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CHIRALITY IN NATURAL SCIENCES: AN APPROACH AT DIFFERENT SCALES

QUIRALIDAD EN LAS CIENCIAS NATURALES: UN ACERCAMIENTO A DISTINTAS ESCALAS

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Abstract

The terms right and left are applicable beyond everyday life and living beings. The fingers on the right hand are arranged in relation to the center of the hand, which is not identical or superimposable to that of the left hand. Both variants are symmetrical versions, but not identical. The spatial arrangement can be observed not only in objects, but also in trajectories. For example, in the bats' flight trajectories. In this article some examples of the chirality condition at different organization levels are defined and some of the recent advances on the subject are mentioned. Understanding the origin of chiral asymmetry found in particles, molecules, and macromolecules, allows us to infer current questions such as chemical evolution, the origin of life, and aspects related to evolution and the development of living beings, among others.

Keywords: Chirality, symmetry, enantiomers, optical activity, biomolecules.

Resumen

Los términos derecha e izquierda son aplicables más allá de la cotidianidad humana y los seres vivos. Los dedos de la mano derecha tienen una disposición respecto al centro de la mano, que no es idéntica o superponible a aquella de la mano izquierda. Ambas variantes son simétricas, pero no idénticas. El arreglo espacial puede observarse no solo en objetos, sino también en trayectorias. Por ejemplo, en las trayectorias del vuelo de los murciélagos. En el presente artículo se definen algunos ejemplos de la condición de quiralidad en distintos niveles de organización y se mencionan algunos de los recientes avances en el tema. Entender el origen de la asimetría quiral encontrada en partículas, moléculas, y macromoléculas, permite inferir preguntas vigentes como la evolución química, el origen de la vida, y aspectos relacionados con la evolución y el desarrollo de los seres vivos, entre otras.

Palabras clave: Quiralidad, simetría, enantiómeros, actividad óptica, biomoléculas.

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1 Introduction

Chirality is a little explored topic at different levels. Therefore, a content was devised to suit, condense and correctly reflect the information reported by science. The topics discussed below are little known in different communities, and it is believed that they can be useful to delve into this subject, especially because chirality is a complex and dynamic system in both science and art. This vision made it possible to analyze the phenomenon at different scales through the trajectory of other works, thus forming a historical and current study. Apparently, the existing information on chirality at different levels is scarce, hence it is important to have a better understanding of the subject.

2 Historical background

In 1815 Jean Baptiste Biot put polarized light into solutions of different organic compounds, noting their hand-style deflection, i.e., a leftward deflection and a rightward deflection, calling them 'optical activity'. Then, Louis Pasteur's experiments in 1848 with single crystals of tartaric acid (Figure 1) were decisive because a set of chiral crystals was held in his hand (Suh et al., 1997). In the 1950s the weak forces were found to be one of the main forces of our universe, bringing with it an answer that is also a question: this fundamental force also shows asymmetry, favoring interaction with left-handed particles (StackExchange, 2020). The possible origin of this behavior is that particles, molecules and everything in our reality behave like helices (which are almost synonymous of chirality) by arranging themselves in space in this way. Hence, a helix is the most reliable representation of chirality. This is not known, but the possible interaction of magnetic fields at the atomic level may be the answer. Shown below is a molecule of tartaric acid (Figure 1), a chemical compound used by Louis Pasteur and his wife Marie Laurent where chiral symmetry was first seen. This was the beginning of specular structural characterization in chemistry.

3 In Physics

In the entropy of the second law of thermodynamics, physics indicates that left and right are nearly equal in their properties, but cosmic rays offer data that may contradict the parity between left and right configurations in the universe. Cosmic rays are believed to originate from the Sun, stars or black holes (Kohler, 2020) and can ionize organic molecules causing chemical reactivity that are not always useful for living systems. When a particle is charged and spins around its own axis and around a nucleus, it produces a magnetic field. So, the magnetic field is a behavior due to the motion of a charged particle. If this motion stops, the magnetic field also vanishes. Maxwell's equations bring together the concepts of electricity and magnetism as two sides of the same coin (Beléndez, 2008). Talking about cosmic radiation is important because when this radiation interacts with some atoms, it forms muons and electrons that interact with molecules of a certain chirality, favoring their synthesis. It would explain the loss of parity in these molecules, although it does not explain why living systems do not respect this parity molecularly (Figure 2).

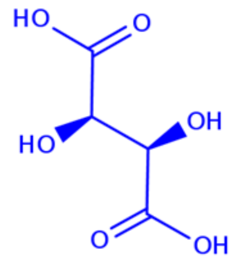

Figure 1. *L* Version with CAS number 87-69-4 and condensed structure $[CH(OH)COOH]_2$ of tartaric acid (C4H6O6 and molecular weight 150,088). D Version has a CAS number 147-71-7 and a condensed structure $HOC(O)CH(OH)CH(OH)CH(OH)C(O)OH$.

The second law of thermodynamics does not respect symmetry either, because it indicates that systems tend to stabilize or condition themselves to the characteristics of the medium which are the conditions of the universe where all reality exists. The ultimate end of everything is disorder and surrender to the conditions of our universe. Weak forces also tend to favor asymmetry. Historically, the polarization of light has been identified for centuries in many cultures. This phenomenon is called 'polarization', because when light passes through a single crystal of Iceland spar, which is calcite, a calcium carbonate generates two points or 'poles' (Craig and Thirunamachandran, 1999). Trilobites had eyes composed of this calcium carbonate (Farace and Aznar, 2011). A preferential coupling to one of the poles by an atom or a part of the molecule could be the answer (Craig and Thirunamachandran, 1999). This answer about the coupling of fundamental particles with radiations and the possible molecular selection in the same molecular evolution of the universe could bring answers, other couplings (Torres-Silva, 2008) and asymmetric molecular selection in the most complex phenomenon that our universe has seen: life. Wu's experiment where parity is violated by weak forces (Wu et al., 1957) is the equivalent to the one we belong to as chiral complex machines.

