Faculty of Science and Technology

Department of Chemistry

The Polarizable Continuum Model Goes Viral!

Extensible, Modular and Sustainable Development of Quantum Mechanical Continuum Solvation Models

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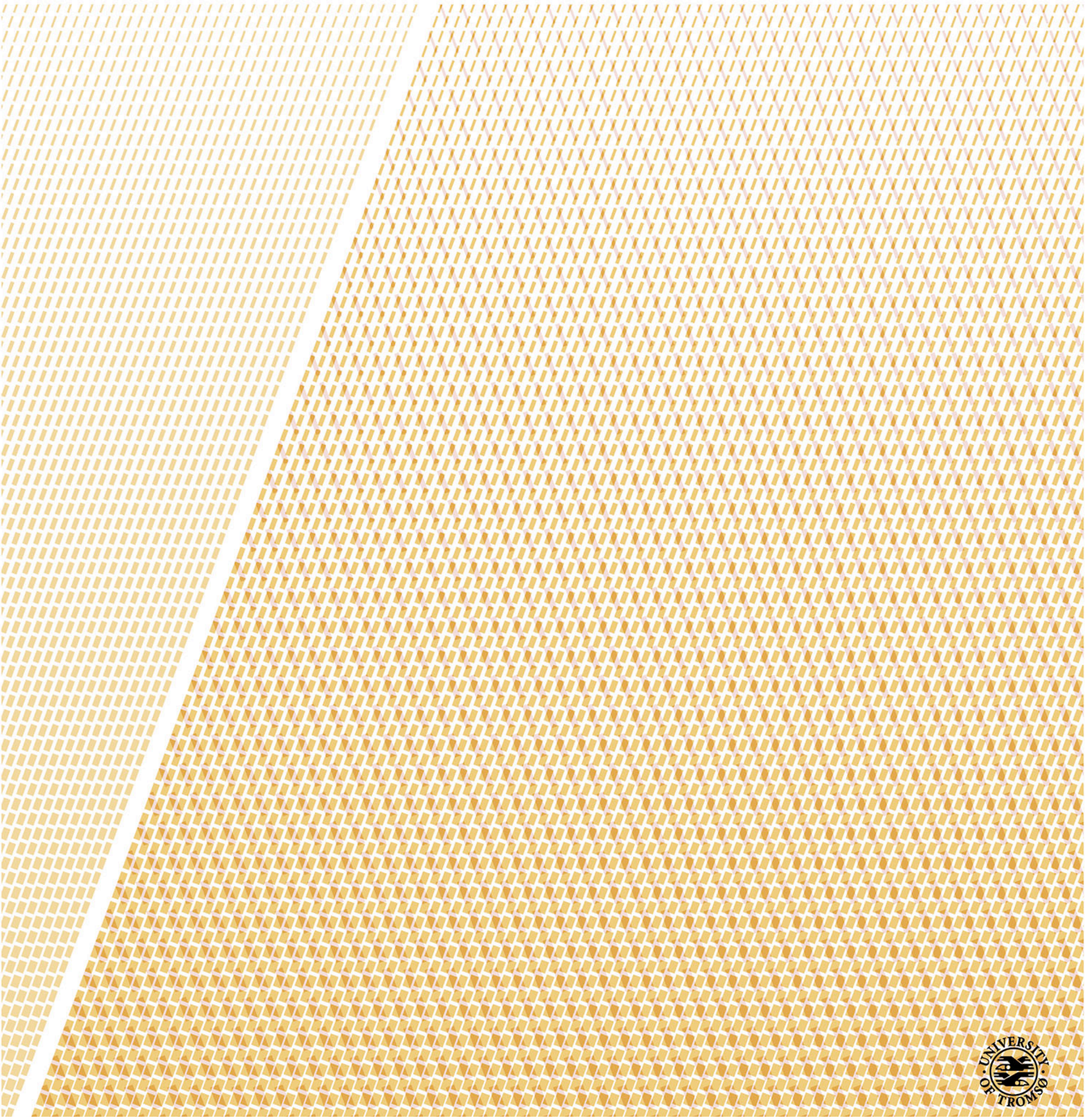
Roberto Di Remigio

A dissertation for the degree of Philosophiae Doctor – January 2017



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THE POLARIZABLE CONTINUUM MODEL GOES VIRAL!

Extensible, Modular and Sustainable Development
of Quantum Mechanical Continuum Solvation Models

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COLOPHON

This document was typeset using LuaLaTeX, with a modified version of the `classicthesis` template developed by André Miede.[*] The style was inspired by Robert Bringhurst's seminal book on typography *The Elements of Typographic Style*[1] and Edward Tufte's work.[2–5] The bibliography was processed using BibLaTeX[†] and Biber.[‡] TeX Gyre Termes provides both the text and display typeface. TeX Gyre Heros is the sans-serif typeface, while Jim Lyles's `Bitstream Vera Mono` is used for monospaced text. Finally, XITS is the typeface for mathematical formulas.

The Polarizable Continuum Model Goes Viral!

[*] https://bitbucket.org/amiede/classicthesis/

[†] https://www.ctan.org/pkg/biblatex

[‡] http://biblatex-biber.sourceforge.net/

Abstract

Synergistic theoretical and experimental approaches to challenging chemical problems have become more and more widespread, due to the availability of efficient and accurate *ab initio* quantum chemical models. Limitations to such an approach do, however, still exist. The vast majority of chemical phenomena happens in complex environments, where the molecule of interest can interact with a large number of other moieties, solvent molecules or residues in a protein. These systems represent an ongoing challenge to our modelling capabilities, especially when high accuracy is required for the prediction of exotic and novel molecular properties. How to achieve the insight needed to understand and predict the physics and chemistry of such complex systems is still an open question.

I will present our efforts in answering this question based on the development of the polarizable continuum model for solvation. While the solute is described by a quantum mechanical method, the surrounding environment is replaced by a structureless continuum dielectric. The mutual polarization of the solute-environment system is described by classical electrostatics. Despite its inherent simplifications, the model contains the basic mathematical features of more refined explicit quantum/classical polarizable models. Leveraging this fundamental similarity, we show how the inclusion of environment effects for relativistic and nonrelativistic quantum mechanical Hamiltonians, arbitrary order response properties and high-level electron correlation methods can be transparently derived and implemented.

The computer implementation of the polarizable continuum model is central to the work presented in this dissertation. The quantum chemistry software ecosystem suffers from a growing complexity. Modular programming offers an extensible, flexible and sustainable paradigm to implement new features with reduced effort. PCMSolver, our open-source application programming interface, can provide continuum solvation functionality to any quantum chemistry software:

continuum solvation goes *viral*. Our strategy affords simpler programming workflows, more thorough testing and lower overall code complexity. As examples of the flexibility of our implementation approach, we present results for the continuum modelling of non homogeneous environments and how wavelet-based numerical methods greatly outperform the accuracy of traditional methods usually employed in continuum solvation models.

Tromsϕ, October 5, 2016

Roberto Di Remigio

Acknowledgments

> Just a perfect day
> You made me forget myself
> I thought I was
> Someone else, someone good
>
> — Lou Reed

It has not been one day, it's been four years. And it's not always been perfect. It is however true that the people I have met and interacted with during this adventure have made me feel *someone good*. I don't feel it's an exaggeration to say that if I have made it this far is also because of *you*. Thus, these few, poorly written lines are a *dedication* of this dissertation to you and an *acknowledgment* of the patience and love you have shown towards me. Thanks for not giving up on me.

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A Grazia, Graziella e al Toblerone, qualcuno sa perché.

Contents

Publications

This thesis is based on the following scientific papers:

Paper I

Four-Component Relativistic Calculations in Solution with the Polarizable Continuum Model of Solvation: Theory, Implementation, and Application to the Group 16 Dihydrides H_2X (X = O, S, Se, Te, Po)
R. Di Remigio, R. Bast, L. Frediani, and T. Saue
J. Phys. Chem. A, 2015, **119**, 5061–5077
DOI: 10.1063/1.4943782

Paper II

Wavelet Formulation of the Polarizable Continuum Model. II. Use of Piecewise Bilinear Boundary Elements
M. Bugeanu, **R. Di Remigio**, K. Mozgawa, S. S. Reine, H. Harbrecht, and L. Frediani
Phys. Chem. Chem. Phys., 2015, **17**, 31566–31581
DOI: 10.1039/C5CP03410H

Paper III

A Polarizable Continuum Model for Molecules at Spherical Diffuse Interfaces
R. Di Remigio, K. Mozgawa, H. Cao, V. Weijo, and L. Frediani
J. Chem. Phys., 2016, **144**, 124103
DOI: 10.1063/1.4943782

Paper IV

Four-Component Relativistic Density Functional Theory with the Polarizable Continuum Model: Application to EPR Parameters and Paramagnetic NMR Shifts
R. Di Remigio, M. Repisky, S. Komorovsky, P. Hrobarik, L. Frediani, and K. Ruud
Accepted for publication in *Mol. Phys.*
DOI: 10.1080/00268976.2016.1239846

Paper V

Open-Ended Formulation of Self-Consistent Field Response Theory with the Polarizable Continuum Model for Solvation
R. Di Remigio, M. T. P. Beerepoot, Y. Cornaton, M. Ringholm, A. H. S. Steindal, K. Ruud, and L. Frediani
Submitted to *Phys. Chem. Chem. Phys.*

Acronyms

AD	automatic differentiation
AO	atomic orbital
API	application programming interface
ASC	apparent surface charge
BCH	Baker–Campbell–Hausdorff
BEM	boundary element method
BIE	boundary integral equation
BO	Born–Oppenheimer
CC	coupled cluster
CC2	approximate coupled cluster singles and doubles
CC3	approximate coupled cluster singles, doubles and triples
CCS	coupled cluster with single substitutions
CCSD	coupled cluster with single and double substitutions
CCSDT	coupled cluster with single, double and triple substitutions
COSMO	conductor-like screening model
CSC	continuous surface charge
DC	Dirac–Coulomb
DFT	density-functional theory
DtN	Dirichlet-to-Neumann
DVCS	distributed version control system
EPR	electron paramagnetic resonance

