In another moment, Alice was through the glass, and had jumped lightly down into the Looking-glass room.... Then she began looking about, and noticed that what could be seen from the old room was quite common and uninteresting, but that all the rest was as different as possible.... How would you like to live in Looking-glass House, Kitty? I wonder if they'd give you milk in there? Perhaps Looking-glass milk isn't good to drink...¹.

Let's start first, like the debaters in ancient times, with the definition of the word chirality. The term comes from the Greek, where χειρ/χέρι (cheir/chéri) means hand. Chirality² is a geometric property (asymmetry of spatial distribution) of a solid object (or spatial arrangement of objects, points, or atoms), which consists in the impossibility of overlapping (identification) with its own mirror image¹; such an object has no elements of symmetry of the second kind (mirror plane, σ = S₁, center of symmetry, i = S₂, rotational-reflection axis, S₂n). However, it can have a rotational axis of symmetry Cₙ. A completely new phenomenon of stereoisomerism is the so-called acamptisomerism, where both isomers are connected by an inversion of the bond angle³. For simplicity in this article, we will use the common chemist's view of chemistry, knowing that both enantiomers of a chiral compound have all the same physicochemical properties except when we "look at or touch" them with something that is itself chiral. A chiral object and its mirror image are referred to as enantiomorphs, in the case of molecules they are called enantiomers.

Fig. 1. Chirality of objects

² Two notations are used in the text to describe symmetric objects. The Hermann-Mauguin notation is preferred in crystallography, while spectroscopy prefers the Schoenflies notation. Thus, for example, the center of symmetry is i (in S), or −1 (in H-M), the mirror plane is σ (in S) and m (in H-M), etc.
For the sake of completeness, we will digress a bit. A little more complicated is the problem of chirality in the crystalline phase, i.e. three-dimensional chirality (but all chirality is three-dimensional). Although the number of possible crystal structures seems to be unlimited, their symmetric arrangement is described by only 230 space groups. Simply put: a space group is the set of all symmetry operations that can be performed on a given crystal structure. When a chiral substance crystallizes in the form of a pure enantiomer, then its crystal structure is called absolute. The absolute structure of the enantiomer belongs to one of the chiral (or Sohncke) groups, of which there are only 65 (tab. 1). Chiral groups are a subset of the 230 groups that obey the symmetry restrictions on chirality, see above.

However, nature "enjoys" certain symmetries, including the fact that there are more right-handed people than left-handed people in the human population. Therefore, not all of these 230 or 65 groups are equally represented. Very often we find monoclinic, triclinic, and orthorhombic groups: $P2_1/c$ (the most common of all 230), $P-1$, or $P2_12_12_1$, of which only $P2_12_12_1$ is chiral because it does not contain a center of symmetry. On the other hand, some spatial groups of higher symmetries (cubic, hexagonal) are only occasionally represented. The distribution of cubic and hexagonal groups in nature is only 1% (ref.3). The reasons for the uneven representation of symmetrical patterns in nature (asymmetry in symmetry) seem to lie in energy preferences.

The determination of the absolute structure of enantiomers, i.e. their exact arrangement in 3D space, is primarily made possible by single-crystal X-ray diffraction analysis, which provides the value of the so-called Flack parameter $x < 0.1$. If the value of $x$ is close to 0, then the found absolute structure is correctly determined, if $x$ is close to 1, then the absolute structure is incorrectly determined and it is necessary to multiply the coordinates of all atoms by $-1$, i.e. to invert the structure through the center of symmetry to the correct absolute configuration. If the value of $x$ is around 0.5, then it is probably a racemate or crystal twin. If an object is superimposable (completely superimposable, identical, E) with its mirror image, it is described as achiral. Objects that occur only in a series of one chiral form are referred to as homochiral (e.g., most natural amino acids, carbohydrates, or steroids).

Chirality, as a phenomenon, gained extraordinary importance especially after the Contergan (thalidomide) affair, when racemic 2-(2,6-dioxopiperidin-3-yl)-1H-isoinol-1,3(2H)-dione was administered to women in the 1950s, as a non-barbiturate hypnotic, to suppress morning sickness in pregnancy. Over time, it was discovered that while the $R$-enantiomer was an effective sedative and antiemetic, the $S$-enantiomer is teratogenic. The problem was that the teratogenicity was kept secret for a long time, resulting in the birth of (probably) tens of thousands of deformed babies. It was later proved that the $R$-enantiomer racemizes in the body, and therefore it is not possible to administer the pure $R$-enantiomer and also the racemate to...