Figure 2. *Nyctinomops laticaudatus* bat colony in flight. The bats leave the caves in a helical, counterclockwise flight, resulting in a 'social convention' (Gardner, 1985). (Image by M. Zozaya Naturalist, under CC BY NC permission).

4 In biological systems

4.1 Microorganisms

Since approximately 3000 million years ago, prokaryotes have lived in bacterial biofilms (Nazar, 2007). This ability to form cooperative collectives serves an important survival strategy when bacteria are exposed to variable and adverse conditions (Finkelshtein et al., 2017); likewise, they present great advantages to protect against environmental perturbations, e.g., humidity, pH, and temperature (Nazar, 2007), and 1000- to 1500-fold resistance to antibiotics (Gohil et al., 2018).

When biofilms are formed, bacteria can use coordinated chemical signals to communicate with each other. This interrelationship works by means of messengers: small molecules that allow bacteria to sense the existing population and respond to different changing environmental conditions. This communication mechanism is called quorum sensing. Gram-negative bacteria use acyl-homoserine-lactone molecules, while in Gram-positive bacteria modified oligopeptides prevail (Nazar, 2007).

The formation of elaborate and convoluted colonies with chiral and/or fractal geometries can be seen in different species, such as *Bacillus subtilis*, which uses flagella (Ingham and Jacob, 2008) and *Paenibacillus vortex*, which also possesses advanced social motility employing chemotactic signaling. *P. vortex* forms swarms with thousands of bacteria with leading groups, called vortices, which cooperatively rotate, thus, the vortex expands in size and moves outward, leaving a trail and originating convoluted colonies with chiral or fractal shapes (Finkelshtein et al., 2017), although the biological basis of the formation is currently not well understood (Ingham and Jacob, 2008).

4.2 Macroorganisms

Chirality in biological systems is a quality typical to all of them. Chirality can be present not only in microscopic systems (since most molecules in living beings are chiral), but also macroscopically, such as in the case of butterfly wings (Figure 3) or the helical shells of different mollusks (Nieto-Ortega, 2014). The same happens in the case of climbing plants that wind in the form of helices on different types of plants, such as trees or shrubs, as well as on various materials such as stakes; the way of doing so is dextrorotatory (to the right), as in the case of the day dondiego, although there are also those that do so by means of a levorotatory twist (to the left), as is the case of the honeysuckle (Pérez Benítez and Arroyo Carmona, 2018). Citing the example of humans, which are structurally chiral, the liver is on the right and the heart on the left, thus showing functional chirality (Hegstrom and Kondepudi, 1990).

Although there is no reason to say that one mirror image is better than the other, there is some preference for one type of chirality over another (Hegstrom and Kondepudi, 1990). For example, an organism prefers functional chirality to use one of its limbs more than the other; an example of this would be that humans use one hand more than the other to perform various activities (Barrera-Calva et al., 2012).

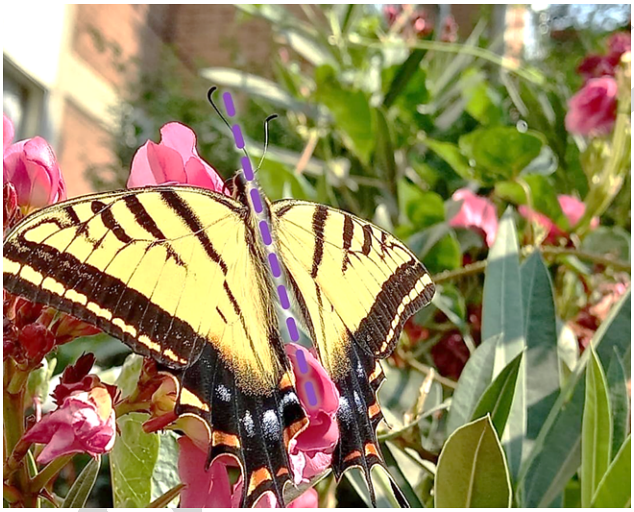

Figure 3. Butterfly 'Xochiquetzal Comet Butterfly'; the plane of bilateral symmetry is pointed out (Image by N. Pacheco-Coronel Naturalista, under CC BY NC permission). Chirality occurs when there are one or more chiral elements, i.e., a chiral axis, plane or center.

Many species use the right hemisphere of the brain to react quickly to new conditions; on the other hand, they use the left hemisphere to control responses that have other alternatives in response to them, thus categorizing their possibilities where ordinarily hemispheric functions have a functional complementarity participation (Barrera-Calva et al., 2012). In humans, the left hemisphere is the responsible of communicative vocalization (including the movement of the tongue, jaw, tongue and lip muscles). However, this is not exclusive to humans; crickets and birds have also been found to possess this chiral property (Barrera-Calva et al., 2012).

A classic example of chirality can be observed in Gastropods due to the direction in which they coil: dextral (clockwise or right-handed) and sinistral (left-handed) (Schilthuizen and Davison, 2005), also known as levorotatory. This chirality originates in early development (Vargas and Zardoya, 2015).

In the third division of larval development when the embryo grows from four to eight cells, mollusks undergo chiral segmentation, i.e., the larval planes are oriented obliquely to the polar axis of the oocyst. When the early division patterns and the direction in which they are oriented are defined, the consequent body asymmetries are determined, i.e., if the division is clockwise, it is a dextral organism; on the other hand, if the case is counterclockwise then the organism will be levorotatory or sinistral (Vargas and Zardoya, 2015).

In the internal anatomy, the internal organs differ in levorotatory and dextrorotatory, since the internal organs are reduced on the side towards which the turn occurs (Vargas and Zardoya, 2015). In certain species these body asymmetries can prevent copulation between the same species, because the genitalia are also inverted with respect to individuals with the opposite chirality (Schilthuizen and Davison, 2005). Therefore, organisms that have an opposite chirality to the majority of those living in a population will have problems finding mates (Schilthuizen and Davison, 2005).

