MOLECULAR FRONTIERS JOURNAL

Making Sense of Helices: Right and Wrong Models in Science and Art

Martin Egli [1] and Shuguang Zhang [2]

Helices are ubiquitous in art and nature. Independent of their pitch and sense of rotation (handedness), helices in sculpture, painting, architecture, scientific illustrations, conference announcements, logos, and advertising are eye-catching and aesthetically pleasing. Helices can turn either clockwise (right-handed helix) or anti-clockwise (left-handed helix). The α-helix formed by L-amino acids and the double helices formed by β-D-2′-deoxyribonucleic acid (A- and B-form DNA) and β-D-ribonucleic acid (A-form RNA) are all right-handed. Artistic license provides the freedom to create helices of any shape and sense; indeed, many helical sculptures do not follow the natural convention observed in proteins and DNA. What is more surprising, given that models of the α-helix and the DNA double helix were published over 70 years ago, is how common left-handed DNA double helices are in the context of scientific papers and books as well as in popular science writing and reporting. In all cases except for left-handed Z-DNA, the use of left-handed helices in scientific illustrations or models is incorrect. Here, we revisit the helix types adopted by peptides, DNA, and RNA, and review examples of right and wrong helical models in science, art, and elsewhere.

Keywords: α-Helix; Double Helix; DNA; Left-Handed; Right-Handed; Peptide; Protein; RNA.

INTRODUCTION

Peptides and DNA both adopt helices, with strands winding around a central axis in a clockwise fashion. The peptide α-helix is single-stranded with amino acid Cα atoms and amide moieties constituting the backbone and side chains protruding outwards[1,2] (Figure 1). In the DNA double helix, base pairs make up the core, and the sugar-phosphate backbones wrap around the base stack (in an anti-parallel manner)[3,4] (Figure 2). The only illustration in the original paper by Watson and Crick depicts a cartoon of the DNA double helix created by Odile Crick: ribbons trace the sugar-phosphate backbones, and rungs indicate base pairs[3]. Nowadays, one encounters more colorful and visually arresting versions of this cartoon DNA on an everyday basis, in advertisements, conference announcements, brochures for genetic testing, and covers of scientific journals and books, to name just a few. Surprisingly often, such cartoons exhibit an important difference from the black-and-white diagram of the DNA double helix published in 1953: the sense of rotation of the ribbons winding around base pairs is anti-clockwise!

Natural peptides and proteins are all composed of α-L-amino acids; DNA and RNA are composed of β-D-2′-deoxyribonucleotides and β-D-ribonucleotides, respectively. The L prefix is short for levorotatory, and the D prefix is short for dextrorotatory. As has been pointed out, levorotation has nothing to do with the optical activity of the amino acids themselves. Instead, it refers to that of the glyceraldehyde stereoisomer, to which amino acids are related by an arbitrary, conventional series of substitutions[8]. In any case, there is nothing left-handed about proteinogenic α-amino acids. Similarly, there is nothing in the configuration of DNA and RNA

[1]Department of Biochemistry, Vanderbilt University, School of Medicine, Nashville, TN 37232-0146, USA. E-mail: martin.egli@vanderbilt.edu, ORCID: https://orcid.org/0000-0003-4145-356X. [2]Laboratory of Molecular Architecture, Media Lab, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA. E-mail: shuguang@mit.edu, ORCID: https://orcid.org/0000-0002-3856-3752.
Published online 22 July 2023; doi:10.1142/S2529732523500086

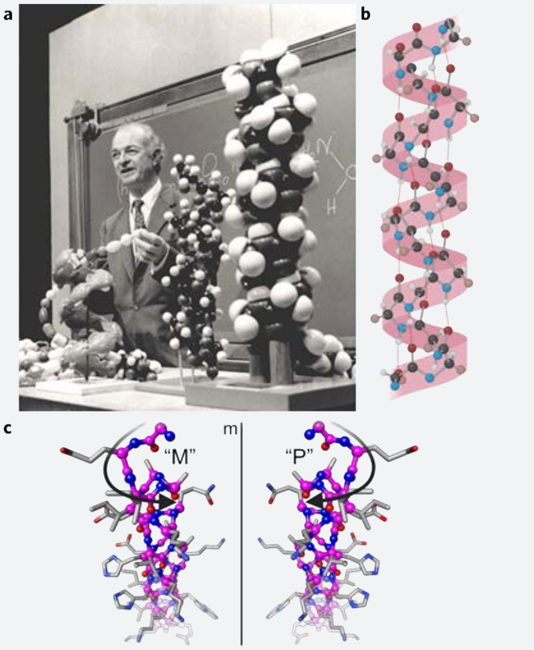

Figure 1. Peptide α-helix. (a) Linus Pauling with models of α-helices. (b) Schematic illustration of the right-handed α-helix with hydrogen bonds indicated by dashed lines. (c) Models of left-handed (Minus) and right-handed (Plus) α-helices (PDB ID 6I1J)[5]. Backbone atoms are shown in ball-and-stick mode with carbon, nitrogen, and oxygen colored in magenta, blue, and red, respectively. Side-chain carbon atoms are shown in stick mode and colored in gray. Arrows indicate the direction of rotation, and m is a mirror plane that converts D-amino acids (left) to L-amino acids (right). Credits: Linus Pauling photograph, https://profiles.nlm.nih.gov/101584639X208; the ball-and-stick α-helix was generated with Biorender, https://www.biorender.com/; the left-handed α-helix was produced with DStabilize[6] from PDB ID 6I1J[5] and UCSF Chimera[7] was used for the figure panel.

nucleotides per se that could be used to relate them to either a left or a right hand. As stated in the first sentence, the sense of rotation of helices composed of either L-amino acids or D-nucleotides is clockwise.

However, compared to the building blocks themselves, helices can be unambiguously designated as either left-handed or right-handed. Thus, by pointing the thumb of the right hand up the helical axis, a helix is right-handed if the strand(s) turns (turn) in the direction indicated by the fingers of the right hand. If the strand(s) turns (turn) in the opposite direction, the helix is left-handed. Therefore, right-handed helices have a clockwise sense of rotation, and left-handed helices have an anti-clockwise sense of rotation. As per the CIP rules that specify molecular chirality, peptides, DNA, and RNA form right-handed P-helices. Those of the opposite sense of rotation are referred to as M-helices[9] (Figure 1c)[5–7]. DNA and RNA duplexes are also homochiral: oligonucleotides composed of either all D-nucleotides or L-nucleotides cannot pair with each other.