FCI	full configuration interaction
FQ	fluctuating charges
GGA	generalized gradient approximation
HF	Hartree–Fock
IEF	integral equation formalism
KS	Kohn–Sham
LDA	local density approximation
LGPL	GNU Lesser General Public License
MBPT	many-body perturbation theory
MD	molecular dynamics
MEP	molecular electrostatic potential
MM	molecular mechanics
MO	molecular orbital
MP	Møller–Plesset
ON	occupation number
PCM	polarizable continuum model
PDE	partial differential equation
PE	polarizable embedding
PES	potential energy surface
pNMR	paramagnetic nuclear magnetic resonance
PTE	perturbation-to-the-energy

PTE(S)	perturbation-to-the-energy with approximate singles substitutions
PTED	perturbation-to-the-energy-and-the-density
PTES	perturbation-to-the-energy with singles substitutions
PWC	piecewise constant
PWL	piecewise linear
QM	quantum mechanics
RHS	right-hand side
SAS	solvent-accessible surface
SCF	self-consistent field
SES	solvent-excluded surface
SOS	sum-over-states
SWIG	switching/Gaussian
TDSCF	time-dependent SCF
vdWS	van der Waals surface
XC	exchange-correlation

Notations, Conventions and Units

A number of notations and typographic conventions has been adopted in order to maintain consistency throughout. We summarize them here. Hartree atomic units are used throughout:[6,7]

$$\mathrm{m_e} = \mathrm{e} = \hbar = 4\pi\varepsilon_0 = 1$$

the unit of length is the Bohr $\mathrm{a_0}$, while that of energy is the Hartree $\mathrm{E_h}$. The speed of light is then:

$$c = 137.035\,999\,074\,\mathrm{a_0}\,\mathrm{E_h}\,\hbar^{-1}$$

Complex conjugation will always be shown using a dagger (†) instead of a star ($*$).

This document makes use of hyperlinks within and without to ease reading and navigation. A numbered citation style was chosen. Citations are color-coded in green, appear (most often) as superscripts and are hyperlinked to the bibliography. Acronyms are color-coded in gray and hyperlinked to the list of acronyms. Finally, URLs and placeholders for URLs are color-coded in orange. They are hyperlinked to the respective online resource.

Basic Notation

u_E	Restriction (trace) of the function u to the set E
$\mathrm{Span}\{\boldsymbol{v}_1, \dots, \boldsymbol{v}_n\}$	Vector space spanned by the vectors $\boldsymbol{v}_1, \dots, \boldsymbol{v}_n$
δ_{ij}	Kronecker symbol: $\delta_{ij} = 1$ if $i = j$ and 0 otherwise
$(u, v)_X$	Scalar product of u and v in the Hilbert space X
$\lVert u \rVert_X$	Norm of u in the normed space X
$O(N)$	A quantity of order N or higher

Vectors and Matrices

$\boldsymbol{v}, \boldsymbol{q}$	Vectors
$\boldsymbol{K}, \boldsymbol{F}$	Matrices
$\mathbb{R}^{m,n}$	Vector space of real-valued $m \times n$ matrices
$\mathrm{Tr}\boldsymbol{A}$	Trace of $\boldsymbol{A}$. For $\boldsymbol{A} \in \mathbb{R}^{n,n}$, $\mathrm{Tr}\boldsymbol{A} = \sum_{i=1}^{n} A_{ii}$
$\overset{\mathrm{Tr}}{=}$	The expression following is to be interpreted as a trace. $\mathscr{E} \overset{\mathrm{Tr}}{=} \boldsymbol{hD} = \mathrm{Tr}\boldsymbol{hD}$
$\overset{\{\mathrm{Tr}\}_T}{=}$	The expression following is to be interpreted as a trace followed by time-averaging over a period T. $\mathscr{E} \overset{\{\mathrm{Tr}\}_T}{=} \boldsymbol{hD} = \frac{1}{T}\int_0^T \mathrm{d}t\,\mathrm{Tr}\boldsymbol{hD}$
$0_N, \boldsymbol{I}_N$	The zero and the identity in an N-dimensional vector space

Operators

$\hat{\mathscr{A}}, \hat{\mathscr{D}}$	Integral operators
$H, \mathit{\Phi}$	First or second quantized N-electron operators

Molecular Quantum Mechanics

r, s, t	General molecular orbital indices
i, j, k	Occupied molecular orbital indices
a, b, c	Virtual molecular orbital indices
κ, λ, μ	One-electron basis functions indices

Introduction

[...] og fordi jeg alltid har hatt en dragning mot det skjulte og hemmelige.

— Karl Ove Knausgård, *Om Høsten*

WHAT ARE THE ELECTRONS REALLY DOING IN MOLECULES?

This question was posed by R. S. Mulliken over a half-century ago[*] and can be considered the fundamental research question behind the development of quantum chemistry. The purpose of quantum chemistry is to provide models based on first principles that can help *understand* and *predict* macroscopic, observable chemical phenomena, such as reaction mechanisms and spectroscopic experiments.[8] As stated by Dirac in his Quantum Mechanics of Many-Electron Systems paper:[9,10]

> *The underlying physical laws necessary for the mathematical theory of a large part of physics and the whole of chemistry are thus completely known, and the difficulty is only that the exact application of these laws leads to equations much too complicated to be soluble. It therefore becomes desirable that approximate practical methods of applying quantum mechanics should be developed, which can lead to an explanation of the main features of complex atomic systems without too much computation.*

Following Dirac's *dictum*, in quantum chemistry we apply physical models based on quantum many-body methods to molecular systems, employ their mathematical realizations and devise computable approximations. The central idea is, in fact, to be able to obtain an

[*] Mulliken chose it as the title for his Gilbert N. Lewis award acceptance speech in 1960.

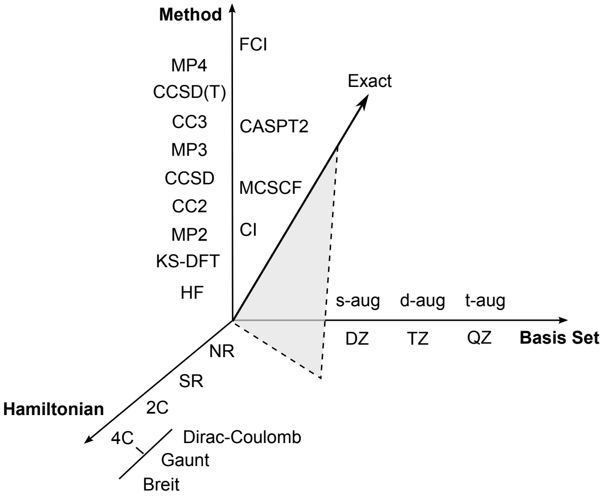


Figure A Pictorial depiction of the concept of *model chemistries* as the three dimensions of quantum chemistry.[12,13] Reproduced from ref. 14 with permission from the PCCP Owner Societies.

algorithmic implementation of the methods that can be applied to interesting chemical systems: model building and software implementations are two closely intertwined aspects in the practice of quantum chemistry.[11]

▶ It is easy to manipulate chemicals in a virtual laboratory. Nowadays quantum chemical methods often complement traditional experimental approaches. They have become invaluable tools in the modern development of chemistry,[15–17] as witnessed by the Nobel prizes awarded in 1998[18] and 2013.[19] The concept of *model chemistries* is at the heart of these successes. Introduced by Pople, theoretical model chemistries are specific combinations of approximations in the basis set and molecular electronic structure methodology.[12] Model chemistries are *systematically improvable* so that it is possible to achieve the heaven of chemical accuracy[*] by relaxing approximations in the model, albeit at an increased computational cost. Figure A presents the usual depiction of this concept as a set of orthogonal axes, where chemical accuracy can be achieved by

[*] A theoretical result is said to be *chemically accurate* if it is within 1 kcal mol^{-1} of the corresponding experimental measurement.

moving away from the origin. Relativity can be considered as the third axis of quantum chemistry: accuracy can be improved on the Hamiltonian, method and basis axes.[13]

The description of the ideas and methods at the basis of quantum chemistry will be the subject of Chapter 1. I will put emphasis on the methods that have been relevant in the work presented in this dissertation.

THE PROBLEM OF SOLVATION

▶ CHEMISTRY CAN BE LARGELY CONSIDERED A *WET* SCIENCE: almost always chemical phenomena happen in a liquid environment.[20] We hereby define a "solution", or more generally an "environment", as a system where the number of solvent molecules exceeds by far the number of solute molecules.[21,22] It is then clear that theoretical and computational approaches to such a problem will necessarily suffer from a *dimensionality disease*. The number of degrees of freedom to be taken into account is, in principle, so large, that even the most powerful computers would have a hard time computing the desired observables. Moreover, on an interpretive level, it would not even be desirable to have such a detailed insight. As is well known from statistical mechanics, microscopic detail cannot account for the macroscopic behaviour.[23,24] To tame this complexity and cure the disease, one must devise *models* that simplify the physical picture, while offering tools for understanding reality and predicting new and exciting phenomena and properties.[8,11,25] One of the earlier attempts at tackling the problem of solvation is due to Onsager. His was a rather crude model, but one that has had a lasting impact and informs much of the developments that will be presented in this dissertation.[26]

BEFORE INTRODUCING OUR MODEL OF CHOICE, let us consider how an environment might affect molecular observables of interest. Environment effects are usually classified as:

DIRECT. These effects stem straightforwardly from the modification underwent by the solute electronic density when interacting with the environment.

INDIRECT. It is common for solutes to exhibit different minimum-energy conformations in different environments. These effects are commonly labelled as indirect.

LOCAL FIELD. Light-matter interactions are also affected by the environment. Local modifications of externally applied fields subtly influence molecular responses.[27,28]

DYNAMIC. The presence of the environment radically influences excited states, since relaxation processes in the medium become important.[29,30]

SPECIFIC. This catch-all category includes all effects stemming from the peculiar solute-solvent pair interactions that cannot be fully described under any of the previous labels. In general, modelling such effects demands an atomistic level of detail.