Among organisms dominated by dextrorotatory chirality, levorotatory individuals seem to exist only as a result of mutations, with very low frequencies (from one in hundreds to one in thousands), although this may vary with the species, even in species where levorotatory and dextrorotatory individuals show a similar proportion, as in the case of the snail *Liguus poeyanus* (Hegstrom and Kondepudi, 1990).

Additionally, genes that are expressed exclusively on one side of the body and that determine some of the asymmetries of gastropods have been described. In a dexotrophic organism, the right side of the body of the organism would express chirality-dependent genes, which would be related to the formation of shell-producing cells, with a higher rate on the right side, or on the left side in the case of levorotrophs. If the asymmetric action of these genes is cancelled, completely symmetrical shells are obtained (Vargas and Zardoya, 2015). Genes that regulate the development of body asymmetries (levorotatory and dextrorotatory) also act in other deuterostomes and vertebrates, therefore, it would seem possible that this cascade of genes was present in a common ancestor of mollusks and deuterostomes, being this the one that established such body asymmetries (Vargas and Zardoya, 2015).

In the few species where chirality has been characterized, it is determined by a single genetic locus with delayed inheritance, meaning that the inheritance factor controlling orientation is maternal (Schilthuizen and Davison, 2005).

5 Cellular Structures

5.1 Membrane

Biological membranes are composed of a double layer or bilayer of lipids (generally phospholipids), the latter containing four sections: two fatty acid chains linked to a glycerol molecule and this in turn to a phosphate; at the other end of the phosphate, molecules such as choline, serine, inosine, ethanolamine, among others, can be found (Figure 4b). The structure of the membrane is a characteristic that continues to explain the diversity of living beings. In 1990, the microbiologists Otto Kandler and Mark Wheelis supported a classification system of living organisms into three domains (Archaea, Bacteria and Eukarya), using membrane composition as one of the main bases (Woese et al., 1990). Although Woese had already developed the use of sequences to classify living organisms, since the 1970s more context was needed to convince the community with his classification system. In the 1990 description, three features are considered to differentiate the domains: cell structure (prokaryote, eukaryote), fatty acid to glycerol binding type (ether, ester) and rRNA type (18S rRNA, 16S rRNA) (Woese et al., 1990).

Homochirality is not apparent in the membrane, but up close it is observed that glycerol presents two configurations: glycerol-1-phosphate (G1P) in Archaea and glycerol-3-phosphate (G3P) in Bacteria and Eukarya, where G1P is an enantiomer (levorotatory) of G3P (dextrorotatory) (Figure 4b). Both molecules are synthesized by dehydrogenases and even though they have equivalent function and localization due to their polarity and molecules bound by both ends, G1DPH and G3DPH dehydrogenases do not share an evolutionary history (Akanuma, 2019). With this background, a dilemma known as 'the lipid split' persisted, i.e., how and when did homochirality originate? In this regard, it is accepted that the origin was heterochiral (a mixture of G1P and G3P), i.e. the Last Universal Common Ancestor (LUCA) had a heterochiral membrane and it has recently been shown, thanks to molecular phylogenetics, that homochirality is modern (Figure 4a). This analysis with bacterial homologs of G1DPH and archaeal homologs of G3DPH concluded that the ancestor of Bacteria did not contain G1DPH, therefore, the G1P molecule in Archaea was selected after its origin and its origin was heterochiral as in LUCA (Akanuma, 2019; Lombard et al., 2012). The latter allows explaining the uniqueness of eukaryotes in presenting a membrane with 3PG when they originated by a process of endosymbiosis, where the archaeon (currently homochiral 1PG) acts as a host for a bacterium (13PG) if this archaeon had a heterochiral membrane.

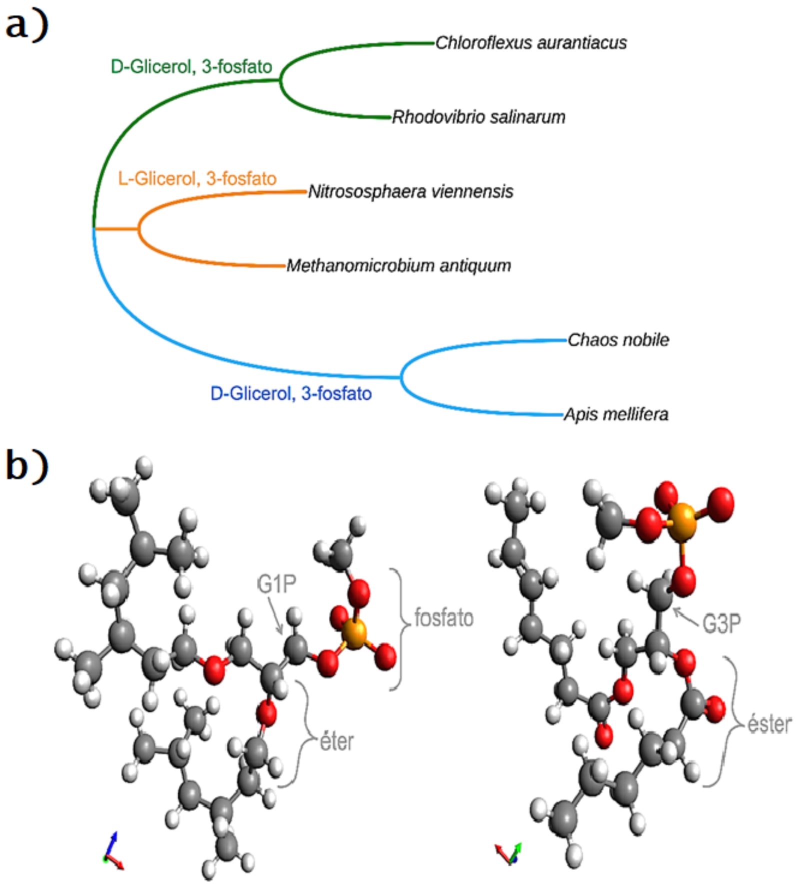

Figure 4. (a) Phylogeny performed with sequence alignment of the three domains (Bacteria in green, Archaea in orange and Eukarya in blue) performed with 2120 positions of the 16S rrna gene, the maximum likelihood method and the GTR evolutionary model in the MEGA X program (Kumar et al., 2018). Enantiomers in each domain are indicated. (b) Chemical structure of phospholipids, G1P (ether in Archaea) and G3P (ester in Bacteria, Eukarya) enantiomers are indicated.

