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Open problem

On quantifying chirality – Obstacles and problems towards unification

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Recently there has been an ever growing interest and activity in the attempts on quantifying chirality which is causing this concept to become a diverse and uncorrelated entity. Possible reasons for this complication are presently discussed. It is shown that it becomes necessary to distinguish between geometric and physical chiralities. For geometrical chiral sets it is necessary to distinguish between equi- and sub-dimensional sets where the metrization of their chirality can be generalized and unified only for equi-dimensional sets. This is accomplished by the method of overlap. For sub-dimensional sets there exists no general and unique mode of quantifying chiralities, except for discrete and finite sets of points such as the corners of polyhedron, for which the approach of Hausdorff distances proves to be an efficient method of quantifying the chirality presented by their distribution. The domain of physical chiralities, although being of natural significance, is still in a premature state of development. Each physical property may have a different chiral measure so that there is no sense in a claim of unification. Equi- and sub-dimensionality exist also for physical chiralities and they can be quantified by the overlap method for equi-dimensional sets.

1. Introduction

In recent years there has been a rapidly growing interest and activity in the domain of structural chirality, in particular concerning the possible metrization of chirality [1–8]. This development, being still in its early stages, is becoming accelerated also by the ever-growing computational ability and technology. Judging from already existing publications it is becoming gradually clearer that this development is bound to face several serious problems concerning the motivation and usefulness of the anticipated ultimum concept of measure of chirality. Unlike many simple physical and geometric properties such as mass, charge, volume, area, length, etc., which are readily quantifiable, the measure of chirality is already becoming diverse and uncorrelated owing to different and inconsistent approaches of quantifying chirality. Moreover, none of the already introduced methods is sufficiently general to propose a measure of chirality for any arbitrarily given chiral object or set. Such lack of generality prevents the formation of a unique metric definition that can be referred to such a question as, "How chiral is any given geometric body?" This difficulty is of substantial nature and it is highly doubtful whether it can be readily overcome, and this is apart from other complications of more technical nature that may exist, such as severe computational difficulties.

It is the purpose of the present article to consider some topological aspects that are involved in this major obstacle towards the unification of chiral measure. Before approaching this subject it may be of interest to notice an obvious motivation for quantifying chirality which is related to the existence of microscopic chirality in nature in the form of chiral molecules and unit cells in crystals [9]. Moreover, the physical effect that leads to this observation, namely optical activity and related effects [10], shows different measurable results for different molecules which strongly indicates the existence of degree of chirality typical to each molecule or unit cell. In view of this it is hardly surprising that there exists strong motivation for quantifying molecular or unit cell chiralities. On the other hand, since molecules or unit cells consist of a finite number of atoms or approximately point-mass nuclei, the geometric representation of a molecule becomes a set of finite number of points to which the problem of quantifying chirality is applied [1,4,5] and a convenient method for this involves the Hausdorff distances [5], first introduced to this domain by Rassat [4]. Such a set may also be regarded as corner points of a polyhedron, the simplest version of which being the tetrahedron. This procedure eventually leads to a question such as, "What is the most chiral tetrahedron?", or to its two-dimensional equivalent: "What is the most chiral triangle?". In contrast to this molecular motivation it would look a little strange to ask: "What is the most chiral potatoe?". As a matter of fact, a perfectly general mode of chiral metrization should be applicable, in principle, to either question.

As things stand now, the geometric aspect of chirality is the main objective in the attempts to quantify chirality. This aspect is treated in section 2 and it is argued that the problem of dimensionality of geometric sets may well be one of the main obstacles that stand in the way towards generalizing and unifying the measure of chirality. But this is not the only problem. The geometric representation of chirality is somewhat over-simplified and even a misleading picture of chirality in nature. In order to appreciate better this argument it is important to notice that the relative positions in space of the massive nuclei in a given molecule are, in fact, an outcome of the spatial distribution of the electronic wave function of the binding electrons throughout the molecule. For this reason it may be more physically justified to ask: "How chiral is the wave-function distribution of the binding electrons in a given molecule?". Such a possible question, premature as it may sound, takes us into the much richer domain of physical chiralities to be discussed in section 3. Let us stress this point a little further by noting that even for the point-mass chiral distribution, if we place n different masses at the corners of some achiral polyhedron, the result will be a chiral molecule due to the physical differences within the massive distribution. Until now, the necessity, as well as the possibility, of quantifying physical chiralities have been largely overlooked with only a few exceptions [7,8].

Before concluding this introduction it ought to be mentioned that the present article is not meant to provide a review of the various methods of quantifying chirality. The interested reader is referred for this to a recent article by Buda et al. [5].