Faced with the problem of describing such a diverse array of effects, two main models have emerged in the past decades, each with its strengths and weaknesses. Both can be classified as *multiscale* (or *focused*) models[19] and hinge on the same idea: treat different parts of the system with different methods and couple these methods by bridging "scales" at the boundary. Figure B schematically portrays the transition from a full QM model of the relevant system to its multiscale representations.

While both models treat the molecular degrees of freedom at the quantum mechanical level, their approach to the microscopic description of the degrees of freedom of the environment differs:

- *Discrete* (or *explicit*) models explicitly treat those degrees of freedom. This is either achieved by a cheaper quantum mechanical method[31] or by molecular mechanics (MM).[32] In the latter approach, commonly dubbed QM/MM, the MM region can either be polarizable[33–35] or non polarizable. While the former method allows for mutual polarization between the QM and MM subsystems, the latter treats the MM region as fixed.

- *Continuum* (or *implicit*) models completely remove the degrees of freedom of the environment from the model, replac-

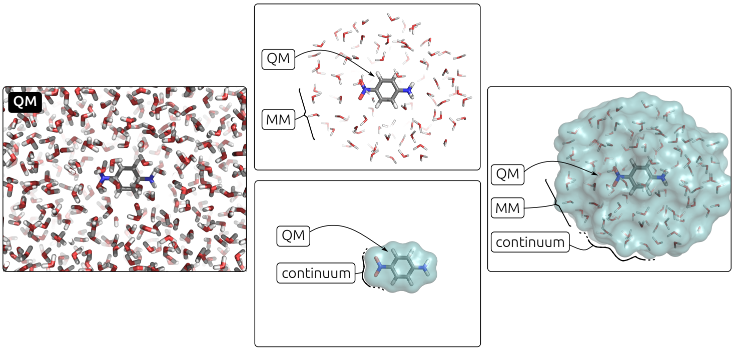


Figure B Pictorial depiction of the transition from quantum mechanical to multiscale models for the aqueous solvation of *para*-nitroaniline. Leftmost panel: a fully quantum mechanical cluster model. Upper central panel: a quantum/classical discrete (explicit) model. Lower central panel: a quantum/classical continuum (implicit) model. Rightmost panel: a quantum/classical mixed explicit/implicit model. Picture reproduced courtesy of Dr. Stefano Caprasecca (MoLEcoLab, Università di Pisa).

ing them with a structureless continuum. Its effect is described, classically, *via* its bulk properties.[26,36]

QM/MM models can capture, albeit approximately, the effect of the atomistic nature of the environment on the active part of the system. However, they demand statistical averaging of environment configurations to yield results of any significance. Moreover, a rather large *cutoff radius* for the MM region is usually required to converge long-range electrostatic interactions.[37] Continuum models avoid both problems at once. Statistical averaging is built into the model *via* their parametrization by means of the environment's bulk properties, such as the permittivity. In addition, long-range electrostatics is treated exactly. Unfortunately, atomistic detail is lost and it is then impossible to recover a satisfactory description of specific effects. To partly alleviate these sources of error, the QM/MM and QM/Continuum methods can and have been successfully combined to yield the three-layer QM/MM/Continuum method.[35,37–39]

Notice that we have deliberately ruled out so-called *cluster* models from the above discussion. These approaches replace the actual physical setting with a suitable truncation of the whole solute+solvent system, the *model system* and treat it within a chosen quantum mechanical level of theory. Cluster models can be used to benchmark more approximate multiscale models, but their description is outside the scope of this dissertation.

Chapter 2 will present an overview of the polarizable continuum model (PCM) for solvation. I will present a nontechnical discussion of the mathematical details of the model and an outline of current methodologies for the solution of the associated governing equations. Borrowing from the work of Lipparini et al.,[40,41] I will introduce a unifying theoretical formalism for QM/Continuum, QM/MM and QM/MM/Continuum models that will be extensively used throughout.

A ROAD TO REALITY OR MOLECULAR RESPONSE PROPERTIES

The experimentalists' view of molecular systems is built mainly around the use of spectroscopic techniques that explore the interaction of light and matter. When a system is exposed to an external perturbing electromagnetic field, it will respond with a detectable change in its properties.[42,43] Characterizing, explaining and predicting a large number of measurable properties requires a synergistic experimental and theoretical approach. *Response theory* is the missing link between theory and these vast classes of experiments, making quantum chemistry a full-fledged virtual laboratory. Response theory allows the description and computation of perturbation-induced changes in observable molecular properties. Electric and magnetic properties, excitation energies and transition moments can easily be calculated in the framework of response theory. *Response functions* are the central concept in response theory. These are built solely by means of *unperturbed* molecular states and energies: no explicit modelling of excited states is needed.

Response theory will be the subject of Chapter 3, where the basic ideas in the computation of response functions will be presented. We will discuss the formulation of the linear response function for quantum/classical polarizable Hamiltonians and show how the variational framework is a powerful theoretical tool.

ACCURATE METHODS FOR ACCURATE PROPERTIES

► THE CONCEPTS OF SYSTEMATIC IMPROVABILITY AND THEORETICAL MODEL CHEMISTRIES are the foundations for the successful practice of quantum chemistry. A balanced description of electron correlation is often necessary to achieve results that are accurate enough for meaningful comparisons with experiments.[15–17] The cost-effective treatment of electron correlation is a challenging problem and a very active line of research in the field. Density-functional theory approaches are cheap and widespread, but their general accuracy is hard to assess. Many-body perturbation theory and coupled cluster approaches are more robust in this respect, albeit at an increased computational cost.

In this dissertation, we are interested in the inclusion of environment effects in *ab initio* models of interesting chemical systems. As already noted, this is a difficult problem, the more so when including electron correlation is necessary to obtain better accuracy. We will describe our approach to this problem in Chapter 4. Treating solvation and electron correlation has been a recurring subject of research in the literature since the inception of continuum models. Once again, we will leverage the variational formulation of classical polarizable models presented in Chapter 2.

1

A Tour of Molecular Electronic Structure Theory

> — electrons deify one razorblade into
> a mountainrange; [...]
>
> — E. E. Cummings

This Chapter presents a brief overview of molecular electronic structure theory with particular emphasis on the methods used in this dissertation. Section 1.1 is a general introduction to the methods of molecular quantum mechanics, relativistic or nonrelativistic. I will provide a brief introduction to the language of second quantization, used throughout the thesis. Section 1.2 presents the mean-field approximation to the molecular electronic structure problem, the workhorse of quantum chemistry. Sections 1.3–1.5 are concerned with the coupled cluster (CC) and many-body perturbation theory (MBPT) methods for the inclusion of electron correlation.

1.1 MOLECULAR QUANTUM MECHANICS

▶ Quantum mechanics is the theory describing the motion and interactions of microscopic particles. In quantum theory every observable of the system is represented mathematically by an operator O in the appropriate Hilbert space of *wave functions*. A wave function ψ is the mathematical object describing the state of the system. In the usual Copenhagen interpretation of quantum mechanics, the modulus square of the wave function $|\psi|^2$ provides the key to predicting experimentally measurable quantities.[44] The wave function ψ is the solution to the Schrödinger equation:

$$H\psi = E\psi \tag{1.1}$$

where H is the *Hamiltonian* operator and E is the energy of the system. The Schrödinger equation is an eigenvalue equation for the Hamiltonian operator and ψ is thus an eigenfunction.[45]

► MOLECULAR QUANTUM MECHANICS IS CONCERNED WITH THE MICROSCOPIC MOTION OF NUCLEI AND ELECTRONS IN MOLECULES and is thus an intrinsically many-body theory. The problem is clearly very complicated to solve, as the number of interactions to be considered is large. Since the nuclei are much heavier than the electrons, the Born–Oppenheimer (BO) or clamped-nuclei approximation is typically assumed. The nuclei are fixed in a specific configuration (called a *molecular geometry*) and treated as static electric sources.[46] This separation of motions results in an electron-only Hamiltonian and an electronic wave function that depends *parametrically* on the nuclear positions. The eigenvalue of this Hamiltonian, also dependent on the nuclear positions, is the potential energy surface (PES) of the system, that is the potential function in which the nuclei move.[47,48] In first quantization, the general expression for the clamped-nuclei, N-electron, molecular electronic Hamiltonian is:

$$H = \sum_{i=1}^{N} h(\boldsymbol{r}_i) + \frac{1}{2}\sum_{i\neq j}^{N} g(\boldsymbol{r}_i, \boldsymbol{r}_j) + V_{\mathrm{NN}}. \tag{1.2}$$

The last term is the nuclear repulsion energy:

$$V_{\mathrm{NN}} = \frac{1}{2}\sum_{A\neq B}^{N_{\mathrm{nuclei}}} \frac{Z_A Z_B}{|\boldsymbol{R}_A - \boldsymbol{R}_B|}, \tag{1.3}$$

a constant shift of the energy scale in the BO approximation. As noted by Saue, the same general expression for the clamped-nuclei Hamiltonian Eq. (1.2) is valid in the nonrelativistic and relativistic no-pair regimes.[13,49] In the nonrelativistic domain one defines the one- and two-electron operators as:[44,47,48]

$$h(\boldsymbol{r}_i) = -\frac{1}{2}\nabla_i^2 + V_{\mathrm{Ne}}(\boldsymbol{r}_i) = -\frac{1}{2}\nabla_i^2 - \sum_{A=1}^{N_{\mathrm{nuclei}}} \frac{Z_A}{|\boldsymbol{R}_A - \boldsymbol{r}_i|} \tag{1.4a}$$

$$g(\boldsymbol{r}_i, \boldsymbol{r}_j) = \frac{1}{|\boldsymbol{r}_i - \boldsymbol{r}_j|}, \tag{1.4b}$$

while in the relativistic regime with the Dirac–Coulomb (DC) approximation they become:[44,50,51]

$$h(\boldsymbol{r}_i) = (\boldsymbol{\beta} - I_4)\mathrm{m_e}c^2 + c(\boldsymbol{\alpha}_i \cdot \boldsymbol{p}_i) + V_{\mathrm{Ne}}(\boldsymbol{r}_i)I_4 \tag{1.5a}$$

$$g(\boldsymbol{r}_i, \boldsymbol{r}_j) = \frac{I_4 \cdot I_4}{|\boldsymbol{r}_i - \boldsymbol{r}_j|} \tag{1.5b}$$

The Dirac matrices, expressed in terms of the vector $\boldsymbol{\sigma}$ collecting the three Pauli spin matrices, were introduced:

$$\boldsymbol{\alpha}_i = \begin{pmatrix} 0_2 & \boldsymbol{\sigma}_i \\ \boldsymbol{\sigma}_i & 0_2 \end{pmatrix}, \quad \boldsymbol{\beta} = \begin{pmatrix} I_2 & 0_2 \\ 0_2 & -I_2 \end{pmatrix}, \tag{1.6}$$

and the operators are implicitly assumed to embed the proper no-pair, positive-energy manifold projectors.[49] Since these are fermionic Hamiltonians, the spin-statistics theorem dictates the corresponding eigenfunctions to be antisymmetric. Using the expansion theorem,[52] we seek the wave function for the N-electron system as a linear combination of N-electron *Slater determinants*.

