

# Bad Language

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chirality · language · stereochemistry · symmetry

**Abstract:** *Bad language in stereochemistry—and elsewhere—can lead to sloppy thinking. In this Essay I review the history of stereochemical concepts and vocabulary in the hope that it may contribute a little to better thinking and communication.*

**B**ad language! “Natural amino acids are almost exclusively left-handed; natural sugars are almost exclusively right-handed.” How often have we read or heard this statement or something like it as part of a prelude to a discussion on the origin of biomolecular homochirality! Left-handed amino acids? What is left-handed about the natural amino acids? That they are conventionally associated with the descriptor prefix *L*? Where is there any resemblance between a molecule of, say, *L*-alanine, and a left hand? There are no good answers to these questions. Although the *L* prefix is short for levorotatory, the levorotation in question has nothing to do with the optical activity of the amino acids themselves but refers rather to the optical activity of the glyceraldehyde stereoisomer to which the  $\alpha$ -amino acids are related by an arbitrary, conventional sequence of substitutions. There is nothing left-handed about it. Similar criticism can be leveled at the right-handedness of the natural sugars. In short, the description of the natural amino acids and natural sugars as, respectively, left- and right-handed has no scientific basis and can easily lead to absurd consequences. Bad language!

Perhaps the trouble stems originally from the now standard use of the words *chiral* and *chirality* in chemistry. Let us repeat Kelvin's original 1893 definition:

“I call any geometric figure or group *chiral*, and say that it has *chirality*, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself. Two equal and similar right hands are homochirally similar. Equal and similar right and left hands are heterochirally similar or allochiral (but heterochirally is better). These are also called enantiomorphs, after a usage introduced, I believe, by German workers. Any *chiral* object and its image in a plane mirror are heterochirally similar.”<sup>[1]</sup>

This is clear. Sixty years later, Kelvin's definitions were rescued from oblivion by the “downfall of parity”, the realization that the laws of physics may not all be mirror-

symmetric and the experimental demonstration that electrons emitted in some radioactive processes, for example,  $\beta$ -decay of  $^{60}\text{Co}$ , are associated preferentially with left-handed spin.<sup>[2]</sup> The universe is *chiral*, in Kelvin's sense of the word.


The concept of *chirality* soon began to be embraced in chemistry as the molecular property associated with the absence of certain symmetry elements. By this time, the  $\alpha$ -helix of the polypeptide chain and the double helix of DNA were already familiar to structurally minded chemists—at least to some of them. The sense of a helix or a screw (right- or left-handed) can indeed be unambiguously defined by reference to the human hand: Point the thumb of the right hand along the helix axis; if the helix turns in the direction indicated by the fingers of the right hand, then it is right-handed; if it turns in the opposite direction, then it is left-handed. It makes no difference whether the thumb points along the upward or downward direction of the helix axis. So a definite handedness, a sense of *chirality*, can be assigned to any given helix.

However, although a molecule of *L*-alanine can certainly be described as *chiral* (according to Kelvin's definition), it is not at all clear how its sense of *chirality* is to be defined in terms of right- or left-handedness. The introduction of the terms *chiral* and *chirality* was taken as an improvement over Pasteur's terms *dissymmetry* and *dissymmetric* and have gradually replaced them in the standard chemical vocabulary. Yet, there may be good reasons for reconsidering the earlier terms and for phrasing the basic concepts in terms of symmetry rather than of handedness or *chirality*. At one level it may seem that there is little to choose between the two. The difference between talking in terms of symmetry or in terms of *chirality* is surely one of emphasis rather than of meaning. When we describe objects (molecules) as *chiral* we may give the impression that there is something special about the property *chirality*; that the presence of *chirality* is worthy of notice, that it is the exception rather than the rule.

But nearly everything in the natural world is *chiral*—not just hands and shoes and the molecules of life but also trees, flowers, seashells, snails, indeed all living things if one looks closely enough. It is difficult to think of anything in the natural world that is not *chiral*—crystals of many minerals provide examples. Apart from these macroscopic objects and a few simple molecules, almost all achiral objects are man-made: tables, picture frames, teacups, all designed and manufactured to be symmetric in a certain sense.

