Monatsh Chem 139, III–IV (2008)
DOI 10.1007/s00706-008-0882-8
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Editorial
Computational chemistry

Received 3 January 2008; Accepted 3 January 2008; Published online 18 January 2008

Computation in science became a discipline in its own right because of the breathtaking development of computational facilities that exceeded all expectations. *Gordon Moore*'s law was formulated in 1965 and predicted a doubling of the number of transistors in integrated circuits every two years. Despite all predictions that the exponential increase in chip complexity would have to come to an insurmountable limit soon it continued until today. This implies a factor of $2^{21} \approx 2 \times 10^6$ since *Moore* made his suggestion. At the same time the costs of computational power fell by about the same factor. Similar exponential increase in capacities and decrease in costs were seen in storage media. Although this fascinating development has been triggered by space missions and the huge market for personal computers, its implications for science were dramatic: Numerically assisted research mainly modeling and computer simulation became topics of comparable importance as experimental science. The possibility of performing highly efficient computations with previously unknown accuracy initiated a second development that was even more impressive than the ''hardware explosion'': New and much more efficient algorithms were conceived and implemented, numerical mathematics became a highly respected and dynamic area. In some disciplines the increase in computational performance due to improved numerical techniques by far exceeded the gain in mere number crunching efficiency thus leading to a total improvement of computational power by factors of 10^{13} and more. This spectacular advancement in computation allowed for addressing new problems and led to substantial progress in finding sufficiently accurate approximate solutions to so-called hard and even some NP-complete problems.

Computational chemistry is a fairly young discipline. Before computers became generally accessible, calculations in physical and theoretical chemistry had to rely on analytical approximations to exact solutions that were mostly lacking the accuracy required for reliable predictions. In the early 1960s the first computers became available for scientific computing. At the University of Vienna we started our first computations on a machine fully equipped with tubes and with a memory of 4 K eight-digit words. The diagonalization of a symmetric 20×20 matrix by means of the *Jacobi* method required more than two hours. The urgent need for increased computing power became most evident in quantum chemistry where all interesting predictions were dependent on an enormous up-scaling of computational capacity. The real break-through in this discipline came in the 1980s when improved algorithmic approaches were assisted by the ''hardware explosion''. Predictions on structures and spectroscopic properties of small and medium size molecular systems became more reliable than most experimental data. Similarly successful were the computations in solid-state quantum chemistry, which developed into an indispensable tool of present-day material sciences. The spectacular progress in quantum chemistry eventually led to the Nobel Prizes in Chemistry 1998, which were awarded to *Walter Kohn* and *John Pople*.

Meanwhile new challenges for computational chemists arose in structural biology were predictions of molecular conformations became an essential requirement for understanding function and regulation

of biological macromolecules. These systems were and still are much too large for direct quantum chemical calculations and empirical methods based on potential energy surfaces – often characterized as molecular mechanics techniques – were developed for computations of macromolecular systems. Two branches of applications of these empirical methods are currently of primary importance: 1) Structure-activity relations in pharmaceutical chemistry and molecular medicine and 2) rational design of protein and nucleic acid molecules with predefined properties. The recent explosion of data from various subdisciplines of molecular genetics – genomics, proteomics, metabolomics, and systems biology – provided new tasks for computational chemistry and computer science. Biochemical kinetics, for example, was an area where scientists relied entirely on analytical approximations and linearized plots for the evaluation of data. The situation has changed completely within the last thirty years: Nowadays, large-scale integration and automated computer driven data fitting techniques dominate. Simulations by high-dimensional dynamical systems as well as methods from discrete mathematics, for example graph theory, are the most frequently applied tools in computational systems biology.

In this special issue we present a representative collection of articles on current problems in computational chemistry. The beginning is made by an overview of general problems written for the non-specialist by *Sax*. The next two papers report highly accurate *ab initio* calculations on small molecules: *Fabian* presents an attempt to compute thermochemical quantities and *Antol et al.* investigate the structures of formamide, protonated formamide, as well as complexes of formamide with alkali metal cations in their ground and electronically excited states. The following two contributions apply *ab initio* density functional theory (DFT) to computations of chemical reaction mechanisms by means of models for reactive complexes: *Marković et al*. study the *Kolbe-Schmitt* reaction of sodium 2-naphthoxide and *Kirchner* investigates ruthenium-mediated C–C coupling reactions of alkynes. The paper by *Delchev et al.* studies intermolecular proton transfer in complexes of uracil with water and methanol molecules. *Karpfen et al.* report conformational analysis of cyclodextrines by means of DFT calculation. The next two contributions present cutting-edge computational research on solid states: *Hafner* reviews DFT calculations dealing with adsorption and reactions of organic molecules on solid surfaces and describes the state of the art in the hierarchy of DFT functionals applied to interactions of molecules and solids. *Puschnig* and *Ambrosch-Draxl* report DFT calculations on semiconductors formed by π-conjugated organic molecules. The two following papers are dealing with quantitative structure-activity relationships (QSAR): *König et al.* study hydrophobic moments for P-glycoprotein inhibitors and *Avram et al.* deal with membrane receptor inhibition by antipsychotic drugs used in schizophrenia treatment. The transition from chemistry to biology in computations is made by a review article by *Schuster* that describes the historical development from biochemical kinetics to structural bioinformatics and computational systems biology, and ends by presenting novel mathematical approaches to gene regulation. The last contribution by *Flamm* and *Hofacker* eventually studies the folding kinetics of ribonucleic acids (*RNA*) by means of a model theory for secondary structures based on empirical parameters determined from thermodynamic and kinetic properties of selected small *RNA* molecules.

Peter Schuster
Peter Wolschann
Issue Editors