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ON A METHOD OF NONLINEAR OPTIMIZATION FOR THE COMPARISON OF SPATIAL STRUCTURE OF MOLECULES

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Abstract: To compare the geometry of two or more geometric structures consisting of N ordered points, and which can be considered as solids in three-dimensional space, we developed a method based on the minimization of a certain comparison function. This function is the sum of squared distances between pairs of elements of the two structures under comparison with the same indices. Distances change when changing the mutual orientation of the structures with all possible shifts and rotations of the structures as rigid bodies. The comparison function is minimized with respect to Euler angles, provided that centers of mass of two compared structures are superposed. The minimization of the comparison function with respect to Euler angles is carried out numerically by the Rosenbrock method. The developed method for comparison of geometric structures is used to solve problems in structural chemistry, that is to compare molecules with the same structural formula in one crystal.

Keywords: Conformer, Euler angles, Rotation Matrix, Optimization, Rosenbrock Method.

MSC: 49M30.

1. INTRODUCTION

This paper is devoted to the theoretical and numerical study of a mathematical model for comparing two molecules in a problem arising in structural chemistry.

This model reduces to comparing two objects consisting of N ordered points with rigid geometry, behaving as solids in $\mathbb{R}^3$. The principle of comparison in this model is based on the optimization of the superposition of these two objects using shifts and rotations. The optimal superposition of these objects involves the minimization of a certain function comparing the geometry of the objects with respect to shifts and rotations. The function is represented as the sum of distance functions between the points of two objects with the same indices. To study the comparison function, we use optimization theory [1]–[4] and Rosenbrock zero-order method [5] to minimize it. The obtained results are used to study the geometry of real molecules.

Molecules of many substances can exist in the form of conformers [6] (conformation – spatial arrangement of atoms in the molecule), where the substance has the same structural formula (with the same connection order of atoms) but different spatial structure. In this case we have the problem of objective comparison of their geometry in space, as the standard characteristics-bond lengths (interatomic distances) and valence angles do not always show differences in the geometry of molecules. In addition, there is a need to compare fragments of chemically different molecules, or the nearest environment of atoms (coordination polyhedra), or other large or small complexes of atoms. For this purpose, we propose our newly developed method of quantitative comparison of the geometry of molecules based on the minimization of a certain comparison function by shifting and rotating molecules. It is proved that the minimum with respect to shifts is achieved by the superposition of some characteristic points, conventionally called centers of mass of molecules. The search for the minimum with respect to angles of rotation is carried out by the Rosenbrock zero order method.

2. MATHEMATICAL MODEL DESCRIPTION

In the following two sections we will give some definitions and prove a theorem.

Definition 1. *A geometric structure, or simply a structure, is a rigid geometric construction of N ordered points in $\mathbb{R}^3$ with coordinates (x_i, y_i, z_i), $i = 1, \ldots, N$, whose motion in $\mathbb{R}^3$ is the same as that of a solid body.*

We assume that to each point of the structure with the number i, corresponds the weight coefficient $w_i \geqslant 0$, and $\sum_{i=1}^{N} w_i = W > 0$. Let $i_k, k = 1, \ldots, K$ be indices of non-zero weights w_i. Then

$$W = \sum_{i=1}^{N} w_i = \sum_{k=1}^{K} w_{i_k} > 0. \tag{1}$$

Let two geometric structures be given, where each consists of N points with coordinates $(x_{1,i}, y_{1,i}, z_{1,i})$ and $(x_{2,i}, y_{2,i}, z_{2,i})$, $i = 1, \ldots, N$. For each fixed index i, the point with coordinates $(x_{1,i}, y_{1,i}, z_{1,i})$ of the first structure corresponds to the point $(x_{2,i}, y_{2,i}, z_{2,i})$ of the second structure.

