseminated by his pupil and successor Democritus of Abdera. This early atomistic philosophy sparked some fierce criticism, but also gained some devoted followers.[41] One of the most significant ancient advocates of atomism was Lucretius, who presented some very clear and compelling empirical arguments for his atomistic views. He also noted that physical properties such as hardness and density are a result of the atom arrangement; his notion of "hooked atoms" nicely corresponds to the modern concept of covalent bonding.[42] His arguments, however, were hardly generally accepted, and the polemic between the critics and followers of atomism was not to reach its final conclusion for almost two millennia.

The close packing of atoms and molecules in crystal structures is widely accepted as one of the fundamental principles governing the assembly of constituents into crystals. Although modern ideas on close packing (particularly in molecular solids), as presented by Kitaigorodskii,[43] are derived from structural data, the notion that crystals are formed by the close packing of constituent particles is much older.

The first mention of this idea appears to be in the encyclopedic work *De subtilitate libri XXI* (21 Books on Subtlety) published in 1550 by Girolamo Cardano. In Book 7 he attempts to explain the hexagonal prismatic shape of quartz crystals as resulting from the close packing of spherical particles, a proposal inspired by the hexagonal arrangement of cells in a honeycomb. The crystals are composed of spherical particles, and since six spheres can be assembled about a central one, adding additional layers of spherical particles must lead to a final crystal with a hexagonal shape. Cardano's view did not meet with much approval and was soon challenged by Giulio Cesare della Scala, who notes that Cardano disregarded the hexagonal pyramids (i.e. rhombohedral faces) of the quartz crystals which he believed to be incongruent with Cardano's model.[44] This purely philosophical debate did not attract much attention, however, and the problem of the packing of spheres was not to be more closely examined until it was addressed from a more belligerent point of view.

Whilst preparing for an expedition to the New World in the 1580s, Sir Walter Raleigh approached a young mathematician in his service, Thomas Harriot, with a practical problem: What is the most efficient way of packing cannonballs in the ship's hull, so that as many as possible can be transported to the New World, where they might prove useful in "dealing" with the native population? Harriot solved the problem in 1591. He seems to have intuitively realized that the closest packing is that which today is referred to as hexagonal closest packing (hcp) and, based on the assumption that cannonballs are to be packed in this manner, he devised a table for calculating the number of cannonballs in trigonal-pyramidal piles.[45]

Most of Harriot's work was never published, and his work on piles of cannonballs would probably be lost in obscurity were it not for his correspondence[46] with his more famous contemporary, Johannes Kepler. The correspondence was initiated by Kepler, who was interested in optics (in order to procure exact astronomical measurements) and had heard of the existence of experts in that field in England. Their correspondence soon took them to a discussion of more general topics—including atomistic theory. Harriot was an ardent atomist and attempted to convince Kepler of the existence of atoms first by explaining the reflection and refraction of light in terms of atoms (which Kepler found implausible, believing they were properties of a glasslike continuum), and later by pointing out that even the most opaque of substances (gold) becomes translucent if thinned out sufficiently. In his argumentation, Harriot pointed out to Kepler the problem of the close packing of spheres, as related to the way in which atoms can occupy space, leaving small pockets of vacuum between them.

After this exchange of letters, Kepler started his own work on the problem of the close packing of spheres. He was soon convinced that the closest assembly of spheres in two dimensions is a hexangular array, immediately reminiscent of a honeycomb. This led him to a question (and also the answer) concerning the shape of snowflakes: Why are snowflakes, before they entangle to form larger plumes, hexagonal in shape?[48] Kepler's observation of the shape of snowflakes can indeed be considered a fortunate one, as this was hardly common knowledge at the time.[49] Only some 60 years earlier Olaus Magnus (Olof Måsson) provided an image of snowflakes (Figure 3) in his book on the history of northern nations,[50] from which it is apparent that he was quite unaware of the hexagonal shape of the crystals of snow. Kepler concluded that the shape of the snowflake is related to the honeycomb geometry—the hexagonal arrangement of spheres provides the closest packing. Such close packing can be extended into three dimensions in the same way as the seeds are packed in a pomegranate. Kepler's choice to base his reasoning on (flat) snowflakes, rather than (polyhedral) quartz crystals as Cardano had, was fortunate, as the objection put forward by della Scala could not be applied.[51]

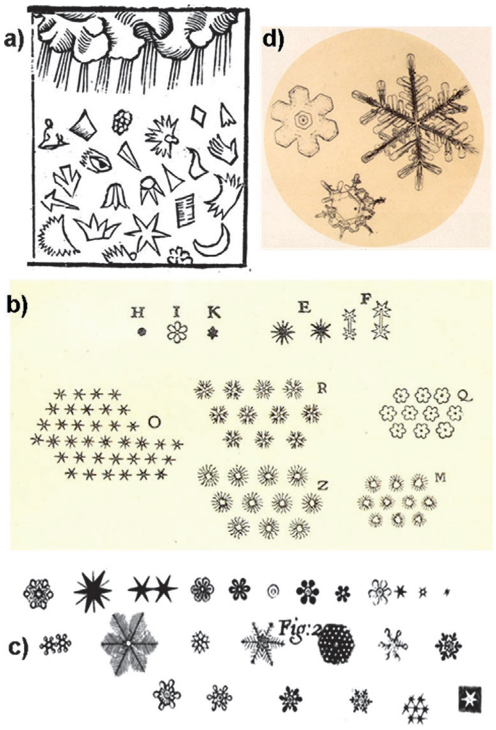

Figure 3. The evolution of the observed shape of snowflakes. a) The earliest (to the best of our knowledge) rendering of snowflakes (1555);[50] note the five-fingered hand on the upper right. b) A more convincing drawing by Descartes (1637).[47] c) Drawings by Hooke of snowflakes seen under a microscope.[29] d) The first (to the best of our knowledge) microphotograph of snowflakes (photographed in Berlin, on December 25, 1892, about noon).[49]

By that time Kepler had completely embraced atomism and regarded matter as composed of spherical atoms. He had considered two different ways in which spheres may pack in two dimensions—a square array and a hexagonal array, noting that the latter provided a closer packing. Extending these planar packings into three dimensions, he deduced that the square array will lead to a cubic arrangement with each sphere surrounded by six neighbors (i.e. primitive cubic packing), whereas the hexagonal array will lead to a more dense packing, in which each sphere is surrounded by twelve neighbors. The latter he claimed to be the closest possible packing of spheres.[52]

Like Cardano and Kepler, Robert Hooke also believed that the atomic nature of matter might explain the regular shapes of crystals. However, while they were content with thinking only of hexagons, Hooke also considered other shapes and noticed that the close packing of spheres might explain all sorts of different shapes one can see on crystals (Figure 4).[29]

Hooke went even further and sketched out more detailed studies to determine how exactly atoms pack in order to create various crystalline bodies. This was to be done by detailed observations on numerous natural and artificial crystals to determine the possible shapes of crystals, and at the same time by construction of all those shapes from spheres.

Hooke never succeeded in completing this most ambitious project. In fact, it took some 160 years of observation of crystals before a more general construction of crystal shapes could be attempted. In 1826 Moritz Ludwig Frankenheim published his attempt to systematize the majority of known crystals on the grounds of their symmetries.[54,55] This led him to the realization that there are only 32 combinations of the

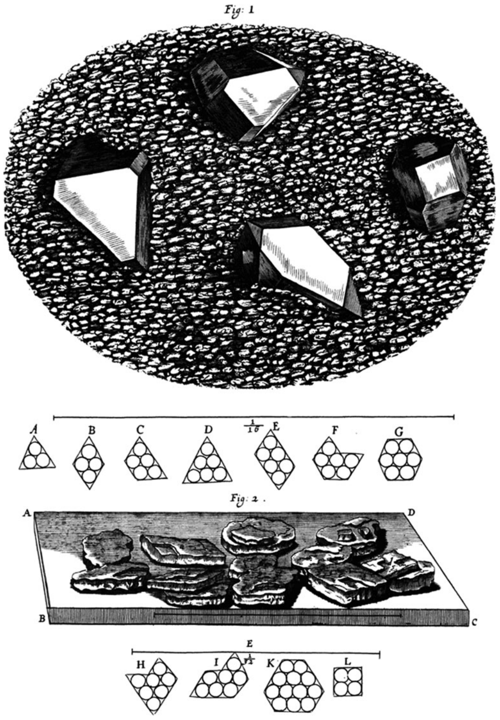

Figure 4. Assembly of spheres leading to different shapes compared to faces of microscopic crystals as observed and deduced by Hooke.[53]

symmetry operations[56] that appear in crystals, and therefore he defined the 32 crystal classes. This insight prompted him to consider the possible ways of the periodical distribution of points (or atoms) in space. He realized that there are 15 different symmetries for the periodic arrangement of atoms in space. In 1848, Auguste Bravais pointed to an error in Frankenheim's derivation, and showed that there are in fact only 14—two of Frankenheim's lattices were identical.[57] Bravais' approach to the problem was mathematically more rigorous, and his result finally the correct one, so the 14 lattices became known as "Bravais lattices", while Frankenheim's contribution is rarely remembered.

