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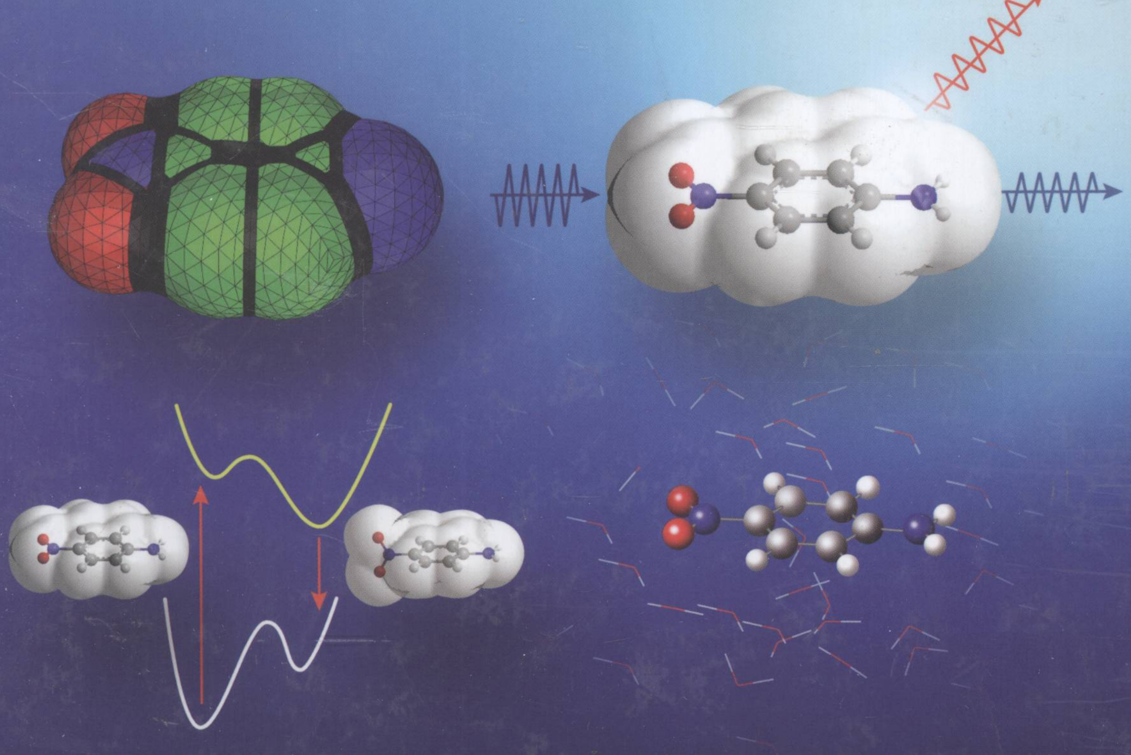

Continuum Solvation Models in Chemical Physics

From Theory to Applications

WILEY

Continuum Solvation Models in Chemical Physics: From Theory to Applications

Edited by

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Preface

The modeling of liquids and solutions with computational tools is a very complex problem which involves several research groups in different parts of the world. Many alternative theoretical models and computational algorithms have been proposed so far. All these models, however, can be classified in two main classes, namely that using an equivalent description for all the components of the system (the solute and the solvent molecules in a dilute solution, the molecules of the different species forming a mixture, etc.), and the other introducing a focused approach, i.e. a hierarchical approach in which the most interesting part of the system is treated at a much more accurate level than the rest. The first class of models include very different approaches which go from classical Molecular Dynamics (MD) and Monte Carlo (MC) simulations to accurate quantum mechanical (QM) calculations on small-medium clusters to ab-initio MD simulation on larger set of molecules.

Also the second class of methods include very different approaches; however, in all of them we can individuate a common aspect, namely the use of a mean-field description for the part of the system encircling the subsystem of real interest. In the application of this class of methods to the study of liquid solutions, the most important mean-field approach is represented by continuum models. In such models, the solute is assumed to be inside a cavity of proper shape and dimension within an infinite continuum dielectric mimicking the solvent.

