On the Definition of Chirality

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In a recent analysis of the chirality of large random supramolecular structures such as spiral diffusion-limited aggregates (DLAs), Katzenelson et al.[1] suggest that the standard definition of Glasgow's Lord Kelvin (I call any geometrical figure, or any group of points, chiral, and say it has chirality, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself)[2] should be modified along with the associated concept of enantiomers. They tentatively propose the following extended definition:

Chirality is the inability to make a structure coincide with a statistical realization of its mirror image; the probe-dependent measure of this inability is the chirality content of the structure.

I would like to discuss this proposal from the standpoint of symmetry and conservation laws in fundamental physics, an approach of which I believe Lord Kelvin, as a physicist, would have approved.

Katzenelson et al.[1] are troubled by the meaning of chirality of an object that can never have an exact enantiomer in practice, such as a DLA. Their concern is misplaced. Kelvin's geometric definition can be expressed in terms of the fundamental operation of parity (space inversion). Provided parity is conserved, as in pure electromagnetic processes, the enantiomers interconverted by the parity operation have exactly the same energy: in the language of modern physics, they are degenerate. As far as physical properties are concerned, chiral objects are distinguished from achiral objects by their ability to support time-even pseudoscalar observables (such as the natural optical rotation angle) with enantiomers showing corresponding observables with *precisely* the same magnitude but opposite sign as required by parity conservation.[3, 4] Precise quantum-mechanical degeneracy of enantiomers is the "gold standard" of the concept and should not be debased. The fact that the exact enantiomer of a given DLA can never be formed in the laboratory (even though it must exist in principle since DLAs are constructed from a finite number of atoms) is irrelevant and should not lead us to abandon perfection as embodied in Kelvin's definition. Why not simply call the clockwise and counterclockwise DLAs *quasi-enantiomers* (or perhaps *statistical enantiomers*) and leave the word enantiomer, unembellished with adjectives such as *virtual*, to describe the mirror-image, as usual? Also, if statistical uncertainty about resolution and the precise positions of atoms is a practical concern, then the same statistical uncertainty should be applied to both enantiomers, not just to the mirror image of one completely determined structure, as stated in the proposed new definition.

At this point it should be mentioned that the conventional mirror-image enantiomers of even small chiral molecules are in fact themselves only quasi-enantiomers since there is a tiny energy difference between them due to the parity-violating weak neutral current interaction.[4-6] Precise degeneracy is recovered if all the particles in the mirror-image molecule are replaced by corresponding antiparticles.[7] However, this imperfection is so small that it can be safely ignored in normal chemistry, but we should be aware of its existence in fundamental work.

Fundamental physics also has something to say about measures of chirality content. Although they may well have practical value in areas such as separation of enantiomers on chiral supports, the measures discussed by Katzenelson et al.[1] and others[8] are of course purely geometrical and appear to have no physical significance at the small chiral molecule level. Chirality content of molecular structures in the form of some fundamental time-even pseudoscalar quantity analogous to, say, energy (a time-even scalar) is in fact a will-o'-the-wisp. Indeed, a hint of this appears in the proposed extended definition of chirality above in which measures of chirality content are recognized to be probe-dependent (e.g., optical rotation angle depends on the wavelength of the incident light beam). The reason that chirality content evaporates under close quantum-mechanical scrutiny is that, neglecting parity violation, chiral molecules are not in stationary states of the Hamiltonian: they oscillate back and forth between the mirror image handed states with an interconversion time proportional to the inverse of the tunneling splitting. This means that any pseudoscalar quantity such as chirality content will average to zero on an appropriate timescale. Chirality content is, however, quantifiable in elementary particle physics where it is a function of the velocity of axially spin-polarized particles relative to the velocity of light and is related to the strength of the weak interaction.[4] This exposes another problem, which the proposed extended definition of chirality shares with Kelvin's original version, since both apply to purely static sources of chirality and so exclude chiral objects, such as circularly polarized photons, where motion is an essential ingredient. The only compelling reason for generalizing Kelvin's definition is to encompass absolute asymmetric synthesis and the concept of chirality in elementary particle physics by including motion-dependent chirality.[3, 4, 7, 9]

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Finally, the analysis of chirality content of spiral DLAs given by Katzenelson et al.[1] appears to be purely two-dimensional. Ignoring the local arrangements of their constituent atoms, these systems are of course achiral in three dimensions. Care needs to be taken in extrapolating any associated physical properties to three dimensions because the physics of chirality in two dimensions is very different from that in three.[10] For example, chiral molecules on an isotropic surface can show new chiroptical phenomena such as huge circular intensity differences in second harmonic scattering, which are generated by pure electric dipole processes.[11]

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Reply to "On the Definition of Chirality"

Further Comments on the Chirality of Large Random Objects

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Prof. Barron has illuminated the question of the chirality of large random objects[1] from an additional point of view, and has added valuable comments to the discussion.[2] The main issue raised is that of geometric versus physical definitions of chirality. It is an important question, which was also addressed recently by Gilat.[3] It is our opinion that these two points of view are correlated and complementary. Thus, we have shown that the *geometric* measure of the degree of centrosymmetricity correlates smoothly with the hyperpolarizability of distorted benzene,[4] that continuous symmetry analysis nicely predicts the melting point of small clusters,[5] that the inhibition efficiency of a series of chiral acetylcholineesterase inhibitors depends linearly on the geometric degree of chirality of these inhibitors,[6] and more. Lord Kelvin has taken in his definition of chirality[7] the strict view of a geometer and not that of a physicist (and here we differ with Barron[2]), and rightly so: symmetry and chirality are strict geometric traits; their physical manifestation is an intimately linked, but totally different story, which may vary wildly with the physical property in question. Optical rotation, mentioned by Professor Barron, is actually a well-known example for this: it can be zero for chiral objects and therefore fails, in principle, to serve as a universal chirality measure. Lord Kelvin's geometric definition is simple in the positive sense and robust: the criterion of nonsuperimposability is general and a sufficient condition for chirality.

It was unnecessary for Barron to "defend" Lord Kelvin (although later on he criticizes Kelvin's definition, see below), because our starting point follows in Kelvin's footsteps with purely geometrical arguments. Our main contribution, as we see it, is to analyze how purely geometric arguments stand vis-à-vis realistic complex structures and the mechanisms of their formation. In fact, our work in reference [1] is a step towards a physical picture of chirality without leaving the safe grounds of geometry. In particular, the issues we emphasized, which have led to the extended treatment of the concept of chirality, are the following:

1. A (large) random object is always chiral even if it had no chiral bias in its construction. However, it is impossible to obtain its enantiomer by repetition of the construction process: the probability of hitting on the exact enantiomer is negligible. The only way to obtain the exact enantiomer is to resort to an alternative *nonrandom*, and therefore artificial construction of a mirror-image object, according to exact guide-lines provided by the original object. In chemistry we have been trained to treat chirality automatically as a structural property which is manifested by a pair of enantiomers. The extension to the always-chiral large random objects, which we call *incidentally chiral objects*,[1] is not trivial. Kelvin's exact superimposability criterion is applicable here as well because it is indifferent to the history of construction; however, its execution is imposable, or at most, artificial. Our link to physical situations is then straightforward: in supramolecular chemistry, randomness leads to chirality, but the enantiomer can never form by the same process (c.f., Ruch's potato[8] and Mislow's analysis of large collections[9]).

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