Frankenheim and Bravais have thus dealt with the problem of arranging points (or spherical atoms) in space. But what if the crystal comprises groups of atoms that need not have any symmetry on their own? This was the question that eventually led Fyodorov to the definition of 230 crystallographic space groups in 1891.[58,59]

Although the shape of crystals was a good argument in favor of the atomistic theory, and the atomistic theory also proved to be a good basis for crystallographic considerations, the opposition to atomism persisted.[60] This is not to be confused with stubbornness or lack of knowledge but rather to the scientific rigor—just because a theory is useful, it is not necessarily correct. The final experimental proof of the atomic nature of matter was not given until the discovery of radioactivity, Einstein's explanation of Brownian motion (experimentally confirmed by Perrin), and the diffraction of X-rays by crystals, which all confirmed the discrete nature of matter.

Crystalloclasts, Periodicity, and Molecules

> "*MOLECULE, n. The ultimate, indivisible unit of matter. It is distinguished from the corpuscle, also the ultimate, indivisible unit of matter, by a closer resemblance to the atom, also the ultimate, indivisible unit of matter. Three great scientific theories of the structure of the universe are the molecular, the corpuscular and the atomic. A fourth affirms, with Haeckel, the condensation or precipitation of matter from ether—whose existence is proved by the condensation or precipitation. The present trend of scientific thought is toward the theory of ions. The ion differs from the molecule, the corpuscle and the atom in that it is an ion. A fifth theory is held by idiots, but it is doubtful if they know any more about the matter than the others.*"
>
> Ambrose Bierce, *The Devils Dictionary*, **1911**

During the 1770s, the young French priest René Just Haüy was spending much of his time in the Parisian botanical garden. He had been interested in science for some time, and had decided to study botany. In order to advance his studies he purchased a copy of Linnaeus' *Systema Naturae*. Soon afterwards he began neglecting his botanical studies and attending the mineralogical lectures presented by Louis-Jean-Marie Daubenton. After he had completed Daubenton's course, mineralogy remained Haüy's sole interest.[61]

Although it was generally known that given minerals prefer to crystallize in certain habits, the variability of crystal habits made this seem to be a less important property, while other properties, such as density, hardness, and even color were considered to be a fundamental basis for classification. It seems therefore a little historic pun that the person to realize the structural basis of crystal habits (to, as it were, see "beyond the habit") was an abbot![62]

According to Georges Cuvier, Haüy made his first discoveries by accident.[63] In 1780, while he was observing a beautiful aggregate of large prismatic calcite crystals, one of the prisms broke off, fell to the ground, and smashed into numerous small pieces. Haüy picked up the pieces, and to his surprise noticed that they were all of the same shape. Furthermore, their shape was not prismatic like the original crystals but rhombohedral, identical to crystals of Icelandic spar (transparent calcite crystals obtained from Iceland). He immediately ran into his study, found a large scalenohedral calcite crystal, hit it with a hammer, and again found that it broke into rhombohedra. A third calcite crystal upon breaking also yielded identical fragments. Thus Haüy reached the conclusion that all calcite crystals comprise rhombohedral calcite molecules.

This nice anecdote probably has no more veracity than Newton's gravitational apple, especially since the experiment with crushing calcite crystals into rhombohedra was performed some years earlier by Torbern Olof Bergman. He published his results in 1779, and this initiated a long correspondence between himself and Haüy. It is therefore evident that Haüy was well aware of Bergman's work at the time that he performed his experiments, which somewhat reduces the verisimilitude of the story of Haüy's accidental smashing of a calcite prism. Unlike Bergman, however, Haüy went further to study other minerals in the same manner and found that many of them break (i.e. are cleaved) into pieces characteristic for that mineral: garnets, rock salt, and pyrite break into small cubes, diamond into octahedra, gypsum and barite into four-sided prisms, and so on. Therefore, the basic constituent units of these minerals must be of those particular shapes. The crystals are then formed as three-dimensional periodical aggregates of their constituent molecules. Variations in the shapes of crystals of the same mineral can therefore be explained as different assemblies of their constituent molecules. In the same way as a number of cubes can be assembled into an octahedron, so also a great number of cubical constituent molecules can be assembled into an octahedral crystal. There is, however, a limitation to the possible faces that can appear on the crystal. Since a crystal is a periodical array of constituents, the only faces that may appear are those whose intercepts on the axes defined by three nonparallel edges of a crystal have a ratio of small integers.[64] This later became known as Haüy's law of integers or the law of rational intercepts.

Haüy's rather destructive approach to the study of crystals was not approved by all of his contemporaries. In his *Cristallographie* of 1783, Jean Baptiste Louis Romé de l'Isle remarked, rather venomously, on the appearance of a novel type of crystallographer, for whom the appellation of "crystalloclast" (i.e. crystal breaker) would be more appropriate![65] Many mineralogists, however, realized the importance of Haüy's work. Daubenton, who was the first one to be acquainted with Haüy's results, encouraged him to submit his work to the Royal Academy (1781), and also included Haüy's theory in his lectures on mineralogy. On the grounds of his papers on the structure of garnets and calcite, Haüy was made a member of the Royal Academy in 1783 (some of Romé de l'Isle's bitterness can perhaps be attributed to the fact that he had applied for membership three years earlier, but was rejected). As a member of the Academy, Haüy could introduce his views to a wider scientific audience, and thus in 1792 he held a course in crystallography which was attended by the chemists Antoine-Laurent de Lavoisier, Antoine François, Count de Fourcroy, Louis-Bernard Guyton de Morveau, and Claude Louis Berthollet, as well as the mathematicians Joseph-Louis Lagrange and Pierre-Simon Marquis de Laplace. Not many crystallographers have ever had the opportunity to lecture to such an illustrious group of "students"! Later on, Haüy's lectures were attended by numerous listeners from all corners of the world, which greatly contributed to the speedy dissemination and acceptance of Haüy's views.[66]

The main impact of Haüy's theory was the introduction of periodicity into crystallography. In the early ideas on the close packing of spheres, the concept of periodicity was implicitly assumed, but it was Haüy who placed emphasis on this point. From Haüy onwards, crystals were considered as aggregates of matter in which this matter repeats periodically.[67] More interestingly, from a purely chemical point of view, postulating that crystals are periodical arrangements of polyhedral units also implies that each unit must have the identical chemical composition as the whole, and, if this unit is indeed the minimal one, it represents a "molecule" of the compound. Haüy was aware of this, and even named the fundamental constituent units "molécules intégrantes",[64] employing the term "molecule" which has since the mid-17th century[68] been applied to denote a group of (connected) atoms. Since molecules have definite geometric (polyhedral) shapes, every chemical substance possesses a characteristic crystalline form. Also, substances differing in chemical composition cannot occur in the same form, (unless their respective "molécules intégrantes" are of very high symmetry, that is, cubes). Although he stressed these chemical implications (and even applied them in practice), Haüy offered very little discussion on the nature of his molecules, referring to their geometry as the only significant property. The shape of the molecules defines the shape of their primary aggregate (kernel, "noyau") from which crystal further lamellary grows into its final crystal habit (Figure 5).

The molecular aspects of Haüy's theory were developed in detail by Dieudonné Sylvain Guy Tancrède de Dolomieu[69] in a tract on "mineralogical philosophy" published in 1801.[70] For Dolomieu an "integrant molecule" represents a "complete individual" and all the chemical properties of a substance are in fact the chemical properties of its molecules, and therefore independent of the physical form of a substance. "Integrant molecules" of lime carbonate can assemble regularly into a crystal, such as calcareous spar, or they can be assembled irregularly as they are in chalk—both are the same substance, comprising the same type of molecule, despite their different physical appearance. In this way Dolomieu expanded the molecular theory beyond regular crystalline bodies, onto formless "earths" and generally all solids.

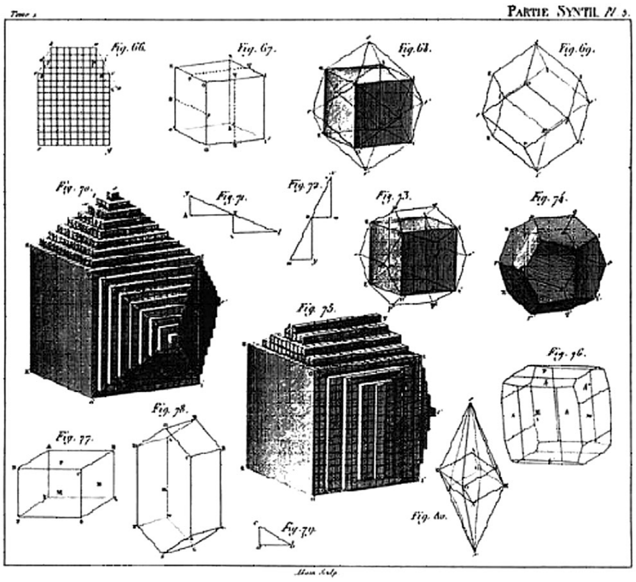

Figure 5. A figure from Haüy's *Traité de mineralogie* (1801) depicting the formation of different habits of pyrite crystals from cubical constituent molecules. Images denoted as Figure 70. and Figure 75. depict the growth of lamellae on a cubic kernel, and images Figure 69. and Figure 73. the placement of the kernel within a rhombic and pentagonal dodecahedron.

