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Preface

This special issue of Biophysical Chemistry is dedicated to the theoretical approaches used to account implicitly for the influence of solvent on biomolecules. One may have the impression that this subject is of interest to theoreticians and computational specialists only. On the contrary, we think that fundamental problems in the treatment of solvation in biomolecular modeling are of interest to a broad range of researchers. Proteins, nucleic acids and other biological molecules perform their functions in a complex aqueous environment. An understanding of a wide variety of phenomena concerning the conformational stability of proteins, as well as protein–protein and protein–ligand association involve the consideration of solvation effects. For example, assessing the relative contribution of hydrophobic and electrostatic interactions in protein–protein recognition in such events is a question of central importance in biology. The complexity of the environment of biomolecules is such that even a qualitative picture extracted from theoretical models may be helpful to further our comprehension of these systems. Nowadays, there is no doubt that computer simulations in which a large number of solvent molecules are treated explicitly represent the most detailed approach to study the influence of solvation on complex biomolecules. However, those methodologies are computationally intensive due to the large number of solvent molecules required to model a bulk solution. Furthermore, computer simulations with explicit solvent molecules are not exempt from approximations. For example, several fundamental questions arise when long-range electrostatic forces are truncated or summed over an infinite periodic array using Ewald techniques. Partly due to these difficulties, it is often desirable to develop different approaches in which the influence of the solvent is incorporated implicitly. Approximate schemes treating the solvent implicitly can provide useful quantitative estimates and remain computationally inexpensive. In addition, such approaches avoid the statistical errors associated with averages extracted from simulations with a large number of solvent molecules. More importantly, implicit solvent models can play an essential role as conceptual tools for analyzing the results of simulations generated with explicit solvent molecules. Implicit solvent models are thus helpful to aid better understanding of the nature of solvation phenomena in general.

The offer to organize and edit a Special Issue of Biophysical Chemistry on solvation was initiated by Professor Anthony Watts. In part, our purpose was to revisit the subject of solvation of biomolecules 5 years after the successful Special Issue edited by A.A. Rashin (Biophysical Chemistry vol 51, number 2,3). Rather than trying to produce a comprehensive review of the whole field, it was decided to focus on one aspect of solvation which has increasing importance, the implicit description of the influence of solvent. This decision was also strongly motivated by the recent advances in the field. We organized this Special Issue with the aim of offering a view of open questions concerning the theoretical treatment of solvent effects in biomolecular simulations. In the following discussions with Professor Anthony Watts, we agreed to link the issue to a Workshop entitled 'Implicit solvent models for biomolecular simulations' held at the Centre calcul Atomique et Moleculaire (CECAM) located

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in Lyon during May 1998. The CECAM workshop was attended by many of the leaders in the field. They responded enthusiastically and kindly agreed to write contributions for the Special Issue of Biophysical Chemistry. As a result, there are 14 contributed papers to the Special Issue.

The first paper presents a theoretical formulation of several central concept pertinent to implicit solvent description. The potential of mean force, thermodynamic integration, free energy decomposition into a non-polar and electrostatic contributions. This is followed by two papers addressing the solvation of non-polar substances and the hydrophobic effect. Then, current issues in electrostatics contribution to solvation and the application of continuum electrostatics are addressed in three papers and statistical mechanical integral equations are discussed and reviewed in two papers.

This ends the first part of the Special Issue which is mostly concerned with formal and theoretical questions. The following papers are devoted to practical implementation and applications. Two papers describe different approaches for quantitative prediction of the hydration free energy and one paper describes a mixed model in which a small number of water molecules in the first hydration shell around a protein are represented explicitly while the influence of the remaining solvent is approximated implicitly. Finally, the Special Issue is ended with three advanced applications of implicit solvent models to biomolecular systems, such as the role of electrostatics in molecule–molecule-associations, the discrimination of misfolded proteins by assessing the influence of solvation on their conformational stability, and the analysis of the various contributions to the heat capacity and compactness of denatured proteins.

We would like to thank Professor Anthony Watts and the staff of Biophysical Chemistry for their help and support, and the CECAM for their hospitality during the Workshop. Lastly, we would like to express our gratitude to all the authors who have contributed to the Special Issue. We hope that you will find this Special Issue useful and interesting.

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Guest Editors