2. Geometric measure of chirality

As mentioned above, the problem of dimensionality may strongly complicate the attempts of quantifying chirality. This point is also discussed by Buda et al. [5] in the context of their presentation of a chiral measure based on the Hausdorff distances. In order to appreciate this point a little better, let us consider any arbitrary collection of geometric properties or sets such as points, linear segments, curves, polygons, surfaces, polyhedra, etc., which may be of use for possible definitions of chiral measures. These properties or sets U_i are usually contained in a space, the dimensionality of which is $d_0 = 2$ or 3. Let us denote the dimensionality of the set U_i by $d(U_i)$ and let us distinguish now between two cases. (a) Sub-dimensional sets which satisfy

$$d(U_i) < d_0 \,. \tag{1}$$

(b) Equi-dimensional sets for which

$$d(U_i) = d_0 \,. \tag{2}$$

For example, a curve U_c in 3d space has $d(U_c) = 1 < d_0 = 3$. The same is true for U_c in $d_0 = 2$. A polyhedron has $d(U_p) = 3 = d_0$, but this example is a little more complex as is demonstrated below. Let us consider a tetrahedron which has a set U_a of 4 corners (or points) where $d(U_a) = 0$; A set U_s of 6 sides where $d(U_s) = 1$; A set U_f of 4 faces, where $d(U_f) = 2$ and a set U_v of one volume where $d(U_v) = 3 = d_0$. Only the last set U_v is equi-dimensional, whereas all other sets or properties or elements are sub-dimensional. It is highly probable that any of these elements can provide for means of defining a measure of chirality of a tetrahedron and, actually, two different properties, the 4 corners [4,5] and the volume [6,7], have already been applied for chiral quantification.

Next let us consider the operation of intersection between any two elements or sets U_i and U_j. Let $U_{ij} = U_i \cap U_j$ then if both U_i and U_j are subdimensional sets, then [11]

$$d(U_i \cap U_j) \leqslant d(U_i), d(U_j) < d_0 \tag{3}$$

if one of the sets, say, U_i is equi-dimensional then

$$d(U_i \cap U_j) = d(U_j) < d(U_i) = d_0 \tag{4}$$

and if both sets are equi-dimensional then

$$d(U_i \cap U_j) = d(U_i) = d(U_j) = d_0\,. \tag{5}$$

The operation of intersection of sets has been proposed as a natural means for metrization of chirality [6,7]. Let U and U^* be two mirror images (enantiomorphs) of a given equi-dimensional set, and let $U \cap U^*$ be their intersection and $V(U \cap U^*)$ be its volume for $d_0 = 3$ or area $S(U \cap U^*)$ for $d_0 = 2$. $V(U \cap U^*)$ or $S(U \cap U^*)$ are now to be maximized by applying rotational and/or translational (RT) transformations on U and/or U^* so that

$$V_0 = V_0(U \cap U^*) = \max[V(U \cap U^*)]\,. \tag{6}$$

Let $v_{\min}$ be defined by

$$v_{\min} = 2[V(U) - V_0] \tag{7}$$

and the volume coefficient of chirality χ_v is given [7] by

$$\chi_v = \frac{v_{\min}}{2V(U)} = \frac{V(U) - V_0}{V(U)}\,. \tag{8}$$

Similarly, for $d_0 = 2$, the area coefficient of chirality is given by

$$\chi_s = \frac{s_{\min}}{2S(U)} = \frac{S(U) - S_0}{S(U)}\,. \tag{9}$$

These, in fact, are the most general measures of chirality for equi-dimensional sets U, for 3d and 2d spaces, respectively.

There are a few interesting topological facts which ought to be realized before applying this definition to actual sets. The most significant question concerns the shape of $U \cap U^*$ of maximal overlap. *Is it chiral or achiral?* This question cannot be readily answered and it is hereby conjectured that for *all convex* sets U it is *achiral*. These include all convex polyhedra and polygons. For the cases where the maximum overlap is chiral there exist *two* maximal overlaps, one being the mirror image of the other [7] and it can be shown [12] (see fig. 1) that a simple translation of U with respect to U^* transforms any chiral intersection $U \cap U^*$ into its mirror image $(U \cap U^*)^*$. The overlap approach to the metrization of geometric chirality is general and unique for all equi-dimensional sets and in this respect the questions of "how chiral is a given polyhedron?" as well as "how chiral is a given potatoe?" can, in principle, be equally well answered, although these may well be uneasy questions to answer.