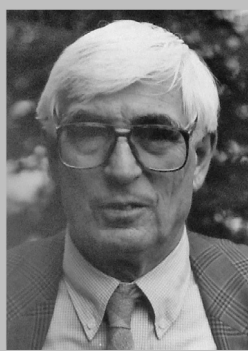
When we talk in terms of symmetry concepts, we should distinguish between the terms *asymmetric* and *dissymmetric*. *Asymmetry* implies the absence of any symmetry; *dissym-*

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metry implies the absence of a particular kind of symmetry, the kind known in group theory as *improper symmetry* or *symmetry of the second kind* (inversion or mirror symmetry). Dissymmetric objects may possess elements of *proper symmetry* such as pure rotational symmetry, a *symmetry of the first kind*, but not elements of improper symmetry. Pasteur, who introduced the term, defined a dissymmetric form as one that is non-superimposable with its mirror image, that is, one that lacks improper symmetry.<sup>[3]</sup> As suggested by the words, here is a fundamental difference between these two kinds of operations, proper and improper. A rotation converts an object into itself in a different position and orientation in space. A rotation can be carried out in infinitesimal steps. It is called a proper operation because it is physically feasible. Reflection converts an object into its mirror image. This process cannot be carried out in infinitesimal steps. It is an all-or-nothing conversion. Here is object, there is mirror image, and there is nothing in between. It is called an improper operation because it is not physically feasible. Only if the object itself possesses inversion or mirror symmetry is it superimposable with its reflection in a mirror. Thus it is not the presence of chirality or handedness that is a special or noteworthy property of objects in general. This property is to be found almost everywhere. Rather, what is special is the presence of certain symmetries in an object that are necessary to confer the property that object and mirror image are superimposable. As Vladimir Prelog put it in a note to the young daughter of a colleague: “The world is chiral and clinal, enjoy symmetry wherever you find it.”

Most natural objects in the world are chiral. To what extent then can we say that different objects are homochiral, that they share the same sense of chirality? To begin with, identical chiral objects are homochiral, by definition. To accept all left hands—yours and mine—as homochiral, we cannot insist on “identical” objects. Some degree of similarity is obviously sufficient. As fellow human beings, we all share a sufficient similarity in the shapes of our hands. Given a collection of human hands—to avoid being too gruesome, let us say plaster casts of human hands—most of us would have no trouble in sorting them into two distinct piles; left hands and right hands. Each pile would consist of homochiral objects. But we cannot push the human aspect of homochirality too far. Apart from convention, it is not easy to see why a left hand should be regarded as having a homochiral relationship with a left shoe.



Jack D. Dunitz (b. 1923) studied chemistry at Glasgow University. After a decade of peripatetic research at Oxford University, Caltech, US National Institute of Health, and the Royal Institution in London, he was appointed Professor of Chemical Crystallography at the ETH Zurich in 1957, a position he held until his retirement in 1990. He has published about 380 scientific papers and is author of “X-Ray Analysis and the Structure of Organic Molecules” (1979, 1995) and “Reflections on Symmetry in Chemistry ... and Elsewhere” (1993) with Edgar Heilbronner.

What about a collection of chiral molecules—molecules of L-alanine, for example? Molecules of L-alanine may exist in solution in several interconvertible conformations. Chemists regard them as homochiral because they share the same spatial configuration of the four bonds formed by the  $\alpha$ -carbon atom. Indeed, there are well established conventions according to which not only L-alanine molecules among themselves are to be classed as homochiral but also as homochiral with molecules of other  $\alpha$ -amino acids with the same spatial arrangement of the four bonds formed by their respective  $\alpha$ -carbon atoms.

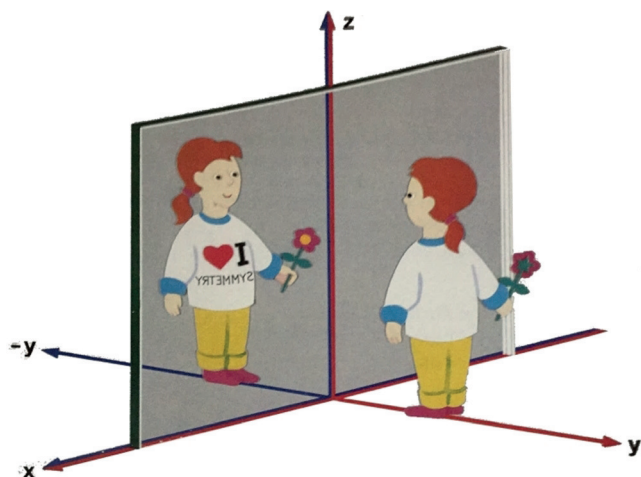
Such a classification principle is provided by the Cahn–Ingold–Prelog (CIP) system,<sup>[4]</sup> according to which the four groups around a tetrahedral centre are put into a priority sequence  $a > b > c > d$  on the basis of certain conventional rules. For alanine,  $a = \text{NH}_2$ ,  $b = \text{COOH}$ ,  $c = \text{CH}_3$ ,  $d = \text{H}$ . The sense of chirality is then assigned by viewing the central atom from the direction opposite to the group of lowest priority, here  $d = \text{H}$ ; if the sense of rotation from  $a$  to  $b$  to  $c$  is clockwise, then the central atom is assigned the chiral descriptor *R* (Latin “rectus”), and if the sense of rotation is anti-clockwise, then the central atom is assigned the chiral descriptor *S* (Latin “sinister”). According to this convention, the natural  $\alpha$ -amino acids all have the chiral descriptor *S*, except L-cysteine, which has the chiral descriptor *R* because the presence of the sulfur atom in the side chain alters the priority sequence. The relationship of the CIP system with handedness is rather remote.

