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Computational Chemistry in Graduation Courses of Chemistry

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Abstract

The experience of the authors on the use of computers on teaching at the various levels of the graduation, in Chemistry and Medicinal Chemistry, ranging from General Chemistry to Drug Design, passing through Computational Chemistry and other courses is presented. The capabilities of computers for revealing the microscopic, unseen, and hidden patterns at all levels of the graduation, and to show how computers are used in research on molecules, materials, and drugs, at higher levels of the graduation, are emphasized. The approach is based on simple ideas and concepts, practical laboratory work, motivational narratives, and clear feedback. New forms of clarifying complex ideas, sometimes presented in a "muddy" way, in particular for Computational Chemistry and Drug Design, are procured.

Keywords: *General Chemistry; Computational Drug Design; Computers in Chemistry.*

1. Introduction

Computational Chemistry is an important part of chemistry research, but usually is judged too difficult to be presented at the graduation level and postponed to master degree or PhD programs. The development of modern computers has retarded the full use of the equations of classical and quantum mechanics that are difficult and tedious to solve even for simple systems. These ideas are very old, and are not fully overcome nowadays. For example, Charles Coulson wrote in 1952: "*In the last twenty-five years the theory of valence has made enormous progress. To a large extent this has been due to the advent of wave mechanics. The result is that a situation has now been reached in which the education of a chemist is not complete unless he knows at least the main lines along which such progress has been achieved. This does not mean that every chemical student should be able to make his own theoretical calculations – this would be ridiculous, and will probably never happen (...)"* (Coulson, 1952). Nowadays, a student can push a button and in a fraction of second obtain results that could take years to achieve, which were impossible to obtain in the 1950's. Our mobile phones have processing capabilities that largely overcome the more powerful and faster computers that lead man to the moon. Since a long time ago it has been proposed to include Computational Chemistry in graduation courses

(Gasyna & Rice, 1999; Hessley, 2004; Ramos & Fernandes, 2005), as well as many activities are being presented (e.g, Bendavid, 2023; Metz et al., 2021; Miorelli et al., 2017; Nassabeh et al., 2014), but the actual fully integrated courses are still somehow scarce (see, e.g., Grushow, 2019; Paselk & Zoellner, 2002, for other examples). In addition, computers are nowadays ubiquitous so it appears that specific courses are not needed anymore. Nevertheless, our opinion is that all students in Chemical graduations must be exposed to computers as working devices, but specific courses on Computational Chemistry, Computer Modeling, and Computer Design of Drugs are useful even for graduations in Chemistry and Medicinal Chemistry.

In our University, one has a successful semester graduation course on Computational Chemistry, and one has various classes related to computers use in Chemistry, namely General Informatics and Drug Design, where the ideas of doing without knowing many of the technical details are subjacent. In fact, one must note that this is the standard in research. It is not possible to build the equipment used in research from scratch, from glassware to spectroscopes, but one can have clear ideas how it works. A similar situation happens with Computational Chemistry: The researchers and students do not need to build from scratch a computer or a software suite. Like the former, they can have clear ideas about the equations, possibilities, and limitations, among other physical-chemical applications.

Students should be exposed early in introductory courses to computers and mobile phones as powerful working objects and not only as ludic ones. But for this goal, one needs to use new and simplified methodologies centered on conceptual ideas and hands-on approaches. This is not only needed but also it is the proper way, as it is not needed anymore to go through hard equations, make difficult implementations in computer languages and carry out tedious calculations. The computers can help in deducing, simplifying, programming, and also taking decisions, while carrying out repetitive calculations. The emphasis must be not on the following tedious calculations, deductions, and simplifications, but on simple and clear ideas about how the things work and how to put computers producing results. Nevertheless, one must not oversimplify, not hide fundamental details, nor put students in the position of mere uncritical users. One must introduce to them the principles, the capabilities and limitations, and also furnish them the tools for development and improving the existing objects.

In this paper, one uses our previous experience on the classes referred to above to propose new ways and views aiming to obtain a correct balance on the discussed hands-on methodologies.

2. Development

A minimum background on the way digital machines work and on their limitations and capabilities are needed. Also, an introduction to a programming language, that can be Phyton, can help in understanding computational thought, algorithmic strategies, and it is very useful in newer environmental programming tools. In Chemistry graduations, computer architecture and

software development must be referred to briefly for showing how digital machines work and therefore revealing their limitations and capabilities, but not as a view on its own.

Computers have many applications in Chemistry (see, e.g, Rodrigues & Caridade, 2022). In what concerns classical and quantum mechanics, our experience shows that the students have extreme difficulty in obtaining clear and general ideas and even the best students can be lost in various mixed ideas. We also verified that students and researchers can manage very complex objects without knowing the simple ideas behind them.

