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Editorial

Postface for Applied Designs in Chemical Structures with High Symmetry

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Probably the best example to start with with regard to structures with high symmetry (SHS) is C_{60} fullerene (buckminsterfullerene) [1], a synthetic form of carbon resembling footballs [2]. Inside of an applicability domain with structure–property relationships applied, designs may serve as tools for the in silico construction of chemical SHS, as well as for the characterization of structure, the classification of series of structures, and property prediction [3]. Investigation into these structures helps us to better understand their natural tendencies to stabilize matter into chemicals, as well as to further develop new classes of highly symmetric chemical compounds. Several experimental [4,5] and theoretical tools [6–8] are now available for this task.

"Applied Designs in Chemical Structures with High Symmetry" (ADCSHS) is a collection of twelve articles.

1. Contributions

Rhombellane was defined by Diudea [9] in the context of distinguishing between cycles, rings, and strong rings. Having in mind the real interest for new potent drug carriers, the potential of these new topologies to be implemented as real chemical structures has been explored further in [10]. ADCSHS gives a group of five papers on this topic ([11–15]). In [11], by using the rhombellane framework, several dual-layer covalent assemblies were designed as potential drug delivery systems. Following a computational study, the authors concluded that the aromatic moieties through stacking interactions, as well as the hydrogen bond donor and acceptor groups on the surface layer, significantly contribute to the ligand binding capacity. They also noted that the immobilization of compounds with pharmaceutical potential could be further enhanced by attachment of functional groups to the aromatic rings. In a subsequent docking study [12], the immobilization of oxindole derivatives was evaluated against immobilization on C_{60}, where, in one instance, an increase up to 4–5 times of the binding constant was noticed.

Docking provides preferred orientation, affinity, and interaction of a ligand in the binding site of a host molecule, and several computer programs are dedicated to do this task. ADCSHS provides two papers on this topic (Refs. [16,17] docking to enzymes' active sites). With the use of AutoDock (v.4 [18] and Vina [19] in [13] and in [14–17]), Dr. Szefler and Dr. Czelen docked several ligands (cisplatin in [13], polyethylenimines derivatives in [14], ChEMBL474807 in [15], oxindole derivatives in [16]) to different hosts (rhombellane homeomorphs and C_{60} in [13–15], nanotubes in [15], 1E9H (CDK2, PDB [20]) and 3QVR (GOx, PDB [21]) enzymes active sites in [16] and in [17]) when similar binding affinities were observed. However, some distinct conclusions were drawn; thus, the highest values of both binding affinity and binding constant were found in the case of carbon nanotubes [15] when compared with the other alternatives (rhombellane homeomorphs and C_{60} fullerene).

COSMO (from COnductor-like Screening MOdel) is a method which has become popular in recent years [22,23] for calculating the electrostatic interaction of a molecule with a solvent [24]. Some challenges and possible solutions in the case of fullerenes are provided in [25]. It was documented in [25] that, from the perspective of the COSMO-RS

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approach, in the case of C_{60}, it is indispensable to distinguish calorimetric contributions to Gibbs free energy of fusion from the fluidization term; classification of solvents into groups with similar values of fluidization term proved to significantly increase the accuracy of the predicted solubility.

In the search for improving the explanatory power of structure–activity relationships, in [26], starting from binding constants of 1:1 β-cyclodextrin complexes with different organic compounds, the authors apply a previously reported approach [27] of non-linear multivariate adaptive regression splines (implemented in STATISTICA v.12 software) on common molecular descriptors calculated from simplified molecular input line entry specification. The study included internal and external validation, which indicated good accuracy of the model, while inclusion of the XlogP (polarity-related descriptor) gives the physical support of the model since the cyclodextrin cavity is hydrophobic.

