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T-hull relations for shape envelopes of molecular contours

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Abstract. Electron density T-hulls have been proposed earlier for the analysis of various molecular shape constraints in solvent–solute interactions and in biomolecular complementarity. Some relations between T-hulls have been applied to relative shape analysis of molecular electron density contour surfaces (MIDCOs). In this contribution, theorems on several additional properties of T-hulls are proven. The results are suitable for comparisons between shape analysis results obtained using different reference molecules, for example, if shape comparisons are carried out using different solvent molecules as shape reference.

Key words: Electron density T-hulls – Molecular contour – Solvent molecules – Shape analysis results

1 Introduction

For a given reference object T, the ordinary *T-hull* $\langle S\rangle_T$ of an object S is the intersection of all rotated and translated versions of T which contain S. Elaboration of the definition and some fundamental properties of T-hulls have been described in Refs. [1–3] and will not be repeated here. The T-hull is a generalization of the α-hull introduced by Edelsbrunner et al. [4]. For α-hulls, the reference objects T are restricted to generalized disks of radius $1/\alpha$; for the more general T-hulls the reference object T can be chosen essentially arbitrarily [1–3]. In Fig. 1, a simple example is shown where the reference object T is a disk; in Fig. 2 a more general example is shown. T-hulls are useful for relative shape characterization of molecules; for example, if object T is chosen as the complement of a body representing the shape properties of the solvent molecule, then the T-hull of a solute molecule S describes the solute molecule encompassing spatial region which is contactable by solvent molecules, and as such $\langle S\rangle_T$ neatly encodes geometrical constraints on solute–solvent interactions.

2 Shape envelopes and *T*-hull relations

In Fig. 2, some of the basic concepts and one of the new results are illustrated by several sketches. This example also illustrates one of the applications of the results

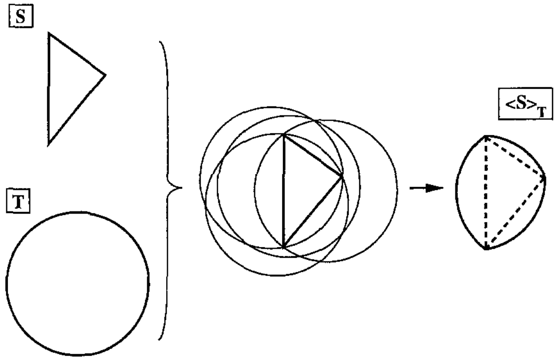

Fig. 1. The generation of the T-hull $\langle S \rangle_T$ of a triangle S using a disk T as reference object. This T-hull $\langle S \rangle_T$ is in fact an α-hull where α is the reciprocal of the radius r of the disk T

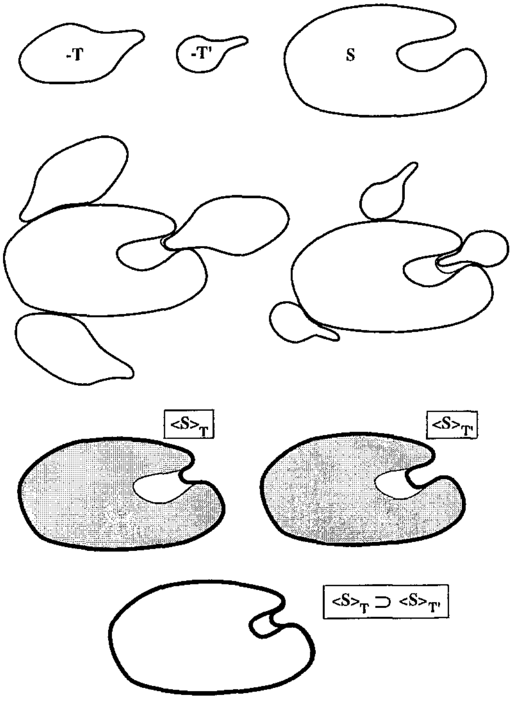

Fig. 2. Illustration of some T-hull relations and the statement of Theorem 1, with respect to complements $T = -(-T)$ and $T' = -(-T')$ of reference objects $-T$ and $-T'$, respectively, taken as representatives of two different solvent molecules, and object S, representing a solute molecule

for the study of relative shapes and sizes of solvent contact surfaces. One may regard objects $-T$ and $-T'$ (where the notation $-T$ stands for the complement of reference object T) as two different solvent molecules. The T-hulls and T'-hulls of various objects, such as $\langle S \rangle_T$ and $\langle S \rangle_{T'}$ of the solute molecule S, are interpreted as the intersections of all those versions of the complements $-(-T) = T$ and $-(-T') = T'$ of the solvent molecules $-T$ and $-T'$ which contain the solute molecule S. Notice that each version of T that contains S corresponds to an arrangement of solvent molecule $-T$ and solute molecule S where the solvent $-T$ and solute S do not overlap. Taking the intersections for all these arrangements, the corresponding T-hull $\langle S \rangle_T$ is obtained. Similarly, the T'-hull $\langle T \rangle_{T'}$ of $-(-T) = T$ is the intersection of all those versions of the complement

$-(-T')=T'$ of the second solvent molecule $-T'$ which contain the complement $-(-T)=\mathrm{T}$ of the first solvent molecule $-T$.