5.2 Cell wall

Most prokaryotes of the Bacteria domain are around either of the two Gram types (positive or negative). In them the arrangement of the cover is quite different, but they coincide in containing a murein cell wall (from Latin *murus* 'wall'), chemically named peptidoglycan. The murein has two sections: several fibers of a polysaccharide alternating N-acetylglucosamine (NAG) with N-acetylmuramic acid (NAM) linked together by a peptide. Some of the amino acids are known as non-canonical because they are not in the list of the 20 universal amino acids in living beings (canonical), some examples are: L-ornithine, L-homoserine and L-hydroxylysine and others that stand out for being dextrorotatory, such as: D-isoglutamate, D-ornithine, D-alanine and D-serine (Vollmer et al., 2008). D-amino acids are also found in some molecules of peptidoglycan-integrated molecules, e.g., teichoic acid (from Greek τειχοζ, teïkhos, 'wall') How and why do these isomeric versions originate? It must be considered that these heterochiral peptides are not synthesized in the ribosome but by enzymes, among them transpeptidases, and the interconversion of L- and D- amino acids is effected by epimerases and racemases enzymes, which belong to the enzyme group of isomerases with the enzyme classification E.C. 5.x.x.x.x. Apparently, the lack of D-amino acids in murein and teichoic acids renders Gram-positive and Gram-negative organisms vulnerable to antimicrobials (Radkov and Moe, 2014).

5.3 Protein complexes

It is common for cells to have extracellular (pili and flagella) and intracellular (cytoskeleton and periplasmic flagella in spirochetes) filamentous structures, or biological particles such as viruses. Some of these fibrillar structures are organized in a helix, thus with an intrinsically chiral conformation. The structure, like the assembly of helical molecules, is the result of selection so homochirality is present in the cell, cell type, or an entire lineage (Satir, 2016). Structures linked to motility are clear examples of a helical polymer: the flagellum and cytoskeleton fibers. Even though the composition and structure of the flagellum are different among the three domains, the common denominator also contains helical fibers. The bacterial flagellum has been by far the most studied and is composed of a tandem flagellin protein attached to the cell body by a hook and ends in a basal body. A rotational feature in the basal body of the flagellum confers motility to the bacterium. Rotation of the flagellum in a basal or minimum energy condition occurs counterclockwise and is reversed as a result of signal transduction, e.g., chemical (toxicants, nutrients) or physical (photons, temperature).

Other helical fibrous structures are the proteins that constitute the cytoskeleton, being actin and tubulin the most widespread among living organisms. It was assumed that the microfilaments of the cytoskeleton were found only in complex cell types (eukaryotes), but proteins homologous to these two proteins have also been found in bacteria and archaea (e.g. MreB, Ftsz and Crenactin). Actin and tubulin are linked to motility, and in eukaryotes they are also related with cell division and motility. An example of the latter is spermatozoa: the microfilaments are helically packed and provide propulsion and allow a twisting motion that can change direction, facilitating crossing in the zona pellucida (Satir, 2016).

Likewise, in prokaryotes the twist of the helical protein MreB is conserved, which implies that the direction of twist of the helical protein is defined since cell division. Also, it has been found that the reference for this twist in MreB is the cell wall, which is opposite to the reticulum that forms the peptidoglycan. It is an opposition that has been found to be conserved even in phylogenetically distant lineages (e.g. phyla as distinct as Proteobacteria and Firmicutes) and is crucial for the fate of the cell shape during division (Wang et al., 2012), recalling that the wall provides cell support. This MreB-peptidoglycan arrangement does not carry over to eukaryotes, because the microfibril helices (actin as homolog of MreB) in eukaryotes are cytoplasmic and radial, without wrapping the bacillus or cocci on the inside (periplasm), as occurs in prokaryotes. The operon for MreB also encodes MreC and MreD, which spatially place MreB with peptidoglycan synthesis proteins (e.g. transglycosylases, transpeptidases) during cell elongation.

6 Macromolecules

6.1 The DNA

DNA (deoxyribonucleic acid) is the main molecule of life, and is the one that carries encoded genetic information typical of different living beings. This molecule is made up of a double strand with two strands composed of successive bonds of the sugar deoxyribose and phosphates (Martínez-Frías, 2010). In general, there are three main families of DNA helices (Figure 5): A-DNA, which can easily form only within certain purine stretches, B-DNA, which is favored by a mixture of sequences (although the exact conformation depends on the particular nucleotide sequence), and Z-DNA, which is favored by alternating purine-pyrimidine steps (Ussery, 2002).

Like proteins, DNA exists under a single chirality. Only the D enantiomer of the sugar is present in nucleic acids, i.e. ,the orientation of DNA and RNA is right-handed, so their most stable conformation is a right-handed helix (Globus and Blandford, 2020). This is extremely important, as living organisms are governed by this preference. However, the helix of the Z-DNA family has a left-handed orientation (Ussery, 2002), which implies that there are different conformations of the DNA helix and therefore different biological functions.