► IN THE LANGUAGE OF SECOND QUANTIZATION, we assume that a complete and orthonormal set of one-particle states is available.[*] These are usually called molecular orbitals (MOs). In general, we would like to embed as many of the symmetries of the system into the one-particle basis. This is accomplished by requiring the one-particle space to be the common eigenbasis for a complete set of suitable, commuting one-particle operators.[52] Any N-particle state can be constructed by distributing particles into one-particle states and accordingly labelling them by the number of particles per one-

[*] Neither completeness nor orthonormality of the one-particle set are necessary assumptions. Relaxing both assumptions would however make the formalism slightly more involved.

particle state present. This is the so-called occupation number (ON) vector representation:

$$|\boldsymbol{n}\rangle = |n_1, n_2, \dots\rangle\,, \tag{1.7}$$

and the span of all ON vectors is called the *Fock space* F^N, a space isomorphic to the Hilbert space H^N of N-particle wave functions. To preserve consistency, the *vacuum* state with no particles:

$$|\mathrm{vac}\rangle = |0, 0, \dots\rangle \tag{1.8}$$

is included in the construction of Fock space. Any N-particle state can be generated by application of *creation* operators $a_i^\dagger$. Creation operators increase the occupation number in the one-particle state i by 1, up to a phase. Conversely, *annihilation* operators a_i, defined as the Hermitian conjugates of the creation operators, decrease occupation in state i by 1, again up to a phase. Clearly, annihilation of any one-particle state in the vacuum yields 0. Pauli's exclusion principle is enforced by the *canonical anticommutation relations*:

$$a_r^\dagger a_s^\dagger + a_s^\dagger a_r^\dagger = 0 \tag{1.9a}$$

$$a_r a_s + a_s a_r = 0 \tag{1.9b}$$

$$a_r^\dagger a_s + a_s a_r^\dagger = \delta_{rs}, \tag{1.9c}$$

showing how the construction of the Fock space representation embeds antisymmetry at the operator level and not in the ON vectors. Finally, the second-quantized molecular electronic Hamiltonian in the Born–Oppenheimer approximation is:[53,54]

$$H = \sum_{rs} h_{rs} a_r^\dagger a_s + \frac{1}{2}\sum_{rstu} g_{rstu} a_r^\dagger a_t^\dagger a_u a_s + V_{\mathrm{NN}} \tag{1.10}$$

where the matrix elements are given as integrals over the chosen one-particle basis:

$$h_{rs} = \int \mathrm{d}\boldsymbol{r} \phi_r^\dagger(\boldsymbol{r}) h(\boldsymbol{r}) \phi_s(\boldsymbol{r}) \tag{1.11a}$$

$$g_{rstu} = \int \mathrm{d}\boldsymbol{r} \int \mathrm{d}\boldsymbol{r}' \,\Omega_{rs}(\boldsymbol{r}) g(\boldsymbol{r}, \boldsymbol{r}') \Omega_{tu}(\boldsymbol{r}') \tag{1.11b}$$

$$\Omega_{rs}(\boldsymbol{r}) = \phi_r^\dagger(\boldsymbol{r}) \phi_s(\boldsymbol{r}). \tag{1.11c}$$

The second-quantized Hamiltonian Eq. (1.10) is thus a *projected* operator, exact only within the subspace determined by the chosen one-particle set.[52,53]

In second quantization, the exact molecular electronic wave function can be written as a linear combination of ON vectors:

$$|\psi\rangle = \sum_{\boldsymbol{k}} C_{\boldsymbol{k}} \, |\boldsymbol{k}\rangle \,, \tag{1.12}$$

also known as the full configuration interaction (FCI) expansion. Among the many properties the exact wave function enjoys, the *variational* property and *size-extensivity* are the ones that are almost always embedded into approximate wave function ansätze.[53] According to the former, the energy is stable with respect to orthogonal variations of the wave function. In practice this guarantees that minimization with respect to the parameters of a well-crafted ansatz will converge from above to the exact energy.[47,48,53] A wave function ansatz enjoying the latter property guarantees that the energy of a system made of noninteracting subsystems is equal to the sum of the energies of the isolated subsystems.[53,55]

Coefficients in the FCI expansion in Eq. (1.12) corresponding to the molecular ground state can be determined by seeking the lowest eigenvalue of the matrix representation of the Hamiltonian in the space of ON vectors. The FCI method is exact, within the chosen one-particle set, but scales exponentially with the number of electrons in the system and thus has very limited practical applications. Approximations can be tailored by appropriate truncations of the N-electron space. In *single-reference* methods, one first determines an approximation to the solution by means of a single ON vector. This ON vector is treated as the *physical* vacuum: vectors in Fock space can be classified according to how different their occupation is from the reference, *i. e.* by *excitation level*.[53,54] A truncated expansion can then be constructed by including only those ON vectors that differ from the reference up to a certain number of excitations. Further details on how these expansions are actually tailored and algorithmically implemented can be found elsewhere.[53] In the rest of this Chapter we will describe how a single ON vector approximation can be constructed, how we can improve on it by means of coupled cluster and many-body perturbation theory and how the properties of the exact wave function are embedded into these ansätze.

1.2 MEAN-FIELD THEORY

► THE IDEA BEHIND MEAN-FIELD THEORY IS SIMPLE: seek the best description of the many-electron wave function using just one Slater determinant. How does one direct this search towards the "best"? We will use the variational principle and optimize the degrees of freedom in our single-determinantal trial wave function accordingly. It is evident that there is no variational freedom in the N-electron space. All variational degrees of freedom reside in the one-electron space, *i.e.* in the space of MOs $\{\phi_r\}$, used to build the determinant $|0\rangle$. The one-electron MOs are thus optimized considering each single electron in the mean field generated by the motion of all other electrons, hence the name of the method. Clearly this neglects parts of the electron– electron interaction energy: *electron correlation*. According to Löwdin, this can be defined as the energy difference between the exact nonrelativistic and the complete-basis set mean-field results for the system under consideration.[56] However, in most cases, it provides a suitable starting approximation for more sophisticated many-body treatments that recover larger portions of the correlation energy.

Starting from an initial guess for the one-particle states, we iteratively refine them by applying suitable rotations. The iterations are carried out until a suitable convergence criterion has been met, *i. e.* the orbitals are *self-consistent*. The unitary rotation operator can be expressed as the exponential of a one-electron, anti-Hermitian operator:

$$U = \mathrm{e}^{-\kappa}, \quad \kappa = \sum_{rs}[\kappa_{rs} a_r^\dagger a_s - \kappa_{rs}^* a_s^\dagger a_r], \quad \kappa^\dagger = -\kappa. \tag{1.13}$$

The energy of the system is now a function of the rotation parameters $\kappa_{rs}, \kappa_{rs}^*$ and setting its gradient $\boldsymbol{E}^{[1]}$ to zero will identify its stationary points. The gradient of the electronic energy can be identified by comparing the Taylor and Baker–Campbell–Hausdorff (BCH) commutator expansions of the Hamiltonian expectation value. For a closed-shell this yields *Brillouin's theorem*:

$$E^{[1]}_{ai} = -f_{ai} = h_{ai} + \sum_j [g_{aijj} - g_{ajji}] = 0, \tag{1.14}$$

where f_{ai} are elements of the *Fock matrix* $\boldsymbol{F}$. The two-electron terms appearing in the Fock matrix are called the Coulomb and exchange integrals, respectively. The stationarity condition implies that the Fock matrix is block-diagonal in the basis of the optimal MOs. In the *canonical representation* one seeks the set of orbitals that make the Fock matrix diagonal. Hence the optimization problem is equivalent to diagonalization of an effective one-electron operator:

$$\boldsymbol{F}\boldsymbol{\phi} = \boldsymbol{\phi}\boldsymbol{\epsilon} \tag{1.15}$$

where the eigenvalues of the Fock matrix are called *orbital energies*.