Continuum solvation models are nowadays widespread computational techniques to study solvent effects on energy/geometry/reactivity and properties of very different molecular systems (from small molecules to very large biochemical systems such as proteins and enzymes).

Continuum solvation models have a quite long history which goes back to the first versions by Onsager (1936) and Kirkwood (1934), however only recently (starting since the 90s) they have become one of the most used computational techniques in the field of molecular modelling. This has been made possible by two factors which will be presented and discussed in the book, namely the increase in the realism of the model on the one hand, and the coupling with quantum-mechanical approaches on the other. The greater realism has also meant an important evolution in the mathematical formalism and in the computational implementation of the continuum models while the QM reformulation of such models has allowed the study of chemical and physical phenomena which were impossible to treat with classical only models. This important evolution of continuum models which has transformed them from empirical or qualitative approaches to accurate and quantitative methods has been realized in the last ten years and only now has real maturity been reached.

In addition to this, the literature on successful applications of these models to real chemical systems and problems has become large enough to stately prove the reliability of these models.

It thus become very interesting to give to both researchers and students a new book in which the analysis of both theory and applications of continuum models is reviewed.

For the first time, solvation continuum models are treated in an up-to-date and coherent way but at the same time using very different points of view coming from experts belonging to very different research fields (mathematicians, theoretical chemists, computational chemists, spectroscopists, etc.).

The book is partitioned into four chapters.

The first chapter focuses on a specific class of continuum solvation models, namely those using as a descriptor for the solvent polarization an apparent surface charge (ASC) spreading on the molecular cavity which contains the solute. This class of methods is central in the whole book (and especially in this first chapter) as during these last years it has become the preferential approach to account for solvent effects in QM calculations. A particular mention, among ASC methods, is for a specific formulation known as Polarizable Continuum Model (PCM). Nowadays, this acronym no longer represents a single computational method but a family of methods which are now available in various QM computational packages.

The physics beyond such a family of PCM models is presented and discussed by **Tomasi** together with an overview on the main features characterizing these models which will be further analyzed in the following chapters.

From a mathematical point of view the PCM models can be unified according to the approach they use to solve the linear partial differential equations determining the electrostatic interactions between solute and solvent. This analysis is presented by **Cancès** who reviews both the mathematical and the numerical aspects of such an integral equation approach when applied to PCM models.

A further analysis of the main numerical aspects related to the computational implementation of such a theory is presented and discussed by **Pomelli** with particular attention given to the definition of the molecular cavity and the sampling of its surface.

The last fundamental aspect characterizing PCM methods, i.e. their quantum mechanical formulation, is presented by **Cammi** for molecular systems in their ground electronic states and by **Mennucci** for electronically excited states. In both contributions, particular attention is devoted to the specific aspect characterizing PCM (and similar) approaches, namely the necessity to introduce an effective nonlinear Hamiltonian which describes the solute under the effect of the interactions with its environment and determines how these interactions affect the solute electronic wavefunction and properties.

In the other two sections of the chapter two further generalizations of PCM models are presented to spatially and dynamically nonlocal media (**Basilevsky & Chuev**) and to a Lagrangian formulation which includes the polarization of the medium as a dynamical variable (**Caricato, Scalmani & Frisch**), respectively. In the first case, the goal is to account for the discreteness of molecular liquids still within a continuum description of the solvent, while in the second case the goal is to describe any kind of time-dependent phenomena exploiting an efficient coupling of continuum models with standard MD simulations, both classical and ab-initio.

The second chapter presents extensions and generalizations of continuum solvation models (mostly of PCM type but not exclusively) to the calculation of molecular properties (both dynamic and static) and spectroscopic features of molecular solutes in different environments of increasing complexity.

