A unification of chirality measures

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A general classification of chirality measures is suggested, based on a new unifying scheme. Two classes of measures - congruity and resolution type - are defined and discussed. All chirality measures so far reported in the literature are found to belong to one of these two classes. At a higher level of unification, a more general construction is suggested that includes congruity and resolution measures as limiting cases. It is shown that congruity measures are nested in clusters of eight, generated by combinations of their possible choice of a reference object (chiral vs. achiral), representation form (optimized vs. factorized) and type of chiral object under consideration (discrete vs. continuous). Each of the eight cases can have an infinite number of variations depending on the choice of averaging scheme. The problem of dimensionality is discussed for congruity measures and is shown to be unresolvable only for the case of chirality measures based on the discrete metric (e.g. overlap measures).

1. Introduction

Since Guye's pioneering work on chirality functions, more than a century ago [1], there has been a continuing interest in the development of methods for the quantification of chirality (for a recent review see [2]). This interest continues unabated (for example, see [3-10]).

An object \( X \) (no matter whether physical or geometrical) is chiral if and only if it is nonsuperposable upon its mirror image \( \overline{X} \) (\( X \neq \overline{X} \)). A chirality measure \( \chi \) that quantifies this property can equal zero if and only if the object is achiral [2]:

\[
\chi(X) = 0 \quad \iff \quad X = \overline{X}.
\] (1)

It has been demonstrated [11] that any two chiral objects in three- and higher-dimensional space can be chirally connected. This has immediate implications for the choice of functions suitable for use as chirality measures: no sign-changing continuous functions, and, in particular, no continuous pseudoscalar functions, \( \eta(\overline{X}) = -\eta(X) \), can be used as chirality measures in three- and higher-dimensions since such functions necessarily have chiral zeroes (\( \eta(X) = 0 \) for \( X \neq \overline{X} \)) and this violates conditions (1). Thus, only sign-preserving functions can be used as chirality measures, and therefore, without loss of generality, we can restrict ourselves exclusively to nonnegative functions:

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It has been recognized [2] that chirality measures can be subdivided into two types: those that gauge the extent to which a chiroid differs from an achiral reference object (measures of the first kind) and those that gauge the extent to which two enantiomorphs differ from one another (measures of the second kind). Subsequently it was demonstrated [6] that the Hausdorff chirality measure [12] and the “continuous symmetry measure” [4] represent special cases within the same class of functions defined within the framework of a unified approach. Still, a more general unification would be highly desirable as “the measure of chirality is already becoming diverse and uncorrelated owing to different and inconsistent approaches of quantifying chirality” [9]. In what follows we introduce such a scheme and demonstrate that all chirality measures suggested so far fit into that unified scheme.

It is shown in section 2 that almost all chirality measures fall into the same class, one in which the degree of chirality of a chiroid $X$ is defined with reference to another, chiral or achiral object $X_{ref}$: the less these two objects match, the more chiral is $X$. We call these congruity-based chirality measures (congruity measures for short). There is, however, one approach [5] that does not fit into this picture and that opens up an entirely new dimension in discussions of chirality. In this approach, the degree of chirality is estimated by the lowest resolution sufficient to recognize that an object is chiral. Following Mezey [5], we call these resolution-based chirality measures (resolution measures for short) and discuss them in section 3. We conclude with section 4, which introduces a construction that unifies congruity and resolution measures.

An important problem is the extent to which chirality measures can be generalized, and, in particular, the extent to which they can be applied to discrete vs. continuous and to sub- vs. equi-dimensional objects [9]. We discuss this below and show that most chirality measures are universal enough to handle this problem, or at least can be easily upgraded to such a universal form.

2. Congruity measures

2.1. DEFINITIONS: DISTANCES AND MEASURES

The measures of this type, which seem to be the most popular ones due to their transparent and natural definition, gauge the chirality of a chiroid $X$ by its degree of nonsuperposability with a given reference object $X_{ref}$. The latter can be either an appropriately selected achiral object $X_o$ (measures of the first kind) or the enantiomorph $\overline{X}$ (measures of the second kind). The choice of $\overline{X}$ as $X_{ref}$ seems to have certain advantages since this object is fully defined by reflection. In the case of an achiral reference object $X_o$, shape and size are not rigidly fixed, and need to be varied depending on the mutual orientation of $X$ and $X_o$. This makes the problem