Another point Dolomieu addressed was that of the simultaneous presence of several different types of molecules. In an aggregate of molecules of one type, molecules of another may appear as "superfluities" or "pollutions". "Superfluities" enter the molecules of the first type without changing their shape, and allow them to assemble into same aggregates as if they were pure. The result is a homogeneous mixture (which can also be considered as a compound), and therefore "superfluities" do not decrease transparency or other properties of the crystals, although they can bring forth new properties, such as color. Coloring agents in colored allochromatic minerals are therefore "superfluities". "Pollutions", on the other hand, take place between the "integrant molecules" upon the formation of a crystal, thus leading to imperfections in their assembly into crystal. Because of this, crystals containing "pollutions" lose their transparency. Other properties of the crystals, such as color, luster, density, and hardness, are also affected, since a crystal containing "pollutions" is no longer a (homogeneous) pure substance but rather a (heterogeneous) mechanical mixture.

Dolomieu's suggestion that a chemical substance, defined by its "molecules", could exist in different solid forms was a revolutionary idea that could hardly be reconciled with the doctrine of the three states of aggregation which was widely accepted in the early 19th century.[5a] It was an important step towards the realization of the existence of polymorphism. Dolomieu, however, was apparently unable to make the next step—the realization that substances of the same composition can have different "molecules".

Same or Different? The Chemist as a Nitpicker

> “*Kakav je to kemičar koji nije cjepidlaka? Ako nije, nek' ide u ekonomiste!*
> *What kind of a chemist is one who is not a nitpicker? He should rather become an economist!*”
> Vladimir Simeon, a physical chemistry lecture (at University of Zagreb), 1999

At the end of the 18th century, the German chemist Martin Heinrich Klaproth continued where Dolomieu had stopped and identified three different crystal forms of calcium carbonate: calcite, aragonite, and vaterite. Differences between these minerals were described in detail in his five-volume book *Beiträge zur chemischen Kenntniss der Mineralkörper* (published 1795–1810).[71] Haüy was interested in this discovery, but was somewhat puzzled by aragonite: unlike calcite it did not shatter into rhombohedra. Klaproth's successor, Eilhard Mitscherlich, started his study of crystals around 1818 and soon recognized that crystals that have the same composition but different morphology (e.g. calcite and aragonite) are not uncommon.[72] However, there are also crystals that have similar morphology but different chemical composition. Dolomite, a mineral described by Dolomieu, is very similar to calcite, but it contains magnesium and calcium rather than only calcium. Accurate measurements by Wollaston showed minor differences in the geometry of the crystals: the rhombohedral angle in calcite is 105°5′, in dolomite 106°15′, while in siderite (iron carbonate) it is 107°0′.[73]

This type of phenomenon was first noticed already by Romé de l'Isle in the late 18th century in cubic alums which form mixed crystals and overgrowths of one crystal on another. Around 1812 Wollaston described more examples of similar crystals with different chemical compositions and he measured slight differences in their interfacial angles. For example, in a series of alkali sulfates (K_2SO_4, Rb_2SO_4, Cs_2SO_4, $(NH_4)_2SO_4$) the interfacial angles differ by several minutes, and in a similar compound, Tl_2SO_4, the corresponding angle differs by a half of a degree.[73] Moreover, a series of phosphates and arsenates also formed similar crystals.

Therefore, there are two apparently opposite phenomena, compounds of the same composition forming crystals of different morphology and compounds of different composition forming crystals of (nearly) the same morphology. For them, Mitscherlich coined the terms “isomorphous” (different composition, same morphology; from Greek ισος = equal and μορφή = shape)[10] and “polymorphous” (same composition, different morphology). Eventually he discovered the law of isomorphism: Compounds that crystallize together probably have similar structures and compositions.[73] That would also mean that compounds with similar composition are likely to grow similar (isomorphic) crystals.

Even elementary substances can crystallize in different ways as Mitscherlich observed for sulfur, which produces different crystals (with different interfacial angles) depending on the conditions of crystallization.[74] He argued that the atoms of the same element may bond in different fashions, resulting in different molecules with different crystal structures. Such examples are diamond, graphite, and soot, all of which are (almost) pure carbon. For this phenomenon, Berzelius in 1841 coined the term “allotropy” (from Greek άλλοτροπία = variability).[10,75]

The discovery of isomorphism had a profound influence on the development of chemistry, which extended beyond the merely conceptual. The different properties of isomorphous compounds enabled Berzelius to obtain the first relatively accurate table of atomic weights.[76] However, Mitscherlich's discovery was only the tip of the iceberg. Many important chemical concepts partly connected with crystallography (the description of the crystal habit used was at the time to describe and identify compounds) came into being during the following several years. The discovery of isomorphism was only a prelude for the discovery of isomerism, one of the central concepts in chemistry.

In 1823 the young German physician Friedrich Wöhler came to Stockholm to work with Jöns Jakob Berzelius, the foremost chemist at the time.[77] Instead of receiving systematic instructions, Wöhler was encouraged to work on his own subject of study: cyanogen and cyanic acid, which he had started investigating as a student at the University of Marburg.[78] In one of his preparations of ammonium cyanate, he noticed some colorless crystals which he could not identify at the time. However, he analyzed cyanic acid and found that its formula is HOCN.[79]

Roughly at the same time, Justus von Liebig at the University of Giessen, pursuing his childhood fascination with explosives,[80] prepared and analyzed an explosive silver fulminate (AgONC),[81] which appeared to have the same chemical formula as Wöhler's silver cyanate (AgOCN).[82] After an initial argument, the two chemists soon agreed that their compounds have the same composition. It was the beginning of a lifelong friendship and collaboration; today we can argue that it was also the beginning of a new era in chemistry. In an editorial in *Annales de chimie et de physique*,[79,83] Joseph-Louis Gay-Lussac stated that if both Liebig's and Wöhler's analyses were correct, “it would be necessary, in order to explain their differences [in properties], to admit a different manner of combination between their elements”. It was the first description of “isomerism”, a term coined a few years later by Berzelius[79,83] (from Greek ισομερης = of the same parts)[10] for compounds with the same atomic composition, but different physical properties. By 1830 several cases of isomerism were described, including tartaric and racemic acid (which played an important role in the development of stereochemistry).

Meanwhile, Wöhler, now back in Germany, realized that the unidentified colorless crystals he had serendipitously obtained in Stockholm were actually urea, which appeared from the isomerization of ammonium cyanate.[84–86] Since instrument-based analytical methods did not yet exist, novel substances were characterized by their chemical and physical properties—the latter including a description of the crystal habit. Crystals of urea were described by Wöhler as “four-sided right-angled prisms, beautifully crystalline”.[79,87] Every crystallographer will recognize in this an early attempt to describe tetragonal crystals; indeed, urea crystallizes in the tetragonal system.

The polymorphism of molecular crystals was also documented for the first time by this same pair of chemists. When its solution is allowed to cool, benzamide initially crystallizes as silky needles; after some time the needles disappear and are replaced by orthorhombic crystals.[88] Many more examples were found in the next years and towards the end of 19th century Wilhelm Friedrich Ostwald stated that in general it is not the most stable but the least stable polymorph that crystallizes first:[89] the rate of crystallization is determined by the activation energy rather than the lattice energy (stability). The physical explanation of the phenomenon was already long overdue. The polymorphism of organic compounds is still a "hot topic" in solid-state chemistry;[71] however, it is also still a poorly explained phenomenon. As for benzamide, its crystallization remained a mystery for some 175 years and was resolved only recently.[90]

Here we should note that isomerism was predicted almost a century before Liebig and Wöhler, by a brilliant Russian chemist and probably the last homo universalis, Mikhail Vasilievich Lomonosov. In his treatise *Elements of Mathematical Chemistry* (1741) he stated that "different molecules must result from the same number of the same atoms, if these be differently combined—there must be formed bodies possessing different properties although having the same composition".[91] However, since Lomonosov's ideas were at least a century ahead of his time, and since he wrote mainly in Russian, his work passed unnoticed and was forgotten, only to be rediscovered at the beginning of the 20th century.[92]

Magical Sunstone, Seafaring, and Asymmetric Molecules

> *“Veður var þykkt og drífanda sem Sigurður hafði sagt. Þá lét konungur kalla til sín Sigurð og Dag. Síðan lét konungur sjá út og sá hvergi himin skýlausan. Þá bað hann Sigurð segja hvar sól mundi þá komin. Hann kvað glöggt á. Þá lét konungur taka sólarstein og hélt upp og sá hann hvar geislaði úr steininum og markaði svo beint til sem Sigurður hafði sagt.*
>
> *The weather was thick and snowy as Sigurður had predicted. Then the king summoned Sigurður and Dagur to him. The king made people look out and they could nowhere see a clear sky. Then he asked Sigurður to tell where the sun was at that time. He gave a clear assertion. Then the king made them fetch the solar stone and held it up and saw where light radiated from the stone and thus directly verified Sigurður's prediction.”*
>
> *Rauðúlfs þáttr* (Icelandic saga, 12th–13th century)

The Vikings were arguably the greatest mariners of the early Middle Ages. Their longships sailed through North Sea, North Atlantic, Mediterranean, and Black Sea. In the 9th century, the Vikings discovered Iceland and settled there. In the following century, Erik Thorvaldsson (Eric the Red) led a group of Icelanders who colonized Greenland, and a couple decades later his son, Leif Eriksson, set forth even further westward, eventually reaching the coast of North America around 1000 AD. The lands the Vikings had named Helluland, Markland, and Vinland are today believed to be Baffin Island, Labrador, and the Gulf of St. Lawrence.