Computational methods to study solvent effects on NMR (**Sadlej & Pecul**) and EPR (**Barone, Cimino & Pavone**) parameters are presented and discussed within the PCM as well their generalizations to hybrid continuum/discrete approaches in which the presence of specific interactions (e.g. solute-solvents H-bonds) is explicitly taken into account by including some solvent molecules strongly interacting with the solute.

Solvent effects on vibrational spectroscopies are analyzed by **Cappelli** using classical and quantum mechanical continuum models. In particular, PCM and combined PCM/discrete approaches are used to model reaction and local field effects.

Rizzo reviews in a unitary framework computational methods for the study of linear birefringence in condensed phase. In particular, he focuses on the PCM formulation of the Kerr birefringence, due to an external electric field yields, on the Cotton-Mouton effect, due to a magnetic field, and on the Buckingham effect due to an electric-field-gradient. A parallel analysis is presented for natural optical activity by **Pecul & Ruud**. They present a brief summary of the theory of optical activity and a review of theoretical studies of solvent effects on these properties, which to a large extent has been done using various polarizable dielectric continuum models.

The inclusion of the environment effects for non-linear optical (NLO) properties is presented within the PCM (**Cammi & Mennucci**) and the multipolar expansion (**Ågren & Mikkelsen**) solvation models. In the first contribution the attention is focused on the connection between microscopic effective properties and macroscopic NLO susceptibilities, whereas in the latter contribution the analysis is extended to treat heterogeneous dielectric media.

The extension of continuum models to complex environments is further analyzed by **Ferrarini** and **Corni & Frediani**, respectively. In the first contribution the use of PCM models in anisotropic dielectric media such as liquid crystals is presented in relation to the calculation of response properties and spectroscopies. In the second contribution, PCM formulations to account for gas-liquid or liquid-liquid interfaces, as well for the presence of a meso- or nano-scopic metal body, are presented. In the case of molecular systems close to metal bodies, particular attention is devoted to the description of the surface enhanced effects on their spectroscopic properties.

The second chapter ends with two overviews by **Stephens & Devlin** and by **Hug** on the theoretical and the physical aspects of two vibrational optical activity spectroscopies (VCD and VROA, respectively). In both overviews the emphasis is more on their basic formalism and the gas-phase quantum chemical calculations than on the analysis of solvent effects. For these spectroscopies, in fact, both the formulation of continuum solvation models and their applications to realistic solvated systems are still in their infancy.

The third chapter focuses on the modelization of solvent effects on ground state chemical reactivity and excited state reactive and non-reactive processes.

The effects of the surrounding medium on the shape of the potential energy surfaces (PES) is discussed by **Cossi & Rega** using the PCM formulation of continuum models while **Soteras, Blanco, Huertas, Bidon-Chanal, & Luque** present an overview of the current status and perspectives of theoretical treatments of solvent effects on chemical equilibria using different versions of continuum solvation model. A different aspect of the modelization of chemical reactivity is given by **Truhlar & Pliego**. In particular, they describe how continuum models can be used to predict the free energy of activation of chemical reactions and the effective potential for condensed-phase tunneling, and they can therefore be combined with variational transition state theory (VTST) to predict chemical reaction rates.

With the other contributions, the focus of the chapter is shifted to electronically excited states and their dynamics and reactivity.

The computational and experimental analysis of time dependent solvatochromic shift in fluorescence spectra of solutes is used by **Ladanyi** to achieve an accurate description of solvation dynamics, i.e., the rate of solvent reorganization in response to a perturbation in solute–solvent interaction.

Electron transfer (ET) reactions are analyzed by **Newton** in terms of continuum solvation models. Their role in the determination of the ET critical parameters (i.e. the solvent reorganization energy and the electronic coupling between the initial and final states) is analyzed using both an equilibrium and nonequilibrium solvation framework.

Photoinduced hydrogen-transfer and proton-transfer chemistry in hydrogen-bonded chromophore-solvent clusters are analyzed by **Domcke & Sobolevski** exploiting an interplay of QM and spectroscopic approaches.

