COMPUTATIONAL CHEMISTRY COLUMN

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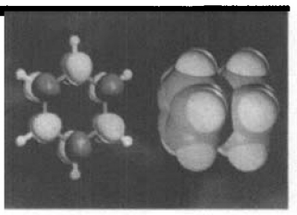

Chimia 46 (1992) 84–85

What is Computational Chemistry? A Tentative Answer

It is now two years that we have initiated this Computational Chemistry (CC) Column in *Chimia* and it is probably time to define with some more details the scope and purpose of the topic it is devoted to. Actually, we did not feel so far this to be a necessity, as there was seemingly a rough consensus among chemists on this subject. However, looking at recent literature [1][2] and discussing with respectable colleagues, we realized that important conceptual differences exist as to the meaning of CC, and that it was time for the editors of this Column to try to clarify the situation.

What is computational chemistry? In our opinion, CC is synonymous with computer-assisted chemistry: *it consists of all the areas of chemistry which benefit from the use of computers.* A somewhat more ambitious, though more restrictive, definition would be: it consists of all the areas of chemistry which are made possible by using computers. We definitely prefer the first formulation as it is more general, encompassing for example applications such as computer-assisted organic synthesis (CAOS): there is no doubt that chemical synthesis may take advantage of CAOS, but it is not made possible through the use of CAOS. Actually, our definition is close to that of *Lipkowitz* and *Boyd* [2], who stated that 'computational chemistry consists of those aspects of chemical research that are expedited or rendered practical by computers'. However, it is at some variance with the formulation of *Counts* [1]: 'the computational chemist is just a chemist whose computational tools and techniques offer a new method of attack in the continuing effort to obtain chemical information'. We feel indeed that the concept of chemical information is ambiguous in this context, as it could be taken in the restrictive sense of the content of chemical data bases, such as the *Chemical Abstracts*, which is obviously what *Counts* did not want to state. By the way, it is interesting to notice that *Counts* does not actually try to define CC itself, but rather the activities of the computational chemist. It is true, however, that as, computational chemists, we are tempted to explain what CC really is by referring to our everyday activities!

Coming back to our tentative definition of CC, it is worthwhile to make it more explicit by reviewing the areas of chemistry which benefit from the use of computers, *i.e.* by trying to make a classification of the various fields of this broad discipline which constitutes CC. Of course, such a classification is always a bit arbitrary, as discrete boundaries do not exist between the various fields of CC, and some methods may belong to different fields. However, it has the advantage of introducing some order into the growing number of applications of CC in virtually every area of chemistry. In our opinion, this classification can be performed under three headings.

1. Structure Elucidation and Analysis

It is an unquestionable fact that computers are today indispensable in this area. Needless to underline the importance of computing in all the applications related to data acquisition and processing in chemical experimentation, be it for diffraction or spectroscopic methods, chromatography, *etc.* This area of CC has even led to a new discipline, chemometrics, defined as 'the use of mathematical and statistical methods: *i*) to design or select optimal measurement procedures and experiments; and *ii*) to provide maximum chemical information by analyzing chemical data' [4]. Special applications such as pattern recognition or exhaustive structure generation should also be classified under this subfield of CC.

2. Chemical Information

The computerized processing of chemical data bases to extract information is a further topic of CC. If a simple on-line text search may not yet be considered as a typical CC activity, the complex search of *e.g.* a pharmacophoric pattern in a 3D-data base or the retrieval of a particular protein fold in a protein structure data base is undoubtedly an important CC area. Also the retrieval of information about reactions and the generation of possible pathways for chemical synthesis (*i.e.* the so-called CAOS applications) is also a prominent domain of CC. Although it would probably be an overstatement to say that CAOS is today an indispensable technique for the synthetic chemist, there are several examples of the important role played by CAOS in 'providing interesting suggestions of synthetic pathways for challenging targets', as recently reported by the 1990 chemistry *Nobel* prize laureate *Corey* [3]. Together with efficient graphical input/output processing and substructure searching procedures, this is a CC area of growing importance.

3. Theoretical Chemistry

Last, but not least, comes theoretical chemistry, the classical area of CC. In this context, theoretical chemistry should not be equated with quantum chemistry, as there are several theoretical methods in this field which are not based on the *Schrödinger* equation. In most cases, the purpose of these methods is to provide *models*, *i.e.* simplified representations of molecules or molecular systems, which help the chemist to rationalize molecular structure-property relationships, hence the name molecular modeling generally given to these applications. Without being exhaustive, let us mention the major topics of theoretical chemistry [5]:

- quantum chemistry: electronic structure and properties
- molecular mechanics: energy minimization, molecular dynamics and Monte Carlo simulations, free energy calculations
- reaction dynamics: dynamics and cross sections of molecular reactive collisions, scattering properties
- molecular graphics: visualization and manipulation of 3D structural models and properties of molecular systems

which have found wide applications in areas such as drug or molecular design, structure-property predictions, *etc.*

As you can see from this long enumeration performed along points *1–3*, computational chemistry suppress, is a broad discipline covering many aspects of chemistry and which continues to extend its importance and applicability. But this is not surprising, since computers have become an integral part in so many human activities, so why should chemistry be excluded?

[1] R.W. Counts, *J. Comput. Aid. Mol. Design* **1987**, *1*, 95.
[2] K.B. Lipkowitz, D.B. Boyd, in 'Reviews in Computational Chemistry', Eds. K.B. Lipkowitz and D.B. Boyd, Verlag Chemie, New York, 1990, p. vii.
[3] E.J. Corey, *Angew. Chem. Int. Ed.* **1991**, *30*, 455.
[4] I.E. Frank, B.R. Kowalski, *Anal. Chem.* **1982**, *54*, 232R.
[5] D.M. Hirst, 'A Computational Approach to Chemistry', Blackwell, Oxford, 1990.

Computerunterstützter Unterricht – Schweiz

Unter dem Patronat des BIGA wurde von interessierten Leuten die Initiative zur Gründung eines schweizerischen CBT-Vereins ergriffen (CBT = Computer Based Training). Das Ziel dieses Vereins syoll das Anbieten von Services in den Bereichen Information, Dokumentation, Beratung usw. sein. Am 11.12.1991 wurde eine Versammlung von an einer Mitgliedschaft interessierten Vertretern von *ca.* 50 Betrieben abgehalten; eine Gründungsversammlung ist auf Anfang April geplant. Mehr Information und Beitrittsformulare sind erhältlich vom Initiativkomitee SFIB, CBT-Schweiz, Erlachstrasse 21, CH–3000 Bern, Tel. (031) 23 0831.