Another approach to quantifying chirality that emerges from the opposite extremum of dimensionality has recently become useful. This approach has been introduced by Rassat [4], developed and implemented by Buda et al. [5] and it is based on the Hausdorff distances (HD) method. The HD approach is highly applicable for discrete and finite sets of points which are the geometric presentations of molecular point masses structures. This mode of chiral measure is extremely sub-dimensional, where $d_0 = 0$ and is not based on the overlap approach. Buda et al. [5] employ this approach to quantify chirality of triangles and tetrahedra which are

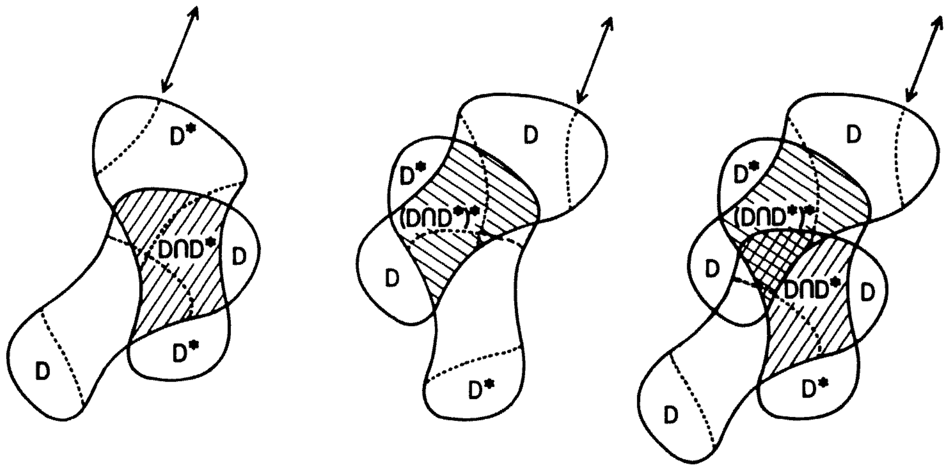

Fig. 1. D and D^* are two enantiomorphs of the same set. In (a) an arbitrary intersection $D \cap D^*$ of these enantiomorphs is shown whereas in (b) the mirror image $(D \cap D^*)$ is shown. In (c) both intersections are shown simultaneously. The direction of the arrow points along the relative translation of D with respect to $D*$ in order to transform $D \cap D^*$ to $(D \cap D^*)^*$.

defined by the relative positions of their corner points. The main problem with the HD approach is that it is limited to finite sets of points and it becomes prohibitively awkward to apply it to infinite and continuous sets of points. For this reason it becomes impossible for the HD method to quantify the chirality of a triangle or a tetrahedron by treating them as convex sets of points. This is true for any continuous set of points, and therefore it is meaningless to ask: "How chiral is a given potatoe?" by applying the HD method. The finite and discrete feature of the HD method severely limits its applicability and therefore it cannot be regarded as a general method of quantifying chirality. Another shortcoming that limits the generality of the HD method in its present form is its lack of applicability to physical chiralities. In view of these deficiencies it becomes doubtful if this approach can become the basis of unification of chiral measure. It is interesting to notice that by applying the constraints of the HD method on the corner points of two enantiomorphs of a given body, being a polygon or polyhedron, it is possible to obtain a so-called [5] "optimal overlap" between the two enantiomorphs. Such a superimposition is actually an overlap between empty sets of points and it has no straightforward relation to the maximal overlap of equi-dimensional sets.

In conclusion, there exists a deep gap between the two approaches described here. The overlap approach is quite general for equi-dimensional sets or bodies, whereas the Hausdorff distances approach is limited to discrete and finite sets of points. This gap between equi and sub-dimensional approaches is hard to bridge and it is causing diversity and inconsistency between different measures of chirality. The overlap approach is only of partial success since it is not applicable to sub-dimensional sets, whereas the Hausdorff distances method is efficient only for discrete and finite sets of zero dimensionality. Actually, the well-motivated attempts to quantify chirality for sub-dimensional sets may be the main cause leading to high diversity and inconsistency of different modes of quantifying chirality.

3. Physical chirality

In contrast to the rapid developments in geometric chirality there has hardly been any interest in the domain of physical chirality which is to be regarded as the natural extension of geometric chirality. There are several reasons for this lack of activity. One of these is probably a certain lack of awareness of its significance. A more obvious reason is probably the anticipated difficulties and complications in the attempts at quantifying physical chirality, in particular at its practical calculation. It is quite feasible that a deeper understanding and insight into the problems of quantifying geometric chirality will become of preliminary help before approaching physical chiralities. For these reasons the discussion carried out here is meant to be more compact and rather incomplete.