Table I

<table>
<thead>
<tr>
<th>Crystal system</th>
<th>Hermann-Maugin notation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triclinic</td>
<td>P1</td>
</tr>
<tr>
<td>Monoclinic</td>
<td>P 121, P 121;1, C 121</td>
</tr>
<tr>
<td>Orthorhombic</td>
<td>P 222, P 222;1, P 2122, P 2121, C 2221, C 2 22, F 2 22, I 2 22, I 2 21 2 1</td>
</tr>
<tr>
<td>Tetragonal</td>
<td>P 4, P 41, P 42, P 43, I 4, I 4 1</td>
</tr>
<tr>
<td>Trigonal</td>
<td>P 3, P 31, P 32, R 3</td>
</tr>
<tr>
<td>Hexagonal</td>
<td>P 6, P 61, P 62, P 63</td>
</tr>
<tr>
<td>Cubic</td>
<td>P 23, F 23, I 23, P 213, I 2 3</td>
</tr>
</tbody>
</table>

Fig. 2. Chirality in nature
pregnant mothers, nor to women and men who do not use contraception6 (however, it is still used under strict conditions9, e.g., against some malignant tumors, inflammations, arthritis or leprosy10).

If the effect of an asymmetric external environment is not taken into account, both enantiomers that make up the racemic mixture should have the same energy, and therefore the formation of both, in any way, will have a 50:50 probability. How is it then possible that in nature, we find single enantiomers, even homochiral series of compounds, and even chiral groupings, such as crystals formed from achiral compounds? Such cases appear to be violations of the symmetry principle formulated by Neuman, Minigerod, and Curie11.

Considerations of where chirality came from on Earth lie somewhere between high physics and philosophy. For the first appearance of chirality, we seem to need nothing less than chirality itself. Chirality and its origin are also an interesting source of poetic philosophical-naturalistic debates between evolutionists and creationists12. To begin with, it should be noted that physics sees possible sources of true and false chirality in parity-breaking gravitational potentials13, the interpretation of which is somewhat beyond the scope of this paper14 since this property can be attributed to any object from elementary particles to galaxies15. If the broken parity in space is the root cause of the fact that, in the end, enantiomers do not have exactly the same energy in the real environment, the homochirality of some series of compounds on Earth may also be the origin of their extraterrestrial origin16. In this context, we can also see Mills' statement that the ratio of enantiomers in a racemate is never exactly 50:50 and that one enantiomer always slightly predominates17.

It is generally accepted that both enantiomers have the same energy, but this is only true for isolated objects (molecules). For crystalline phases and similarly, for solvated molecules (multiparticle systems), the question of energy equality is at least debatable, because "enantiomers" may show different reactivity during interactions with a chiral environment, but we are already departing from the properties of mere enantiomers and must take into account the formation of non-achiral supramolecules (clusters). However, there are also special systems – polar smectic phases of fractured liquid crystals, which are characterized by spontaneous deracemization and the formation of macroscopically chiral domains in a system that is composed entirely of achiral molecules18, as we discuss below.

Violation of (spatial) parity is a fundamental property of particle and atomic chirality that is used to deal with the complex phenomenon of asymmetry in the universe. However, at the molecular level, numerous experiments indicate that the energy differences associated with parity violation alone do not cause the strengthening and propagation of homochirality19. However, parity (and P-symmetry) is broken by weak interactions. Asymmetric transformations carried out under conditions far from equilibrium reveal the existence of nonlinear autocatalysis, which is stochastic in nature. In any case, and from a global perspective, chirality appears to be a unifying feature of our observable environment with evolutionary implications20.

"Spontaneous" deracemization (mirror symmetry breaking) is a challenging, multidisciplinary topic in current chirality research. In the absence of any chiral inducers, an achiral substance or racemic mixture can be transformed into an enantiomerically enriched or even homochiral state by selective energy input, e.g., chemical potential, irradiation, mechanical milling, ultrasonic waves, thermal gradients, etc. (ref.22). Let's take a closer look at some of the possibilities of such "deracemization", i.e., the transformation of a stable racemic state into an asymmetric non-racemic one. A transformation that has attracted the attention of natural scientists and philosophers for years because it is intrinsically related to life on Earth23 and is an important process in pharmacology, supramolecular chemistry, nanoscience, and other fields. Logically, deracemization processes must also be seen in the context of epimerization, when one epimer is transformed into another, because polarized radiation, keto-enol tautomerism, chiral catalysis, and enzymes (epimerases) are also involved. It is clear that spontaneous racemization is also related to the described phenomena24.