A careful look at Figure 2 in Pauling et al.[2] reveals that the depicted model of the α-helix with 3.7 amino acids per turn is left-handed. Although Pauling and associates were aware at the time of the publication that peptides are composed of L-amino acids, they showed a peptide with amino acids of the opposite (wrong) chirality. Thus, the authors made an arbitrary choice and illustrated their landmark paper with a left-handed α-helix, the mirror image of the natural α-helix[10–12]. The model of the γ-helix with 5.1 amino acids per turn shown in Figure 3 of the original paper is right-handed, but not of relevance as a secondary structural element of the 3D structure of proteins, contrary to the 3_{10} helix, which was barely mentioned in the 1951 paper[11].

A left-handed double helix, so-called Z-DNA, exists in cellular DNA but is limited to specific GC-rich regions[15,16]. Phosphate groups in the backbone of Z-DNA cannot be traced with a smooth ribbon, but follow a *zigzag* pattern that gave the double helix its name[4,17,18] (Figure 2). Even among chemists and molecular biologists, the left-handed Z-form of DNA has remained somewhat of an obscurity. For most, DNA structure is synonymous with the canonical right-handed B-form double helix that features 10 base pairs per turn. Fewer will be familiar with its somewhat fatter cousin, the right-handed A-form, which features 11 base pairs per turn and is also the standard conformation adopted by double-stranded RNA. More importantly, the familiar cartoons of DNA double helices that quite often display the wrong sense of rotation are clearly not meant to depict Z-DNA because the backbones are always depicted as smooth ribbons.

Besides the double-helical structures with antiparallel orientation of strands, nucleic acids can adopt three-stranded (e.g., the RNA triplex[19] with PDB ID code 7JNH; http://www.rcsb.org), four-stranded (e.g., the human telomeric DNA quadruplex[20] with PDB ID 1K8P), and even five-stranded motifs[21] (the G/isoG DNA pentaplex with PDB ID 2LUJ). In all cases, such structures exhibit a clockwise sense of rotation of the strands. Moreover, parallel-stranded DNA[22] (PDB ID 7T6Y) and RNA[23] double helices (PDB ID 4JRD) are also right-handed.

To conclude: α-helices in proteins and DNA double helices are right-handed. Illustrations and sculptures of left-handed helices may be artistically pleasing, but chemically and biologically, they make no sense.

PEPTIDE AND DNA SUPRAMOLECULAR STRUCTURES

Right-handed α-helices and DNA adopt left-handed supramolecular structures. DNA forms a left-handed coil around

Figure 2. DNA double helices. The photograph shows (from left to right) Alexander Rich, a CPK model of left-handed Z-DNA, a CPK model of right-handed B-DNA, and Francis Crick. Credit: Shuguang Zhang, MIT. The photograph is flanked by schematic illustrations of Z-DNA (left) and B-DNA (right) generated with Biorender https://www.biorender.com/.

the histone proteins in nucleosome core particles (Figure 3a)[13]. Peptides form left-handed coiled coils[24]; an example of a parallel-stranded, left-handed coiled coil is depicted in Figure 3b. Independent of the higher-order structures observed for proteins and DNA in cellular environments, the underlying secondary structure motifs—α-helix and double helix, respectively—remain right-handed.

SCREWS, SNAILS, AND SPIRALS

Virtually all screws are right-handed, and the use of left-handed screws is only indicated for very specific applications, for example, in machinery where operation could loosen the right-handed type. Some 85% of humans are right-handed, allowing them to apply more torque to tighten right-handed screws. Thus, just like peptide and DNA helices, screws are right-handed.

The terms spiral and helix are often treated like synonyms, but they clearly differ in their mathematical definitions. A helix is a curve on a cylinder surface whereby the angle between the curve and a plane perpendicular to the axis is constant. Hence, the distance from the axis for a point moving along the helix does not change (Figure 4a). A point moving along a spiral rotates about a fixed point while continuously increasing the distance from that point. This is beautifully illustrated by snail shells (Figure 4b). We owe it to Jack Dunitz that we refer to the peptide and DNA secondary structures as helices (α-helix and double helix, respectively) rather than spirals. He suggested to Linus Pauling the designation "helix"[12,25] instead of "spiral configuration of the polypeptide chain" used by Pauling and Corey in their initial publication[1].

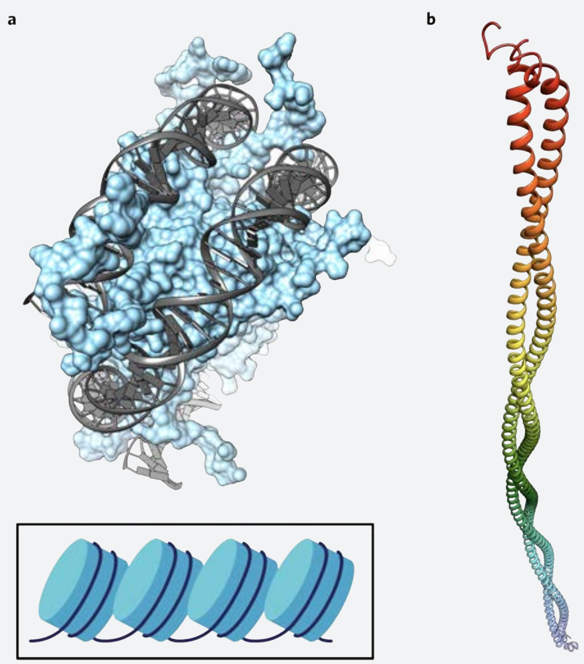

Figure 3. Left-handed supramolecular structures adopted by DNA and peptides. (a) Crystal structure of the nucleosome core particle from chicken (PDB ID code 1EQZ)[13]. A right-handed DNA (gray) forms a left-handed coil around the histone octamer (light-blue surface rendering). Inset: schematic of four consecutive nucleosome core particles. The DNA (black string) wraps around histone protein cores (light blue cylinders) in a left-handed fashion. (https://www.biorender.com/). (b) A left-handed coiled coil formed by right-handed α-helices from rabbit tropomyosin protein (PDB ID 2TMA)[14]. The parallel-stranded coiled coil is shown in rainbow coloring from blue (N-termini) to red (C-termini).