In the Viking age the compass was not known, and navigation relied on the observation of the positions of the sun, moon, and stars. Therefore, clear weather for at least part of the day was required for the reliable determination of the ship's position. In the far North, however, clear weather is rather uncommon, making celestial navigation all but impossible. Then how did the Vikings manage to cross vast expanses of the Atlantic and North Sea and safely return home? For many centuries, it remained a mystery.

It is known from the Nordic sagas that the Vikings used a "magic sunstone" (Icelandic: "sólarstein"), which showed them the position of the sun even in the most foul weather, thus enabling safe navigation over great distances. In the late 11th century Viking power (and seafaring) began to wane, and after the invention of the compass around 1300 the sunstone fell out of use and its "magic" was forgotten. The sunstone was actually Icelandic spar, a transparent single crystal of calcium carbonate, and its "magic" a phenomenon today known as birefringence.[93] When held in an appropriate orientation, a birefringent crystal be used to locate the source of light rays (i.e. the sun) even when it is obscured by clouds or fog. How this was done remained a mystery, which was solved only recently.[94]

The scientific study of birefringence started centuries after the sunstone and its "magic" had been forgotten, although the first person to describe the phenonenon was actually of Viking descent. While studying a crystal of Icelandic spar, the Danish physician Rasmus Bartholin (Erasmus Bartholinus) noticed with astonishment that a double image is seen when one looks through the crystal.[95] The curious phenomenon was named double refraction (or birefringence) and was explained only some 130 years later. The wave nature of light was confirmed by Thomas Young's diffraction experiment; in 1803 he wrote the treatise *Experiments and Calculations Relative to Physical Optics*[96] in which he also gave an early explanation of birefringence.

On a late afternoon in Paris in 1808 Étienne-Louis Malus was gazing through a crystal of Icelandic spar at light reflected from glass windows of the Palais Luxembourg and was perplexed: instead of seeing two equally bright images, he observed that one image was much brighter. Apparently, something happened with the light upon reflection. Malus gave a tentative explanation which was in accord with the wave theory of light: the reflected light was plane-polarized.[97] He soon devised the first polarizers and polariscopes which were based on the reflection of an (unpolarized) light beam at a certain angle (later known as Brewster's angle). Experimenting with polarized light soon became fashionable, and new discoveries followed, particularly in studies conducted by two of Malus' compatriots: François Jean Dominique Arago and Jean-Baptiste Biot.[98] The former first observed a color change when a plane-polarized beam passed through a crystal of quartz (1811); the latter observed optical rotation (i.e. optical activity) of quartz crystals (1812) and some organic substances (e.g. turpentine oil, citrus and laurel extracts, solutions of camphor, sugar, etc.; about 1815).[96] Furthermore, he noted that organic compounds retain their optical activity regardless of the state of aggregation; that is, sugar is dextrorotatory both in crystals and in solution. Molten quartz, however, is optically inactive. Biot concluded that the optical rotation of organic compounds is a molecular property, while optical rotation of quartz is a property of the crystals—a result of the packing of the molecules.[99,100] Moreover, he also stated that the cause of optical activity is asymmetry. Therefore, organic molecules are asymmetric, while quartz crystals are asymmetric arrangements of symmetric molecules.[101] A few years later Sir John William Herschel noted hemihedral faces on quartz crystals: There are two types of crystals, with either left- or right-handed hemihedral faces, and they are mirror images (i.e. enantiomorphic). Herschel also correlated the sense of optical rotation with hemihedry: left-handed crystals are levorotatory and right-handed ones are dextrorotatory. One of the first structure–property relationships, proposed by Biot, was confirmed.

A compact and robust polarizer, the Nicol prism (a device consisting of a diagonally split and rejoined single crystal of Icelandic spar and making use of its birefringent properties), coincided with the advent of routine polarimetry in the 1830s. It was also the beginning of a new branch of science, crystal optics, which was pioneered by Arago, Biot, and Sir David Brewster in the first half of the 19th century. The observation of crystals under polarized light offered a first glimpse into the internal structure of crystals, and remained the only method capable of doing so until the discovery of X-ray diffraction.[102,103]

An Unlikely Gift from Dionysus: Stereochemistry

> “In vino veritas
> In wine [there is the] truth”
> Gaius Plinius Secundus, (Pliny the Elder), *Naturalis Historia*, ca. 79.

The Ancient Greeks believed that the god Dionysus descended from Mount Olympus to teach them the art of making wine. According to modern archaeology, he might have descended to Asia Minor (present-day eastern Turkey) some 7000 years ago. Together with wine he gave mankind another valuable but long-unrecognized gift, the long-ignored substance known as tartar (potassium hydrogen tartrate), which is found in old wine barrels and amphorae (Figure 6). Lucretius[13] and Pliny the Elder[15] were familiar with tartar: it had a sour taste and burned with a purple flame, and in their time was used for the preparation of a dozen remedies.[15] It was more closely studied during the Middle Ages. The Persian alchemist Abu Mūsā Jābir ibn Hayyān (known in Europe by his latinized name Geber) first realized, about 800 AD, that tartar is a salt and isolated free tartaric acid (albeit in a relatively impure form).[104] Pure tartaric acid (and quite a number of other organic acids) was isolated by Carl Wilhelm Scheele in the 1770s.[99,100] The compound was sought after as an ingredient of many cosmetics and remedies (e.g. Rochelle salt and tartar emetic), so many wineries soon turned into tartaric acid factories.

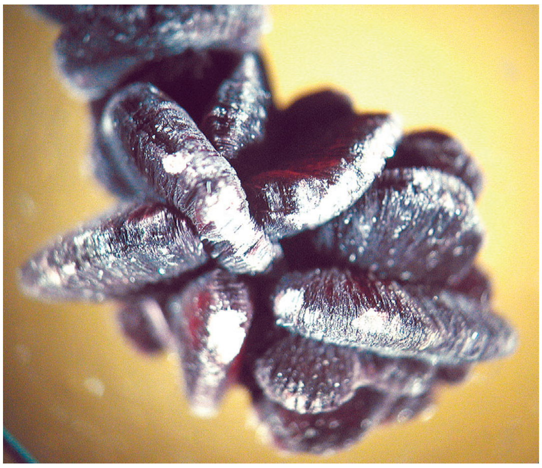

Figure 6. Crystals of tartar found in a bottle of Macedonian red wine (*T’ga za jug*, vintage 2003). The sample is colored wine-red by tannins present in the beverage; pure tartar is colorless. The mussel-shaped aggregates consist of tiny platelike single crystals of potassium hydrogen tartrate, as confirmed by single-crystal X-ray diffraction (by K.M.). The sample was provided by Kristijan A. Kovač.

Around 1818 Paul Kestner, a tartar manufacturer from Thann (France) noticed that besides tartaric acid, a small quantity of another substance crystallized in his barrels. At first he thought it was oxalic acid; however, soon he realized it was something novel and produced larger amounts of the substance by boiling a saturated solution of tartaric acid. In 1826 he gave a sample to Gay-Lussac, who determined its formula to be $C_4H_6O_6$, the same as tartaric acid. He named the novel compound racemic acid (from Latin *racemus* = a bunch of grapes).[105]

Chemical differences between tartaric and racemic acid (and also between their salts, tartrates and racemates) were slight, and puzzled the contemporary chemists. This was one of several examples of isomeric compounds known at the time; many of salts of the two similar acids were isomorphous. Also, the compounds were cheap and easily obtainable (in the early 19th century the chemical industry was only in its infancy and few chemically pure compounds could be purchased), salts were easy to prepare, and large crystals were easy to grow. Therefore, it was a perfect system for the study of two novel, little understood, and possibly connected phenomena: isomerism and isomorphism. In the 1830s Biot measured the optical activity of tartaric acid and its salts (they are dextrorotatory); racemic acid and its salts were optically inactive. Seeking the root of the difference between the isomers, Berzelius prompted Mitscherlich to study the crystal symmetry of tartrates and racemates.[99]

Crystals of tartaric acid and its salts turned out to be hemihedral and optically dextrorotatory; racemic acid and its salts were found to be optically inactive and their crystals holohedral. Two salts, however, did not conform: sodium ammonium tartrate and sodium ammonium racemate formed identical crystals and apparently differed only in their optical activity. Mitscherlich was confused and hesitated to publish his work for a whole decade. Eventually, he was overtaken by Frédéric Hervé de la Provostaye who published a similar study in 1841.