In terms of structural features, B-DNA has double strands running in opposite directions and an asymmetric structure with alternating major and minor grooves, the number of base pairs per helical turn is 10.5 and the width of its helix is ∼ 2nm. On the other hand, A-DNA is favored in many solutions that are relatively devoid of water. Unlike B-DNA, its helix is wider (∼ 2,3 nm), the number of base pairs per helical turn is 11 and the plane of the base pairs is tilted about 20° with respect to the helix axis (Lehninger et al., 2008).

The structure of Z-DNA changes radically in the first two, and the most obvious distinction will be a helical rotation to the left. The width of its helix is 1.8 nm, it has 12 base pairs per helical turn, and the structure appears thinner and more elongated, taking on a zigzag appearance. This form of Z-DNA is difficult to observe, as it is highly unstable (Lehninger et al., 2008).

Regarding biological functions, A-DNA plays an important role in transcription and Long Terminal Repeat (LTR) sequences such as the sequence found in human immunodeficiency virus (HIV). Short stretches of purines have been found to exist in genomes that probably form A-DNA conformations in much greater abundance than would be expected for mononucleotide composition, ranging from about a quarter of the genome in bacteria to almost half of the DNA in eukaryotes (Ussery, 2002). B-DNA is sequence-dependent, and rigid (or flexible) sequences can serve as sites for protein binding and the formation of specific complexes, whereas Z-DNA may play an important role as an enhancer in transcription and terminal differentiation. It can be found in prokaryotes, eukaryotes and viruses. In some eukaryote genomes, 10 % or more regions with the Z-DNA configuration may be present (Ussery, 2002). In living cells, most DNA is found in a mixture of A-DNA and B-DNA, with some small regions capable of forming Z-DNA (Ussery, 2002).

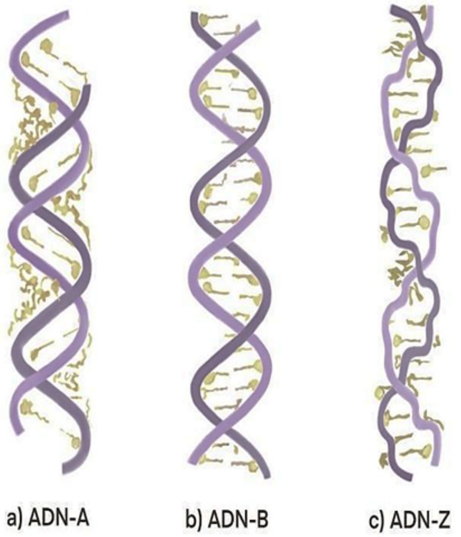

Figure 5. Different DNA helix configurations: (a) A-DNA, (b) B-DNA and (c) Z-DNA are presented with a longitudinal view.

6.2 The RNA

The importance of chirality in RNA lies in the fact that prebiotic chemistry was essentially racemic. The chiral element in RNA is a sugar that undergoes particularly rapid racemization under the warm, humid conditions in which prebiotic chemistry presumably took place (Sandars, 2005). Its replication is only successful if homochiral nucleotide monomers are used. In the presence of racemic monomers, replication is inhibited, thus homochirality preceded the RNA world by a pre-RNA world in which selection operated using some other type of genetic material without the chiral constraints of RNA (Bailey, 2000).

However, enantiomeric cross-inhibition by RNA stops the polymerization process, preventing the formation of long polymers. Thus, Sandars (2005) has shown that under certain circumstances enantiomeric cross-inhibition could be the driving force for a chiral bifurcation leading to homochiral polymers.

It should be noted that the polymer likes to adopt a helical shape for structural reasons in both cases (PNA and RNA). In the case of PNA, the choice of orientation is random or triggered by an external influence. In contrast, the RNA polymer is forced to adopt an orientation determined by that of the constituent monomers (Sandars, 2005).
. Although this may well not be the system that nature used, it represents one possible way in which homochirality could have evolved.

6.3 Chlorophylls and bacteriochlorophylls

Chlorophylls and bacteriochlorophylls are optically active molecules with several chiral centers, necessary for their natural biological function and the assembly of their supramolecular complexes (Senge et al., 2014). They are cyclic tetrapyrroles with a central Mg, a five-part isocyclic ring and a long-chain esterifying alcohol at C17 (Patty et al., 2017).

The central magnesium atoms of chlorophylls (Chls) and bacteriochlorophylls (BChls) are in most cases penta-coordinated, resulting in the formation of a new stereochemical center and the possibility of two different types of chlorophyll-ligand interaction (Senge et al., 2014).

Bacteriochlorophylls do not normally occur as 'isolated' pigments in monomeric and/or free form. In their functional state, they are often bound to apoprotein side chains. This is facilitated by axial ligands, which allow important interactions with the apoprotein environment, aiding the organization of chlorophyll proteins and modulating their electronic properties (Senge et al., 2014). Like most amino acids and proteins, any tetrapyrrole complex containing a protein, even achiral, becomes optically active.

7 Biomolecules

Life on Earth exists because biomolecules (sugars and amino acids) are mainly in their predominant homochiral form (Breslow, 2011). The two mirror images of a chiral molecule are called enantiomers. The enantiomers of amino acids and sugars are called L- or D- (Cava et al., 2011). Living beings have an exclusive affinity for L-amino acids in ribosomal protein synthesis, and for D-sugars (D-ribose) in nucleotides (Sasabe and Suzuki, 2018). If proteins with L-amino acids had random D- enantiomers, they would have variable conformations. However, this is not something that occurs in actual biology because specific enzymes produce the L-amino acids, and the same is true for sugars (Breslow, 2011).

7.1 Sugars

Sugars have a generic formula of $C_nH_{2n}O_n$. Most sugars are optically active because they have asymmetrically substituted carbons. The relative position of the first asymmetric carbon in the sugar chain determines whether the sugar is D- or L-. Sugars such as ribose and glucose have more than one chiral center and are classified based on the configuration of the chiral center farthest from the carbonyl group (Breslow, 2011).