First, we shall prove an elementary property of T-hulls, illustrated in Fig. 1.

Theorem 1. *If T and T' are two reference objects such that*

$$\langle T\rangle_{T'}=T, \tag{1}$$

then for the respective T-hull and T'-hull of S, the relation

$$\langle S\rangle_T \supset \langle S\rangle_{T'} \tag{2}$$

holds.

Proof. If $\langle T\rangle_{T'}=T$, then T is an intersection of some versions of T'. Then, indeed, every version of T is an intersection of some versions of T'. Consequently, $\langle S\rangle_T$, that is an intersection of some versions of T, is also an intersection of some versions of T', where each version of T' contains S. However, this latter intersection does not necessarily involve all versions of T' which contain S. By contrast, $\langle S\rangle_{T'}$ is an intersection of all versions of T' which contain S. Consequently, relation (2), $\langle S\rangle_T \supset \langle S\rangle_{T'}$, follows. Q.E.D.

For the general case, this result cannot be made stronger by replacing the sign of inclusion with the sign of equality in relation (2). The following example shows that if $\langle T\rangle_{T'}=T$, then $\langle S\rangle_T=\langle S\rangle_{T'}$ is not necessarily true. If, for bounded reference sets T and T', $T'\supset T$, $T'\supset S$, but S does not fit within any version of T, that is, if $T_v \not\supset S$ for every version T_v, then $\langle S\rangle_{T'}$ is bounded and $\langle S\rangle_T$ is the empty intersection, that is, the full space. Consequently, $\langle S\rangle_T \supset \langle S\rangle_{T'}$, but $\langle S\rangle_T \neq \langle S\rangle_{T'}$. It is easy to find other examples.

Based on this theorem, the property $\langle T\rangle_{T'}=T$ suggests a simple method for predicting some of the results of relative shape analysis with reference to one solvent from a relative shape analysis with reference to another solvent. If T_1 and T_2 are the complements of shape representations of the two solvent molecules, and if the condition $\langle T_1\rangle_{T_2}=T_1$ holds, then according to the proven theorem, $\langle S\rangle_{T_1}\supset\langle S\rangle_{T_2}$. This means that the second solvent is at least as "accommodating" for the actual shape of the solute molecules S as the first solvent, and one can *a priori* expect stronger attractive interactions between the solute and the second solvent than those between the solute and the first solvent.

The family of versions T_v of reference object T can be chosen in a variety of ways; some choices have been described in [1,2]. Whereas the most important transformations within the chemical context are the combinations of 3D translations and rotations, nevertheless, various constrained motions, as well as additional freedoms, such as reflections, have been considered [1,2].

In many instances, the constraints can be described by group theoretical means. For example, we might consider a group $\boldsymbol{G}$ of geometric transformations G, a subgroup of affine transformations, such as rotations, translations, reflections, collineations, and combinations thereof.

Two versions, T_v and $T_{v'}$, of reference object T are considered $\boldsymbol{G}$-equivalent if both T_v and $T_{v'}$ are derived from reference object T by an allowed transformation. The set of $\boldsymbol{G}$-equivalent versions T_v of T is denoted by

$$V(T,G)=\{GT:G\in\boldsymbol{G}\}. \tag{3}$$

Set $V(T, G, S)$ is a subset of $V(T, G)$, containing all those versions T_v from $V(T, G)$ which contain set S:

$$V(T, G, S) = \{T_v \in \mathrm{V}(T, G) \colon S \subset T_v\}. \tag{4}$$

The G-constrained T-hull $\langle S \rangle_T$ of S is

$$\langle S \rangle_T = \bigcap_{T_v \in V(T, G, S)} T_v. \tag{5}$$

Theorem 2. *If for objects S, S', and reference object T the relations $S \subset S' \subset T$ hold, then for the respective T-hulls*

$$\langle S \rangle_T \subset \langle S' \rangle_T, \tag{6}$$

with $\langle S \rangle_T = \langle S' \rangle_T$ if $S' \subset \langle S \rangle_T$.

Proof. Since $S \subset S'$, there can be no more $T_{v'}$ versions containing S' than T_v versions containing S, and one has

$$V(T, G, S) \supset V(T, G, S'). \tag{7}$$

Consequently, the intersection of all $T_v \in V(T, G, S)$ will be a subset of the intersection of all $T_{v'} \in V(T, G, S')$, hence

$$\langle S \rangle_T \subset \langle S' \rangle_T, \tag{8}$$

thereby proving the main assertion of the theorem.