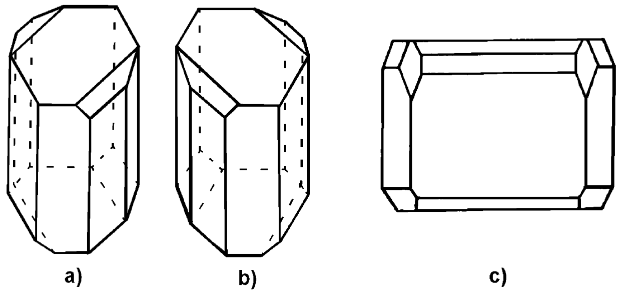

Figure 7. Crystals of a) dextrorotatory sodium ammonium tartrate, b) levorotatory sodium ammonium tartrate, and c) optically inactive sodium ammonium racemate. While (a) and (b) are hemihedral and enantiomorphic to each other, (c) is holohedral.

The tartrate/racemate quandary intrigued Louis Pasteur,[106,107] at the time a student of Biot. He carefully repeated the experiments[108] and was soon delighted to find hemihedral faces on crystals of sodium ammonium tartrate, a detail missed by both Mitscherlich and de la Provostaye (Figure 7 a). However, crystals of sodium ammonium racemate were also hemihedral; the bulk sample was actually a mixture of crystals with "left" and "right" hemihedral faces (Figure 7 a,b). Pasteur separated the "left" and "right" crystals using a magnifying glass and tweezers; a solution of the "left" crystals was levorotatory and a solution of the "right" ones was dextrorotatory! Dissolving equal masses of "left" and "right" crystals produced an optically inactive solution. Pasteur then isolated the free acids from both the "right" and "left" salts: the former was identical to tartaric acid, while the latter displayed an opposite sense of optical rotation. Their crystals also had "left" and "right" hemihedral faces.

Using these data, the 25-year-old Pasteur made the following conclusions:[109,110]

1) Racemic acid is not a pure compound, but a mixture of equal amounts of "left" and "right" tartaric acid which differ only in the sense of optical rotation. The optical rotation of the two compounds is therefore cancelled out, and racemic acid appears to be optically inactive.
2) The optical activity of organic compounds, their solutions, and liquids is a result of a lack of symmetry (i.e. dissymmetry) of the molecules.[111]
3) The optical activity of crystals whose solutions (or melts) are optically inactive, for example, quartz and sodium chlorate, is a result of the dissymmetric packing of non-dissymmetric molecules.
4) Just like their crystals, molecules of "left" and "right" tartaric acid are mirror images (i.e. enantiomers).

Urged by the aged Biot, Pasteur presented his discovery before the French *Académie des sciences* in 1848.[110] In the following years he continued studies of crystal and molecular asymmetry on many compounds, including optically active and racemic malates and aspartates.[107] In 1853, he prepared the third, optically inactive, isomer of tartaric acid, today known as *meso*-tartaric acid.

Pasteur's discovery of molecular chirality[113] added the third dimension to chemistry; this was the beginning of stereochemistry.[99,113,114] In the following decades, the concept of a molecule grew from a formula (1D) into a graph (2D), and finally, at the close of 19th century, into a 3D object. The tetrahedral model of the carbon atom proposed by van't Hoff[115,116] and Le Bel[117,118] in 1874; Werner's model of octahedral coordination compounds (1893);[119] and Emil Fischer's monumental work on the stereochemistry of sugar[120,121] and molecular projections[122] (1890s) all stem from Pasteur's crystallographic work. The spontaneous resolution (first noticed by Pasteur for sodium ammonium racemate) into the left and right enantiomers upon crystallization was, and still is, the basis for separating enantiomers in the laboratory and in the chemical and pharmaceutical industry.[100,114]

It is perhaps worth noting that the discovery of molecular chirality was purely serendipitous; Pasteur's original intention was to study isomorphism and tartrates/racemates were merely a convenient system.[106] While it can be argued that Pasteur was simply lucky,[99,113,114] it was his keen eye for detail (i.e. talent for nitpicking) and open-mindedness which led to the discovery that had eluded such accomplished scientists as Mitscherlich and de la Provostaye. Or, as Pasteur himself put it, "chance favors a prepared mind".[123]

However, the special role of tartar in the development of stereochemistry did not end with the 19th century. While Fischer's designation of relative configurations was arbitrary and intended as a bookkeeping device only, the anomalous dispersion of X-rays permitted the experimental determination of absolute configurations, which was pioneered in the 1940s by J. M. Bijvoet.[124] The first compound whose absolute configuration was determined was, no surprise, rubidium sodium tartrate.[125] The divine nature of tartar (indeed a gift from Dionysus) was proven once again in the age of X-ray diffraction.

Dead or Alive? A Trip into Metaphysics

> “*Der Kristall ist ein chemischer Friedhof.*
> *A crystal is a chemical cemetery.*”
> Leopold Ružička

This unfortunate remark[126] gained the 1939 Nobel Laureate L. Ružička a certain level of notoriety, at least among crystallographers. As often stated, these words reflect a typical mid-20th century chemist's opinion and, unfortunately, this view still persists among many present-day synthetic chemists. However, one just can't ignore the similarities between a crystal and a cemetery (Figure 8): the regular, periodic, and (mostly) static array of tombstones is indeed reminiscent of a 2D crystal. A trained crystallographer would easily recognize symmetry elements and "lattice planes", and may even be tempted to use Miller indices to locate a particular grave.

However, crystals were not always considered as "dead". Lucretius proposed a correct, albeit sketchy, mechanism of crystal growth: the bodies grow as many atoms are attached to them, and shrink when many atoms are detached (although he never explicitly mentioned crystals!).[127] This is probably the first description of a chemical equilibrium, a concept devel-

Figure 8. The regular array of tombstones in Memorial Cemetery in Ružička's hometown, Vukovar, Croatia.[138]

oped in the second half of the 19th century and intimatly connected with precipitation/crystallization. Unfortunately, Lucretius' work was forgotten for many centuries, and later philosophers developed more esoteric ideas.

The medieval theologian John Duns Scotus, known as *Doctor Subtilis*, believed that crystals are alive. Similarly to plants, crystals grow, and "die" when dissolved or melted. This view persisted for centuries and is still reflected in Linneaus' *Systema Naturae*.[22] However, discoveries in chemistry, physics, and geology in the 18th and 19th centuries dissmissed the notion of "living" crystals.[128] Instead, a static picture emerged of regularly placed atoms, not unlike a cemetery,[129] and the Age of X-rays only confirmed this. However, modern cutting-edge research in solid-state chemistry and physics challenges this view: today crystals are designed for many special purposes. Materials science is concerned with the design of crystals with exceptional electrical[130] or magnetic properties[131] (so-called functional materials), which often involve reversible phase transitions;[132] solid-state phase transitions are a sub-field of research on their own and include study of reaction mechanism;[133] many dynamic phenomena such as proton transfer,[134] electron transfer,[135] and magnetic exchange interactions[136] are most conveniently studied in crystals; there are many chemical reactions that take place in single crystals, some of them reversible; finally, template-directed solid-state synthesis takes place in specifically designed crystals.[137]

There is no unequivocal definition of life; we can only describe it. An object is considered "alive" if it exibits all or most of the following phenomena: homeostasis (which reminds us of Le Chatelier's principle), organization (living organisms consist of cells; both crystals and viruses have *unit* cells), metabolism (not found in crystals and viruses), growth (depends on definition; crystals *do* grow), adaptation (none observed among crystals), response to stimuli (do piezoelectricity and pyroelectricity count?), reproduction (just think of crystal seeds and "crystalloclasts"). Therefore the boundary between living and inanimate worlds is rather arbitrary.

While we firmly stick to the opinion that crystals are inanimate objects,[139] we believe that they are also dynamic entities and instrument-based methods that provide only a "static" picture are insufficient for their in-depth study. If crystals are to be understood as "chemical cemeteries", the study of their dynamics would be akin to "chemical necromancy".