An overwhelming majority of snails are right-handed, and it was shown that formin *Lsdia1* is the handedness-determining gene in the freshwater snail *Lymnaea stagnalis*[26]. Studies with the land snail species *Bradybaena similaris* using both the dextral wild-type found in nature and a laboratory-maintained racemic strain (producing a 1:1 mixture of left- and right-handed snails) established that

Figure 4. Helix versus spiral. (a) Karlskirche in Vienna, Austria. Cylindrical towers on the left and the right are decorated with left- and right-handed helices, respectively. (b) Sinistral (left) and dextral (right) morphs of the land snail Bradybaena similaris with left- and right-handed spiral patterns of shells, respectively. Credits: Eric Hong, https://unsplash.com/photos/Ka8xLwYVY4E (Karlskirche) and https://phys.org/news/2019-02-right-left-handed-gene-story-snail.html (snails).

the main difference between the two was in the expression level of the *diaph* gene[27]. However, in keeping with the theme of the dominance of the right-handed pattern seen so far, we note that, like protein and DNA helices, snails occur almost exclusively in the right-handed form in nature.

HELICAL STAIRCASES

For reasons described above for the α-helix, spiral staircases should really be referred to as helical staircases. Thus, we can compare the direction of rotation in helical staircases with the helical structures of peptides and DNA. The helical staircase shown in Figure 5a is left-handed, as one's left hand is on the handrail on the way up. Although a person moves in a clockwise direction when climbing upstairs, the handrail forms a left-handed helix. The helical staircase shown in Figure 5b is right-handed, as one's right hand is on the handrail on the way up. Although a person moves in an anti-clockwise direction when climbing upstairs, the handrail forms a right-handed helix. An architecturally fascinating case of adjacent ("twinned") left- and right-handed helical staircases is depicted in Figure 5c. Right-handed helical staircases are more common in contemporary buildings, as right-handers can hold on to the handrail with their preferred hand on the way up. Still, comparisons with spirals, snails, and spiral staircases are best avoided in the context of α-helical peptides and double-helical DNA.

MECHANICAL MOLECULAR MODELS

In their pursuit of the fundamental structural principles of proteins and nucleic acids, Pauling as well as Watson and Crick were keenly aware of the power of mechanical molecular models (Figure 1). Irrespective of the material used to build such models, plaster, paper, cardboard, metal, wood, and later plastics, building a 3D model and holding it in one's hands allows a much different interaction with its stereochemical properties than merely looking at the 2D version in a publication or on a screen. The first scenario also makes it easier to distinguish between left- and right-handed helices. By comparison, keeping the two apart based just on an illustration requires mental rotations of the model that can lead to errors. Mechanical molecular models were commonplace in chemistry and molecular and structural biology for many decades and have been described as cognitive facilitators and augmentations[28]. Simply put, phone and computer screens cannot completely replace a physical molecular model. Such molecular models can still serve an important role in undergraduate and graduate teaching. Our conclusion is strongly supported by the fact that many illustrations of proteins and DNA display helices with the wrong sense of rotation. For a biomolecular helix to be meaningful, it needs to be right-handed. To quote Henry David Thoreau: "The question is not what you look at, but what you see".

SCIENTIFICALLY CORRECT AND INCORRECT HELIX CHIRALITY

We emphasize here that peptides and nucleic acids and the helices they form are chiral. The reason for stressing this is not to give the impression that chirality is something special or rare. Rather, we want to provide users of helices in art, science, and elsewhere with a consumer guide to create

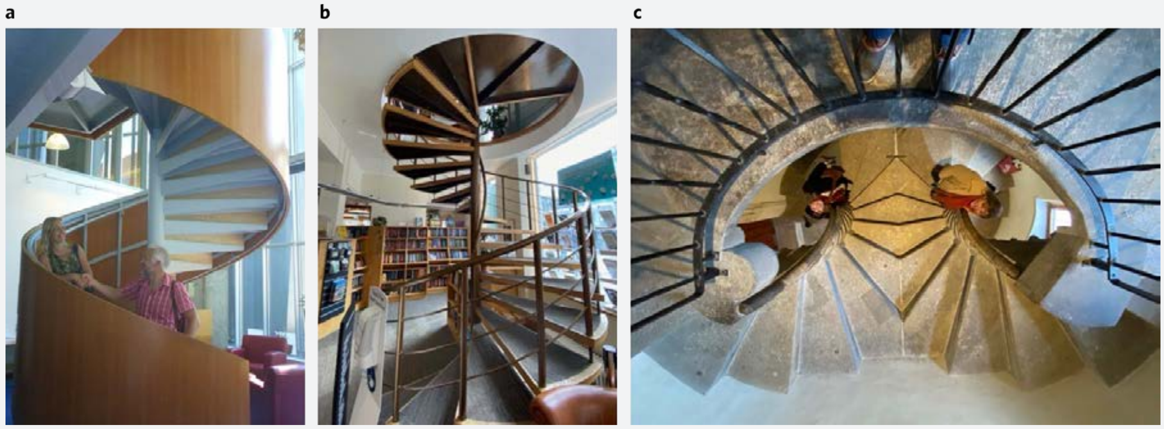

Figure 5. Helical staircases. (a) Left-handed: 5th floor, Satata Center, MIT, Cambridge, MA. (b) Right-handed: Cambridge University Press bookstore at the corner of Trinity Street and St. Mary Street, Cambridge, UK. (c) Racemic, left- and right-handed: Zwillingswendeltreppe, Grazer Burg, Graz, Austria. Credits: Shuguang Zhang.

Figure 6. Helices in currency. (a) The face of the 2003 British two-pound coin shows a right-handed DNA double helix with A:T and G:C base pairs. The correct helical sense was carefully checked by scientists at the MRC-Laboratory of Molecular Biology, Cambridge, UK. The coin was minted to commemorate the 50th anniversary of the discovery of the DNA double helix. (b) The edge of the same coin shows an incorrect left-handed DNA double helix that was designed without input from scientists. (c) The back of the Turkish five-lira banknote. The DNA double helix is left-handed and of the B-form, which is incorrect. Left-handed Z-DNA[30] adopts a very different structure (Figure 2, left).

scientifically correct helices and to be able to readily distinguish between correct and incorrect artwork. It has been pointed out that chirality is more the rule than the exception: "The world is chiral and clinal, enjoy symmetry wherever you find it" (Vladimir Prelog). Thus, almost everything in the natural world is chiral, not just the molecules of life and hands but also flowers, trees, shells, minerals, and so forth. Conversely, most achiral objects are man-made—think of furniture, cups, and buildings, just to name a few[8,29].