Let the geometry of the two structures be the same. Take any two points given by the vectors $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$, which are equally positioned with respect to the corresponding geometric structure. In particular, as $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$, we can take the points of the corresponding structures with the same indices. Then the identical points can be matched through the rotations until the two structures coincide. If the structures under consideration have different geometry, it is natural to formulate the problem of optimal "superposition" of structures by means of various shifts and rotations of one structure relative to another as solid bodies.

The criterion of optimal superposition of two geometric structures will be related to the minimum with respect to shifts and rotation angles (Euler angles [7]) of the comparison function of the form

$$U(\mathbf{r}_{1,0}, \mathbf{r}_{2,0}, \varphi, \theta, \psi) = \sum_{i=1}^{N} w_i |\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})|^2, \tag{2}$$

where the vectors $\mathbf{r}_{1,i}$ and $\mathbf{r}_{2,i}$ determine the position of points in the first and the second structure; the vectors $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ determine the displacement of the first and the second structures to the corresponding points; $Q = Q(\varphi, \theta, \psi)$ is the rotation matrix

$$\begin{pmatrix} \cos\psi\cos\varphi - \sin\psi\sin\varphi\cos\theta & -\cos\psi\sin\varphi - \sin\psi\cos\varphi\cos\theta & \sin\psi\sin\theta \\ \sin\psi\cos\varphi + \cos\psi\sin\varphi\cos\theta & -\sin\psi\sin\varphi + \cos\psi\cos\varphi\cos\theta & -\cos\psi\sin\theta \\ \sin\varphi\sin\theta & \cos\varphi\sin\theta & \cos\theta \end{pmatrix}$$

corresponding to Euler angles ψ, θ, φ (the angle of precession, the angle of nutation, and the angle of rotation, respectively).

Thus, the function U of the form (2) is the sum of the distances between the homonymous points of two geometric structures with weights w_i after matching the points determined by the vectors $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ and after rotation of the second structure relative to the first one. We will examine some problems of minimizing the comparison function of two structures of the form (2).

3. MINIMIZING THE COMPARISON FUNCTION OF GEOMETRIC STRUCTURES

We show that by superposing some characteristic points of two geometric structures, it is possible to reduce the problem of minimization of the comparison function with respect to a full set of variables to finding the minimum of the function U with respect to rotation angles φ, θ, ψ.

Here we give a more complete and rigorous formulation and the proof of the idea proposed in [8].

Theorem 2. *The minimum of the function U is achieved at the point corresponding to "centers of mass" of two geometric structures. "Centers of mass" are determined by the vectors*

$$\mathbf{r}_{j,0} = \frac{1}{W} \sum_{i=1}^{N} w_i \mathbf{r}_{j,i}, \quad j = 1, 2. \tag{3}$$

Proof. In function (2) let us fix the angles φ, θ, ψ, and therefore we fix the matrix Q. Thus, we consider the function (2) with respect to the variables $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$. With respect to these variables, the function is convex and quadratic, so its minimum on $\mathbf{r}_{1,0}$, $\mathbf{r}_{2,0}$ is achieved at the points where the derivative is zero. Thus, we obtain the equations

$$\frac{\partial U}{\partial \mathbf{r}_{1,0}} = 0, \quad \frac{\partial U}{\partial \mathbf{r}_{2,0}} = 0. \tag{4}$$

Differentiating, we have

$$-2\sum_{i=1}^{N} w_i(\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})) = 0, \tag{5}$$

$$2Q^T\sum_{i=1}^{N} w_i(\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})) = 0. \tag{6}$$

Due to the non-degeneracy of the matrix Q^T, the equation (6) is equivalent to (5). By solving (5) with respect to $\mathbf{r}_{1,0}$, we obtain

$$\mathbf{r}_{1,0} = \frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{1,i} - Q\Big(\frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{2,i} - \mathbf{r}_{2,0}\Big). \tag{7}$$

For the expression in the bracket (8) to equal zero, we choose vector $\mathbf{r}_{2,0}$ from the condition

$$\mathbf{r}_{2,0} = \frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{2,i}. \tag{8}$$

Then from (7), it follows

$$\mathbf{r}_{1,0} = \frac{1}{W}\sum_{i=1}^{N} w_i\mathbf{r}_{1,i}. \tag{9}$$

As noted above, equations (5) and (6) are equivalent. Therefore, the points $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ obtained from (8) and (9) satisfy equations (4), and the function (2) with fixed angles φ, θ, ψ attains its minimum at $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$. The theorem is proved.