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[3] W. L. Bragg, *Nature* **1912**, *90*, 410.
[4] a) D. Schwarzenbach, *Acta Crystallogr. Sect. A* **2012**, *68*, 57–67; b) S. W. Wilkins, *Acta Crystallogr. Sect. A* **2013**, *69*, 1–4; c) W. A. Hendrickson, *Acta Crystallogr. Sect. A* **2013**, *69*, 51–59; d) J. M. Thomas, *Angew. Chem.* **2012**, *124*, 13120–13132; *Angew. Chem. Int. Ed.* **2012**, *51*, 12946–12958.
[5] a) H. Kubbinga, *Acta Crystallogr. Sect. A* **2012**, *68*, 2–29; b) J. N. Lalena, *Crystallogr. Rev.* **2006**, *12*, 125–180; c) J. Lima-de-Faria, *Historical Atlas of Crystallography*, International Union of Crystallography and Kluwer Academic Publishers, Dordrecht, London, **1990**.
[6] P. Groth, *An Introduction to Chemical Crystallography*, Wiley, New York, **1906**.
[7] W. C. Pei, *Bull. Geol. Soc. China* **1932**, *11*, 109–146.
[8] F. D'Errico, C. Gaillard, V. N. Misra, *Collection of non-utilitarian objects by Homo erectus in India. In Hominidae. Proceedings of the 2nd International Congress of Human Paleontology* (Ed.: Giacomo Giacobini), Editoriale Jaca Book, Milan, **1989**, pp. 237–239.
[9] For example, a total of 23 minerals (including subvarieties such as beryl and emerald) are mentioned in the Bible (Exodus 28:17–20; Exodus 39:10–13, Ezekiel 28:13, Tobit 13:16–17).
[10] H. G. Liddel, R. Scott, *A Greek-English Lexicon*, Clarendon, Oxford, UK, **1940**.
[11] Such as: "Solibus indomitum glacies Alpina rigorem/sumebat nimio iam pretiosa gelu/nec potuit toto mentiri corpore gemmam,/sed medio mansit proditor orbe latex./auctus honor; liquidi crescunt miracula saxi,/et conservatae plus meruistis aquae." ; from a collection of poems by Claudianus at http://penelope.uchicago.edu/Thayer/E/Roman/Texts/Claudian/Carmina_Minora*/home.html.
[12] Unfortunately, ancient philosophers were for the most part content with reporting and re-reporting stories that were told and known by everybody, rather than ever bothering to look whether there was really some truth in them. The water droplet in crystal is an example of this, but it was hardly the only one. Pliny reports of mountains of magnets upon which one with iron nails in his boots gets stuck, but also of mountains of reverse magnets that repel iron and on which the same one can never step. Also he mentions that a magnet loses its power if rubbed with garlic. This "fact" was generally believed until the end of the 16th century when William Gilbert disproved it by actually trying it and seeing that garlic has no effect on magnets; see G. Gilbertus, *De Magnete, Magneticisque Corporibvs et de Magnete Telure Physiologia Nova*, Petrus Short, London, **1600**. W. Gilbert, *De Magnete* (Engl. Transl.: P. Fleurty Mottelay), Dover Publications, New York, **1958**. More amusing examples of prescientific beliefs regarding the properties of crystals can be found in G. F. Kunz, *Curious Lore of Precious Stones*, Halcyon House, New York, **1913**.
[13] T. Lucretius Carus, *De rerum natura*, manuscript, ca. 54 BC. An English translation is available free of charge at http://www.perseus.tufts.edu/hopper/text?doc=Perseus%3atext%3a1999.02.0131.
[14] A. L. Mackay, *Symmetry* **1990**, *1*, 3–17.

[15] G. Plinius Secundus, *Naturalis historia*, manuscript, ca. 77 AD, Pliny the Elder, *The Natural History* (English translation: J. Bostock), Taylor & Francis, London, **1855**; also available free of charge at http://www.perseus.tufts.edu/hopper/text?doc=Plin.+Nat.+toc&redirect=true. Rocks, minerals, and precious stones are discussed in the last two books.

[16] J. F. Healy, *Pliny the Elder on Science and Technology*, Oxford University Press, Oxford, **1999**.

[17] V. Biringuccio, *De La Pirotechnia Libri X*, Venetiis, **1540**. V. Biringuccio, *The Pirotechnia* (English translation: C. S. Smith, M. T. Gnudi), Dover Publications, New York, **1942**.

[18] G. Agricola, *De Re Metallica Libri XVII.*, Basileae, **1556**. G. Agricola, *De Re Metallica* (English translation: H. C. Hoover, L. H. Hoover), Dover Publications, New York, **1950**.

[19] Georg Bauer published most of his work under the latinized name *Georgius Agricola* (Latin *Agricola* = German *Bauer* = peasant, farmer).

[20] He reports, for example, that ruby neutralizes poisons and purifies "air that is corrupted by pestilant vapour", diamonds become brittle if wetted by the blood of a (male) goat, emeralds are found in griffins' nests and prevent epilepsy, and that an emerald "worn during coitus breaks in many places".

[21] In the tenth edition of *Systema Naturae* Linaeus took it upon himself to systematize not only plants but also animals and minerals. He is often quoted to have said "Deus creavit, Linnaeus disposuit" (God created, Linnaeus organized); Brightwell, *A Life of Linnaeus*, John van Voorst, London, **1868**.

[22] C. Linnaei, *Systema Naturae per Regna Tria Naturae secundum Classes, Ordines, Genera, Species*, Editio Decima, Laurenti Salvii, Holmiae, **1758**.

[23] C. Gessner, *De rerum Fossilium, Lapidum et Gemmarum*, Zurich, **1564**.

[24] The decision was possibly prompted by the 1654–1655 plague epidemic which claimed the lives of over two hundred students from his school.

[25] H. Kermit, "The Life of Niels Stensen" in *K. Ascani, H. Kermit, G. Skytte, Niccolò Stenone (1638–1686): anatomista, geologo, vescovo*; atti del seminario organizzato da Universitetsbiblioteket i Tromsø e l'Accademia de Danimarca, "L'Erma" di Bretschneider, Rome, **2002**, pp. 17–22.

[26] N. Steno, *De solido intra solidum naturaliter contento Dissertationis Prodromus, sub signo Stellae*, Florence, **1669**.

[27] This was also the Stensen's last great contribution to science. Afterwards he studied theology, was ordained as a priest in 1675, and was made a bishop in 1677. After his death in 1686 he was venerated as a saint in Hildesheim. He was officially beatified by the Roman Catholic Church in 1988.

[28] It has been proposed that he may have traced the outline of the crystal on paper, see U. Burchard, *Mineral. Rec.* **1998**, *29*, 517–583.

[29] R. Hooke, *Micrographia: or some Physiological Descriptions of Minute Bodies Made by Magnifying Glasses*, J. Martyn and J. Allestry, London, **1665**.

[30] By means of a (disgusting) experiment Hooke also noticed that the crystals grown from urine are those of pure water "Tasting several cleer pieces of this *Ice*, I could not find any *Urinous* taste in them, but those few I tasted, seem'd as *insipid* as water.".

[31] The name of the instrument is derived from the Greek word γωνία (angle). Note that it is written with omega, rather than omicron, and the little typo (γονυ means knee) can have rather embarrassing connotations. In 1810 Wollaston wrote to an acquaintance, who apparently made the mistake, "you seem disposed to bend the knee and worship your little idol", and later naming his instrument "-ometer". For more unsavory details on this typo, see Ref. [28].

[32] E. H. Kraus, *Am. Mineral.* **1918**, *3*, 126–130.

[33] Vauquelin's original name was "glycinia" (also written "glucinia", and "glicinia") due to the sweet taste. Berylium metal was obtained from its oxide by F. Wöhler in 1828. K. A. Walsh, D. J. Kaczinski, "History of Beryllium" in K. A. Walsh, *Beryllium Chemistry and Processing*, ASM International, Materials Park, OH, **2009**, pp. 7–18.

[34] W. H. Wollaston, *Proc. R. Soc. London* **1809**, *1*, 337.

[35] H. D. Deas, *Centaurus* **1959**, *6*, 129–148.

[36] W. H. Wollaston, *Philos. Trans. R. Soc. London* **1809**, *99*, 253–258.

[37] In English literature the name фёдоров can often be found transliterated as Fedorov, due to the similarity of the "soft o" (ë) to the letter "e". The transliteration Fyodorov, employed here, provides a closer approximation to the original pronunciation.

[38] However, already in 1874 William Hallowes Miller improvized a similar instrument by mounting a small Wollaston-type goniometer onto a larger one.

[39] It may be argued that the demise of optical goniometer began with the discovery of X-ray diffraction. While the study of the crystal morphology lost its appeal (at least for chemists) and was supplanted by interest in the internal structure, that is, atomic arrangement in the crystal, the optical goniometer still remained in widespread use, although as an instrument of secondary importance. It was still used for preliminary examination. Measurements using X-ray cameras require the precise alignment of the crystal along its axes, and indexing of faces is necessary for analytical absorption correction. It was only after the advent of automatic, computer-controlled diffractometers in the 1970s that the optical goniometers fell out of use.

[40] Posidonius and Strabo, however, mention a certain Mochus the Phoenician who supposedly lived in 12th or 13th century BC as the founder of atomism. There is, however, no real evidence that this mysterious proto-philosopher ever existed.

