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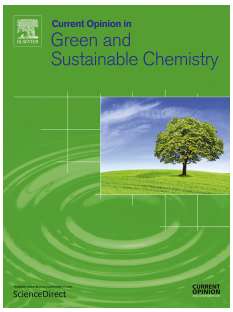

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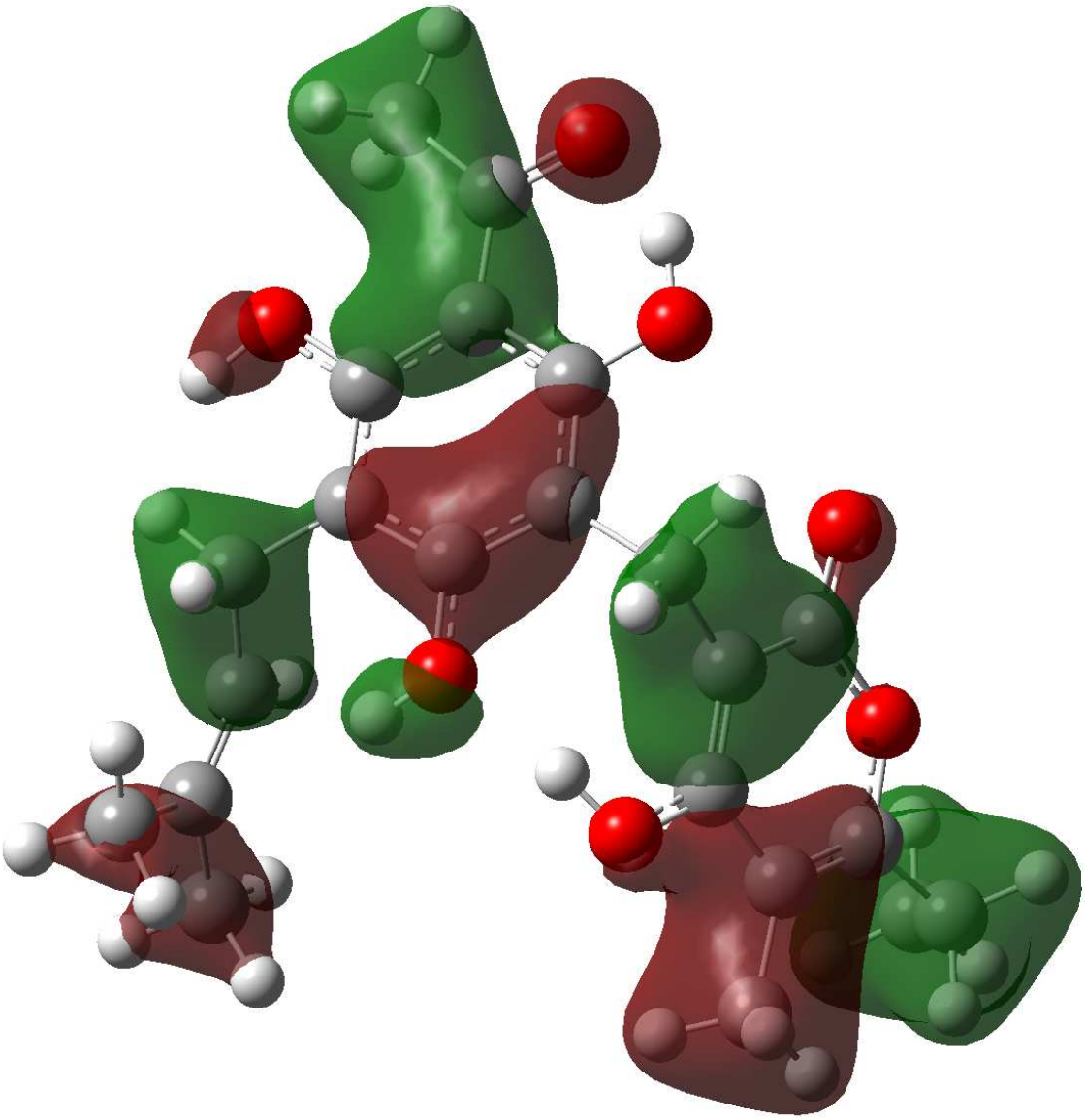

Incorporating information on green chemistry into theoretical chemistry courses

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Abstract

One of the key objectives of green chemistry is the design of environmentally benign substances. The design of new substances with specific properties relies on the knowledge of the properties of their molecules, which are investigated with the methods of theoretical chemistry. Therefore, cross-disciplinarity between the two areas is important, both in chemistry practice and for the educational level. The current work explores ways of attracting students' attention to the challenges of molecular design, through an overview of the issues that are relevant to the chemical industry.

Keywords: green chemistry education; learner active engagement; molecular design; quantum chemistry methods; theoretical chemistry education.