A DIFFERENT APPROACH IS TAKEN IN DENSITY-FUNCTIONAL THEORY (DFT), where the electron density is the central quantity in the theory, instead of the wave function. The Hohenberg–Kohn theorems[57,58] and their relativistic counterparts[59,60] establish the energy as a *functional* of the density. The Kohn–Sham (KS) approach to DFT takes us a step further by assuming the density of the system to be equal to that of a fictitious, noninteracting system once again described by a single Slater determinant.[61] We rewrite the energy as a sum of five terms:

$$E[\rho] = T_s[\rho] + V_{\text{ext}}[\rho] + J[\rho] + E_{\text{xc}}[\rho] + V_{\text{NN}} \tag{1.16}$$

the first four of which are functionals of the density. The first term $T_s[\rho]$ is the kinetic energy of the fictitious noninteracting system. The second and third terms in Eq. (1.16) represent, respectively, the classical interaction of the electrons with the external potential (including the nuclear attraction potential) and the classical Coulomb interaction of the density with itself:

$$V_{\text{ext}}[\rho] = \int \mathrm{d}\boldsymbol{r} V_{\text{ext}}(\boldsymbol{r})\rho(\boldsymbol{r}) \tag{1.17a}$$

$$J[\rho] = \frac{1}{2}\int \mathrm{d}\boldsymbol{r} \int \mathrm{d}\boldsymbol{r}' \rho(\boldsymbol{r})g(\boldsymbol{r},\boldsymbol{r}')\rho(\boldsymbol{r}') \tag{1.17b}$$

The fourth term in Eq. (1.16) is the exchange-correlation (XC) functional. This term accounts for the nonclassical part of the two-electron interaction: electron exchange and electron correlation. Moreover, it also corrects for the self-interaction present in $J[\rho]$ and the error introduced in the evaluation of the kinetic energy. The exact form of this functional is not known and a number of parametrized approximations exist.[62] In the local density approximation (LDA), the functional is expressed in terms of an *energy density*, e_{xc}, which is a local function of the density:

$$E_{\mathrm{xc}}^{\mathrm{LDA}}[\rho] = \int \mathrm{d}\boldsymbol{r} e_{\mathrm{xc}}(\rho(\boldsymbol{r})). \tag{1.18}$$

In the generalized gradient approximation (GGA), the energy density is a local function of both the density and the norm of its gradient:

$$E_{\mathrm{xc}}^{\mathrm{GGA}}[\rho] = \int \mathrm{d}\boldsymbol{r} e_{\mathrm{xc}}(\rho(\boldsymbol{r}), \zeta(\boldsymbol{r})), \quad \zeta(\boldsymbol{r}) = \boldsymbol{\nabla}\rho \cdot \boldsymbol{\nabla}\rho. \tag{1.19}$$

Finally, in *hybrid* functionals, some proportion of the HF exchange is included:

$$E_{\mathrm{xc}}^{\mathrm{hybrid}}[\rho] = E_{\mathrm{xc}}^{\mathrm{GGA}}[\rho] + \gamma E_{\mathrm{x}}^{\mathrm{HF}}[\rho] \tag{1.20}$$

The KS-DFT state is optimized by the same iterative process described above. Repeated diagonalizations of the KS matrix are carried out until self-consistency is reached. The KS matrix:

$$f_{rs} = h_{rs} + \sum_j [g_{rsjj} - \gamma g_{rjjs}] + f_{\mathrm{xc};rs}. \tag{1.21}$$

contains an XC one-electron contribution due to the in addition to the other terms contained in the Fock matrix. The functional derivative of the XC functional enters in the definition of this additional term:

$$f_{\mathrm{xc};rs} = \int \mathrm{d}\boldsymbol{r} \Omega_{rs}(\boldsymbol{r}) v_{\mathrm{xc}}(\boldsymbol{r}), \quad v_{\mathrm{xc}}(\boldsymbol{r}) = \frac{\delta E_{\mathrm{xc}}[\rho(\boldsymbol{r})]}{\delta\rho(\boldsymbol{r})}. \tag{1.22}$$

Notice moreover the exact exchange admixing factor γ in the two-electron part of the KS matrix.

How are MOs constructed? The usual approach is to expand them in a basis of one-particle, atom-centered basis functions of known functional form:

$$\phi_r(\boldsymbol{r}) = \sum_{\alpha=1}^{N_{\text{basis}}} C_{\alpha r}\chi_\alpha(\boldsymbol{r}) \tag{1.23}$$

and optimize the expansion coefficients in the SCF procedure. Choosing the one-particle MO space is then equivalent to choosing the one-particle atomic orbital (AO) space. The functional form of the AO basis is chosen to strike a balance between a physically accurate description of the short-range Coulomb interaction and algorithmic robustness and efficiency.[53] The usual choice, also adopted in this dissertation, is to use bases of Gaussian functions.[63,64]

1.3 THE COUPLED CLUSTER ANSATZ

In the coupled cluster method we construct our correlated wave function as an exponential mapping on top of a single reference function:[53,54,65,66]

$$|\mathrm{CC}\rangle = \mathrm{e}^{T}\,|\mathrm{HF}\rangle\,. \tag{1.24}$$

Out of convenience we assume, here and in the following, that the reference function is a closed-shell HF wave function. The *cluster* operator appearing in the exponential is given as:

$$T = \sum_{u=1}^{\mathscr{M}} T_u = \sum_{u=1}^{\mathscr{M}} \sum_{\mu_u} t_{\mu_u}\tau_{\mu_u} \tag{1.25}$$

that is, as a truncated sum of excitation operators, τ_{μ_u}, times the corresponding cluster amplitudes, t_{μ_u}. Here μ_u is the μ-th excitation at the u-th excitation level and $\mathscr{M}$ is the truncation level. One of the main strengths of the CC model is its size-extensivity which stems directly from the exponential nature of the wave operator.[53,54]

The CC method is not a variational but a *projective* method. Chosen the truncation level $\mathscr{M}$, one projects the nonrelativistic Schrödinger equation for this ansatz on the excitation manifold which comprises the reference function and all possible excited determinants, up to the chosen truncation order:

$$\langle \mathrm{HF}|\mathrm{e}^{-T}H\mathrm{e}^{T}|\mathrm{HF}\rangle = E_{\mathrm{CC}} \tag{1.26a}$$

$$\langle \mathrm{exc}|\mathrm{e}^{-T}H\mathrm{e}^{T}|\mathrm{HF}\rangle = 0 \tag{1.26b}$$

where $\langle \mathrm{exc}|$ means any of the excited determinants in Fock space compatible with the excitation level truncation. Notice that we have also performed a *similarity transformation* of the Hamiltonian operator. This leads to the *linked* form of the CC equations, which is manifestly size-extensive term-by-term. Use of similarity transformed operators is ubiquitous when dealing with CC theory and we introduce the following notation for it:

$$\overline{O} = \mathrm{e}^{-T}O\mathrm{e}^{T} \tag{1.27}$$

The cluster operator is not Hermitian. Hence, the similarity transformation will not, in general, preserve any of the symmetries, such as hermiticity, that the bare operators might have possessed. Similarity-transformed operators can be expanded in a BCH commutator series:

$$\overline{O} = O + \tilde{O} = O + [O, T] + \frac{1}{2}[[O, T], T] + \dots \tag{1.28}$$

It can be shown that the BCH expansion of the similarity-transformed Hamiltonian *exactly* truncates after the four-fold nested commutator, greatly simplifying algebraic derivations and manipulations.[53]

Introducing the Møller–Plesset (MP) partitioning of the Hamiltonian leads to further insight:

$$H = F + \Phi = \sum_{r} \epsilon_r a^{\dagger}_r a_r + (g - V_{\mathrm{HF}}), \tag{1.29}$$

where F if the Fock matrix and Φ is the fluctuation potential, expressed as the difference between the full two-electron interaction and its Hartree–Fock (HF) mean-field approximation:

$$V_{\mathrm{HF}} = \sum_{i} [g_{rsii} - g_{riis}] a^{\dagger}_r a_s. \tag{1.30}$$

Given our initial assumption on the reference function, the Fock operator is diagonal and expressed in terms of spin-orbital energies and number operators. Its similarity transformation truncates after the second term and has a relatively compact form:

$$\overline{F} = F + \sum_{u=1}^{\mathscr{M}} \sum_{\mu_u} \epsilon_{\mu_u} t_{\mu_u} \tau_{\mu_u} \tag{1.31}$$

where ϵ_{μ_u} is the difference in orbital energies between the occupied and virtual spin-orbitals of excitation u. For the fluctuation potential the similarity transformation truncates after the fifth term, including up to four-fold nested commutators.

WE HAVE ALREADY REMARKED THAT THE CC METHOD IS NOT VARIATIONAL. It is however possible to introduce a fully variational Lagrangian that leads to the same amplitudes equations.[67–72] Let us call $\mathscr{E}(\boldsymbol{\eta})$ the definition of the energy for the given quantum chemical method. The *amplitudes* $\boldsymbol{\eta}$ are determined by a set of stationarity conditions $\boldsymbol{\Omega}(\boldsymbol{\eta}) = 0$. Direct minimization of $\mathscr{E}(\boldsymbol{\eta})$ is thus a *constrained* optimization. Introducing a set of Lagrange *multipliers* $\bar{\boldsymbol{\eta}}$ lets us recast the problem as an unconstrained minimization of the Lagrangian:

$$\mathscr{L}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}) = \mathscr{E}(\boldsymbol{\eta}) + (\bar{\boldsymbol{\eta}}, \boldsymbol{\Omega}(\boldsymbol{\eta}))_W, \tag{1.32}$$

where $(\cdot, \cdot)_W$ denotes the scalar product in the vector space W. The governing equations are then obtained by differentiation with respect to both sets of parameters:

$$\frac{\partial \mathscr{L}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}})}{\partial \bar{\boldsymbol{\eta}}} = \boldsymbol{\Omega}(\boldsymbol{\eta}) = 0 \tag{1.33a}$$

$$\frac{\partial \mathscr{L}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}})}{\partial \boldsymbol{\eta}} = \frac{\partial \mathscr{E}(\boldsymbol{\eta})}{\partial \boldsymbol{\eta}} + \left(\bar{\boldsymbol{\eta}}, \frac{\partial \boldsymbol{\Omega}(\boldsymbol{\eta})}{\partial \boldsymbol{\eta}}\right)_W = 0 \tag{1.33b}$$