Thus, the minimum of the function (2) corresponds to the shift of the "centers of mass" of geometric structures, determined by the formulae (9) and (8) into the coordinate center. The function (2) can now be viewed as a function of rotation angles

$$U(\varphi, \theta, \psi) = \sum_{i=1}^{N} w_i|\mathbf{r}_{1,i} - \mathbf{r}_{1,0} - Q(\varphi, \theta, \psi)(\mathbf{r}_{2,i} - \mathbf{r}_{2,0})|^2, \tag{10}$$

where $\mathbf{r}_{1,i}, \mathbf{r}_{2,i}$ are given as coordinates of geometric structures, and "centers of mass" $\mathbf{r}_{1,0}$ and $\mathbf{r}_{2,0}$ are calculated by formulae (9) and (8). The minimum of function (10) is determined by the rotation angles φ, θ, ψ.

Let the minimum of function $U = U(\varphi, \theta, \psi)$ of the form (10) be attained at the point $(\varphi_0, \theta_0, \psi_0)$. The measure of proximity of two geometric structures will be represented by the value

$$s = \Big(\frac{U(\varphi_0, \theta_0, \psi_0)}{W}\Big)^{1/2}. \tag{11}$$

This value can be considered as a quantitative characteristic of the proximity of geometric structures since it is the average distance between points with the same indices in two structures after "superposition".

We call two structures "approximately equal" if

$$s = \Big(\frac{1}{W} \min_{\varphi,\theta,\psi} U(\varphi, \theta, \psi)\Big)^{1/2} = \Big(\frac{U(\varphi_0, \theta_0, \psi_0)}{W}\Big)^{1/2} \leqslant s_0, \tag{12}$$

where s_0 is a given value (in applications, it is determined by the practical situation in consideration). We call the inequality $s \leqslant s_0$ the criterion of proximity of structures. When carrying out numerical calculations, the value of s may contain a computational error.

We note that if the minimum point is not unique and there is a point $(\varphi_1, \theta_1, \psi_1)$ such that $U(\varphi_1, \theta_1, \psi_1) = U(\varphi_0, \theta_0, \psi_0)$, then the value of s does not change and the nonuniqueness of the minimum point does not affect the criterion of proximity of structures.

Thus the comparison of the geometry of two geometric structures can now be split into three stages: 1) the displacement of the center of mass of each of the geometric structures into the center of the coordinates; 2) minimization of function (10) with respect to the angles; 3) calculation of function s of the form (12), and the conclusion about the proximity of the structures.

To compare the two structures in accordance with the algorithm 1)–3), a numerical determination of the minimum of the comparison function $U(\varphi, \theta, \psi)$ with respect to the rotation angles after the superposition of the centers of mass of the structures is carried out below.

4. NUMERICAL SOLUTION OF THE OPTIMIZATION PROBLEM

This section presents the results of a computational experiment comparing geometric structures by minimizing the comparison function (10). Since the comparison function (10) is not convex, we applied zero-order Rosenbrock method [5] for its numerical minimization. This method was effectively used to solve problems in structural chemistry [8]. The program implementing the comparison algorithm 1)–3) uses the optimization library program [9] to minimize the comparison function (10) by the Rosenbrock method.

