On the Complexity of Molecular Graphs

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Abstract

We studied the complexity of molecules using approaches based on the topological complexity, that is, the complexity of the corresponding molecular graphs. Several measures of the topological complexity, such as those introduced by Bertz and Randić or based on the number of spanning trees, are briefly reviewed. Comparison is made between these measures of topological complexity for selected molecular graphs.

1. Introduction

The concept of complexity is a rather difficult notion to define [1]. Some even stated that nobody knows how to define complexity [2]. This did not stop publishing company John Wiley and Sons, Inc. of New York to start an international journal entitled *"Complexity"* (Harold Morowitz, Editor-in-Chief; John L. Casti, Executive Editor) with an aim to provide global coverage of all aspects of the science of complexity in a readable, topical and informative way.

The manifestations of complexity can be found everywhere in the nature and in all kinds of human activities [1, 3-5]. Therefore, no wonder that this concept and the related theory, that is, the complexity theory, are discussed even in science fiction [6], where they are called by the author, Michael Crichton, *"the science of the twenty-first century"*. Some authors are trying to use it for studying so diverse problems as the complexity of poems [7] and the origin of life [8]. Hence, it is not surprising that there are many attempts in the literature to define and quantify complexity [9, 10].

The word *complexity* is made up from the Latin roots: *com* (meaning *together*) and *plectere* (meaning *to plait*). In Webster's Ninth New Collegiate Dictionary (Merriam-Webster Inc., Springfield, MA, 1985, p. 269) *complexity* is defined as 1: *the quality or state*

of being complex, 2: *something complex,* while the term *complex* is defined *as a whole made up of complicated or interrelated parts.* This agrees with our understanding of complexity: A system is complex if it consists of many components interacting with each other in many different ways with an outcome that these interactions sometimes lead to unexpected collective properties (fashionably called as *emergent properties* [1]). Therefore, the increasing complexity is associated with the increasing number of components in a system and the versality of their interactions. However, it must be emphasized that complexity is related to nonlinear systems, since linear systems cannot be complex because the principle of superposition makes sure that the whole behaves in precisely the same manner as the sum of its components. This is the reason why linear systems are completely solvable and also why they are deprived of any surprises. In other words, linear systems are "dull-systems".

Since complexity is a difficult concept to define and since people have an intuitive feeling about it, complexity appears to be a fuzzy concept. However, there are many fuzzy concepts in chemistry that are nevertheless very useful chemical notions [11]. The first such fuzzy concept that comes to our mind, which permeates the whole chemistry for more than a century, is aromaticity. This did not prevent chemists to attempt to quantify aromaticity [12]. Similar situation is happening with complexity. Chemists are freely using terms *complex* and *complexity* in describing molecules and their reactions. Therefore, it is not unexpected that the contemporary chemical literature contains a number of attempts to define and to quantify complexity of molecules and reaction paths [e.g, 13-32]. Here we are interested in a topological complexity of molecular graphs and its relationship to structural complexity of molecules. It is of interest to note that Prelog, a Croatian Nobel Laureate 1975, was among the first who used the terms "topology" and "topological" in chemistry [33], although in a different context. Nowadays these are standard terms in a chemists' vocabulary [34, 35]

This report is structured as follows. In the next section we give several measures of topological complexity. The third section contains a comparison between various complexity measures for selected molecular graphs. The report ends with our concluding remarks.

2.   Some measures of topological complexity

In this section we consider several approaches to quantification of topological complexity. In order to simplify the presentation we will use throughout the report the apparatus of (chemical) graph theory [36, 37].