We all know that the right foot cannot fit into a left shoe and that a left-handed nut cannot be screwed onto a right-handed bolt, and vice versa. However, many creators of helices seem to be ignorant of chirality and then arbitrarily use either a right- or a left-handed helix. With this article, we wish to alert readers to the issue of helical chirality and urge them to pay close attention to the correct handedness of a helix. Depicting a left-handed helix or double helix with the intent to represent standard protein or nucleic acid secondary structure, respectively, is fundamentally wrong and embarrassing.

Examples of right-handed and left-handed helices are depicted in Figures 6 (currency), 7 (sculpture, jewelry, and objects of art), 8 (architecture), 9 (plants and animals), 10 (scientific publications), and 11 (websites and company logos). Incorrect left-handed DNA duplexes have appeared on the covers of prestigious journals and classic books. Thus, the cover of the first British edition of James Watson's "The Double Helix" depicts an incorrect left-handed double helix (Figure 10a). The cover of the first US edition of the book showed the correct right-handed model (Figure 10b). The cover of the September 9, 2010, issue of *Nature* displayed an incorrect left-handed DNA double helix (Figure 10c).

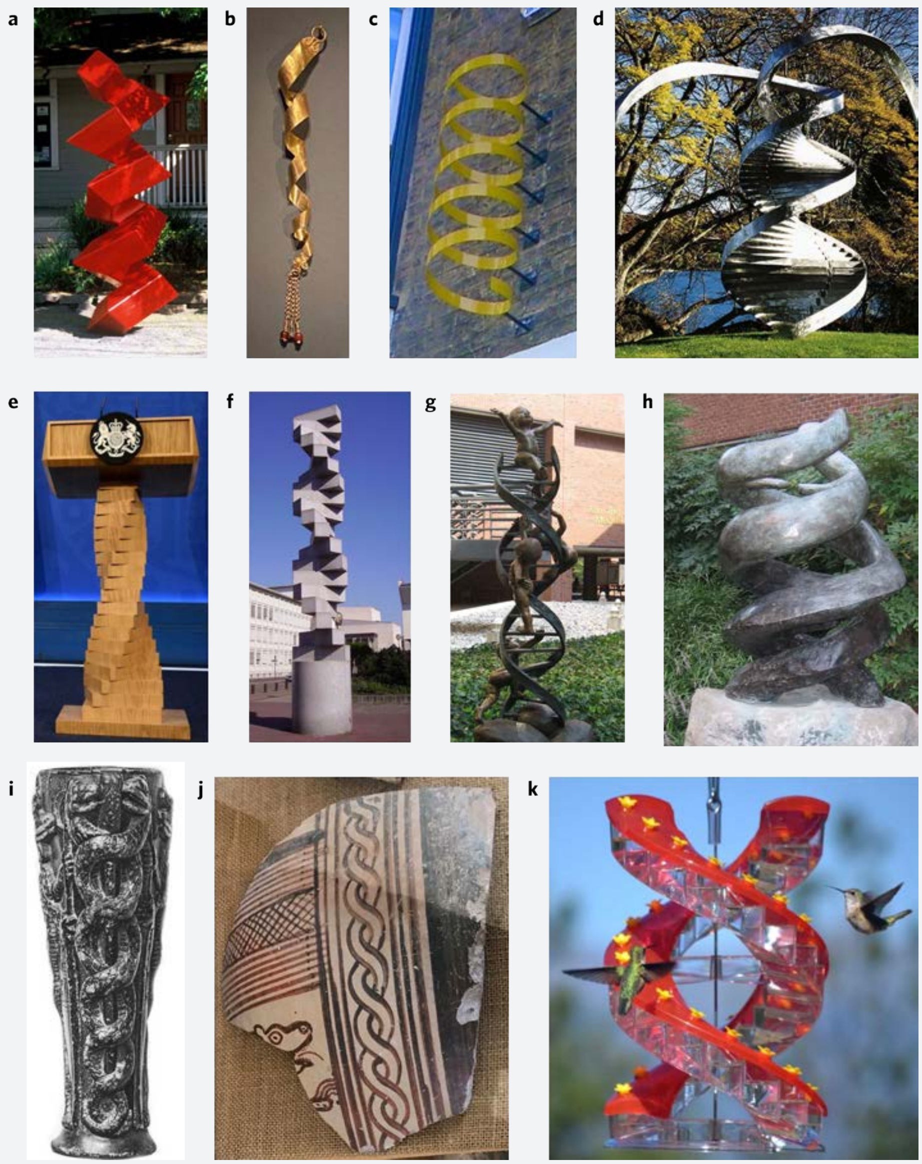

Figure 7. Helices in sculpture, jewelry, and objects of art. (a) α-Helix in front of Linus Pauling's boyhood home on 3945 SE Hawthorne Blvd, Portland, OR. (b) Right-handed golden helix jewelry made by a Macedonian artist in ancient Greece (~350 BC) on display in the Archeological Museum of Thessaloniki, Greece. (c) The Golden Helix was installed by Francis Crick above the door of his house in Cambridge, UK in 1951, shortly after the discovery of the right-handed peptide α-helix by Linus Pauling. Crick did not replace it with the right-handed DNA double helix that he discovered with Jim Watson. (d) Right-handed double helix sculpture "Spirals Time—Time Spirals" by artist Charles Jencks and donated by Jim Watson on the campus of Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. (e) Right-handed double-helix lectern used by former British prime minister Liz Truss. (f) Left-handed double helix sculpture ("Endlose Treppe") by Swiss artist Max Bill, located in Ludwigshafen, Germany. (g) The incorrect left-handed DNA double helix sculpture in front of the Robinson Research Building, Vanderbilt University Medical Center, Nashville, TN. (h) Right-handed double helix sculpture in front of Light Hall, Vanderbilt University Medical Center, Nashville, TN. (i) The caduceus, a right-handed double helix of snakes, symbol of God Ningishzida, on the libation vase of Sumerian ruler Gudea, ca. 2,100 BC. The caduceus represents the magic wand of Hermes or the Roman Mercury and serves as the symbol of medicine in more recent depictions[31]. Both right-handed and left-handed versions of intertwined snakes exist randomly. The caduceus of the Surgeon General of the United States Army is left-handed and the Star of Life symbol that identifies emergency medical services features a blue six-pointed star with a right-handed helical (snake) Rod of Asclepius. (j) Left-handed double helix on a pottery fragment from the Minoan civilization (~2,000 BC), on display in the Archeological Museum of Thera, Santorini, Greece. (k) Left-handed double-helix hummingbird feeder.