We show the effectiveness of the comparison algorithm 1)–3), proposed above, on the examples used in structural chemistry. We consider a molecule with ordered

Table 1: Atoms' coordinates in three molecules of lactide, $C_6H_8O_4$ in angstroms

№		$x_{1,i}$	$y_{1,i}$	$z_{1,i}$	$x_{2,i}$	$y_{2,i}$	$z_{2,i}$	$x_{3,i}$	$y_{3,i}$	$z_{3,i}$
1	O_1	1.766	4.283	0.385	0.200	-0.513	-2.171	6.816	1.823	4.003
2	O_2	2.955	2.955	1.996	2.448	-2.053	-2.144	9.027	3.243	3.260
3	O_3	2.874	3.825	3.672	3.350	-0.669	-3.593	9.104	2.088	1.387
4	O_4	1.522	2.776	-1.187	-0.400	-1.489	-0.297	6.466	3.285	5.606
5	C_1	2.066	3.097	-0.164	0.254	-1.527	-1.308	7.233	2.801	4.814
6	C_2	3.090	2.264	0.556	1.185	-2.645	-1.687	8.682	3.202	4.678
7	C_3	2.817	3.643	2.484	2.352	-1.106	-3.090	8.697	2.182	2.513
8	C_4	2.595	4.753	1.482	0.947	-0.650	-3.414	7.819	1.166	3.179
9	C_5	1.890	5.940	2.053	0.925	0.679	-4.086	7.087	0.283	2.207
10	C_6	2.977	0.803	0.267	1.510	-3.571	-0.548	9.045	4.516	5.263

structure of atoms (points) as a geometric structure. When comparing molecules, we are be interested in differences in the spatial structure of molecules with the same structural formula.

In the examples considered below, the results of comparison of molecules with lactide $C_6H_8O_4$ structure are shown, investigated in paper [10], consisting of $N = 10$ main atoms (4 atoms of oxygen, 6 atoms of carbon). The coordinates of hydrogen atoms were not taken into consideration in this calculation since the accuracy of their determination is lower than that of other atoms and their presence is insignificant for the problem of comparison of molecules. The geometry of these molecules is shown in Fig. 1. The coordinates of the molecules were obtained on the basis of X-ray diffraction data. In the experiment, the superposed atoms in the molecules are assigned the weight $w_i = 1$.

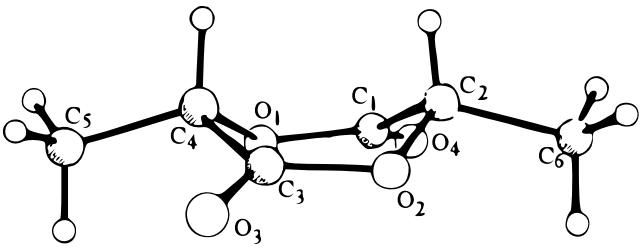

Figure 1: Positions of the C and O atoms in the lactide molecule, $C_6H_8O_4$.

Example 3. Comparison of three lactide molecules.

In Table 1, the coordinates of oxygen atoms $O_j, j = 1, \ldots, 4$ and of carbon $C_j, j = 1, \ldots, 6$ in angstroms in three symmetrically independent (they are present in one crystal) molecules of lactide $C_6H_8O_4$ are shown.

The application of the comparison algorithm 1)–3) to compare molecules 1 and

2, 1 and 3, 2 and 3 yields the results given in Table 2. The points of minimum with respect to the rotation angles obtained for these calculations are also given in Table 2.

Practical experience in the study of conformation of molecules based on the results of the comparison of a significant number of structures [11], [12] led to the following conventional classification of the molecules according to the value of the proximity measure (in chemistry it is called the proximity characteristic): $s \leqslant s_0 = 0,1$ Å – the molecules are approximately, or substantially, identical, $0,1$ Å $< s \leqslant 0.2$ Å – molecules are close, $s > 0,2$ Å – the molecules are different.