The chirality and helicity of substances, non-achiral supramolecules or crystals, can be influenced or even enhanced in many ways, for example by irradiation with different wavelengths of electromagnetic radiation or by circularly polarized radiation25,26, while the creation of polarized light can be seen through, among other things, selective absorption and scattering (light coming from the sky is partially polarized), reflection at the so-called "Brewster" angle, birefringence, sometimes combined with reflection, where the birefringence can be natural or induced by a strong electric field. As a historical reminiscence at the level of illumination, let us recall the practice of the Vikings, who, without knowing why, at
that time, searched for the position of the sun (source of polarized radiation) for navigation under cloudy skies using "sólsteinn", sunstone, a crystal of Icelandic birefringent calcite or limestone (polarization analyzer)\textsuperscript{27}. In the cosmic scenario, it is believed by some that the action of polarized quantum radiation in space, such as circularly polarized photons or spin-polarized particles, may have induced asymmetric conditions in primitive interstellar media, resulting in terrestrial biogenic homochirality\textsuperscript{28}. The application of ultrasound may also have similar effects in the formation of chiral complexes\textsuperscript{29}.

Weak electrical interactions differ from others in that they can distinguish the chirality of the particles involved\textsuperscript{30-31}. However, these forces alone are not sufficient for deracemization\textsuperscript{32}. It is useful to note that these general features can be illustrated considering the evolution of a chemical system that is initially far from equilibrium. Examples are systems breaking chiral symmetry and oscillatory systems where a stationary state can be seen when the change in entropy is minimal. Calculating the rate of entropy production per unit volume is then the easiest for homogeneous chemical systems where all elementary reaction steps are known\textsuperscript{33}. Polar interactions can result in chirality being affected by pH (ref.\textsuperscript{34}).

In autocatalytic reaction systems, where the presence of a small amount of (chiral) reaction product in enantiomeric excess can help generate a much larger enantiomeric excess of the resulting product (Soai reaction)\textsuperscript{35}. This reaction is a unique laboratory demonstration of absolute kinetically controlled asymmetric synthesis, i.e. the spontaneous formation (automultiplication) of an enantiomerically enriched product, even in the absence of any other chiral inducers or physical forces\textsuperscript{22}. A comparable possibility is the "inoculation" of the spontaneous crystallization of an achiral substance that forms chiral crystals with the first chiral crystal (from a supramolecular point of view, the first synthon), often multiplied by one-way mixing\textsuperscript{36}. In such events, which are actually self-assembly, phenomena such as filtering (correction) of errors, molecular recognition, and cooperativity apply because, if such an event occurs, it must be advantageous in terms of the energy (entropy) of the resulting product. All conceivable non-covalent interactions have a place here.

The formation of chiral crystals of an achiral substance is possible when the achiral substance itself forms a chiral crystal cell during crystallization\textsuperscript{37}. Examples of such enantiomorphic crystals are quartz, gypsum, olivine, clinopyroxenes, clinoamphiboles\textsuperscript{1}, or sodium chlorate, and organic compounds such as benzophenone, phenol, and many others. In nature, a chiral crystal can initiate both enantioselective crystallization and a chiral reaction, even in the solid phase\textsuperscript{38}.

A similar case is the formation of uniform chiral crystals starting from an almost racemic mixture of levorotatory and dextrorotatory crystals. Dissolution and recrystallization processes based on considerations of the solubility of small and larger crystals according to the Gibbs-Thomson rule (Stefan problem)\textsuperscript{39}, coupled with racemization in a stirred solution, lead this near-equilibrium system to uniform chirality in the solid phase\textsuperscript{40} (Ostwald ripening\textsuperscript{41-44}), explained either by looking at the mean field approximation (Lifshitz-Slyozov-Wagner (LSW) theory) or by the many-particle theory based on the solution of the diffusion equation in the quasi-static approximation\textsuperscript{45}.