L- enantiomers of sugars are known as rare sugars because they are not found very often in nature. However, these rare sugars have great potential in the food and pharmaceutical industries (Chen et al., 2020). For example, they are used as antiviral drugs for treating serious viral diseases, such as HIV or hepatitis (Helanto et al., 2009), and although L-sugars have not been found in biological processes, experiments have been done to determine whether some L-sugars contribute to total energy metabolism (Livesey and Brown, 1995).

7.2 Amino acids

Proteins are formed from 20 essential amino acids, which are α-amino acids. The general structure of an amino acid consists of a carboxyl group ($-COOH$) and an amino group ($-NH_2$) attached to the α carbon, which in turn is attached to a hydrogen ($-H$) and a side chain (R group) (Genchi, 2017). Amino acids generally have a single chiral center (Breslow, 2011), which is precisely the carbon (Figure 6). Enantiomers of amino acids are called L- or D- depending on the optical activity of the glyceraldehyde isomer on which the amino acid can be superimposed. Both enantiomers are produced by chemical synthesis, but most enzymes exhibit marked selectivity and, because of this, many biochemical processes use and produce particular enantiomers (Cava et al., 2011).

Although L-amino acids are the most common in living organisms, D-amino acids have been found to play a role in some biological processes, such as D-aspartate, which is an important regulator of adult neurogenesis, and D-serine which acts as a co-agonist of N-methyl D-aspartate-type glutamate receptors in the brain, and which are involved in learning, memory, and behavior in mammals. Also, D-amino acids are known to have been used as nutrients to support bacterial growth, regulate bacterial spore germination, and are components of the bacterial cell wall (Cava et al., 2011).

There are three theories to try to explain the presence of D-amino acids in the proteins of living beings. The first is that it may result from the direct incorporation of a D-amino acid into the peptide chain (produced, for example, by an amino acid racemase). The second is that it may be due to nonenzymatic racemization associated with aging or disease. And the third is that it may be due to a post-translational enzymatic modification (Genchi, 2017).

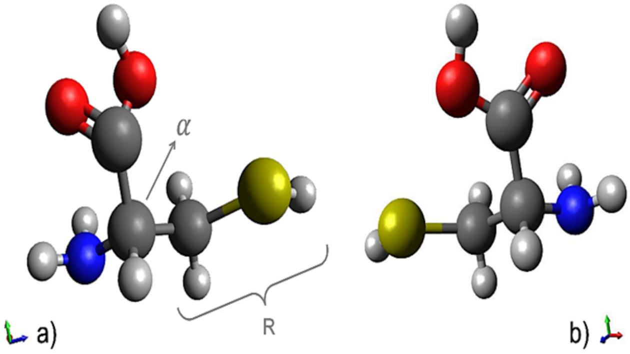

Figure 6. Cysteine amino acid in its enantiomeric versions (mirror images): dextrorotatory (a) and levorotatory (b).

7.2.1 Amino acid racemization

Racemization is a reversible first order reaction that can be described by Equation 1 (Bada, 1985).

$$\text{L-amino acid} \leftrightarrows \text{D-amino acid} \qquad (1)$$

It was more than a century ago when it was first observed that amino acids underwent racemization when heated in highly acidic and basic solutions. In the early 20th century, racemization of amino acids into peptides and proteins was first observed in alkaline solutions at elevated temperatures. Racemization can also occur at neutral pH and at rates that are comparable to those under acidic pH and in dilute bases. In addition, racemization is detected in proteins from both fossils and living organisms (e.g., mammals), so it has even been suggested that racemization could be the basis of a useful dating method for determining the age of organisms (Bada, 1985).

Amino acid racemases and D-amino acid oxidases (DAO) are the enzymes responsible for the synthesis and degradation of D-amino acids. As L-amino acids are the predominant amino acids in living organisms, they act as the substrate for the generation of D-amino acids and what racemases do is to change the stereochemistry of the chiral α-carbon in amino acids to convert L-amino acids into D-amino acids (Genchi, 2017).

7.2.2 Origin of homochirality in sugars and amino acids

Achiral compounds can crystallize in chiral structures. Enantiomorphic minerals such as quartz are optically active. These types of minerals, whether from space or Earth, could have served as prebiotic chiral nurseries due to surface-mediated chirality transfer, providing an excess of L-amino acids or D-sugars in the prebiotic Earth (Evans et al., 2012).

Generally, any chemical reaction that forms a product with a chiral center will produce equal amounts of L and D enantiomers, known as a racemic mixture, but this is not always the case: Frank's autocatalytic kinetic model for an asymmetric synthesis suggests that a slight excess of one enantiomer can influence and favor the synthesis of that enantiomer over its optical antithesis (Evans et al., 2012). At present, it is still uncertain what processes led to the change from a racemic world to the homochiral world in which we live (Sasabe and Suzuki, 2018).

Organic compounds, including some amino acids, have been found in some meteorites that have fallen to Earth. In the meteorite that fell near Murchison, Australia in 1969, five α-methyl amino acids were found, and all had a small but significant excess of what were described as L- enantiomers (or S enantiomers). One idea to explain this is that racemic mixtures of α-methyl amino acids formed in the Kuiper belt that were then selectively broken down by unshielded right-handed circularly polarized light, and the α-methyl amino acids with an excess of L- enantiomers reached Earth via chondrites (Breslow, 2011).

7.3 Other low molecular weight biomolecules

Thalidomide, antibiotics and amphetamines are examples of drugs with one or more chiral centers that are indicated by the prefixes R and S. The chiral versions of thalidomide have different effects on the human body: the S version is teratogenic, and the R version has tranquilizing properties (Elder et al., 2021). Examples of antibiotics are ofloxacin and its R-version, levofloxacin (Maia et al., 2018). Another example is chloramphenicol, which presents two chiral centers (there are S,S and R,R versions) and inhibits protein synthesis, therefore, it is a bacteriostatic antibiotic. This antibiotic is used only in developing countries for some meningitis and conjunctivitis; however, its use is restricted due to its toxic effects and the development of antimicrobial resistance.