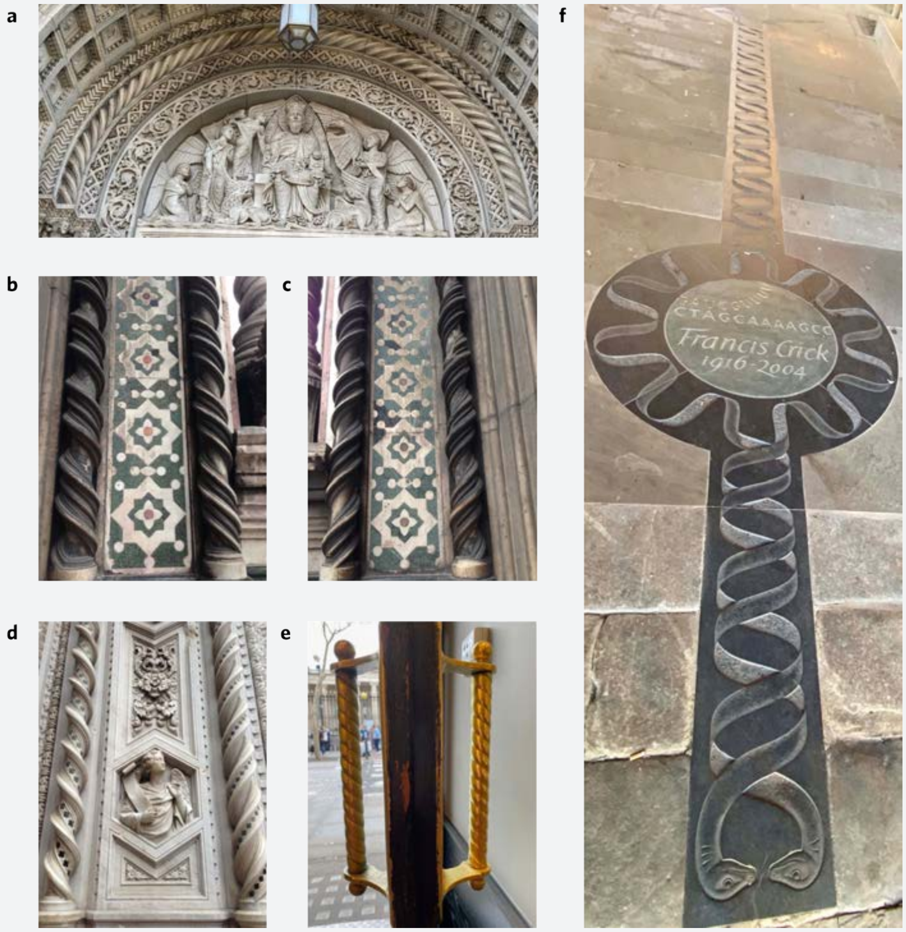

Figure 8. Helices in architecture. (a) The arch above the main portal of the 12th-century Siena Cathedral, Siena, Italy, contains a continuous left-handed helix. (b) Left-handed helix on the facade of the 14th-century Florence Cathedral (Duomo), Florence, Italy. (c) Right-handed helix on the facade of the Duomo. (d) Left- and right-handed helices on the facade of the Duomo. (e) Left-handed helical door handles at the Starbucks store across from the British Museum in London, UK. (f) Right-handed DNA double helix Memorial to Francis Crick in the Great Gate of Gonville & Caius College (University of Cambridge, Cambridge, UK), unveiled in April of 2013.

Extra attention should be paid to depictions of helices to celebrate the anniversary of the discovery of the DNA double helix. Unfortunate examples of incorrect left-handed double helices in this context are shown in Figures 6b, 10d, and 10i. Relying on commercial stock images for illustrating articles should not prevent one from checking their correctness. The fantasy cartoon rendering of the three-dimensional structure of a protein in Figure 10e is a case in point. No natural protein folds by adopting three left-handed and a right-handed helix connected by loops. Conference banners often use flashy imagery, and an example of an incorrect left-handed DNA double helix used to announce a 2023 scientific meeting is shown in Figure 10g.

Many well-known research institutions and biotech companies also use incorrect left-handed DNA double helices to illustrate topics such as genetics, genomes, or discovery in newsletters, web blogs, and even in logos. Selected examples are shown in Figure 11 and include seminar announcements (Figure 11a), websites (Figure 11c, e, f), and logos (Figure 11b, d). The logo of the Eagle's DNA beer brand served in the Eagle Pub in Cambridge, UK, is a particularly embarrassing case: it depicts a left-handed DNA double helix carried by an eagle. Even after a few beers, the fact remains that this is not the secret of life that James Watson and Francis Crick found as per their announcement to the crowd in the Eagle Pub on February 28, 1953.