2.1.   The approach of Bertz

The Bertz approach is based on the following formula [15-18, 28, 29]:

$$C = 2n \log_2 n - \Sigma\, n_i \log_2 n_i \qquad\qquad (1)$$

where the complexity of a molecular graph is denoted by C, n is stands for the number of selected graph-theoretical invariants that breaks down into equivalence classes i and n_i is the number of equivalent invariants in a given class i. Note that $n=\Sigma n_i$. Bertz established that the optimal invariant to use is the number of pairs of adjacent edges in a molecular graph G. If G is transformed into a line graph L(G), then n is simply the number of edges in L [38]. The first part of eq. (1) roughly approximates structural characteristics of G (size, branching, cyclicity, etc.), while the second part reflects the symmetry of G in terms of equivalent adjacent edges. Therefore, eq. (1) represents a balance between the structural and symmetry features of a molecular graph. Bertz introduced his approach for use in synthesis planning and analysis of synthetic strategies [15, 16, 28, 29, 39].

Eq. (1) represents a clever modification of the information-theoretic formula derived by Bonchev and Trinajstić [13], denoted by BT, to study the concept of molecular branching:

$$BT = n \log_2 n - \Sigma\, n_i \log_2 n_i \qquad\qquad (2)$$

where n is the number of pairs of vertices in a molecular graph, which in terms of the vertex-number V is $\begin{pmatrix} V \\ 2 \end{pmatrix}$ and n_i is the number of pairs of vertices at a given distance i.

Bertz modified eq. (2) by adding to it $n\ log_2\ n$ which prevented the result BT=0 when all pairs of adjacent edges in a structure are equivalent, which is the case for graphs representing propane, isobutane, cycloalkanes, benzene, annulenes, etc.

Formula (2) is related to the information-theoretic formula proposed by Mowshowitz [40]:

$$I = - \Sigma\, p_i \log_2 p_i \qquad\qquad (3)$$

where p_i is the number of orbits of the automorphism group of a graph. Mowshowitz called eq. (3) the relative complexity of graphs. All of the above formulas are related to the Shannon formula [41] for an information content of a system. Rashevsky [42] was the first to apply Shannon formula to graphs.

2.2. The approach based on spanning trees

A purely graph-theoretical approach to the complexity of graphs is based on the concept of a spanning tree, that is, the complexity of a molecular structure can be given in terms of the number of the corresponding spanning trees [43-45]: The most complex structure possesses the highest number of spanning trees. A spanning tree of a graph G is a connected acyclic subgraph containing all the vertices of G. In the case of trees, the spanning tree is identical to the tree itself. Therefore, the number of spanning trees can only be used as a quantitative measure of complexity for polycyclic graphs. The interest in spanning trees is related to several chemical problems such as the use of spanning trees in calculation of the magnetic properties of conjugated systems by means of the ring-current model [46-49] in the framework of π-electron molecular orbital theory [50].

The number of spanning trees can be obtained by means of the Laplacian matrix in several ways [24]. The Laplacian matrix $L=L(G)$ of a graph G is defined as [50-52]:

$$L = D - A \qquad (4)$$

where D is a diagonal matrix whose entries are the vertex-degrees and A is the adjacency matrix of G. The diagonalization of the Laplacian matrix of G with V vertices produces V real eigenvalues. The set of Laplacian eigenvalues is usually referred to as the Laplacian spectrum and denoted by $\{x_1(L), ..., x_1(L)\}$. The smallest member of the Laplacian spectrum is always zero. This is a consequence of the special structure of the Laplacian matrix.

The most important application of the Laplacian matrix of a graph G is in the matrix-tree theorem for spanning trees [52]: Let G be a graph with V vertices and let $t(G)$ denote the number of spanning trees contained in G. Then:

$$t(G) = \det | (L)_{ij} | \qquad (5)$$

where $(L)_{ij}$ is the submatrix of L derived by deleting row i and column j. The value of $t(G)$ can be computed in integer arithmetic by simple elimination techniques. Sofware packages like mathematica or maple could be used for computing efficiently $t(G)$.