[41] It is less known that atomism was also present in ancient Indian philosophy, see A. Berrydale Keath, *Indian Logic and Atomism*, Clarendon Press, Oxford, UK, **1921** and M. Gangopadhyaya, *Indian atomism: History and sources*, K. P. Bagchi, Calcutta, India, **1980**.

[42] "What seems to us the hardened and condensed/Must be of atoms among themselves more hooked,/Be held compacted deep within, as 'twere/By branch-like atoms—of which sort the chief/Are diamond stones, despisers of all blows,/And stalwart flint and strength of solid iron,/And brazen bars, which, budging hard in locks'/Do grate and scream." (translated by William Ellery Leonard).

[43] A. I. Kitaigorodskii, *Organicheyskaya kristallokhimiya*, Izdateljstvo Akademii Nauk SSSR-a, Moscow, **1955**; A. I. Kitaigorodskii, *Organic Chemical Crystallography*, Consultants Bureau, New York, **1961**.

[44] De la Scalla (latinized as Julius Caesar Scaliger) seems to have been quite infuriated by Cardano's work. In 1557 he published a vast (over 1000 pages long) book, *Exotericarum exercitationum liber XV. De Subtilitate, ad Hieronymum Cardanum* (The 15th book of exoteric exercises: On Subtlety, contrary to Girolamo [Hieronymus] Cardano), as a rebuttal of the entire Cardano's *De Subtilitate*.

[45] B. Kahr, *Cryst. Growth Des.* **2011**, *11*, 4–11.

[46] The correspondence lasted two years (1606–1608) from which period five letters survive—two by Harriot and three by Keppler: J. A. Lohne, *Internationales Kepler Symposium, Weid der Stadt; Germany, 1971*, Hildesheim, **1973**, pp. 187–215.

[47] R. Descartes, *Discours de La méthode pour bien conduire sa raison, et chercher la vérité dans les sciences*, Ian Maire, Leiden, **1637**.

[48] J. Kepler, *Strena, seu de Nive Sexangula*, apud Godefriedum Tambach, Frankfurt on Main, **1611**.

[49] An excellent account of early studies of snowflakes' shapes can be found in G. Hellmann, *Schneekrystalle: Beobachtungen und Studien*, Rudolf Mückenberger, Berlin, **1893**.

[50] O. Magnus, *Historia de gentibus septentrionalibus*, Rome, **1555**.

[51] Of course, from the modern point of view, Kepler's explanation for the shape of snowflakes was almost entirely wrong—neither are water molecules spheres, nor is the crystal structure of ice anything akin to close-packed.

[52] This was the famous Kepler conjecture which remained unproven until 1998 (the proof was published in 2005); T. C. Hales, *Ann. Math* **2005**, *162*, 1065 – 1185.

[53] Note that from his constructions of various shapes from spheres it follows that only certain angles are possible on crystals. Unfortunately, Hooke never mentioned this fact. Had he done so, the discovery of the law of constant angles would be attributed to him, as his *Micrographia* predates Stensen's *De solido* by four years.

[54] M. L. Frankenheim, ISI *Enzyklopadische Zeitung Oken* **1826**, *5*, 497 – 515.

[55] M. L. Frankenheim, ISI *Enzyklopadische Zeitung Oken* **1826**, *6*, 543 – 565.

[56] That is, 32 symmetry point groups. He did not use the term point group; however, as the mathematical definition of group was given by Galois in 1829, and was generally unknown until 1846.

[57] A. Bravais, *Etudes Crystallographiques*, Gauthier-Villars, imprimeur-libraire, Paris, **1866**.

[58] I. I. Shafranovskiy, *(Y)Evgraf Stepanovich Fyodorov*, Izdatelstvo Akademii Nauk, Moscow, **1963**.

[59] R. V. Galiulin, *Crystallogr. Rep.* **2003**, *48*, 899 – 913; R. V. Galiulin, *Kristallografiya* **2003**, *48*, 965 – 980.

[60] The concept of atoms was resuscitated by J. Dalton at the very beginning of the 19th century, but the existence of atoms and molecules was "officially" accepted only at the 1st International Congress of Chemists, in Karlsruhe, in 1860. However, many prominent chemists still loathed the theory and disputed existence of atoms until the end of 19th century.

[61] M. P. Shakolskaya, I. I. Shafranovskiy, *Rene Zhjust Gayui*, Izdatelstvo Nauka, Moscow, **1981**.

[62] He is usually referred to as Abbé Haüy, since he had been appointed as an honorary canon of Notre Dame. A further meaning of the word habit is the distinctive set of garments worn by members of a religious order.

[63] G. Cuvier, *Mémoires de L'Académie Royale des Sciences* **1829**, *8*, cxiii – clxxiii.

[64] R. J. Haüy, *Essai d'une théorie sur la structure des crystaux*, Gogué & Né de La Rochelle, Paris, **1784**.

[65] "Des Novateurs en Crystallographie, qu'on peut avec raison nommer Cristalloclastes (brise-cristaux), s'imaginet avior fait une grande découverte en nous annoçant qu'il *n'y a point de troncatures, que la Nature ne tronque piont, & c*." Preface to: J.-B. L. Romé de L'Isle, *Cristallographie, ou Description des formes propres a tous les corps du regne minéral, dans l'état de combinaison saline, pierreuse ou métallique*, Paris, **1783**, p. xxvii.

[66] W. Whewell, *Hystory of the Inductive Sciences, Vol. III.*, London, **1847**, pp. 215 – 252.

[67] This categorical view was somewhat ameliorated in the past decades due to the discovery of quasicrystals.

[68] P. Gassendi, *Syntagma philosophiae Epicuri*, Lyon, **1646**.

[69] Usually known simply as Déodat du Dolomieu, he is better known as the discoverer of dolomite, which was named after him.

[70] D. Dolomieu, *Sur la Philosophie Minéralogique et sur l'Espèce Minéralogique*, Bossange, Masson, and Besson, Paris, **1801**.

[71] D. Braga, F. Grepioni, L. Maini, M. Polito, *Struct. Bonding (Berlin)* **2009**, *132*, 25 – 50.

[72] E. Mitscherlich, *Ann. Chim. Phys.* **1821**, *18*, 350 – 450.

[73] S. I. Morrow, *J. Chem. Educ.* **1969**, *46*, 580 – 583.

[74] He thus discovered monoclinic sulfur (which crystallizes above 96 °C).

[75] R. Winderlich, *J. Chem. Educ.* **1948**, *25*, 500 – 505.

[76] All previous tabulations were erroneous: while the relative atomic weight of hydrogen was designated as 1, the weights of carbon and oxygen were calculated as 6 and 8, respectively. Therefore, the molecular formula of water was believed to be HO, rather than H_2O. It was Berzelius who corrected this.

[77] J. Wisniak, *Chem. Educ.* **2000**, *5*, 343 – 350.

[78] G. B. Kauffman, S. H. Chooljian, *Chem. Educ.* **2001**, *6*, 121 – 133.

[79] F. Wöhler, *Ann. Phys. Chem.* **1825**, *3*, 177 – 224.

[80] He was expelled from gymnasium (high school) after detonation of one of his fulminate samples, F. Kurzer, *J. Chem. Educ.* **2000**, *77*, 851 – 857.

[81] J. Liebig, *Ann. Chim. Phys.* **1824**, *25*, 285 – 311.

[82] The formulae of the isomeric cyanic acid and fulminic acid are today known to be HOCN and HCNO. Some time later, Wöhler and Liebig together prepared and described a third isomer, isocyanic acid, HNCO.

[83] G. B. Kauffman, R. D. Myers, *J. Chem. Educ.* **1975**, *52*, 777 – 781.

[84] F. Wöhler, *Ann. Phys. Chem.* **1828**, *88*, 253 – 256.

[85] P. S. Cohen, S. M. Cohen, *J. Chem. Educ.* **1996**, *73*, 883 – 886.

[86] S. Esteban, *J. Chem. Educ.* **2008**, *85*, 1201 – 1203.

[87] J. Liebig, F. Wöhler, *Ann. Phys.* **1830**, *20*, 394.

[88] F. Wöhler, J. Liebig, *Ann. Pharm.* **1832**, *3*, 249 – 282.

[89] W. Ostwald, *Z. Phys. Chem.* **1897**, *22*, 289 – 330.

[90] J. Thun, L. Seyfarth, J. Senker, J. E. Dinnebier, J. Breu, *Angew. Chem.* **2007**, *119*, 6851 – 6854; *Angew. Chem. Int. Ed.* **2007**, *46*, 6729 – 6731.

[91] B. N. Menschutkin, *J. Chem. Educ.* **1927**, *4*, 1079 – 1087.

[92] Lomonosov also stated that matter consists of atoms, which combine into molecules, at the time when the concept of the atom virtually didn't exist. Moreover, he explicitly used the terms "atom" and "molecule" in their modern sense. Among his other precocious theories, he stated the law of conservation of matter (nearly half a century before Lavoisier!), considered heat as atomic motion, and made significant contributions to physics, astronomy (he proposed that Venus has an atmosphere), geography, and Russian literature (he compiled the first Russian grammar). M. Muratov, *Lomonosov* (Croatian Transl.: S. Kranjčević), Matica Hrvatska, Zagreb, **1947**.