At first let us recall that a physical chirality is related to the presence of asymmetry in the spatial distribution of any physical property such as mass or charge density or the distribution of $|\psi|^2$, the electronic wave function or of $(\psi\Omega\psi^*)$, Ω being any relevant quantum operator. It is quite clear that the same dimensional qualifications exist for physical as for geometric chirality. There are equi- as well as sub-dimensional physical sets and, as a matter of fact, the chiral quantification of equi-dimensional physical sets has already been proposed [7] and this is performed in an analogous way to the overlap method [7,8]. On the other hand, the HD method in its present form is inapplicable to any physical chirality, not even for discrete and finite sets of varying mass points. Actually, as has already been mentioned, the chiral measure of a molecular or unit cell structure may well be more relevant to $|\psi|^2$, or $(\psi\Omega\psi^*)$, continuous distributions throughout the molecule rather than to the relative locations of the nuclear masses. But even so, the massive distribution throughout the molecule is also of physical rather than geometric nature. These may well be strong arguments in favour of physical rather than geometric chiralities, but they are also quite premature for a rapid development in view of may practical problems. For instance, in many partical cases the exact distribution of $|\psi|^2$ is only crudely known, and therefore hardly usable. In addition, it is important to emphasize that in contrast to geometric properties such as volume, area and length which are homogeneously distributed, physical properties can well be inhomogeneous. This introduces certain topological complications which make the problem even less accessible. For example, it is quite meaningless to describe an inhomogeneous physical set as convex or simply connected. Nevertheless, like in the case of geometric chirality of equi-dimensional sets, there also exist for physical chiralities two possibilities of maximal overlap, namely, being achiral or chiral. For the second case there are also two overlaps, one being the mirror-image of another. Another important point is that for physical chiralities, even of equi-dimensional sets, it is meaningless to look for uniqueness of chiral measure since for any physical property, say i, there exists a different measure χ_i. Moreover, it may be quite possible that given a physical chiral set be characterized as L with respect to one property and as D or achiral with respect to another [7]. For these reasons it is senseless to strive for a unification of different physical chiral measures, and each one stands independently on its own. Nevertheless unification can be accomplished, in principle, for each physical chirality of equi-dimensional sets by employing the overlap method.

Before concluding this section it may be of importance to mention the subject of chiral interaction introduced recently by the same author [13,14]. There exist many devices such as windmills and Crookes' radiometer which interact with various media such as wind or radiation and as a result they begin to rotate in one preferred direction out of two possible ones. A necessary condition for such devices is that their surface of contact with the medium be chiral. For such devices the chiral distribution of the physical property is *on a surface* and therefore they are to be considered as sub-dimensional sets. It is of special interest to notice that for Crookes' radiometer the physical chirality is not in the shape but rather in the colors of the wings of the device, namely, black and silver. In fact, the chirality is in the distribution of the physical property of optical absorption over the surface of the wings which comes in contact with the light radiation. The phenomenon of chiral interaction has been extended to microscopic systems such as soluble proteins [14] but as yet it has not been verified by experiment. The possible presence of such modes of chiral interaction extends considerably the significance of physical chiralities.

In addition let us also recall that there exists the physical effect of rotation of the vector polarization of light by chiral molecular structure [10]. Similar effect exists also in the scattering of polarized electrons by chiral molecules [15].

4. Conclusions

As indicated throughout this article, its main purpose is to present and discuss various problems and difficulties that stand as obstacles toward possible generalization and unification of chiral metrization. The phenomenon of chirality is to be categorized into geometric and physical chiralities. For geometric chirality it is shown that there exist two kinds of chiral sets, namely, equi- and sub-dimensional sets where the metric of chirality can be generalized and unified only for equi-dimensional sets and this is accomplished by the overlap method [6,7]. For this case the shape of maximum overlap can be either chiral or achiral, whereas for chiral overlap there exist two enantiomorphs of the same overlap that can be transformed from one to another by a pure translation. It is conjectured that for convex chiral sets the maximum overlap is *achiral.*

In the case of discrete and finite sets of points, being sub-dimensional of $d_0 = 0$, there exists the method of Hausdorff distances [5] for quantifying the chiral distribution of these points. This approach cannot be readily generalized beyond zeroth dimensionality, which severely limits its generality. This approach is useful for quantifying the geometric chirality of molecular structures.

The concept of physical chirality, being well less developed, is also discussed in brief. It is shown that physical chiral sets can also be characterized as equi- or sub-dimensional. The chirality of equi-dimensional physical set can be quantified by the overlap method [7,8] using a slight extension of the geometric overlap for possible inhomogeneous distributions of physical properties. On the other hand, the Hausdorff distances approach is not readily applicable for chiral quantification of sub-dimensional discrete sets of physical nature such as the point-mass distribution throughout a molecule. The quantification of physical chirality, being specific for each physical property, cannot, in principle, be generalized to a unified mode of physical chiral measure.

Note added in proof

The conjecture mentioned in the present article concerning the shape of $U \cap U^*$ for the maximal overlap has recently been proven to be *achiral* for convex sets U. This theorem will be presented in a forthcoming article by G. Gilat and Y. Gordon.

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