The CC Lagrangian can thus be expressed as:

$$\begin{aligned}\mathscr{L}(t,\bar{t})_{\mathscr{M}} &= \langle \mathrm{HF}|\overline{H}|\mathrm{HF}\rangle + \sum_{u=1}^{\mathscr{M}}\sum_{\mu_u}\bar{t}_{\mu_u}\langle\mu_u|\overline{H}|\mathrm{HF}\rangle \\ &= E_0 + \sum_{u=1}^{\mathscr{M}}\bar{t}_{\mu_u}\epsilon_{\mu_u}t_{\mu_u} + \langle\mathrm{HF}|\overline{\Phi}|\mathrm{HF}\rangle \\ &+ \sum_{u=1}^{\mathscr{M}}\langle\bar{t}_u|\overline{\Phi}|\mathrm{HF}\rangle\end{aligned} \tag{1.34}$$

where $E_0 = \sum_i \epsilon_i$ is the sum of the one-electron orbital energies and the shorthand notation for the Lagrangian multiplier state (left CC state) was introduced:

$$\langle\bar{t}_u| = \sum_{\mu_u}\bar{t}_{\mu_u}\langle\mu_u|\,. \tag{1.35}$$

Differentiation of the Lagrangian with respect to the multipliers correctly yields the amplitudes equations, while differentiation with respect to the amplitudes leads to the governing equations for the multipliers:

$$\Omega_{\mu_q}(t,\bar{t}) = \epsilon_{\mu_q}t_{\mu_q} + \langle\mu_q|\overline{\Phi}|\mathrm{HF}\rangle = 0 \tag{1.36a}$$

$$\begin{aligned}\bar{\Omega}_{\mu_q}(t,\bar{t}) &= \epsilon_{\mu_q}\bar{t}_{\mu_q} + \langle\mathrm{HF}|[\overline{\Phi},\tau_{\mu_q}]|\mathrm{HF}\rangle \\ &+ \sum_{u=1}^{\mathscr{M}}\langle\bar{t}_u|[\overline{\Phi},\tau_{\mu_q}]|\mathrm{HF}\rangle = 0\end{aligned} \tag{1.36b}$$

While the multipliers are not needed for the evaluation of the CC energy, their calculation is mandatory when expectation values and molecular properties in general are sought. The CC expectation values are formed using the left and right CC states and we introduce the following notation:

$$O(t,\bar{t})_{\mathscr{M}} = \langle\mathrm{HF}|\overline{O}|\mathrm{HF}\rangle + \sum_{u=1}^{\mathscr{M}}\langle\bar{t}_u|\overline{O}|\mathrm{HF}\rangle \tag{1.37}$$

Explicit expressions for truncated CC models can be found in Appendix A.2

1.4 MANY-BODY PERTURBATION THEORY

Perturbation theory offers an alternative method to recover the correlation energy missing in the mean-field approximation.[44] The single determinant optimized in the mean-field approximation is used as zeroth-order wave function and the perturbation series is developed considering the fluctuation potential in the Møller–Plesset partitioning of the Hamiltonian as the perturbation.[48,53] Notice that the partitioning of the Hamiltonian is not unique and other choices are available.[54]

As shown by Koch et al., the MBPT series can be derived from a CC ansatz for the wave function. This ensures term-by-term size-extensivity of the energy at all orders.[53] The governing equations (1.36a)–(1.36b) are expanded in terms of the fluctuation potential. Energy corrections are identified from the corresponding order expansion of the CC Lagrangian and retaining only terms complying to the $2n+1$ and $2n+2$ rules, *vide infra*.[69,70,74] A superscript index in square brackets - $[i]$ - will denote an i-th order contribution.

It is clear from the stationarity conditions that $t^{[0]}_{\mu_u} = 0$, $\forall u$ and $\bar{t}^{[0]}_{\mu_u} = 0$, $\forall u$. Thus cluster operators can be of order 1 and higher. We introduce the following notation for the i-th order cluster operators and multipliers states:

$$T^{[i]}_u = \sum_{\mu_u} t^{[i]}_{\mu_u} \tau_{\mu_u}, \quad \langle \bar{t}^{[i]}_u | = \sum_{\mu_u} \bar{t}^{[i]}_{\mu_u} \langle \mu_u | \tag{1.38}$$

To first order, one has:

$$\epsilon_{\mu_2} t^{[1]}_{\mu_2} = -\langle \mu_2 | \boldsymbol{\Phi} | \mathrm{HF} \rangle = -\langle \mathrm{HF} | [\boldsymbol{\Phi}, \tau_{\mu_2}] | \mathrm{HF} \rangle = \epsilon_{\mu_2} \bar{t}^{[1]}_{\mu_2} \tag{1.39}$$

which shows that singles and triples amplitudes are of second and higher order. For the former this is a consequence of Brillouin's condition, valid for the reference closed-shell determinant. For second order singles, doubles and triples one obtains:

$$\begin{aligned} \epsilon_{\mu_q} t^{[2]}_{\mu_q} &= -\langle \mu_q | [\boldsymbol{\Phi}, T^{[1]}_2] | \mathrm{HF} \rangle \\ &= -\langle \bar{t}^{[1]}_2 | [\boldsymbol{\Phi}, \tau_{\mu_q}] | \mathrm{HF} \rangle = \epsilon_{\mu_q} \bar{t}^{[2]}_{\mu_q} \end{aligned} \tag{1.40}$$

According to the $2n+1$ and $2n+2$ rules, energy corrections up to fifth order can be obtained from amplitudes and multipliers up to second order:

$$E^{[1]} = \langle \mathrm{HF}|\boldsymbol{\Phi}|\mathrm{HF}\rangle \tag{1.41a}$$

$$E^{[2]} = \langle \mathrm{HF}|[\boldsymbol{\Phi}, T_2^{[1]}]|\mathrm{HF}\rangle \tag{1.41b}$$

$$E^{[3]} = \langle \bar{t}_2^{[1]}|[\boldsymbol{\Phi}, T_2^{[1]}]|\mathrm{HF}\rangle \tag{1.41c}$$

$$E^{[4]} = \langle \bar{t}_2^{[1]}|[\boldsymbol{\Phi}, T^{[2]}]|\mathrm{HF}\rangle + \langle \bar{t}_2^{[1]}|\frac{1}{2}[[\boldsymbol{\Phi}, T_2^{[1]}], T_2^{[1]}]|\mathrm{HF}\rangle \tag{1.41d}$$

$$\begin{aligned} E^{[5]} = {} & \langle \mathrm{HF}|\frac{1}{2}[[\boldsymbol{\Phi}, T^{[2]}], T^{[2]}]|\mathrm{HF}\rangle + \langle \bar{t}_2^{[1]}|[[\boldsymbol{\Phi}, T^{[2]}], T_2^{[1]}]|\mathrm{HF}\rangle \\ & + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}_u^{[2]}|[\boldsymbol{\Phi}, T^{[2]}]|\mathrm{HF}\rangle \\ & + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}_u^{[2]}|\frac{1}{2}[[\boldsymbol{\Phi}, T_2^{[1]}], T_2^{[1]}]|\mathrm{HF}\rangle \end{aligned} \tag{1.41e}$$

Since the triples first appear to second order, the coupled cluster with single and double substitutions (CCSD) energy is correct to third order in the fluctuation potential. The triples contributions to the fourth and fifth order corrections to the energy are given as:

$$E_T^{[4]} = \langle \bar{t}_2^{[1]}|[\boldsymbol{\Phi}, T_3^{[2]}]|\mathrm{HF}\rangle \tag{1.42a}$$

$$\begin{aligned} E_T^{[5]} = {} & \langle \bar{t}_1^{[2]}|[\boldsymbol{\Phi}, T_3^{[2]}]|\mathrm{HF}\rangle + \langle \bar{t}_2^{[2]}|[\boldsymbol{\Phi}, T_3^{[2]}]|\mathrm{HF}\rangle \\ & + \langle \bar{t}_3^{[2]}|[\boldsymbol{\Phi}, T_2^{[2]}]|\mathrm{HF}\rangle + \langle \bar{t}_3^{[2]}|[\boldsymbol{\Phi}, T_3^{[2]}]|\mathrm{HF}\rangle \\ & + \frac{1}{2}\langle \bar{t}_3^{[2]}|[[\boldsymbol{\Phi}, T_2^{[1]}], T_2^{[1]}]|\mathrm{HF}\rangle\,. \end{aligned} \tag{1.42b}$$

These expressions form the basis for the development of reduced-scaling CC schemes were the double and triple excitations are treated approximately. These are the subject of the next Section.

1.5 APPROXIMATE COUPLED CLUSTER METHODS

The CCSD scheme, which scales as N^6, is really successful in recovering a large portion of the correlation energy, but as hinted at in the previous Section, is only correct to third order in perturbation theory. Triple excitations are needed to get higher accuracy, but the full coupled cluster with single, double and triple substitutions (CCSDT) model, with its steep N^8 scaling, is unfeasible for all but the smallest systems. One way around this problem is to exploit the perturbation theory expression for the fourth and fifth order energy corrections of Eqs. (1.42a)–(1.42b) to guide the construction of approximate schemes for the inclusion of higher excitations. These schemes can either be *iterative* or *noniterative*.

► IN THE ITERATIVE SCHEMES, one approximates the amplitude equations for the higher excitation to be correct up to a given order in perturbation theory. For the development of iterative schemes, we assume that $T_1 = O(0)$ and use T_1-transformed operators:

$$\check{O} = \mathrm{e}^{-T_1} O \mathrm{e}^{T_1}. \tag{1.43}$$

Since T_1 is a one-electron operator, the T_1-transformation does not affect the particle rank of the electronic Hamiltonian,[53,75] see Appendix A for details. The assumption that T_1 is of zeroth order is contrary to the usual MP approach but highlights the role of the singles amplitudes as orbital optimization parameters. In the approximate coupled cluster singles and doubles (CC2) method, the amplitudes equations are:[53,76]

$$\epsilon_{\mu_1} t_{\mu_1} + \langle \mu_1 | \check{\Phi} + [\check{\Phi}, Q_2] | \mathrm{HF} \rangle = 0 \tag{1.44a}$$

$$\epsilon_{\mu_2} t_{\mu_2} + \langle \mu_2 | \check{\Phi} | \mathrm{HF} \rangle = 0 \tag{1.44b}$$

and are obtained from the CCSD equations by retaining only first order terms in the doubles equations. The approximate doubles cluster operator was introduced:

$$Q_2 = -\sum_{\mu_2} \epsilon_{\mu_2}^{-1} \langle \mu_2 | \check{\Phi} | \mathrm{HF} \rangle \, \tau_{\mu_2} \tag{1.45}$$

and we shall refer to it as quasi-T_2. The CC2 Lagrangian is constructed based on the approximate equations obtained for the singles and doubles:[53,76]

$$\begin{aligned}\mathscr{L}(t,\bar{t})_{\mathrm{CC2}} &= E_0 + \sum_{u=1}^{2} \bar{t}_{\mu_u}\epsilon_{\mu_u}t_{\mu_u} \\ &+ \langle \mathrm{HF}|\check{\Phi} + [\check{\Phi}, Q_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_1|\check{\Phi} + [\check{\Phi}, Q_2]|\mathrm{HF}\rangle + \langle \bar{t}_2|\check{\Phi}|\mathrm{HF}\rangle\end{aligned} \tag{1.46}$$