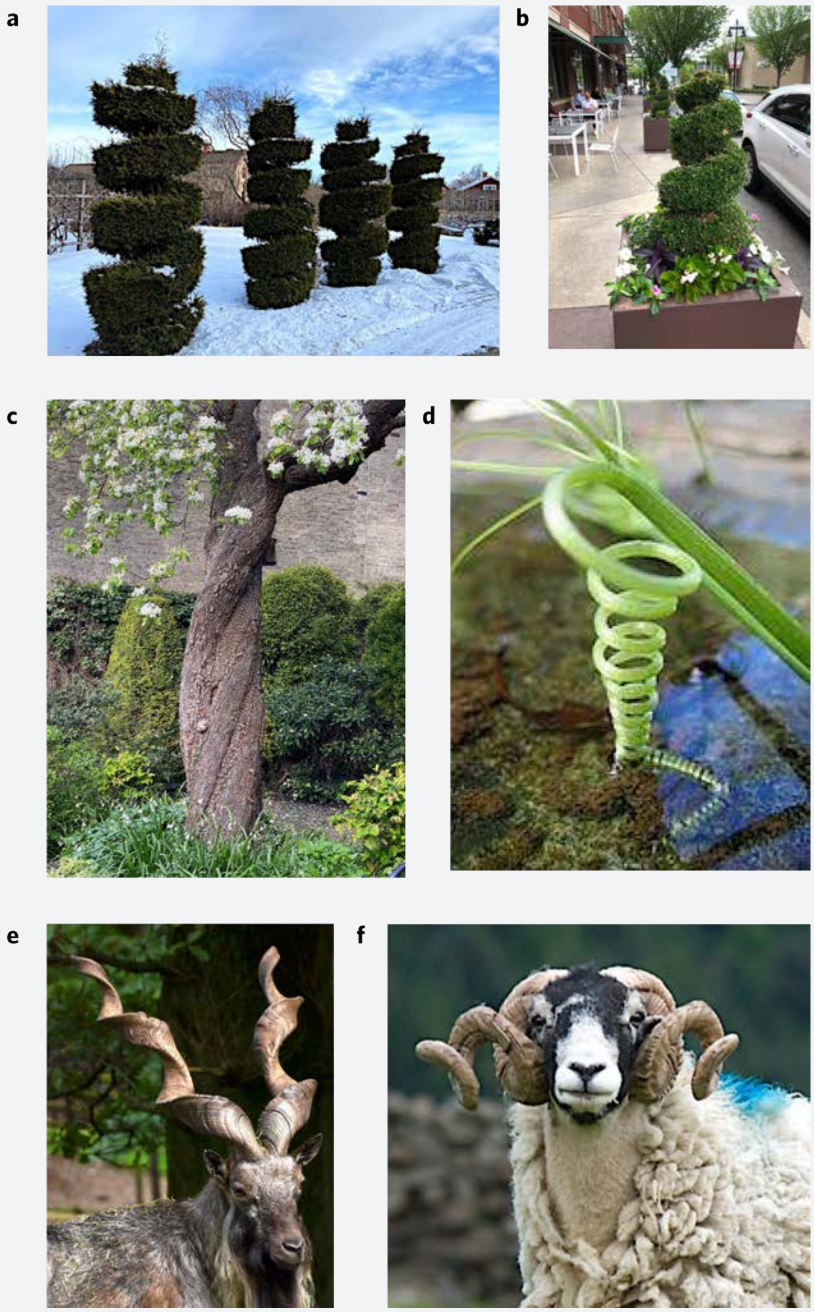

Figure 9. Helices in plants and animals. (a) Right-handed helix trees. A structural biologist in Leksand, Sweden, cut his trees in honor of the protein α-helix. (b) Potted plants trimmed in the shape of right-handed single helices outside Whole Foods Market in Nashville, TN. (c) Two intertwined trees seem to form a right-handed double helix outside Francis Crick's former home on Portugal Place, Cambridge, UK. (d) Left-handed helical tendril in a climber plant. Most twining plants exhibit right-handed helical growth independent of their hemispheric location. (e) Kashmir or flare-horned markhor, a goat-antelope with helix-shaped horns. The animal's right horn is left-handed, and its left horn is right-handed. (f) In contrast, this Curly horn Swaledale ram has a left horn that is left-handed and a right horn that is right-handed. Nature is fascinatingly complex.