We touch all the aspects of the use of computers in Chemistry (see Figure 1) and our approach starts with simple ideas, (hopefully) clear ones, dichotomies, motivational narratives on the importance and aesthetics of the matters, and a strong component on experiments and on discussing results. In the classes where practical experimentation is lower, the emphasis is on the former and we try other strategies as “flipped classrooms”. Feedback is always done and dialogue with students is procured. The results (measured as approval rates and anonymous inquiries) are very good. Some examples, and our views will appear next.

2.1 Unveiling the Patterns: Periodic Properties in General Chemistry

The periodic table, with its neatly arranged elements is, as well known, a cornerstone of Chemistry. But beyond its rows and columns lie hidden patterns, the "periodic properties" of atoms, dictating their behavior and shaping the world around us. Periodic properties like atomic radii, ionization energy, and electronegativity reflect the organization of electrons around the nucleus. These trends reveal a captivating story about electron filling across periods, driven by fundamental quantum mechanical principles. By understanding these patterns, students can predict physical and chemical properties, explain trends in reactivity, and visualize the invisible forces shaping molecules. But the journey beyond rote memorization requires active engagement, as it is well known. This is where Computational Chemistry steps in, transforming the classrooms into computational laboratories. One can use software to visualize electron clouds, calculate ionization energies, or simulate reactions.

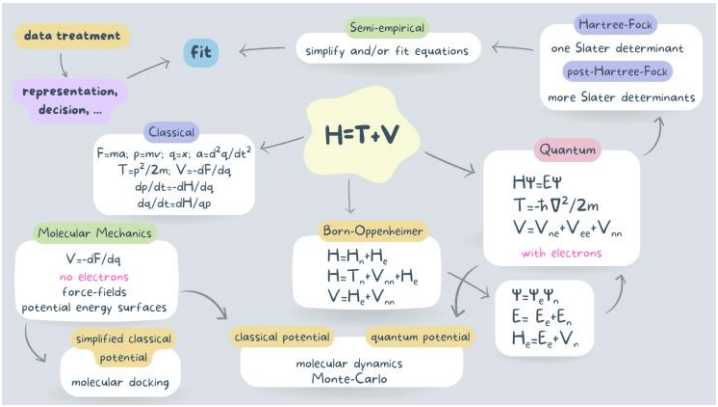

Figure 1. A general view of the computational methods in chemistry

This is done with online software tools such as WebMO (2024). The benefits are multifaceted. Visualization tools bring abstract concepts to life, improving spatial reasoning and conceptual understanding. Interactive simulations allow students to explore "what-if" scenarios, testing their predictions and deepening their grasp of cause-and-effect relationships.

2.2. Bridging the Invisible: Demystifying Chemical Bond

The world around us, from the vibrant colors of nature to the life-sustaining reactions within our bodies, exists due to the invisible dance of atoms held together by chemical bonds. Understanding these bonds is fundamental to grasping both the microscopic intricacies and macroscopic wonders of chemistry. However, traditional methods often paint an incomplete picture, leaving students yearning for a deeper glimpse into the hidden forces at play. This is where the magic of computational chemistry unfolds, offering an invaluable tool to illuminate the world of chemical bonds in undergraduate classrooms.

At its core, a chemical bond is a lowering of potential energy achieved when atoms share or exchange electrons. Computational tools transcend limitations of simple models, allowing students to visualize electron clouds, delve into molecular orbitals, and even simulate bond formation in real-time. Imagine watching electrons shift, feeling the tug of attraction and repulsion, and witnessing the birth of a molecule – a powerful experience that transforms theoretical concepts into tangible realities. Tools such as WebMO (2024.) are used in conjunction with other free ones such as ORCA (Neese et al., 2020), GAMESS (Schmidt et al., 1993), and wxMacmolPLT (Bode & Gordon, 1998).

2.3. Unveiling the Hidden: Infrared Spectroscopy and Computational Chemistry

Everything vibrates with unseen energy, and hidden within these vibrations lies a wealth of information about the molecules that make up our universe. Even at 0K, molecules vibrate. Infrared (IR) spectroscopy, the ability to analyze these vibrations, empowers us to unveil the identities and functionalities of molecules. However, interpreting the complex "fingerprint" of an IR spectrum can be daunting. This is where computational chemistry steps in, offering a powerful tool to enhance the understanding and application of IR spectroscopy.

Each molecule vibrates in unique ways, resulting in a distinct pattern of absorption frequencies in the IR spectrum. This "fingerprint" serves as a signature, allowing us to identify and analyze unknown molecules. However, interpreting the complex interplay of various functional groups and their corresponding peaks within the spectrum can be challenging for students. This is where Computational Chemistry comes to the rescue. By simulating the vibrations of molecules using sophisticated software, it empowers students to visualize and understand the origin of each peak in the IR spectrum. Imagine visualizing the atoms dancing, picturing the stretching and bending of bonds, and directly correlating these movements to the corresponding energy levels observed in the spectrum. This interactive approach transforms the abstract concept of vibrational modes into a tangible and engaging experience.