Some enterobacteria can degrade R,R-(-)-chloramphenicol as a microbial resistance strategy and through metabolic pathways not applicable for S,S-(+)-chloramphenicol. Recently, a form of resistance to the S,S version has been found through its racemization to the metabolizable R,R form (Elder et al., 2021).

8 Conclusions

Chirality is an essentially geometrical property that comes from molecules and has physicochemical relevance. In living systems, other unicellular organisms such as eukaryotes and metazoans to social behavior have this symmetry. Especially in living systems, it is relevant that mirror symmetry gives distinct physical and chemical properties. In this respect, the origin of chirality in biology is a necessary question to answer.

This review has tried to solve and approach this question from thermodynamic and emergent properties, where chirality does have relatively measurable changes in our simulations and some of our experiments. The fact that L-amino acids and D-sugars are the main compounds of the living evolutionary machinery allows to assume molecular evolutionary mechanisms and molecular natural selection. This approach from molecular biophysics is giving some answers, and therefore we continue looking for the relevance of chirality in living systems through our research.

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References

Akanuma, S. (2019). *Astrobiology: From the Origins of Life to the Search for Extraterrestrial Intelligence*, chapter The Common Ancestor of All Modern Life, pages 91–103. Springer.

Bada, J. (1985). *Chemistry and Biochemistry of the Amino Acid*, chapter Racemization of Amino Acids, pages 399–414. Springer Netherlands.

Bailey, J. (2000). Chirality and the origin of life. *Acta Astronautica*, 46(10-12):627–631. Online:https://bit.ly/3UdWQYE.

Barrera-Calva, E., Pineda-Ledezma, R., and Barrera-Mera, B. (2012). De la quiralidad elemental a la complementariedad funcional determinante de la hermosura como producto de la interacción hemisférica cerebral. *Archivos de Neurociencias*, 17(2):79–84. Online:https://bit.ly/3FeRk3B.

Beléndez, A. (2008). La unificación de luz, electricidad y magnetismo: la"síntesis electromagnética"de maxwell. *Revista Brasileira de Ensino de Física*, 30:2601.1–2601.20. Online:https://bit.ly/3ETdEP1.

Breslow, R. (2011). The origin of homochirality in amino acids and sugars on prebiotic earth. *Tetrahedron letters*, 52(32):4228–4232. Online:https://bit.ly/3GV4qEw.

Cava, F., Lam, H., De Pedro, M., and Waldor, M. (2011). Emerging knowledge of regulatory roles of d-amino acids in bacteria. *Cellular and Molecular Life Sciences*, 68(5):817–831. Online:https://bit.ly/3ue7tQt.

Chen, M., Wu, H., Zhang, W., and Mu, W. (2020). Microbial and enzymatic strategies for the production of l-ribose. *Applied microbiology and biotechnology*, 104(8):3321–3329. Online:https://bit.ly/3VG6yUU.

Craig, D. and Thirunamachandran, T. (1999). New approaches to chiral discrimination in coupling between molecules. *Theoretical Chemistry Accounts*, 102(1):112–120. Online:https://bit.ly/3VGF6pO.

Elder, F., Feil, E., Pascoe, B., Sheppard, S., Snape, J., Gaze, W., and Kasprzyk-Hordern, B. (2021). Stereoselective bacterial metabolism of antibiotics in environmental bacteria-a novel biochemical workflow. *Frontiers in microbiology*, 12:738. Online:https://bit.ly/3OMMj5E.

Evans, A., Meinert, C., Giri, C., Goesmann, F., and Meierhenrich, U. (2012). Chirality, photochemistry and the detection of amino acids in interstellar ice analogues and comets. *Chemical Society Reviews*, 41(16):5447–5458. Online:https://rsc.li/3OQ7m7t.

Farace, C. and Aznar, L. (2011). Origen, evolución y extinción de los trilobites. INEC. Online:https://bit.ly/3VFE39H0.

Finkelshtein, A., Sirota-Madi, A., Roth, D., Ingham, C., and Ben Jacob, E. (2017). *Biocommunication: Sign-Mediated Interactions between Cells and Organisms*, chapter Paenibacillus vortex: a bacterial guide to the wisdom of the crowd, pages 257–283. World Scientific.

Gardner, M. (1985). *Izquierda y derecha en el cosmos*. Salvat Editores.

Genchi, G. (2017). An overview on d-amino acids. *Amino Acids*, 49(9):1521–1533. Online:https://bit.ly/3GTwwA2.

Globus, N. and Blandford, R. (2020). The chiral puzzle of life. *The Astrophysical Journal Letters*, 895(1):L11. Online:https://bit.ly/3irGzSL.

Gohil, N., Ramírez-García, R., Panchasara, H., Patel, S., Bhattacharjee, G., and Singh, V. (2018). *Book review: quorum sensing vs. quorum quenching: a battle with no end in sight*. Frontiers Media SA.

Hegstrom, R. and Kondepudi, D. (1990). The handedness of the universe. *Scientific American*, 262(1):108–115. Online:https://bit.ly/3OO4VSA.

Helanto, M., Kiviharju, K., Granström, T., Leisola, M., and Nyyssölä, A. (2009). Biotechnological production of l-ribose from l-arabinose. *Applied microbiology and biotechnology*, 83(1):77–83. Online:https://bit.ly/3uenRAD.

Ingham, C. and Jacob, E. (2008). Swarming and complex pattern formation in paenibacillus vortex studied by imaging and tracking cells. *BMC microbiology*, 8(1):1–16. Online:https://bit.ly/3VnyhK3.