Some of the research carried out under the framework of the GEMNS project (Self-navigated integrin receptors seeking 'thermally-smart' multifunctional few-layer graphene-encapsulated magnetic nanoparticles for molecular MRI-guided anticancer treatments in 'real time' personalized nanomedicine) from the EuroNanoMed-II, PN III, ERA-NET program (ID 57, Grant no. 8/2015, Director Prof. Mircea V. Diudea) was highlighted in [28]. The authors of [28], combining data from Chemoffice (v. 2005) software with tools from Mathematica (v. 5.0) software constructed QSAR models using the AutoQSAR (v. 2009) software. Hypotheses were derived from QSARs, and finally, a merged (combined from two) hypothesis was formulated. Based on their study, the authors concluded that a mathematical model based on Riemann surfaces can be built in order to screen and characterize polymers with gene transfer properties.

At over fifty years since its formulation [29], density functional theory is has become a very powerful tool for molecular and materials modeling. As a typical case study of its capabilities, in [30], dimensionless ratio, elastic constants, shear modulus, Young's modulus, bulk modulus, ductile–brittle transition, material anisotropy, and Poisson's ratio, as functions of applied pressure, are calculated for TiV alloys with symmetric structures under high pressure. The authors of [30] were able to extract from their computations a series of important specific information, for example, that the symmetric crystal structure of the TiV alloy produces structural phase transitions when the applied pressure exceeds 42.05 GPa, which was found to be the critical pressure of the structural phase transition.

Molecular conformation as a subproblem of the geometrical shaping of molecules is essential for the expression of biological activity, and two typical examples are sugars [31] and amino acids [32]. In [33], the author stresses the connection between geometrical orthogonalization and molecular alignment. In [33], it is shown that while the eigenproblem arises when topological adjacencies are represented into the Hessian, molecular alignment is achieved when projections of the geometrical adjacencies follow a transformation which maximizes its principal components.

2. Perspectives

As later studies showed [34,35], similarity invokes symmetry (and vice versa) in certain details, and there is plenty of research on the formulation of the eigenproblem in chemistry. Moving from the molecular level to macroscopic level requires a change in perspective regarding the objects subjected to the symmetry analysis [36,37]. Molecular clusters are an interesting case of similarity symmetry, the topology being taken to the next level [38].

Even if the primary use of symmetry is to predict or explain properties such as dipole moment and allowed spectroscopic transitions, there is an increasing number of studies [39–43] recognizing and documenting the role of symmetry in the biological manifestations of chemical compounds since the control of the symmetry in synthetic molecules increases the ability to provide therapies with minimal side effects.

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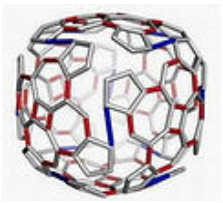
Acknowledgments: Since most of the papers from ADCSHS are written by authors who know, collaborated with, or were guided by Mircea V. Diudea (b. 11 November 1950; d. 25 June 2019), a memoriam is in its place here. Mircea Vasile Diudea received his B.Sc. and M.Sc. in Chemistry from the Faculty of Chemistry, Babeş-Bolyai University of Cluj-Napoca (1974), and his Ph.D. in Chemistry (1977) from the Institute of Chemistry Cluj-Napoca. He started to work as chemist at 'Terapia' drug factory (in 1974), then as a researcher at the Chemical-Pharmaceutical Institute of Cluj-Napoca (in 1980), finally taking a position at the Department of Chemistry from Babeş-Bolyai University (in 1987). He was the founder and the president of the European Society of Mathematical Chemistry (ESMC). Writing over 450 papers (most of them on molecular topology) and several books, including [44,45], Diudea succeeded in having a positive and emancipative influence on others. He kept correspondence and had fruitful collaborations with other well-known scientists in his field, resulting in the following works: [46–64], to enumerate just a few of the results of his fruitful collaborations. Twenty-seven students graduated under his supervision. The author of this editorial is grateful for the help received from M. V. Diudea, as his former Advisor (in Chemistry), being the first of his graduates enrolled in his open PhD positions.



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M. V. Diudea in 2007

Conflicts of Interest: The author declares no conflict of interest.

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