Introduction

The term "Green Chemistry", as adopted by the IUPAC Working Party 'Synthetic Pathways and Processes on Green Chemistry', is defined as "the invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances". 'Design' is thus one of the key concepts and the design of environmentally-benign substances has a key role. The design of a new substance requires reliable predictions of its properties. The properties of a substance depend on the properties of its molecules. The more we know about the properties of molecules, the more we can understand the behaviour of substances and predict the properties of molecules and substances that have not yet been synthesised. The most refined tools for knowing the properties of molecules are those provided by quantum chemistry and realised through computational chemistry. It would appear obvious to infer that interfaces between green chemistry and theoretical/computational chemistry are important both in chemistry practice and at educational level. The latter would imply the incorporation of information about green chemistry into theoretical chemistry courses and about quantum chemistry into green chemistry courses. The information to be incorporated does not need to reach high levels of specialisation, as the objective is that of building a viable background for professional interactions between theoretical chemists and specialists working on the design of new environmentally-benign substances; in this perspective, theoretical chemists can provide information about molecules of interest to experts working on substance design for the industry, while the latter experts can pose challenging research questions to theoretical chemists.

The realization pathways of the envisaged incorporation of information are largely to be explored. Descriptions of in-class practical implementations are not yet available. Even the incorporation of information on computer-aided substance-design into the chemistry

engineering curriculum is not always finalised, for a variety of reasons; as Gani [1] noted in 2015, "Despite the early enthusiasm and substantial effort, there is a general feeling in the chemical engineering community at this time that research activities on chemical product design have been flagging and that there is no consensus on what needs to be emphasized in teaching". He identifies the fact that "the issues in chemical product design are multidisciplinary in nature" [1] as the main challenge. Providing information across disciplines and specialisation areas at both education and training levels has the potential to contribute to address this challenge.

The current work proposes to highlight some threads that can be utilised to inform students about the challenges of the design of environmentally-benign substances as required by the industry. It is therefore more apt for the presentation of basic information to students taking a theoretical chemistry course, but it can also be utilised to provide information to chemistry students who are not majoring in chemical engineering but who need to know about the main questions and practices of modern chemistry. Because of the explorative character of this work, the references are not limited to the last two years, but span through the recent history of green chemistry and theoretical/computational chemistry. This is generally in line with the acknowledged importance of historical perspectives in chemistry and science education; for theoretical chemistry courses in particular, it responds to the advantages of information on the recent history as a means to stimulate creativity [2]. It is envisaged that a quick literature review for the last decades is expedient to highlight the importance of molecular design for the industry and, simultaneously, to provide an overview of questions to be addressed. Within a theoretical chemistry course, an overview of selected crucial issues (without going into the technical-engineering parts of each of them) would be sufficient to convey the message of the importance of theoretical models and computational studies for the chemical industry and to stimulate possible interests for the students' choice of future careers. Particular attention is here also given to the works which utilise quantum chemistry information or propose its incorporation into future approaches for industry-related molecular design, because this aims at 'bridging the gap' between theoretical chemistry and the chemical industry (in particular, green chemical industry) and improving the quality of molecular design.

The design of molecules and substances

Product design has become increasingly important in the last two decades [e.g., 1, 3, 4]. Actually, "a large portion of the research currently performed in the chemical industries is devoted to product design, that is, the search for new materials with specifically tailored properties" [5]. Green chemistry aims at replacing substances that have negative effects on human health and on the environment with substances that are inherently benign (which requires the consideration of the biological, environmental, health and safety related properties [6]). The fact that environmental friendliness becomes a major target-characteristic in the design of a new substance has led to the 'benign-by-design' concept, introduced nearly at the onset of green chemistry [7] and developed into one of its *leit-motifs* [e.g., 8-10].

The fast development of computers' power in the last decades has drastically changed the design of new molecules and chemical products, from a once intuition based, trial-and-error practice into a rational, computer-aided design [11]. The pharmaceutical industry has steadily utilised rational drug design to improve the properties of existing biologically active molecules (enhancing desired activity, decreasing undesirable side effects) or to design novel molecules with specific activities. Because of the delicate role of pharmaceuticals for human health, the design needs to give careful attention to the finest details of molecular structures

and to Quantitative Structure Activity Relationships (QSAR, [4, 6, 11]). The design of substances for other purposes relies on the analogous Quantitative Structure Properties Relationships (QSPR, [4, 6, 11, 12]). Several relevant descriptors to be used in QSAR and QSPR are obtained from quantum mechanical studies of molecules.

Most Computer-Aided Molecular Design (CAMD) approaches so far utilised in the industry are combinatorial in nature. They can be defined as: "Given a set of building blocks and a specified set of target properties, determine the molecule or molecular structure that matches these properties" [13]. CAMD generates a large number of molecular structures with desired properties from the building blocks (structural groups) [14] and involves a rapid search through millions of possible structures [11]. Fast-screening methods have a number of advantages, but they may also entail risks [8]. The incorporation of quantum chemistry descriptors and results is viewed as a promising development for the future [6, 11, 15-17].