2.3.   The approach based on connected subgraphs of a molecular graph

Bertz and co-workers [28, 29] and Bonchev [53] independently introduced an approach based on the subgraphs of a molecular graph. Bertz and co-workers proposed to use as the complexity indices the number of kinds of subgraphs $N_s(G)$ and the total number of connected subgraphs $N_t(G)$ of G. The latter was also proposed by Bonchev. However, they did not take into account all subgraphs but only connected (chemically-meaningful) subgraphs such as a single vertex (representing carbon atom of methane), two vertices

connected by an edge (representing carbon skeleton of ethane), three vertices connected as a chain (representing carbon skeleton of propane), four vertices connected either as a chain (representing carbon skeleton of butane) or a star (representing carbon skeleton of isobutane), a three-membered cycle (representing carbon skeleton of cyclopropane), etc. The graph itself is counted as a subgraph, because in the formal graph theory [36] G is its own subgraph.

It should be also noted that that the number of methane subgraphs (N_m) of G is equal to the number of vertices (V) in G: $N_m = V$. Similarly, the number of ethane subgraphs (N_e) is equal to the number of edges (E) in G: $N_m = E$. A chain-like structure of n-alkane trees allows one to derive formula for obtaining the N_t and N_s numbers: $N_t = V (V+1)/2$ and $N_s = V$, respectively. A cyclic structure of n-cycloalkane graphs leads to formula for obtaining the N_t and N_s numbers: $N_t = V^2 + 1$ and and $N_s = V +1$, respectively.

There is a problem with the N_t number, since it includes also the number of spanning trees. The number of spanning trees is a rather explosive quantity even for not too large graphs. For example, the modestly sized coronene graph has 423,381 spanning trees. Then, the N_t number will be even larger. Bertz and Wright were aware of this problem when they stated that N_t *"is conceptually simple, and it is practical for small molecules, but it quickly becomes unwieldy for large ones"* [29]. It is a rather difficult problem to compute all subgraphs of a graph and to compute only chemically-meaningful subgraphs is only slightly less involved computational problem. Therefore, it appears that it is much easier to obtain the N_s number, since it is enough to detect a single subgraph of each class of subgraphs.

2.4. The approach of Randić

The approach of Randić [30] is based on the concept of augmented vertex-degree [54]. The augmented degree for a given vertex is obtained by adding to its degree a half of the degrees of the nearest neighbors, a quarter of the degrees of the next nearest neighbors, and so on. The Randić complexity index is then given as the sum of the augmented vertex-degrees for symmetry non-equivalent vertices.

Computations using the Randić approach can be carried out by the augmented distance matrix:

$$\mathbf{D'} = \left\{ \begin{array}{l} (\mathbf{D'})_{ii} = \text{the vertex-degree} \\ \\ (\mathbf{D'})_{ij} = d_i/2^{\ell_{ij}}; \ i,j = 1,...V; \ i<j \end{array} \right. \tag{6}$$

where d is the vertex-degree, V the total number of vertices and ℓ_{ij} the distance between the vertex i and neighbors j. The augmented distance matrix is a non-symmetric matrix.

3. Comparison between measures of topological complexity for selected molecular graphs

We selected four sets of simple molecular graphs to compare topological complexity measures discussed in the previous section. We first give in Table 1 five isomeric hexane-trees and their complexity indices.

From Table 1 we learn the following. The C index increases roughly with *branching* (branching is reflected in the vertex-degrees higher than two; trees with vertex-degrees one and two are not branched): **A < C< D < E**. For the equally branched graphs it decreases with *symmetry*: **C < B**. This is confirmed in all studied isomeric alkane-trees and was also observed by Bertz. However, the C index is not a pure branching index, because symmetry decreases it. For example, the more branched tree **D** (C=21.02) has a smaller value of the C index than a less branched tree **B** (C=21.22). This is so because **D** is a more symmetric structure than **B** which lowers the value of its C index below that of **B**, although not by much.