[93] More about Icelandic spar and its role in the history of science, see L. Kristjánsson, *Iceland spar and its influence on the development of science and technology in the period 1780 – 1930*, University of Iceland, Reykjavik, **2010** and L. Kristjánsson, *Hist. Geo. Space Sci.* **2012**, *3*, 117 – 126.

[94] G. Ropars, G. Gorre, A. Le Floch, J. Enoch, V. Lakshminarayanan, *Proc. R. Soc. London Ser. A* **2012**, *468*, 671 – 684.

[95] E. Bartholin, *Experimenta crystalli islandici disdiaclastici quibus mira & insolita refractio detegitur*, Copenhagen, Denmark, Daniel Paulli, **1669**, *Experiments with the double refracting Iceland crystal which led to the discovery of a marvelous and strange refraction* (English translation: W. Brandt), Westtown, Pa., **1959**.

[96] O. Krätz, E. Vaupel, *Angew. Chem.* **2007**, *119*, 24 – 51; *Angew. Chem. Int. Ed.* **2007**, *46*, 24 – 51.

[97] B. Kahr, K. Claborn, *ChemPhysChem* **2008**, *9*, 43 – 58.

[98] B. Kahr, O. Arteaga, *ChemPhysChem* **2012**, *13*, 79 – 88.

[99] E. L. Eliel, *Croat. Chem. Acta* **1996**, *69*, 519 – 533.

[100] H. A. M. Snelders, *J. Chem. Educ.* **1974**, *51*, 2 – 7.

[101] In today's language, "asymmetric" molecules are chiral, and "symmetric" means achiral. We are also quite aware that the

molecule SiO_2 does not exist in the solid or melt, therefore it *can't* be chiral.

[102] B. Kahr, J. M. McBride, *Angew. Chem.* **1992**, *104*, 1 – 28; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1 – 26.

[103] A. Shuktenberg, Y. O. Punin, B. Kahr, *Optically Anomalous Crystals*, Springer, Dordrecht, **2007**.

[104] It was a common practice among 13th century European alchemists to sign their texts as "Geber", to give their works more relevance. Many books by "Geber" are today believed to have been written in the 13th century (since Arabic or Greek originals cannot be found) by a collection of anonymous European authors, commonly known as "Pseudo Geber". Some of them were identified as Paul of Taranto and Rodogero Hispalensi ("Geber Hispanicus"). However, it appears that tartaric acid was discovered by the original Geber.

[105] This is one of the earliest examples of isomerism, and probably the first isomerization reaction which preceded the famous Wöhler's synthesis of urea.

[106] H. D. Flack, *Acta Crystallogr. Sect. A* **2009**, *65*, 371 – 389.

[107] R. G. Kostyanovsky, *Mendeleev Commun.* **2003**, 1 – 6.

[108] Y. Tobe, *Mendeleev Commun.* **2003**, 1 – 2.

[109] L. Pasteur, *Leçons de chimie profesées en 1860*, Société Chimique de Paris, Paris, **1860**. An English translation is available free of charge at http://web.lemoyne.edu/~giunta/pasteur60.html.

[110] L. Pasteur, *Ann. Chim. Phys.* **1848**, *24*, 442 – 459.

[111] The term "dissymmetry" should be distinguished from "asymmetry". While the latter implies the lack of any symmetry elements (other than identity), dissymmetric molecules may posses symmetry axes. Therefore both asymmetric and dissymmetric molecules are chiral; the latter may actually possess quite high symmetry (M. Farina, C. Morandi, *Tetrahedron* **1974**, *30*, 1819 – 1831). For further discussion on asymmetry and dissymmetry, see M. Hargittai, I. Hargittai, *Mendeleev Commun.* **2003**, 1 – 2.

[112] While Pasteur originally used the term "dissymmetric", Lord Kelvin proposed the modern term "chiral" in 1880s. More detailed definitions and descriptions of chirality can be found in: V. Prelog, *Chirality in Chemistry*, Nobel Lecture, December 12, 1975; L. D. Barron, *Space Sci. Rev.* **2008**, *135*, 187 – 201; J. Jonas, *New J. Chem.* **1997**, *21*, 1251 – 1253; "Molecular Chirality": K. Mislow, *Top. Stereochem.* **1999**, *22*, 1 – 82.

[113] G. Nagendrappa, *Resonance* **2007**, *12*, 38 – 48.

[114] Z. Derewenda, *Acta Crystallogr. Sect. A* **2008**, *64*, 246 – 258.

[115] J. H. Van't Hoff, *Arch. Neerl. Sci. Exactes Nat.* **1874**, *9*, 445 – 454.

[116] E. W. Meijer, *Angew. Chem.* **2001**, *113*, 3899 – 3905; *Angew. Chem. Int. Ed.* **2001**, *40*, 3783 – 3789.

[117] J. A. LeBel, *Bull. Soc. Chim.* **1874**, *22*, 337 – 347.

[118] R. G. Kostyanovsky, *Mendeleev Commun.* **2004**, *14*, 229 – 230.

[119] K.-H. Ernst, E. R. W. P. Wild, O. Blacque, H. Berke, *Angew. Chem.* **2011**, *123*, 10970 – 10977; *Angew. Chem. Int. Ed.* **2011**, *50*, 10780 – 10787.

[120] E. Fischer, *Syntheses in the purine and sugar group*, Nobel lecture, December 12, **1902**.

[121] H. Kunz, *Angew. Chem.* **2002**, *114*, 4619 – 4632; *Angew. Chem. Int. Ed.* **2002**, *41*, 4439 – 4451.

[122] R. Hoffmann, P. Laszlo, *Angew. Chem.* **1991**, *103*, 1 – 16; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1 – 16.

[123] "Dans les champs de L'observation le hasard ne favorise que les esprits préparés". Pasteur probably said this while giving a lecture at the University of Lille on December 7, 1854.

[124] a) J. M. Bijvoet, *Proc. Kon. Ned. Akad. Wet. B* **1949**, *52*, 313 – 314; b) J. M. Bijvoet, *Nature* **1954**, *173*, 888 – 891.

[125] The choice of rubidium sodium tartrate was not random. In the 1940s state-of-art X-ray crystallography required a relatively simple molecule (i.e. comprising few atoms) of known stereochemistry able to grow large single crystals. Since the determination of absolute configuration is based on anomalous dispersion, the presence of a heavy atom, rubidium, was required to obtain a measurable anomalous dispersion.

[126] J. D. Dunitz, V. Schomaker, K. N. Trueblood, *J. Phys. Chem.* **1988**, *92*, 856 – 867.

[127] For truly matter coheres not, crowds not tight,/Since we behold each thing to wane away,/And we observe how all flows on and off,/As 'twere, with age-old time, and from our eyes/How eld withdraws each object at the end,/Albeit the sum is seen to bide the same,/Unharmed, because these motes that leave each thing/Diminish what they part from, but endow/With increase those to which in turn they come,/Constraining these to wither in old age,/And those to flower at the prime (and yet/Biding not long among them). Thus the sum/Forever is replenished, and we live/As mortals by eternal give and take. (Translated by William Ellery Leonard).

[128] However, this view was not universal. Biologist Ernst Haeckel believed that crystals are alive and in the early 20th century wrote a book on the subject. See E. Haeckel, *Crystal Souls—Studies of Inorganic Life* (Engl. Transl:. A. Mackay), *Forma*, **1999**, *14*, 1 – 204.

[129] Or, more appropriate, a 3D version of a cemetery.

[130] a) V. Podzorov, *Nat. Mater.* **2010**, *9*, 616 – 617; b) C. Goh, M. D. McGehee, *The Bridge* **2005**, *35*, 33 – 39; c) J. J. Novoa, M. Deumal, J. Jornet-Somoza, *Chem. Soc. Rev.* **2011**, *40*, 3182 – 3212; d) J. S. Brooks, *Chem. Soc. Rev.* **2010**, *39*, 2667 – 2694.

[131] a) E. Coronado, P. Dey, *Chem. Rev.* **2004**, *104*, 5419 – 5448; b) E. Collet, M.-H. Lamee-Cailleau, M. Buron-Le Cointe, H. Cailleau, M. Wulff, T. Luty, S.-Y. Koshihara, M. Meyer, L. Toupet, P. Rabiller, S. Techert, *Science* **2003**, *300b*, 612 – 615.

[132] a) R. G. Hicks, *Nat. Chem.* **2011**, *3*, 189 – 191; b) J. S. Miller, *Chem. Soc. Rev.* **2011**, *40*, 3266 – 3296.

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[138] The Vukovar Memorial commemorates the victims of the Battle of Vukovar in 1991, and could not have been the inspiration for Ružička's remark. Having died in 1976, Ružička did not survive to witness the devastation of his hometown after the demise of Yugoslavia.

[139] Among others, for purely practical reasons: slicing, grinding, and irradiating living creatures is considered cruel and atrocious.