Preface

Electrostatics is one of the primary forces in the physical realm and is pivotal in most of the processes occurring at the nanometric scale. In Biology, its importance cannot be overstated since it is one of the major responsible factors of molecular recognition, which is at the basis of Life as we know it. Describing electrostatic phenomena at the atomistic level can be a daunting task, especially when investigating complex multi-scale phenomena or when genomic data are processed. An approximation which often proves useful is the so-called *continuum* approach. Matter is described partly at the atomistic detail and partly as a continuum, endowed with constitutive properties. One of these properties is the dielectric permittivity, which accounts, in a mean field fashion, for a collective reaction of the considered media, both at the atomic and the electronic levels.

The continuum description of the matter frequently entails a piecewise constant permittivity and therefore the definition of one or more surfaces separating regions where it is uniform is needed. These surfaces can be very complex and their calculation involved and time-consuming. Leveraging a combination of the values of Geometry Processing with those of Computational Biology can be extremely beneficial to both fields. These were the leading topics of the Computational Electrostatics for Biological Applications (CEBA) international meeting, organised in Genova from July 1 to 3, 2013.

CEBA joined researchers in computational disciplines aiming at discussing and exploring different approaches to improve the electrostatics calculations mainly in the Molecular Biology field. The workshop covered both theoretical and numerical aspects mostly devoted to the solution of the Poisson–Boltzmann equation (PBE) as well as novel geometric approaches to molecular surface creation and applications to the NanoBiotechnology field. Different thematic sessions were organised with the specific aim of fostering interdisciplinary exchange between the members of the different scientific communities. This book builds upon the outcomes of the workshop.

CEBA was co-organized by the Department of Drug Discovery and Development of the Italian Institute of Technology and by the Shape Modelling Group of the Institute of Applied Mathematics and Information Technology of the Italian

National Research Council (CNR). Due to a true belief in the power of an interdisciplinary approach to the description of complex physical and biological problems, CEBA was co-located with the Eurographics Symposium on Geometry Processing 2013, (3–5 July 2013), a premier venue for exchanging research results on a wide range of topics related to the creation of mathematical foundations and practical algorithms for the processing of complex geometric data sets and models. The full CEBA programme, including videos of the lectures, can be found at http://electrostaticszone.eu/index.php/ceba-meeting.

This book collects a number of contributions that were discussed and extended after the workshop. The covered topics range from theoretical and numerical aspects of the solution of the PBE, to possible alternative models, to surveys and comparisons among geometric models of molecular surfaces, including their discretization and computational issues. The book also includes a number of chapters addressing applications, mostly in Biology and Biophysics.

The first chapter, *Electrostatics Models for Biology*, is kind of introductory. Here, Sazanavets et al. give an interesting **historical perspective on the evolution of continuum electrostatics models** since the early twentieth century, up to the introduction of Finite Difference Poisson–Boltzmann solvers. They also cover applications of this model in the field of Molecular Biology and give an outlook about their role in the post-genomic era. Then, Forsman and co-workers in the chapter *Classical Density Functional Theory of Ionic Solutions* review the basic structure of **classical density functional theory**, as an alternative to the differential approach inherent in the PBE, and more prone to the inclusion of ion–ion correlation in the treatment of electrolytic solutions.

Chapter 3, *A Comprehensive Exploration of Physical and Numerical Parameters in the Poisson–Boltzmann Equation for Applications to Receptor–Ligand Binding*, authored by Sørensen et al. is a practical and comprehensive guide for the scientist who wants to achieve a more insightful control on the use of the PBE in a context which is very relevant, for instance, in the Drug Discovery perspective.

The ensuing three chapters report on different **numerical techniques** aimed at improving quality, speed and robustness of electrostatic calculations. Boschitsch and Fenley, in *The Adaptive Cartesian Grid-Based Poisson–Boltzmann Solver: Energy and Surface Electrostatic Properties* present a solver where an unevenly spaced Cartesian grid adapts its local resolution based on the underlying geometry of the molecular surface. Huang and Baulin report on an efficient and stable method to solve PBE with steep gradients. Jaydeep Bardhan, in *Boundary-Integral and Boundary-Element Methods for Biomolecular Electrostatics: Progress, Challenges, and Important Lessons from CEBA 2013* very nicely revisits the main themes treated in CEBA in the perspective of solving the electrostatic problem via Boundary-Integral Equations and Boundary Element Methods, some less widespread alternatives to the differential PBE.

In Chap. 7, *The Accuracy of Generalized Born Forces*, Fogolari et al. give an overview of the *Generalized Born Approach*, which is often used in lieu of the PBE and against which it is compared. Chapters 8–10 represent the contributions given in CEBA that concerned the **geometric approaches to the construction of the**

molecular surface. In *State-of-the-Art and Perspectives of Geometric and Implicit Modeling for Molecular Surfaces*, Patanè and Spagnuolo give a general description of how implicit geometric modelling can be useful in the construction of the molecular surface. Both Dias and Gomes in *Triangulating Molecular Surfaces with Millions of Atoms* and Decherchi and Rocchia in *Building and Analysing Molecular Surfaces: A Tutorial on NanoShaper* give a computational perspective on geometric models when these entail the processing of large models. Dias and Gomes focus on methods to triangulate and visualise models built for millions of atoms on a desktop computer, while Decherchi and Rocchia give a tutorial on a tool that builds the molecular surface according to several different definitions using an efficient ray-casting approach.

The contribution of Zoppè and Loni is an intriguing description of how **intuitive visualisation** of biomolecules can help in conveying a great deal of information to the non-expert and can be used for dissemination to communities with different backgrounds.

The last chapters consider **application studies**, where different techniques are used on real case systems.

In *Using Structural and Physical–Chemical Parameters to Identify, Classify and Predict Functional Districts in Proteins*: *The Role of Electrostatic Potential*, Neshich et al. identify a correlation between what they call "nano-environment" descriptors and local structural and functional protein features such as catalytic sites. Among these descriptors, the local electrostatic potential, which they estimate by means of PBE, plays a major role. The study of Marracino et al. titled *Evaluation of Protein Electrostatic Potential from Molecular Dynamics Simulations in the Presence of Exogenous Electric Fields: The Case Study of Myoglobin*, considers the effects of an external electric field on a biomolecule by means of explicit solvent molecular dynamics simulation. Vitale and Amodeo in *Self-Inclusion Complexes of Mono-functionalized Beta-Cyclodextrins as Host–Guest Interaction Model Systems and Simple and Sensitive Testbeds for Implicit Solvation Methods*, identify a simple system that is used to compare different implicit solvation models. Finally, in Chap. 15, *Modeling Protein–Ligand Interaction with Finite Absorbing Markov chain*, Pacholczy et al. use the PBE calculated energies within the Stochastic Roadmap Simulation and finite absorbing Markov chain frameworks to estimate protein–ligand binding affinity.

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