If $S' \subset \langle S \rangle_T$, then S' is contained in every version $T_v \in V(T, G, S)$, hence

$$V(T, G, S) \subset V(T, G, S'). \tag{9}$$

Consequently, if $S' \subset \langle S \rangle_T$, then the intersection of all $T_{v'} \in V(T, G, S')$ will be a subset of the intersection of all $T_v \in V(T, G, S)$, hence

$$\langle S \rangle_T \supset \langle S' \rangle_T. \tag{10}$$

That is, if $S' \subset \langle S \rangle_T$, then combining relations (8) and (10) gives

$$\langle S \rangle_T = \langle S' \rangle_T. \qquad \text{Q.E.D.} \tag{11}$$

Note that the case of equality, $S \subset S' \subset \langle S \rangle_T$ implying $\langle S \rangle_T = \langle S' \rangle_T$, is Theorem 3 of Mezey [3].

Since $S \subset \langle S \rangle_{S'}$ always holds, and if $S \subset S' \subset T$, then $\langle S \rangle_{S'} \subset T$, hence

$$S \subset \langle S \rangle_{S'} \subset T, \tag{12}$$

consequently, we may replace S' by $\langle S \rangle_{S'}$ in Theorem 2 to yield

Corollary. *For $S \subset S' \subset T$,*

$$\langle S \rangle_T \subset \langle \langle S \rangle_{S'} \rangle_T, \tag{13}$$

with $\langle S\rangle_T = \langle\langle S\rangle_{S'}\rangle_T$ *if* $\langle S\rangle_{S'} \subset \langle S\rangle_T$. *The special case* $S' = T$ *yields Theorem 1 of Mezey* [3].

Theorem 3. *For* $S \subset S' \subset T$, *the relation*

$$\langle S\rangle_T \subset \langle S\rangle_{\langle S'\rangle_T} \tag{14}$$

holds, with

$$\langle S\rangle_T = \langle S\rangle_{\langle S'\rangle_T} \tag{15}$$

if

$$\langle S\rangle_T = \langle S'\rangle_T. \tag{16}$$

Proof. The intersection of members of set $V(\langle S'\rangle_T, G, S)$ is such that these members are allowed G-transforms of intersections of members of set $V(T, G, S')$. That is, the set $\langle S\rangle_{\langle S'\rangle_T}$ is an intersection of certain G-transforms $T_{v'} = G'T$, $G' \in \boldsymbol{G}$, where each such GT transform contains S:

$$S \subset T_v = G'T. \tag{17}$$

The family $V(\langle S'\rangle_T, G, S)$ of these $T_{v'} = G'T$ transforms is a subset of the family $V(T, G, S)$ of versions T_v of T fulfilling the condition

$$S \subset T_v = GT. \tag{18}$$

That is, for the family $V(T, G, S)$ of all allowed G-transforms $T_v = GT$ which contain set S, the following holds:

$$V(T, G, S) \supset V(\langle S'\rangle_T, G, S). \tag{19}$$

Consequently, for the corresponding intersections

$$\langle S\rangle_T \subset \langle S\rangle_{\langle S'\rangle_T} \tag{20}$$

holds, and this proves the main assertion of the theorem.

If $\langle S\rangle_T = \langle S'\rangle_T$, then $\langle S\rangle_{\langle S\rangle_T}$ is the intersection of various allowed transforms $G < \langle S\rangle_T$ of $\langle S\rangle_T$, and this intersection cannot exceed $\langle S\rangle_T$ itself:

$$\langle S\rangle_T \supset \langle S\rangle_{\langle S\rangle_T}. \tag{21}$$

Comparison of this relation to relation (20) taken with $S' = S$ yields

$$\langle S\rangle_T = \langle S\rangle_{\langle S\rangle_T}. \qquad \text{Q.E.D.} \tag{22}$$

Setting $S' = S$ in the main result of the theorem yields Theorem 2 of Mezey [3]. Theorem 1 of this work can also be regarded as a special case of Theorem 3 proven here: if $\langle S'\rangle_T = S'$, then by renaming T as T', and renaming S' as T, Theorem 1 follows.

For iterated T-hulls the following notation is useful:

$$\langle S\rangle_T = \langle S\rangle_{\text{sub}}(T). \tag{23}$$

Corollary. *For a series of nested sets,*

$$S^{(0)} \subset S^{(1)} \subset S^{(2)} \subset S^{(3)} \subset \cdots S^{(k)} \subset T, \tag{24}$$

the relation

$$\langle S^{(0)}\rangle_T \subset \langle S^{(0)}\rangle_{\text{sub}}(\langle S^{(1)}\rangle_{\text{sub}}(\langle S^{(2)}\rangle_{\text{sub}}(\langle S^{(3)}\rangle \cdots \text{sub}(\langle S^{(k)}\rangle_{\text{sub}}(T))\cdots))) \tag{25}$$

holds.

3 Summary

The T-hull, a generalization of the convex hull of objects according to a "bias" with respect to a reference shape T, offers a new tool for molecular shape analysis. Several properties of T-hulls are proven, offering shortcuts when comparing shape analysis results obtained with different reference shapes, for example, with respect to different solvent molecules.

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