Again, online software tools such as WebMO (2024) is used with other free software as ORCA, (Neese et al, 2020), GAMESS (Schmidt et al., 1993), and wxMacmolPLT (Bode & Gordon, 1998).

2.4. Computers as tools of research: Computational Chemistry and Drug Design

As stated in the introduction, Computational Chemistry is an important part of chemistry research. More than that, fundamental. Nowadays, chemists and medicinal chemists rarely go to the laboratory to develop new molecules, materials, or drugs without some previous calculations and visualizations. Moreover, also previous browsing of the literature using different methods and databases, but also with computers. In what concerns Medicinal Chemistry various methods of Computational Drug Design are available centered on the ligand or on the target, ranging from virtual screening of candidates to new drugs to guide this research of artificial intelligence (AI), ranging from various forms of molecular modeling and fitting tools. Both Computational Chemistry and Computational Drug Design are full of methods mixed with a thorough jargon and difficult equations.

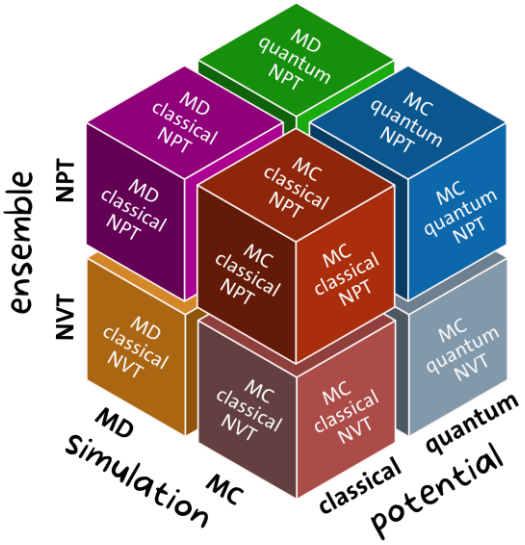

Figure 2. Methods of simulation, ensembles, and forms of obtaining the potential.

As an example of our approach, one presents a new way of making a first introduction of some complex ideas to Drug Design students (see Figure 2): (1) Classical *versus* Quantum; (2) Molecular Dynamics (MD) *versus* Monte Carlo (MC); and (3) *ensemble* NVT *versus ensemble* NPT. They have difficulty in seeing clear differences from methods of simulation and forms of obtaining the potential because they usually are exposed to very complex information about the methods, about solving Schrodinger equation, and force fields without being exposed to the simpler ideas and concepts behind them.

3. python4chemistry: Tools for Chemistry Students

In recognition of the growing importance of interdisciplinary approaches in science education, a new distance learning course titled "python4chemistry" has been developed. The course focuses on more elaborate tools, aiming to provide a simple approach to complex subjects providing foundational skills of Python programming and its application to chemical projects. It delves into core libraries enabling students to manipulate, analyze, and visualize chemical data effectively. A relevant point is the capability of creating craft informative visualizations like bar charts, heatmaps, and 3D plots, effectively communicating complex relationships and trends within their data.

Furthermore, the course explores Cheminformatics to leverage the power of computers in chemical research. Participants will gain the ability to represent molecules *in silico* (computationally), calculate molecular properties, and perform similarity searches for identifying compounds with desired characteristics.

Finally, the course introduces the exciting field of Machine Learning in the context of chemistry. Participants will be exposed to fundamental concepts of machine learning algorithms and their potential applications in chemical research tasks such as predicting reaction outcomes, property prediction, and materials design. Through hands-on exercises, researchers will gain a foundational understanding of these powerful tools and their potential to revolutionize chemical discovery and education.

Being prepared as a facultative course and fully at distance, it offers flexibility and accessibility for students with busy schedules or geographical limitations. It requires a strong commitment by the students and a high degree of self-discipline and time management skills to navigate coursework and complete assignments independently. Despite these challenges, the course encompasses engaging activities, clear learning objectives, and effective communication strategies leading to major benefits of online tools and molecular simulations to create a positive learning experience for students in undergraduate chemistry.

4. Conclusions

In this paper, we presented our experience on using computers on teaching at the various levels of the graduation, in Chemistry and Medicinal Chemistry, ranging from General Chemistry to Drug Design, passing through Computational Chemistry and other courses. We emphasized in this work the capabilities of computers for revealing the microscopic, unseen, and hidden patterns at lower levels at all levels of the graduation, and to show how computers are used in research on molecules, materials, and drugs at higher levels of the graduation. Our approach is based on simple ideas and concepts, practical laboratory work, motivational narratives, and clear feedback. New forms of clarifying complex ideas, sometimes presented in a “muddy” way, in particular for Computational Chemistry and Computational Drug Design, are envisaged. Some examples of concrete applications are presented.

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