The analysis of values of the residuals $\Delta r_i = |\mathbf{r}_{1,i} - \mathbf{r}_{2,i}|, i = 1, \ldots, 10$, that is, the distances between atoms with the same indices in both molecules after the superposition (at the point of minimum of the comparison function U), and the value $s_0 = 0.1$ Å allows us to conclude that the first and the third molecules, as well as the second and the third are almost identical in geometry, since in both cases $s < s_0$. The greatest differences are between the first and the second molecules ($s = 0.11$ Å$> s_0$); these molecules can be considered as close. One can see from Table 2 that the atoms of the substituents (atoms outside the cycle) have the maximum residuals. To better identify these differences, an additional calculation was made: when molecules were matched with respect to atoms from cycles (calculation with weight multipliers $w_i = 0$ for substituents). In this case, we got $s < 0.04$ Å. This means that the cycles within the molecules are almost the same.

Example 4. Identification of the molecule own symmetry.

On the basis of the comparison algorithm 1)–3), the self-symmetry of the lactide molecule was tested. The assumed second-order axis of symmetry passes through the center of the cycle vertically. To apply the comparison algorithm 1)–3), a "second" molecule was formed in which the atomic numbering order was changed compared to the original molecule. Due to the supposed symmetry, atom №1 of the second molecule must correspond to atom №2 of the first one, atom №5 must correspond to atom №7, etc. The total renumbering of atoms in the "second" molecule is given in Table 3. The results of comparison of "two" molecules are given in the same table. Since the comparison characteristic in this case is $s = 0.009$ Å$< s_0 = 0.1$ Å, the molecules are considered equal and therefore, the original molecule has its own second-order symmetry with high accuracy.

Table 2: The values of "residuals" Δr_i, characteristics s and rotation angles $\varphi_{\min}$, $\theta_{\min}$, $\psi_{\min}$ for the point of minimum of the comparison function

Atom	Δr_i for molecules 1 and 2 $w_i = 1$	Δr_i when combining molecules 1 and 2 by cycles	Δr_i for molecules 1 and 3 $w_i = 1$	Δr_i for molecules 2 and 3 $w_i = 1$
1 O_1	0.020	0.009	0.011	0.015
2 O_2	0.040	0.021	0.044	0.004
3 O_3	0.156	0.138 $w = 0$	0.076	0.081
4 O_4	0.188	0.210 $w = 0$	0.098	0.090
5 C_1	0.040	0.051	0.039	0.011
6 C_2	0.056	0.064	0.016	0.043
7 C_3	0.046	0.036	0.038	0.009
8 C_4	0.059	0.049	0.029	0.038
9 C_5	0.149	0.127 $w = 0$	0.113	0.041
10 C_6	0.176	0.196 $w = 0$	0.139	0.049
s	0.111	0.043	0.073	0.047
$\varphi_{\min}$	73,9°	253,6°	80,4°	27,8°
$\theta_{\min}$	111,0°	249.4°	157,5°	74,8°
$\psi_{\min}$	-42,0°	138.6°	59,0°	-51,0°

Table 3: The value of "residuals" Δr_i, characteristic s and the rotation angles $\varphi_{\min}$, $\theta_{\min}$, $\psi_{\min}$ for the minimum value of comparison functions when checking the own symmetry of the molecule

Atom	Permutation of atoms	Δr_i of the molecule 1 and of the molecule 1 with permutation
1 O_1	2 O_2	0.008
2 O_2	1 O_3	0.008
3 O_3	4 O_4	0.012
4 O_4	3 O_3	0.012
5 C_1	7 C_3	0.011
6 C_2	8 C_4	0.008
7 C_3	5 C_1	0.011
8 C_4	6 C_2	0.008
9 C_5	10 C_6	0.006
10 C_6	9 C_5	0.006
$s = 0.009$		
$\varphi_{\min} = 71{,}6°$ $\theta_{\min} = 216{,}8°$ $\psi_{\min} = 108{,}4°$		

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