Laage, Burghardt & Hynes present and discuss analytic dielectric continuum nonequilibrium solvation treatments of chemical reactions in solution involving conical intersections. Their analysis shows that theories of the rates of mechanisms of the chemical reaction in solution have to incorporate the fact that the solvent can be out of equilibrium with the instantaneous charge distribution of the reacting solutes(s).

Persico & Granucci focus on the nonadiabatic dynamics of excited states in condensed phase. Static environmental effects are discussed in terms of the change of the PES with respect to the isolated molecule, while dynamic effects are described in terms of transfer of energy and momentum between the chromophore (or reactive centre) and the surrounding molecules.

The third chapter ends with two contributions on the effects of the environment on the excitation energy transfers (EET) between chromophores.

In the first contribution, **Huxter & Scholes** present a review of the recent evolution of theory of EET in condensed phase from their earliest and simple formulation, based on the Forster theory to the most recent advances of theoretical and computational methods based on continuum solvation models. In the second contribution, **Curutchet** reviews the recent developments of PCM towards accurate theoretical investigations of EET in solution. In particular, the modelization of the various contributions of solvent effects in the chromophore–chromophore electronic coupling is presented using quantum-mechanical approaches.

The fourth chapter presents extensions and generalizations of continuum models to classical molecular dynamics simulations, to layered and to hybrid methods as well as to methods which can be considered as alternative to continuum models to account for the environment effects.

In more detail, **Orozco, Marchán & Soteras** review recent implementations of continuum models in the context of MD or MC calculations, to study solvent effects on the conformational space of large, flexible molecules. **Vreven & Morokuma** outline the formalism of the ONIOM method and how it can be extended to include solvation effects, both implicitly (using a ONIOM-PCM combination) and explicitly (using a ONIOM supra-molecular description). **Mikkelsen** covers the theoretical background of the multiconfigurational self-consistent field response methods for calculating molecular properties of molecules interacting with a structured environment using a hybrid QM/MM approach. **Milani, Tommasini, Del Zoppo & Castiglioni** compare Raman and infrared experiments in condensed phase with the results obtained using both a quantum supra-molecular approach and a simplified electrostatic embedding scheme.

Aguilar, Sánchez, Martín, & Fdez. Galván review the ASEP/MD method, acronym for Averaged Solvent Electrostatic Potential from Molecular Dynamics, showing how this method combines aspects of quantum mechanics/molecular mechanics (QM/MM) methods with aspects of continuum models.

Sato presents an alternative method to both continuum solvation models and hybrid QM/MM or ONIOM approaches. This is represented by the "reference interaction site model" (RISM) formalism when combined to a QM description of the solute to give the RISM-SCF theory.

As shown in this brief description of the contents, the book aims to present the main aspects and applications of continuum solvation models in a clear and concise format, which will be useful to the expert researcher but also to Ph.D. students and postdoctoral workers.

To this end, the presentation of the various contributions follows a step-by-step scheme in which the physical bases of the models come first followed by an analysis of both mathematical and computational aspects and finally by a review of their applications to different physical–chemical problems. For all the parts of the book two reading levels will thus be possible: one, more introductory, on the given theoretical issue or on the given application, and the other, more detailed (and more technical), on specific physical and numerical aspects involved in each issue and/or application. In such a way, the reader will first be introduced to a given subject through a general description of the problem (with more emphasis on those aspects which are more directly related to the presence of the solvent), and then she/he will discover how continuum models can be extended and generalized to properly describe such a problem. In parallel, possible limitations or incompleteness of these models are pointed out with indications of future developments.

Ending this Preface we would like to give our sincere thanks to all the colleagues who are (or have been) part of the PCM group in Pisa in the last years and have also contributed to this book: Chiara Cappelli, Marco Caricato, Stefano Corni, Maurizio Cossi, Luca Frediani, and Christian Pomelli.

The final and most important acknowledgement goes however to Professor Jacopo Tomasi who greatly contributed to the formation of our scientific and personal growth.

Benedetta Mennucci and Roberto Cammi.