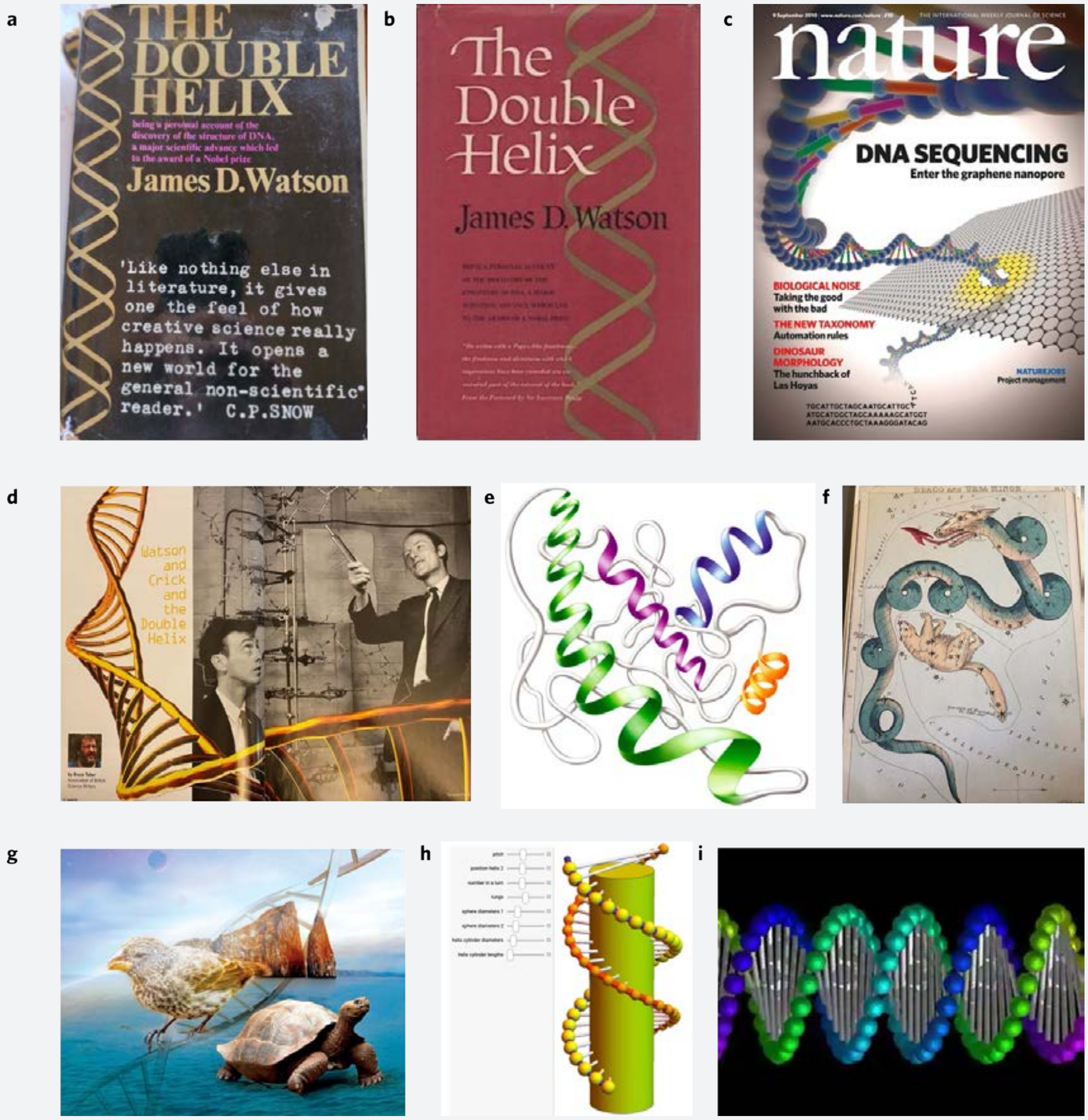

Figure 10. Helices in scientific publications. (a) Cover of the first British edition of James Watson's "The Double Helix". It depicts an incorrect left-handed DNA double helix. (b) The cover of the first US edition of the book showed the correct right-handed model. (c) The cover of Nature of September 9, 2010 467(7312) displayed an incorrect left-handed DNA double helix. (d) Overlay of an incorrect left-handed DNA double helix onto the 1953 photo of Watson and Crick. The article was published in "DNA 50: The Secret of Life" in 2003, on the 50th anniversary of the discovery of the DNA double helix. (e) An Alamy stock image from their posttranslational photo and image selection shows a protein cartoon with one correct right-handed α-helix (purple) and three incorrect left-handed α-helices (blue, green, and orange). Such a protein does not exist in nature. Extra care should be applied when selecting stock images, free or copyrighted, from websites. For example, the site https://pixabay.com/images/search/dna/ features hundreds of images of incorrect, left-handed DNA double helices. (f) A card from the 1820s on display in the British Royal Observatory Museum, Greenwich, UK. It depicts the Draco and Ursa Minor constellations, and when held up to the light, the pin holes in such cards reveal the patterns of constellations. The dragon features both right-handed and left-handed turns. (g) The on-line conference banner for the Origins 2023 meeting in Quito, Ecuador, organized by the International Society for the Study of the Origin of Life (ISSOL) and the International Astronomical Union (IAU) shows an incorrect left-handed DNA double helix. (h) Incorrect left-handed double helix model from the WOLFRAM Demonstrations Project. (i) This illustration depicting an incorrect left-handed double helix accompanied the article "DNA's double helix: 60 years since life's deep molecular secret was discovered" by Brenda Maddox in the 22 February 2013 edition of The Guardian.

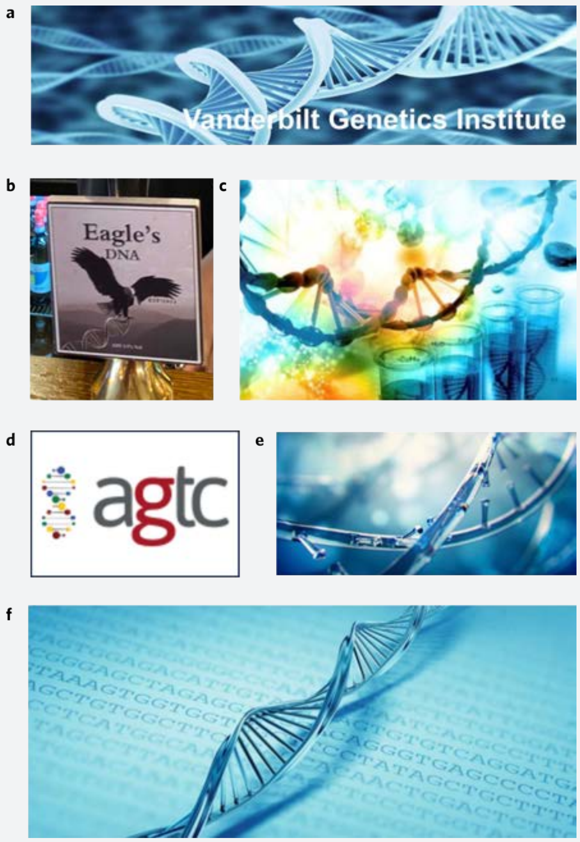

Figure 11. Incorrect left-handed DNA double helices in websites and company logos. (a) The E-mail logo and seminar announcements by the Vanderbilt Genetics Institute use a left-handed DNA double helix. (b) The logo of Eagle's DNA beer brand depicts a left-handed DNA double helix. On February 28, 1953, Francis Crick announced in the Eagle pub "We discovered the secret of life". Cheers to that—but better with right-handed DNA! (c) The Biomedcentral BMC Publishing company shows a left-handed DNA double helix on its website. (d) The logo of the biotech company AGTC Genetic Therapy uses a left-handed DNA double helix. (e) The Oxford News Blog, published on October 30, 2017, on "The origin of the first genomes" used an illustration that depicts a left-handed DNA double helix. (f) An online article on August 17, 2012, reported a breakthrough on DNA information storage capacity by scientists at Harvard University's Wyss Institute. The article was illustrated with a left-handed DNA double helix.

CONCLUSIONS

The essential point we wanted to convey in this article is that almost all peptide and protein α-helices and nucleic acid double helices are right-handed. Exceptions to this rule are mirror-image enzymes and RNAs with inverted chirality, that is, composed of D-amino acids and L-ribonucleotides, respectively[32]. Illustrators and artists creating models of helices should bear in mind the following quotations to avoid taking the wrong turn. "La droite et la gauche—ce n'est pas la même chose!" (Pierre Mauroy, French Prime Minister 1981–1984), and "If you can't imitate it, don't copy it!" (Yogi Berra, New York Yankees catcher and master of the malapropism).

ACKNOWLEDGMENT

Dedicated to the memory of our mentors and advisors, Professors Jack Dunitz, Vladimir Prelog, and Alexander Rich, for their teachings in the field of structural chemistry.

CONFLICT OF INTEREST

Martin Egli and Shuguang Zhang declare that they have no conflict of interest relating to the content of this article.