A remarkable opinion can be seen in the so-called natural orbital chirality of the Earth, which is mainly caused by the right-handed rotation of the Earth around its axis of rotation (including precession) and the right-handed rotation of the Earth around the Sun, creating an effective rhythmic right-handed force field in space and time, which can lead, for example, to the primordial crystallization of the "seed" of one of the enantiomers\textsuperscript{46}. There are considerations that the mentioned field is not even necessary if there is a simple statistical fluctuation\textsuperscript{47}, even on a miniature scale, e.g. according to the model proposed by Frank\textsuperscript{48}. However, it has been shown that strong laminar rotational mixing is sufficient as the only source of chiral discrimination for the formation of homochiral supramolecular gels\textsuperscript{49}, as well as homochiral crystals, whether from solution or melt\textsuperscript{50}. Equilibrium systems are applied both during uniform mixing of the crystallizing mixture\textsuperscript{51} and during grinding (e.g., in a ball mill), during a process called Viedma ripening\textsuperscript{52}, when the product is completely deracemized. A necessary condition for successful deracemization is the ability of the given substance to exist in a racemic state in the form of a conglomerate, i.e. to form a racemic mixture of enantiomerically pure crystals. Only about 15 % of all known chiral compounds have this ability, including biologically important substances such as aspartic acid\textsuperscript{53}.

A process that can look like witchcraft is thus used, for example, in the production of pharmaceuticals\textsuperscript{54}.

Another way to separate enantiomers is to convert them into diastereomers, which already have different physicochemical properties. The formation of diastereomers does not have to be exclusively based on a covalent bond. For example, it can also be based only on solvation with a chiral solvent or environment (chiral chromatography), or co-crystallization with one enantiomer of a chiral substance, as already mentioned. The separation of enantiomers on chiral membranes is also related\textsuperscript{55}. Enantiomers can also be separated using enzymes or directly by cell cultures or organisms that selectively convert only one of the enantiomers\textsuperscript{56}, a process in which the dynamic formation of diastereomers from enantiomers is quite legitimately conceivable.

The quest to understand the origin of chirality in biological systems has sparked an intense search for nonlinear effects in catalysis and ways to enhance slight enantiomeric excesses in racemates to form optically pure molecules. The amplification of chirality in polymer
systems as a result of cooperative processes has been and continues to be studied intensively. A subtle interplay of noncovalent interactions such as hydrogen bonding, π-π stacking, and hydrophobic interactions have also been shown to be sufficient to observe chirality enhancement in small molecules. The so-called "matrix-assisted enhancement of chirality" is a phenomenon where, for example, using the above-mentioned π-π stacking enhanced by suitable properties of the environment, molecules that are either chiral or achiral are stacked on top of each other, but with a certain restriction of free mobility, so that they form chiral, e.g., helical formations. In the case of chiral entities, the "sergeant-and-soldiers" principle is even applied, where several sergeants can control the movements of a large number of cooperative soldiers so that even the few chiral or sterically rigid supramolecular components can control the supramolecular helicity of the resulting supramolecule because it is even energetically advantageous for the components to obey only one of the helices, which in the case of non-coordination of the "sergeants" can even alternate in the resulting aggregate. An example of such behavior can be the stacking of porphyrin units with chiral and structurally rigid substituents, which in solution after a certain time when measuring the chiroptical properties, reach another unchanged state, which shows a specific optical rotation of tens of thousands of units. Later it was found that the stacking of synths can be of type J or H, depending on the chirality of the substituent. Chiral aggregates were observed by electron microscopy, and calculations showed the advantage of one of the helices for a given aggregate.

The article hints at the complexity and breadth of the topic of chirality, chiral coordination, association, and interaction and does not claim to be an exhaustive overview. There are many more sophisticated attempts to initiate homochirality such as the application of plasma, optical rotation of tens of thousands of units and structurally rigid substituents, which in solution after a certain time when measuring the chiroptical properties, reach another unchanged state, which shows a specific optical rotation of tens of thousands of units. Later it was found that the stacking of synths can be of type J or H, depending on the chirality of the substituent. Chiral aggregates were observed by electron microscopy, and calculations showed the advantage of one of the helices for a given aggregate.

The article hints at the complexity and breadth of the topic of chirality, chiral coordination, association, and interaction and does not claim to be an exhaustive overview. There are many more sophisticated attempts to initiate homochirality such as the application of plasma, polarized particles, spins... (ref.) However, we have tried to point out fundamental questions and research results, the importance of which will probably only be appreciated by our children's children

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