Contents

1

Modern Theories of Continuum Models

1.1 The Physical Model

Jacopo Tomasi

1.1.1 Introduction

As the title indicates, this chapter focuses on methodological problems relating to the description of phenomena of chemical interest occurring in solution, using methods in which a part of the whole material system is described by continuum models.

The inclusion in the book of this introductory section has been motivated by the remarkable advances of continuum methods. Their extension to more complex properties and to more complex systems makes it necessary to have a more detailed understanding of the way in which physical concepts have to be further developed to continue this promising line of investigation. The relatively simple procedures in use for three decades to obtain with a limited computational effort the numerical values of some basic properties, such as the solvation energy of a solute in very dilute solution, are no longer sufficient.

To appreciate the basic reasons why continuous models are so versatile and promising for more applications, however, we have to consider again the simple systems and the simple properties mentioned above. The best way to gain this initial appreciation is to contrast the procedures given by discrete and continuum methods to obtain the solvation energy in a very dilute solution.

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1.1.2 Solvation Energy

The Discrete Approach

The material model consists of a large assembly of molecules, each well characterized and interacting according to the theory of noncovalent molecular interactions. Within this framework, no dissociation processes, such as those inherently present in water, nor other covalent processes are considered. This material model may be described at different mathematical levels. We start by considering a full quantum mechanical (QM) description in the Born–Oppenheimer approximation and limited to the electronic ground state. The Hamiltonian in the interaction form may be written as:

$$\hat{H}^{\text{tot}}(r_{\text{M}}, r_{\text{S}}) = \hat{H}^{\text{M}}(r_{\text{M}}) + \hat{H}^{\text{S}}(r_{\text{S}}) + \hat{H}^{\text{SS}}(r_{\text{S}}) + \hat{H}^{\text{MS}}(r_{\text{M}}, r_{\text{S}}) \tag{1.1}$$

In extremely dilute solutions only a single solute molecule M is sufficient and so $\hat{H}^{\text{M}}$ refers to a single molecule only. The number of solvent molecules S is in principle infinite, but the physics of the system is sufficiently well described by a finite, albeit large, number n of S units.

The third term of the Hamiltonian, $\hat{H}^{\text{SS}}$, represents the interactions between such molecules, and the last term, $\hat{H}^{\text{MS}}$ the interactions between M and the n solvent molecules. The coordinates $(r_{\text{M}}, r_{\text{S}})$ apply to both electrons and nuclei. Nuclear coordinates have to be explicitly considered, because the mobility of solvent molecules is a very important factor in liquid systems, and changes in their internal geometry, due to the intermolecular interactions, may also play a role.

The formulation of the Hamiltonian given in Equation (1.1) has introduced considerable simplifications in the formulation of the problem (the existence of specific molecules and their persistence has been acknowledged) but the computational problem remains formidable. Approximations are unavoidable.

The system is described as an assembly of interacting molecules whose motions are governed, in a semiclassical approximation, by a potential energy surface (PES) of extremely large dimensions related to the positions of all the nuclei of the system, internal nuclear motions within single molecule being for the moment still allowed. The approach used for the characterization of small clusters, i.e. searching first for the minimum energy conformation of the PES, cannot be used here. The physics of solvation is remarkably different. Solvation energy and related properties (solvent effects on the solute geometry are an example) are averaged properties and we are compelled to perform a suitable average upon the energies corresponding to all the accessible conformations of the whole molecular system.

Statistical thermodynamics gives us the recipes to perform this average. The most appropriate Gibbsian ensemble for our problem is the canonical one (namely the isochoric–isothermal ensemble N, V, T). We remark, in passing, that other ensembles such as the grand canonical one have to be selected for other solvation problems). To determine the partition function necessary to compute the thermodynamic properties of the system, and in particular the solvation energy of M which we are now interested in, of a computer simulation is necessary [1].

We do not enter into the description of Monte Carlo of Molecular Dynamics methods, as these details are not important for our discussion. There are other more general aspects of computer simulations to consider here.