Kohler, S. (2020). Cosmic rays as the source of life's handedness. *AAS Nova Highlights*, page 6575. Online:https://bit.ly/3FiruvP.

Kumar, S., Stecher, G., Li, M., Knyaz, C., and Tamura, K. (2018). Mega x: molecular evolutionary genetics analysis across computing platforms. *Molecular biology and evolution*, 35(6):1547–1549. Online:https://bit.ly/3UmHGQW.

Lehninger, A., Nelson, D., and Cox, M. (2008). *Lehninger principles of biochemistry*. Freeman.

Livesey, G. and Brown, J. (1995). Whole body metabolism is not restricted to d-sugars because energy metabolism of l-sugars fits a computational model in rats. *The Journal of nutrition*, 125(12):3020–3029. Online:https://bit.ly/3VnQC9O.

Lombard, J., López-García, P., and Moreira, D. (2012). The early evolution of lipid membranes and the three domains of life. *Nature Reviews Microbiology*, 10(7):507–515. Online:https://go.nature.com/3H3GqPw.

Maia, A., Tiritan, M., and Castro, P. (2018). Enantioselective degradation of ofloxacin and levofloxacin by the bacterial strains labrys portucalensis f11 and rhodococcus sp. fp1. *Ecotoxicology and environmental safety*, 155:144–151. Online:https://bit.ly/3ERggNd.

Martínez-Frías, M. (2010). Estructura y función del adn y de los genes. i tipos de alteraciones de la función del gen por mutaciones. *SEMERGEN-Medicina de Familia*, 36(5):273–277. Online:https://bit.ly/3XMwZtW.

Nazar, J. (2007). Biofilms bacterianos. *Revista de otorrinolaringología y cirugía de cabeza y cuello*, 67(1):161–172. Online:https://bit.ly/3AZhBjR.

Nieto-Ortega, B. (2014). *Quiralidad en Estructuras Supramoleculares: Espectroscopías de Dicroísmo Circular (ECD, VCD y ROA)*. PhD thesis, Universidad de Málaga.

Patty, C., Visser, L., Ariese, F., Buma, W., Sparks, W., van Spanning, R., Röling, W., and Snik, F. (2017). Circular spectropolarimetric sensing of chiral photosystems in decaying leaves. *Journal of Quantitative Spectroscopy and Radiative Transfer*, 189:303–311. Online:https://bit.ly/3ivtNCQ.

Pérez Benítez, A. and Arroyo Carmona, R. (2018). Enseñando helicidad y quiralidad con vasos de unicel. *Educación Química*, 12(3):133–137. Online:https://bit.ly/3OTAYAD.

Radkov, A. and Moe, L. (2014). Bacterial synthesis of d-amino acids. *Applied microbiology and biotechnology*, 98(12):5363–5374. Online:https://bit.ly/3VnwmoO.

Sandars, P. (2005). Chirality in the rna world and beyond. *International Journal of Astrobiology*, 4(1):49–61. Online:https://bit.ly/3VpemdY.

Sasabe, J. and Suzuki, M. (2018). Distinctive roles of d-amino acids in the homochiral world: chirality of amino acids modulates mammalian physiology and pathology. *The Keio journal of medicine*, 68(1):1–16. Online:https://bit.ly/3FfD6Q9.

Satir, P. (2016). Chirality of the cytoskeleton in the origins of cellular asymmetry. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 371(1710):20150408. Online:https://bit.ly/3uaUcIC.

Schilthuizen, M. and Davison, A. (2005). The convoluted evolution of snail chirality. *Naturwissenschaften*, 92(11):504–515. Online:https://bit.ly/3Ukp8Rh.

Senge, M., Ryan, A., Letchford, K., MacGowan, S., and Mielke, T. (2014). Chlorophylls, symmetry, chirality, and photosynthesis. *Symmetry*, 6(3):781–843. Online:https://bit.ly/3FfHXAR.

StackExchange (2020). Why does the weak force distinguish left and right handedness? StackExchange. Online:https://bit.ly/3VIyJTc.

Suh, I., Park, K., Jensen, W., and Lewis, D. (1997). Molecules, crystals, and chirality. *Journal of chemical education*, 74(7):800. Online:https://bit.ly/3OR2oaz.

Torres-Silva, H. (2008). Electrodinámica quiral: eslabón para la unificación del electromagnetismo y la gravitación. *Ingeniare. Revista chilena de ingeniería*, 16(ESPECIAL):6–23. Online:https://bit.ly/3EUvCRj.

Ussery, D. (2002). Dna structure: A-, b-and z-dna helix families. *Encyclopedia of life sciences*, pages 1–7. Online:https://bit.ly/3ESD92J.

Vargas, P. and Zardoya, R. (2015). *El aárbol de la vida: sistemaática y evolucioón de los seres vivos*. CSIC.

Vollmer, W., Blanot, D., and De Pedro, M. (2008). Peptidoglycan structure and architecture. *Journal of chemical education*, 74(7):149–167. Online:https://bit.ly/3ivIJ3u.

Wang, S., Furchtgott, L., Huang, K., and Shaevitz, J. (2012). Helical insertion of peptidoglycan produces chiral ordering of the bacterial cell wall. *Proceedings of the National Academy of Sciences*, 109(10):E595–E604. Online:https://bit.ly/3OND6Kn.

Woese, C., Kandler, O., and Wheelis, M. (1990). Towards a natural system of organisms: proposal for the domains archaea, bacteria, and eucarya. *Proceedings of the National Academy of Sciences*, 87(12):4576–4579. Online:https://bit.ly/3EJiRJ6.

Wu, C., Ambler, E., Hayward, R., Hoppes, D., and Hudson, R. (1957). Experimental test of parity conservation in beta decay. *Physical Review*, 105(4):1413. Online:https://bit.ly/3ON4qZa.