The CC2 method brings the scaling of the CCSD method down to N^5 in the iterative step. From the approximate CC2 Lagrangian we can derive the multipliers equations:

$$\begin{aligned}\epsilon_{\mu_1}\bar{t}_{\mu_1} &+ \langle \mathrm{HF}|[\check{\Phi}, \tau_{\mu_1}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\Phi}, \tau_{\mu_1}] + [[\check{\Phi}, \tau_{\mu_1}], Q_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{\Phi}, \tau_{\mu_1}]|\mathrm{HF}\rangle = 0\end{aligned} \tag{1.47a}$$

$$\epsilon_{\mu_2}\bar{t}_{\mu_2} + \langle \mathrm{HF}|[\check{\Phi}, \tau_{\mu_2}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\Phi}, \tau_{\mu_2}]|\mathrm{HF}\rangle = 0 \tag{1.47b}$$

Formally, CC2 expectation values can be computed using the expression for the CCSD (see Appendix A.2) and the approximate amplitudes and multipliers:

$$\begin{aligned}O(t,\bar{t})_{\mathrm{CC2}} &= \langle \mathrm{HF}|\check{O}|\mathrm{HF}\rangle + \langle \bar{t}_1|\check{O}|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_1|[\check{O}, Q_2]|\mathrm{HF}\rangle + \langle \bar{t}_2|[\check{O}, Q_2]|\mathrm{HF}\rangle \\ &= O(t,\bar{t})_{\mathrm{CCS}} + \langle \bar{t}_1|[\check{O}, Q_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{O}, Q_2]|\mathrm{HF}\rangle\end{aligned} \tag{1.48}$$

The approximate coupled cluster singles, doubles and triples (CC3) model is constructed analogously. Starting from the CCSDT amplitudes equations in the T_1-transformed representation, we retain only second order terms in the triples equation:[53,73,77,78]

$$\epsilon_{\mu_1}t_{\mu_1} + \langle \mu_1|\check{\Phi} + [\check{\Phi}, T_2] + [\check{\Phi}, Q_3]|\mathrm{HF}\rangle = 0 \tag{1.49a}$$

$$\begin{aligned}\epsilon_{\mu_2}t_{\mu_2} &+ \langle \mu_2|\check{\Phi} + [\check{\Phi}, T_2]|\mathrm{HF}\rangle \\ &+ \langle \mu_2|\frac{1}{2}[[\check{\Phi}, T_2], T_2] + [\check{\Phi}, Q_3]|\mathrm{HF}\rangle = 0\end{aligned} \tag{1.49b}$$

$$\epsilon_{\mu_3}t_{\mu_3} + \langle \mu_3|[\check{\Phi}, T_2]|\mathrm{HF}\rangle = 0 \tag{1.49c}$$

In complete analogy with CC2, the quasi-T_3 operator was introduced:

$$Q_3 = -\sum_{\mu_3} \epsilon_{\mu_3}^{-1} \langle \mu_3 | [\check{\Phi}, T_2] | \mathrm{HF} \rangle \, \tau_{\mu_3}. \tag{1.50}$$

The CC3 Lagrangian is constructed based on the approximate amplitude equations (1.49):[53,73,77,78]

$$\begin{aligned} \mathscr{L}(t,\bar{t})_{\mathrm{CC3}} = E_0 &+ \sum_{u=1}^{3} \bar{t}_{\mu_u} \epsilon_{\mu_u} t_{\mu_u} + \langle \mathrm{HF} | \check{\Phi} + [\check{\Phi}, T_2] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_1 | \check{\Phi} + [\check{\Phi}, T_2] + [\check{\Phi}, Q_3] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_2 | \check{\Phi} + [\check{\Phi}, T_2] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_2 | \frac{1}{2} [[\check{\Phi}, T_2], T_2] + [\check{\Phi}, Q_3] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_3 | [\check{\Phi}, T_2] | \mathrm{HF} \rangle \end{aligned} \tag{1.51}$$

The CC3 method brings the scaling of the CCSDT method down to N^7 in the iterative step. We can now derive the CC3 multipliers equations:

$$\begin{aligned} \epsilon_{\mu_1} \bar{t}_{\mu_1} &+ \langle \mathrm{HF} | [\check{\Phi}, \tau_{\mu_1}] | \mathrm{HF} \rangle + \langle \bar{t}_1 | [\check{\Phi}, \tau_{\mu_1}] + [[\check{\Phi}, \tau_{\mu_1}], T_2] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_2 | [\check{\Phi}, \tau_{\mu_1}] + [[\check{\Phi}, \tau_{\mu_1}], T_2] + [[\check{\Phi}, \tau_{\mu_1}], Q_3] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_3 | [[\check{\Phi}, \tau_{\mu_1}], T_2] | \mathrm{HF} \rangle = 0 \end{aligned} \tag{1.52a}$$

$$\begin{aligned} \epsilon_{\mu_2} \bar{t}_{\mu_2} &+ \langle \mathrm{HF} | [\check{\Phi}, \tau_{\mu_2}] | \mathrm{HF} \rangle + \langle \bar{t}_1 | [\check{\Phi}, \tau_{\mu_2}] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_2 | [\check{\Phi}, \tau_{\mu_2}] + [[\check{\Phi}, \tau_{\mu_2}], T_2] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_3 | [\check{\Phi}, \tau_{\mu_2}] | \mathrm{HF} \rangle = 0 \end{aligned} \tag{1.52b}$$

$$\epsilon_{\mu_3} \bar{t}_{\mu_3} + \langle \bar{t}_1 | [\check{\Phi}, \tau_{\mu_3}] | \mathrm{HF} \rangle + \langle \bar{t}_2 | [\check{\Phi}, \tau_{\mu_3}] | \mathrm{HF} \rangle = 0 \tag{1.52c}$$

CC3 expectation values can be computed as follows:

$$\begin{aligned}
O(t,\bar{t})_{\mathrm{CC3}} &= O(t,\bar{t})_{\mathrm{CCS}} + \langle \bar{t}_1 | [\check{O}, T_2] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_2 | [\check{O}, T_2] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_2 | [\check{O}, Q_3] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_3 | [\check{O}, Q_3] + \frac{1}{2}[[\check{O}, T_2], T_2] | \mathrm{HF} \rangle \\
&= O(t,\bar{t})_{\mathrm{CCSD}} + \langle \bar{t}_2 | [\check{O}, Q_3] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_3 | [\check{O}, Q_3] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_3 | \frac{1}{2}[[\check{O}, T_2], T_2] | \mathrm{HF} \rangle
\end{aligned} \tag{1.53}$$

▶ Finally, one can construct *noniterative* methods, where the expensive N^7 step for the inclusion of connected triples is calculated as a one-off correction on top of the converged CCSD energy. The expression for the correction is based on the fourth and fifth order triples energy corrections Eqs. (1.42a)–(1.42b), but is computed using the converged CCSD singles and doubles amplitudes,[79–87] here and in the following denoted by a $*$ superscript. Since the left and right CC states differ, symmetric and asymmetric variants of the noniterative corrections exist.

The ΛCCSD[T][88] and CCSD[T][79] methods only include the fourth order correction Eq. (1.42a). The former uses both the left and right state, while the latter uses only the right state and can be obtained from the former by replacing the multipliers with the amplitudes:[73,88]

$$E_{\Lambda[\mathrm{T}]} = {}^{*}E^{[4]}_{\Lambda[\mathrm{T}]} = \langle \bar{t}^{*}_2 | [\Phi, T^{*}_3] | \mathrm{HF} \rangle \tag{1.54a}$$

$$E_{[\mathrm{T}]} = {}^{*}E^{[4]}_{[\mathrm{T}]} = \langle t^{*}_2 | [\Phi, T^{*}_3] | \mathrm{HF} \rangle \,. \tag{1.54b}$$

The ΛCCSD(T)[83–85] and CCSD(T)[80] methods also include the first of the fifth order triples corrections in Eq. (1.42b):

$$E_{\Lambda(\mathrm{T})} = {}^{*}E^{[4]}_{\Lambda[\mathrm{T}]} + {}^{*}E^{[5]}_{\Lambda(\mathrm{T})} = \langle \bar{t}^{*}_{1} | [\boldsymbol{\Phi}, T^{*}_{3}] | \mathrm{HF} \rangle \tag{1.55a}$$

$$+ \langle \bar{t}^{*}_{2} | [\boldsymbol{\Phi}, T^{*}_{3}] | \mathrm{HF} \rangle \tag{1.55b}$$

$$E_{(\mathrm{T})} = {}^{*}E^{[4]}_{[\mathrm{T}]} + {}^{*}E^{[5]}_{(\mathrm{T})} = \langle t^{*}_{1} | [\boldsymbol{\Phi}, T^{*}_{3}] | \mathrm{HF} \rangle \tag{1.55c}$$

$$+ \langle t^{*}_{2} | [\boldsymbol{\Phi}, T^{*}_{3}] | \mathrm{HF} \rangle \tag{1.55d}$$

once again, the symmetric method can be obtained from the asymmetric variant by replacing multipliers with amplitudes in the left state.