And what about a collection of potatoes? We can agree that potatoes are chiral; they do not show improper symmetry, in fact, they don't show any symmetry at all yet there is no obvious property of potatoes that makes it possible to divide them into two homochiral classes.

Even if we can divide a collection of chiral objects (hands, shoes,  $\alpha$ -amino acid molecules) into two homochiral classes, there is still the problem of whether and how we can ascribe to them a definite sense of chirality or handedness. Earlier I described how this can be done for a helix or a screw, by reference to our right hand. There is also a perfectly unambiguous way by which to describe the handedness of a three-dimensional coordinate system. By convention this is usually taken as a right-handed system. Point the thumb of the right hand along the **a** direction and the stretched index finger along the **b** direction; then to form a right-handed triple **a**, **b**, **c**, the **c** axis is taken in the direction of the middle finger pointed forward. In crystallography, it is mandatory to describe the crystal axes and atomic coordinates in terms of a right-handed system. If the absolute sense of a chiral or polar crystal expressed in this way needs to be reversed, then the atomic coordinates must be inverted ( $x_i, y_i, z_i \rightarrow -x_i, -y_i, -z_i$ ) but not the coordinate axes. Note that reversing the directions of one axis or all three axes changes the handedness of the coordinate system, whereas reversing the directions of two of the axes preserves the handedness. In an orthogonal axis system, reversal of one axis corresponds to reflection through the plane of the other two axes; reversal of two axes corresponds to rotation of  $180^\circ$  about the third axis; reversal of all three axes corresponds to inversion through the origin. (The formal mathematical criterion is the sign of the

determinant of the transformation matrix: +1 for retention of the sense of handedness, -1 for its reversal. This criterion holds in  $n$ -dimensional space, thus providing a generalization of the concept of preservation or reversal of sense of handedness to spaces with any number of dimensions, even though human hands are decidedly three-dimensional objects. For example, in two- or four-dimensional space, inversion through the origin is an operation that preserves the sense of handedness, although in three-dimensional space, inversion through the origin reverses the sense of handedness.)

These considerations should help to clarify the classic puzzle: Why does reflection in a mirror seem to reverse right and left but not up and down? (Figure 1). The answer is that



**Figure 1.** Reflection in a mirror. Reproduced from E. Heilbronner, J. D. Dunitz in *Reflections on Symmetry in Chemistry ... and Elsewhere*, Helvetica Chimica Acta, Basel, **1993**, pp. 70.

reflection in a mirror does not simply change right into left. It changes a right-handed coordinate system into a left-handed one. For example, if the  $x$  and  $z$  axes are chosen in the plane of the mirror, then the direction of the  $y$  axis is reversed by reflection in the mirror. If the  $y$  axis points from the mirror towards the observer, then in the mirror image it points away from the observer. The person that we see in a mirror is not ourself; it is our mirror image. Because we lack a plane of symmetry, this mirror image is not superimposable with

ourself. Compare the image that you see in a mirror with a photograph of yourself. The two are similar but different. Mirror reflection seems to reverse right and left but it really reverses the forward and backward directions of the  $y$  axis and leaves the other two axes unaltered—an improper operation. Right and left are interchanged by mirror reflection but not the directions of the  $x$  and  $z$  axes; East stays East and West stays West. Reflection in the mirror changes you into your mirror image, not merely right hand changed to left hand but also every molecule in your body changed into its enantiomer. “Perhaps looking-glass milk isn’t good to drink,” wondered Alice. Bad language? But it was written in 1871 just a few years after the discovery by Wislicenus that there are two lactic acids that appear to be identical except that solutions of the two substances rotate the plane of polarized light in opposite senses!<sup>[5]</sup> Alice seems to have known a lot of chemistry for a child of her time.

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### Conflict of interest

The authors declare no conflict of interest.

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