Hexane trees					
Indices	A	B	C	D	E
Bertz	12.00	21.22	19.22	21.02	29.79
Bonchev-Trinajstić	32.24	28.63	27.38	23.48	22.59
Randić	12.10	21.94	17.82	9.75	19.50
N_t	21	24	25	28	30
N_s	6	8	8	7	8

Table 1.   Isomeric hexane-trees and their complexity indices

The BT index changes considerably with size of the longest path which is reflected in the appearance of larger distances, e.g., the distance of the length 5 in *n*-hexane-graph **A**. Therefore, the decreasing distances result in smaller values of the BT index. This is well-reflected in the case of the isomeric hexane-trees and other studied alkane-trees. It is noted that in this case the BT index diminishes with increasing symmetry: **D < C < B**. The increasing branching also results in decreasing the value of the BT index: **E < D < C < A**.

n-Alkane trees / Indices	—	∧	∨∧	∧∧	∧∨∧	∧∧∧	∧∨∧∨	∧∧∧∧	∧∨∧∨∧
Bertz	1	0	2.00	7.51	12.00	19.22	25.02	33.30	40.00
Bonchev - Trinajstić	0	2.75	8.76	18.47	32.24	50.37	73.09	100.60	133.08
Randić	1.50	5.25	6.38	11.44	12.10	17.67	18.02	23.82	24.01
N_t	3	6	10	15	21	28	36	45	55
N_s	2	3	4	5	6	7	8	9	10

Table 2. Complexity indices for lower n-alkanes

Since branching should increase complexity, this result is counterintuitive. The moving of the branch to the center of a tree also produces somewhat smaller values of the BT index: $C < B$.

The Randić index appears to be very sensitive to symmetry. It decreases considerably with increasing symmetry, that is, with decreasing number of equivalent vertices: D (2)$<A$ (3)$< C$ (4); E (4) $< B$ (5). If the number of equivalent vertices is the same, than the Randić index increases with branching: $C < E$.

The N_t number increases with branching: $A < B, C < D < E$, and symmetry: $B < C$. The N_s number cannot be used to rank hexane-trees according to their complexity because in words of Bertz ["this number was not intended for fine graduations such as hexane isomers, but for a rough appraisal, where it seems to be valid."

In the case of n-alkane-trees all considered indices increase with size (see Table 2). The C index increases with size because the number of pairs of adjacent bonds increases. The BT index increases because the total number of distances increases. The Randić index increases in groups of two (propane and butane; pentane and hexane; heptane and octane, etc.) reflecting the number of vertices in different environment. For example, in propane there are two end-vertices (one type of vertices) and one central vertex (the second type of vertices). In butane there are again two end-vertices and two central vertices. Thus, propane and butane possess the Randić indices which differ slightly. The same is encountered for the duo of pentane and hexane, their indices also differ slightly. However, there is a jump in the value of their indices in comparison with the values of the preceding duo of propane and butane. This is so because the duo of pentane and hexane possesses three different types of vertices and hence the jump in the value of their indices. The N_t and N_s numbers for n-alkanes clearly increase with the number of atoms (see above formulas for computing these numbers for n-alkanes). Each n-alkane in the series has the N_t number which is made up from the N_t number of the preceding n-alkane and its own size in terms of the number of vertices (carbon atoms).. For example, the N_t number of nonane (45) is equal to N_t (octane) + 9.

In Table 3 we give all molecular graphs with four vertices and their complexity indices. The C index orders these graphs as follows: $F < G < I < H < J < K$. It increases with branching ($G > F$) and with cyclization ($K > J > I$; $H > G$). In the case of graphs I and H: $I < H$. The relationship between them is the result of the different influence of branching and symmetry on the C index in this case. Graph I has smaller value of C for two reasons: it is less branched and more symmetric than H. But the effect of branching is stronger. This can be seen from the computation of the C index for these graphs:

$$C(H) = 2 \cdot 5 \log_2 5 - (2 \log_2 2 + 1 \log_2 1) = 23.22 - 4.00 = 19.22$$

$$C(I) = 2 \cdot 4 \log_2 4 - 4 \log_2 4 = 16.00 - 8.00 = 8.00$$

Graphs	$\mathcal{N}$	$\bigwedge$	$\underset{\triangle}{\bigwedge}$	$\square$	$\boxed{\diagup}$	$\boxtimes$
Indices	F	G	H	I	J	K
Bertz	2.00	4.75	19.22	8.00	36.00	43.02
Bonchev - Trinajstić	8.76	6.01	5.51	5.51	3.90	0.00
Randić	6.38	7.50	13.75	4.50	12.00	7.50
No. of spanning trees	1	1	3	4	8	16
N_t	10	11	18	17	33	64
N_s	4	4	7	5	9	10

Table 3.   All molecular graphs with four vertices and their complexity indices

We already stated that the first part of the eq. (1) reflects branching and the second part symmetry. From above is seen that the branching is reponsible for the higher value of the C index for **H**.