The categories of individual molecules relevant in the chemical industry are reactants, products, solvents and catalysts. They can all be targets of molecular design. However, as remarked by Deva and co-authors [17], "Although the problem of designing solvents and catalysts for reactive systems has garnered considerable attention, focus on the problem of design of reactants and products has been lacking". The same authors developed an algorithm to design reactants and products by optimizing dominant structure-dependent properties; they utilised 2D-type molecular descriptors (topological indexes), but also propose to extend the algorithm to incorporate 3D-type and quantum chemistry descriptors [17].

Solvents are used for a variety of purposes in the chemical industry: process materials, extracting agents, and as process liquids in process industries, pharmaceutical industries, and solvent-based industries [18]. Computer-aided design of solvents, aimed at designing solvents with the properties needed for a certain function or process, started since the early stages of molecular design. The target properties of a solvent-to-be-designed may be various: the solubility it enables for the solute of interest [5, 6, 19, 20], the reaction rate it enables for the reaction that will take place within it [15, 21, 22] and its separation capacity and selectivity [15, 23-25]. Several methods have been developed to improve the design, with two main approaches [26]: multi-level generate-and-test methods [e.g., 20, 28] or optimisation procedures [11, 14, 20-24, 27-32]. However, when designing solvents for a specific process, it is very often difficult to relate the performance of the process to a specific solvent property [26], Attempts to overcome this problem focus on integrating solvent design and process design, proposing methodological approaches of general type, or for entire categories of processes [11, 14, 18-20, 23, 26, 33-39], or for specific processes [25, 40-46].

Quantum chemistry approaches proved expedient for the calculation of rate constants in solvents under design-exploration [15]. The most commonly used screening models in solvent design are conductor-like screening models (COSMO, [47–51]), which employ electronic surface charge distributions that are calculated through quantum chemistry approaches [15]. The reliability of solvent design depends on the accuracy of the predictive models used to estimate solvent physical properties [20, 28]. Quantum chemistry calculations can predict many properties of a molecular structure that is being designed to be used as a solvent. Quantum chemistry models for solute-solvent interactions such as the polarisable continuum models (PCM, [52, 53]), or – when expedient – also the consideration of explicit solvent molecules around a solute molecule of interest, can provide relevant information on the interactions between the solvent being designed and that solute.

Catalysis is one of the pillars of green chemistry [54] and is included in its 12 principles [55]. Molecular modelling has been utilised extensively in the design of environmentally benign catalysts [1, 8, 11, 54]. Like for the case of solvents, the design targets specific properties, such as improved selectivity [1]. The "benign by design" concept applies also to the design of catalysts [56]. Catalysts mimicking those of nature are considered particularly promising [57].

Industrial products cover a vast scope. Some of them have already been objects of rational molecular design, such as foaming agents [58, 59], adsorbents [60], and substitutes for CFC [61]. The simultaneous design of product and process is given specific attention [63–66], as it aims at identifying molecules corresponding to optimum process performance [65].

The improvement of molecular design methods is one of the major challenges of green chemistry, the chemical industry, and chemical research in general [1, 4, 67, 68]. A standing major challenge is the need to develop more accurate predictive capabilities for the properties of compounds in order to apply the optimization methodologies [67]. Quantum chemistry has the best predictive capabilities attained so far in modern chemistry.

Conclusions

The design of new substances with desired properties involves the design of new molecules enabling the substances to have those properties. The design relies on the prediction of the properties of not-yet-synthesised molecules. Theoretical chemistry methods are the methods enabling the best currently possible predictions. The outline in the previous section is functional to acquaint students taking a theoretical/quantum chemistry course with the molecular design challenges of the chemical industry. It is also suggested that the familiarisation is pursued in a way that maximises students' active engagement, following the approach described in [69], where different students, or small groups of students, select specific themes, search for the literature and try to organise the material into a coherent discourse. It is also suggested that students are invited to pay specific attention to the quantum chemistry contributions highlighted in the literature, or to those that they consider possible on the basis of what they are learning in the course. Finally, it is suggested as particularly important that this exercise is also carried out in higher education in those regions where theoretical/computational chemistry research is still scarce and the very teaching of theoretical chemistry poses challenges because of the scarcity of experts, like in many parts of Sub-Saharan Africa. Stimulating the awareness of the relevance of computational and quantum chemistry for the industry and for sustainable development is likely to encourage greater attention to this area of chemistry, both from postgraduate students and from academic authorities.

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Highlights

- The design of benign substances is a key issue in green chemistry.
- The design of substances with desired characteristics relies on the design of their molecules.
- Computer-aided molecular design is largely utilised for the design of substances.
- Quantum chemistry approaches enable the best prediction of the properties of not-yet-synthesised molecules.
- It is important to design options to familiarise students learning quantum chemistry with its potentialities for the design of benign substances.