ORCID

Martin Egli https://orcid.org/0000-0003-4145-356X
Shuguang Zhang https://orcid.org/0000-0002-3856-3752

REFERENCES

1. Pauling, L. & Corey, R.B. Two hydrogen-bonded spiral configurations of the polypeptide chain. *J. Am. Chem. Soc.* **72**, 5346 (1950).
2. Pauling, L., Corey, R.B. & Branson, H.R. The structure of proteins: two hydrogen-bonded helical configurations of the polypeptide chain. *Proc. Natl. Acad. Sci. USA* **37**, 205–211 (1951).
3. Watson, J.D. & Crick, F.H.C. Molecular structure of nucleic acids: a structure for deoxyribose nucleic acid. *Nature* **171**, 737–738 (1953).
4. Egli, M. DNA and RNA structure. In: Blackburn, G.M., Egli, M., Gait, M.J. & Watts, J.K. editors. *Nucleic Acids in Chemistry and Biology*. 4th ed. (R. Soc. Chem., Cambridge, UK, 2022). pp. 20–95.
5. Boyle, A.L. et al. Selective coordination of three transition metal ions within a coiled-coil peptide scaffold. *Chem Sci.* **10**, 7456–7465 (2019).
6. Malik, A.J., Aronica, P.G.A. & Verma, C.S. DStabilize: a web resource to generate mirror images of biomolecules. *Structure* **28**, 1358–1360 (2020).
7. Pettersen, E.F. et al. UCSF Chimera—a visualization system for exploratory research and analysis. *J. Comput. Chem.* **25**, 1605–1612 (2004).
8. Dunitz, J.D. Bad language. *Angew. Chem. Int. Ed.* **58**, 1248–1250 (2019).
9. Cahn, R.S., Ingold, C. & Prelog, V. Specification of molecular chirality. *Angew. Chem. Int. Ed.* **5**, 385–415 (1966).
10. Dunitz, J.D. Pauling's left-handed α-helix. *Angew. Chem. Int. Ed.* **40**, 4167–4172 (2001).

11. Eisenberg, D. The discovery of the α-helix and β-sheet, the principle structural features of proteins. *Proc. Natl. Acad. Sci. USA* **100**, 11207–11210 (2003).
12. Egli, M. & Zhang, S. How the α-helix got its name. *Nat. Rev. Mol. Cell Biol.* **23**, 165 (2022).
13. Harp, J.M., Hanson, B.L., Timm, D.E. & Bunick, G.J. Asymmetries in the nucleosome core particle at 2.5 A resolution. *Acta Crystallogr. D Struct. Biol.* **56**, 1513–1534 (2000).
14. Phillips, G.N., Jr. Construction of an atomic model for tropomyosin and implications for interactions with actin. *J. Mol. Biol.* **192**, 128–131 (1986).
15. Herbert, A., Alfken, J., Kim, Y.G., Mian, I.S., Nishikura, K. & Rich, A. A Z-DNA binding domain present in the human editing enzyme, double-stranded RNA adenosine deaminase. *Proc. Natl. Acad. Sci. USA* **94**, 8421–8426 (1997).
16. Herbert, A. Z-DNA and Z-RNA in human disease. *Commun. Biol.* **2**, 7 (2019).
17. Wang, A.H.J. et al. Molecular structure of a left-handed double helical DNA fragment at atomic resolution. *Nature* **282**, 680–686 (1979).
18. Krall, J., Nichols, P., Henen, M., Vicens, Q. & Vögeli, B. Formation and stabilization of Z-DNA and Z-RNA. *Molecules* **28**, 843 (2023).
19. Torabi, S.F. et al. RNA stabilization by a poly(A) tail 3'-end binding pocket and other modes of poly(A)-RNA interaction. *Science* **371**, eabe6523 (2021).
20. Parkinson, G.N., Lee, M.P. & Neidle, S. Crystal structure of parallel quadruplexes from human telomeric DNA. *Nature* **417**, 876–880 (2002).
21. Kang, M., Heuberger, B., Chaput, J.C., Switzer, C. & Feigon, J. Solution structure of a parallel-stranded oligoisoguanine DNA pentaplex formed by $d(T(iG)_4T)$ in the presence of Cs^+ ions. *Angew. Chem. Int. Ed.* **51**, 7952–7955 (2012).
22. Luteran, E.M. & Paukstelis, P.J. The parallel-stranded d(CGA) duplex is a highly predictable structural motif with two conformationally distinct strands. *Acta Crystallogr. D Struct. Biol.* **78**, 299–309 (2022).
23. Safaee, N. et al. Structure of the parallel duplex of poly(A) RNA: evaluation of a 50-year-old prediction. *Angew. Chem. Int. Ed.* **52**, 10370–10373 (2013).
24. Woolfson, D.N. Understanding a protein fold: The physics, chemistry, and biology of α-helical coiled coils. *J. Biol. Chem.* **299**, 104579 (2023).
25. Dunitz, J.D. La Primavera. *Helv. Chim. Acta* **96**, 545–563 (2013).
26. Abe, M. & Kuroda, R. The development of CRISPR for a mollusc establishes the formin *Lsdia1* as the long-sought gene for snail dextral/sinistral coiling. *Development* **146**, dev175976 (2019).
27. Noda, T., Satoh, N. & Asami, T. Heterochirality results from reduction of maternal *diaph* expression in a terrestrial pulmonate snail. *Zoological Letters* **5**, 2 (2019).
28. Charbonneau, M. The cognitive life of mechanical molecular models. *Studies in History and Philosophy of Biological and Biomedical Sciences* **44**, 585–594 (2013).
29. Dunitz, J.D. & Heilbronner, E. *Reflections on Symmetry in Chemistry ... and Elsewhere*. (VCH Publishers, Basel, 1993).
30. Herbert, A. & Rich, A. The biology of left-handed Z-DNA. *J. Biol. Chem.* **271**, 11595–11598 (1996).
31. Finn, R., Orlans, D.A. & Davenport, G. A much misunderstood-caduceus and the case for an aesculapion. *The Lancet* **353**, 1978 (1999).
32. Xu, Y. & Zhu, T.F. Mirror-image T7 transcription of chirally inverted ribosomal and functional RNAs. *Science* **378**, 405–412 (2022).