The BT index decreases with cyclicity (i.e., the increasing number of cycles in the structure): $K < J < I = H < F$ or G. This is also the order of increasing simplicity of molecular graphs with four vertices. The most complex graph in this group is **K**. Since it is also the complete graph possessing only distances of the length one, its BT index equals zero. In general, complete graphs will always possses zero value of the BT index.

The Randić index is not sensitive to cyclicity ($I < K = G < J$) and is too sensitive to symmetry ($K < J < H$). The numbers of spanning trees give the following complexity order of graphs in Table 3: $F = G < H < I < J < K$. However, the number of spanning trees suffers from several problems. It cannot be used for acyclic structures, cannot discriminate isomeric structures (e.g., anthracene and phenanthrene posses the same number of spanning trees, 204) and often produces an astronomical number of spanning trees. For example, the number of spanning trees for buckminsterfullerene [57-59] is 375,291,866,372,898,816,000. It is evidently impractical to work with this number.

n-Cycloalkane / Indices	△	▢	⬠	⬡	⬠(7)	⬢(8)	⬡(9)	◯(10)
Bertz	4.75	8.00	11.61	15.51	19.65	24.00	28.53	33.22
Bonchev - Trinajstić	0	5.51	10.00	22.83	33.29	54.61	72.00	102.64
Randić	4.00	4.50	5.00	5.25	5.50	5.63	5.75	5.81
No. of spanning trees	3	4	5	6	7	8	9	10
N_t	10	17	26	37	50	65	82	101
N_s	4	5	6	7	8	9	10	11

Table 4. Complexity indices for lower n-cycloalkanes

The N_t number order graphs in Table 3 as **F < G < I < H < J < K**. This order agrees with the chemical intuition. The N_s number gives the following complexity order: **F = G < I < H < J < K**, which the same order as one given by the C index and the N_t number, except for **F = G**.

Finally, we considered *n*-cycloalkane graphs with up to n=10. Their complexity indices are given in Table 4. In the case of cycloalkanes again all considered complexity indices increase with the size of the structure.

The Bertz index increases because the number of pairs of adjacent edges increases, but C(*n*-cycloalkane) is always bigger than C(*n*-alkane) for the same number of vertices. The BT index increases because the total number of distances also increases, but not to extent as in the corresponding *n*-alkane. Thus, the BT index of a given *n*-cycloalkane is always smaller than its value of the corresponding *n*-alkane. The Randić index increases rather slowly because all vertices in a cycle share the same environment, that is, every vertex in a cycle is connected to other vertices in the same way. Because of that the Randić index for a given *n*-cycloalkane is always smaller then for the corresponding *n*-alkane. The number of spanning trees for *n*-cycloalkanes is equal to n, because the number spanning trees for any cycle is identical to its size. The N_t number increases with the size squared (plus one) and the N_s number linearly with size plus one (see above formulas for computing these numbers for *n*-cycloalkanes).

4. Concluding Remarks

We compared several measures of the topological complexity for selected sets of molecular graphs. It appears that the total number of connected subgraphs and the C index are the most suitable measures at present to study the topological complexity. The number of spanning trees is also a useful measure of complexity, although in some cases, especially in the case of isomers, it does not give results in agreement with chemical intuition. For example, graphs representing p-, o- and m-xylylene all have the same number of spanning trees, that is, 6. Unfortunately, the number of connected subgraphs is a difficult quantity to compute for larger systems and this fact limits its use. Since the C index is much simpler to compute, it appears to be at present [60] very useful complexity index.

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