

PREFACE

Advances in computer hardware together with recent enormous progress in linear scaling algorithms and developments in theory make molecular modeling attractive research tool for various fields starting from gas-phase reactivity of simple chemical molecules, through nanochemistry, to enzymology and pharmacology. Studies of kinetics and dynamics frequently involve modeling of the short-lived intermediates and transition states. These studies are conceptually demanding and are still stirring the scientific community. A compilation of reviews from different but related fields collected together in this volume can facilitate the knowledge transfer and interdisciplinary cooperation. Molecular modeling of dynamic processes of systems of increasing complexity is reviewed by experts in computational chemistry, wherever possible in collaboration with experimentalists. The first five chapters are devoted to progress in studies of gas phase reactions as well as catalysis and reactivity of the organic reactions. They also present novel approaches allowing to study dynamics of chemical reactions. In the following chapters dynamics of more complex systems like DNA constituents or polymerization reactions and phenomena such as charge transfer in biological systems are presented. The remaining, about half of the book will addresses kinetics of biosystems, including mechanisms of enzymatic reactions, whole protein motions concluding with tunneling contribution to the reaction dynamics.

The presented volume starts with very thorough chapter devoted to Ca^{2+} reactivity by Manuel Yáñez and his coworkers. Based on the most up-to-date knowledge from both experimental and theoretical studies the most fundamental issues regarding this important and common metal ion behavior are discussed. Ca^{2+} binding energies as well as created basicity scale based on the gas-phase DFT calculations deserve a special attention. It is followed by the contribution from Kyrychenko and Waluk that presents recent developments in computational modeling of hydrogen-bonding induced phenomena and excited-state properties in a series of biologically relevant bifunctional proton donor–acceptor heteroazaaromatic compounds. The authors show how the structure and dynamics of these complexes change gradually going from gas-phase calculations, via solvation simulation to the computations where lipid membrane environment is included. It is a very nice example of using MD simulations to explore hydrogen-bonding modes and the factors controlling their photochemistry and photophysics in the studied molecules of biological importance. The third chapter by Maksić and coworkers constitutes a nice continuation of the previous contribution as it also aims at describing an ultrafast phenomena in photochemistry and photobiology by the use of dynamics simulations. The authors present an overview of computational methods adequate for studying fast photodissociation process, among which a recently developed hybrid nonadiabatic photodynamics QM/MM method seems to be a promising tool for approaching such problems. In the following chapter the

predictive power of quantum mechanical methods in designing catalysts for asymmetric applications as exemplified with an organocatalyzed aldol reaction and a sulfur-ylide promoted aziridination is presented. The next chapter takes the readers into the world of chemical reactions and their representations using empirical force fields. The importance of the dynamics of bond-breaking and bond-forming processes is emphasized and the application of four different approaches is illustrated. Two novel ones, Molecular Mechanics for Proton Transfer (MMPT) and Adiabatic Reactive Molecular Dynamics (ARMD) are tested against several systems including the large biological ones. This chapter closes the first section devoted to the reactivity of small systems and available approaches capable of exploring dynamics and kinetics of reaction they take part in. The proceeding chapter opens up another section focused on more complex systems as it touches the molecular modeling of polymerization reactions. The authors present limitations of the available methods and give an overview of problems which may arise while using various levels of approximation. In the following chapter, Leszczynski and coworkers provide an important review on *ab initio* based kinetics simulation technique and show its performance on the example of the proton transfer reaction in DNA bases, nucleotides and their complexes with metal ions in the presence of water molecules. DNA theme is further explored in the chapter by Kubař and Elstner. It is devoted to the charge transfer (CT) in DNA, the computational framework developed for treating the main factors influencing it in this important biological system is presented. The CT process is also the focus of attention in the chapter by Civasotto and Anisimov. The authors present semiempirical linear scaling quantum-mechanical methods and their application to studies of CT using quantum mechanical molecular dynamics simulations in explicit water. The first chapter of the second half of the presented volume introduces the readers to the world of enzymatic systems by presenting the quantum theory of enzymology with the special emphasis on the role of the transition state structures. In the proceeding account the authors (Ramos and coworkers) review MD simulations in the study of metalloproteins. The most common obstacles and the available methods helping to solve the problems are presented. The next chapter by Liu provides a nice overview of QM/MM methodology and its application on enzymatic catalysis. It is followed by the work of Tuñón and coworkers in which on the example of lactate dehydrogenase the evolution of techniques and methods allowing for simulation of chemical reaction catalyzed by an enzyme is shown. This chapter constitutes also a nice illustration of possible shortcomings of all approaches chosen so far to study this particular enzymatic system. The topic of the role of protein dynamics and its impact on the kinetics and catalysis is further explored in the next chapter by McGeagh and Mulholland. Several examples of reactions catalyzed by enzymes are presented along with the applied QM/MM schemes.

In the subsequent chapter Cao and coworkers review their computational approach for studying transport mechanism in the membrane protein and show how theoretical studies can constitute a complementary tool towards deeper understanding of a biological problem. Another example of how MD methods can support experimental studies is presented in the next chapter by Liedl and

coworkers. The authors illustrate the applicability of different simulation techniques in drug discovery process. The following chapter is an introductory review for contributions focused on tunneling phenomena in enzymes. The contribution by Siebrand and Smedarchina provides a new model – analysis tool allowing to determine, based on the observed kinetic isotope effect and its temperature dependence, whether the tunneling process occurs via adiabatic or non-adiabatic mechanism. The theoretical background of quantum effects is further discussed in the subsequent chapter by Meana-Pañeda and Fernández-Ramos. Using Variational Transition State Theory the authors propose an alternative approach for taking into account large curvature tunneling mechanism, especially for large systems. Enzymatic H-tunneling reactions and the role of so-called promoting vibrations are reviewed in the last chapter of this volume by Scrutton and coworkers. The effect of the fluctuations coupled to the reaction coordinate in enzyme kinetics is illustrated by several biological H-transfers.

The presented studies do not only provide very useful information regarding the most recent achievements in computational chemistry and show the usefulness and applicability of the employed approaches but they also outline the major limitations of current simulations and draw possible future perspectives. There is a constant need for force fields improvement and development in order to guarantee the reliable models for simulating target molecules. The existing computational tools and theoretical frameworks require an ongoing feedback from the experiment for better understanding of factors governing dynamics and kinetics and the link between them in many systems, especially enzymes. And not only classical methods suffer from certain shortcomings, also quantum approaches necessary to study phenomena which explanation is only available by using higher level theories need more accurate and at the same time reasonable models with respect to the complexity and the cost of computations. Despite of listed limitations the field of molecular modeling is advancing at an easy to notice and acknowledge speed and its impact on the current knowledge status in such areas as photochemistry, material science, enzymology, or biophysics is growing and its role will definitely continue to be crucial in resolving many existing and long-lived puzzles.

Lodz
March 2010

Agnieszka Dybala-Defratyka
Piotr Paneth

Kinetics and Dynamics

From Nano- to Bio-Scale

Paneth, P.; Dybala-Defratyka, A. (Eds.)

2010, XVIII, 530 p., Hardcover

ISBN: 978-90-481-3033-7