Results from noniterative methods can be rationalized within the framework of MBPT.[73,88–91] From Eqs. (1.39)–(1.40), one can derive which MBPT terms are included in the corrections:

$$\begin{aligned} {}^{*}E^{[4]}_{\Lambda[\mathrm{T}]} &= \langle \bar{t}^{[1]}_{2} | [\boldsymbol{\Phi}, T^{[2]}_{3}] | \mathrm{HF} \rangle + \langle \bar{t}^{[2]}_{2} | [\boldsymbol{\Phi}, T^{[2]}_{3}] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}^{[2]}_{3} | [\boldsymbol{\Phi}, T^{[2]}_{2}] | \mathrm{HF} \rangle + O(6) \end{aligned} \tag{1.56}$$

and similarly for ${}^{*}E^{[4]}_{[\mathrm{T}]}$. The MBPT terms included in ${}^{*}E^{[5]}_{\Lambda(\mathrm{T})}$ can be seen to be:

$${}^{*}E^{[5]}_{\Lambda(\mathrm{T})} = \langle \bar{t}^{[2]}_{1} | [\boldsymbol{\Phi}, T^{[2]}_{3}] | \mathrm{HF} \rangle + O(6) \tag{1.57}$$

and similarly for ${}^{*}E^{[5]}_{(\mathrm{T})}$.

2

Continuum Solvation Models

> L'acqua è la forza che ti tempra,
> nell'acqua ti ritrovi e ti rinnovi:
> — Eugenio Montale, *Falsetto*

Developments of the polarizable continuum model (PCM), a continuum solvation model, are at the heart of this dissertation. This Chapter is a brief exposition of the major points of the PCM we have worked upon in the thesis. Continuum models have a venerable history in quantum chemistry: Onsager's model[26] appeared in 1936 and the first form of the PCM entered the stage in 1981.[36] Section 2.1 will offer a heuristic "derivation" of continuum models. While it cannot be thought as formally rigorous, it highlights the major physical insights that have informed the creation of continuum models. Section 2.2 will present the formulation of the model. Section 2.3 will be devoted to the numerical strategies used in solving the PCM equation. I will show how a variational approach can facilitate the formulation of quantum/classical polarizable Hamiltonians in Section 2.4. Appendix A contains much of the mathematical details omitted from the exposition in this Chapter.

Still nowadays much research activity is expended on the PCM.[92–94] I will point out throughout the Chapter to developments outside our group that are particularly interesting.

2.1 CONTINUUM SOLVATION MODELS: WHY AND HOW

► THE BASIC IDEA OF IMPLICIT MODELS IS TO REPLACE THE ENVIRONMENT WITH A STRUCTURELESS CONTINUUM. The continuum will interact *classically* with the explicit part of the multiscale model, an interaction mediated by some macroscopic property of the bulk material the continuum represents. Thus, continuum models bypass both problems plaguing explicit models we mentioned in the Introduction, namely:

1. the statistical averaging of environment configurations, and
2. the MM region electrostatics cutoff radius choice.

Following Tomasi, we introduce the complete system Hamiltonian in the BO approximation:[21,22]

$$H(\boldsymbol{r}_\mathrm{S}, \boldsymbol{r}_\mathrm{E}) = H_\mathrm{S}(\boldsymbol{r}_\mathrm{S}) + H_\mathrm{E}(\boldsymbol{r}_\mathrm{E}) + H_\mathrm{SE}(\boldsymbol{r}_\mathrm{S}, \boldsymbol{r}_\mathrm{E}) \tag{2.1}$$

The Hamiltonian features solute terms, marked by the S subscript, environment terms, marked by the E subscript, and interaction terms. The coordinates $(\boldsymbol{r}_\mathrm{S}, \boldsymbol{r}_\mathrm{E})$ refer to *both* nuclei and electrons. The interaction term is given by the usual Coulomb electrostatic Hamiltonian.

One can replace the pure environment and interaction terms with their classical counterparts and obtain the quantum/classical, possibly *polarizable*, Hamiltonian for an explicit QM/MM model. This brings about the first important point: the need for statistical averaging. Whenever a large number of degrees of freedom is involved, one can access macroscopic observables of the system by the appropriate averaging of the microscopically detailed motion over phase space trajectories or on the appropriate statistical ensemble.[23] The need for ensemble averages leads us to the following observations:

1. the need for *macroscopic* parameters, absent from the microscopic Hamiltonian Eq. (2.1), in carrying out statistical simulations.
2. Chosen a thermodynamic ensemble, the basic energetic quantity is accordingly determined. For example, the Gibbs free energy G is intrinsically related to the (NpT) ensemble.

3. Even atomistic simulations will lead to results that are essentially averages. The discrete picture of the system has been replaced by some continuous distribution function.

These observations strongly suggest that one can perform the averaging step *before* embarking into the solution of the quantum mechanical problem and replace the full Hamiltonian with an *effective* Hamiltonian in which the environment degrees of freedom are properly averaged.[95,96] The solute-environment interaction term would then be replaced by a term only depending on the solute degrees of freedom, represented by the averaged, continuous response functions of the solvent. This is the physical setting of the PCM and is schematically depicted in Figure 2.1.

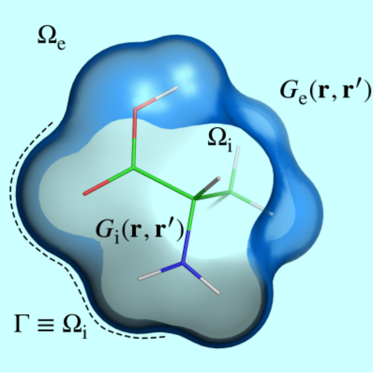


Figure 2.1 The physical setting of the PCM. The molecular solute, represented by its, possibly quantum mechanical, charge density ρ_i is enclosed in a *cavity* Ω_i. The boundary of the cavity $\Gamma \equiv \partial\Omega_i$ is a continuously differentiable 2-manifold. We assume the material properties of the cavity to be those of vacuum, hence characterized by the Green's function $G_i(\boldsymbol{r},\boldsymbol{r}') = \frac{1}{|\boldsymbol{r}-\boldsymbol{r}'|}$. The cavity is carved out of an infinite, structureless, continuum characterized by its Green's function $G_e(\boldsymbol{r},\boldsymbol{r}')$ and fully covering the external subdomain Ω_e.

The solute molecule is enclosed in a *cavity* inside the structureless continuum representing the solvent and the basic energetic quantity is a *free energy*:[97–99]

$$G = G_{\mathrm{cav}} + G_{\mathrm{el}} + G_{\mathrm{dis}} + G_{\mathrm{rep}} + G_{\mathrm{Mm}}(T). \tag{2.2}$$

The decomposition of the solute free energy takes into account the different physical origins of the different solute-solvent interactions. G_{cav} is the cavity formation free energy, a constant as long as the solute geometry does not change.[97,100] The second term G_{el} is the most important one in the framework of continuum models. It accounts for the mutual electrostatic polarization of solute and solvent, see Section 2.2. The third and fourth terms account for dispersion (G_{dis}) and repulsion (G_{rep}) interactions, respectively.[101,102] Finally, $G_{\mathrm{Mm}}(T)$ accounts for the collective molecular motions of the solute-solvent system. It explicitly depends on the temperature T and can be calculated from the solution partition function, see ref. 98 for further details.

In this dissertation, we focused exclusively on the purely electrostatic component of the interaction energy, completely neglecting the other terms. While a balanced description of solvation chemistry certainly demands a proper treatment of all solute-solvent interactions, especially when non homogeneous environments are studied,[103,104] it is also true that the electrostatic component is the most numerically relevant, especially when considering energy differences between different electronic states.

2.2 CONTINUUM ELECTROSTATICS AS A BOUNDARY INTEGRAL PROBLEM

The molecular solute, represented by its charge density ρ_{i} is enclosed in a *cavity* Ω_{i}. The boundary of the cavity $\Gamma \equiv \partial\Omega_{\mathrm{i}}$ is a 2-manifold and is assumed to be continuously differentiable. The cavity is carved out of an infinite, structureless, continuum characterized by the bulk properties of the solvent. The continuum fully spans the external subdomain Ω_{e}, see Fig. 2.1. The source charge density is not assumed to be continuous: both classical point multipoles and quantum mechanical charge densities can be treated within the model. However, we assume that its support is entirely within the cavity, $\mathrm{Supp}(\rho_{\mathrm{i}}) \subseteq \Omega_{\mathrm{i}}$. This assumption is, of course, false for quantum mechanical charge densities. It can however be proven that the errors induced by this *charge penetration* are not severe.[105–107]

Formulated as such, the PCM is a well-known problem in classical electrostatics: find the electrostatic potential in space generated by a charge distribution confined in a cavity in a *polarizable* continuous medium.[108,109] In the mathematical literature on partial differential equations (PDEs), it is usually referred to as a *transmission* problem.[110,111]

Given the partition of Euclidean space $\mathbb{R}^3$ outlined above, we want to find the solution $u(\boldsymbol{r})$ to the following set:

$$\begin{cases} L_{\mathrm{i}}u = \nabla^2 u = -4\pi\rho_{\mathrm{i}} \text{ in } \Omega_{\mathrm{i}} & (2.3a) \\ L_{\mathrm{e}}u = 0 \text{ in } \Omega_{\mathrm{e}} & (2.3b) \\ [u] = u_{\mathrm{e}} - u_{\mathrm{i}} = 0 \text{ on } \Gamma & (2.3c) \\ [\partial_L u] = \partial_{L_{\mathrm{e}}} u - \partial_{L_{\mathrm{i}}} u = 0 \text{ on } \Gamma & (2.3d) \\ |u(\boldsymbol{r})| \leq C\|\boldsymbol{r}\|^{-1} \text{ for } \|\boldsymbol{r}\| \to \infty & (2.3e) \end{cases}$$

Eqs. (2.3c) and (2.3d) are the *jump conditions*, expressed in terms of trace operators for the solution u and its *conormal* derivative. For notational simplicity, we will use the symbols $\partial_{L_{\mathrm{e}}}$ and $\partial_{L_{\mathrm{i}}}$ for the latter and only give it in explicit form when needed. Further mathematical details and technical results on the definition of function traces and their use in setting up the proper normal and conormal derivatives can be found in the excellent book by Sauter et al.[111] The fundamental solutions, or Green's functions, for the elliptic differential operators L_{i} and L_{e} will be denoted by $G_{\mathrm{i}}(\boldsymbol{r}, \boldsymbol{r}')$ and $G_{\mathrm{e}}(\boldsymbol{r}, \boldsymbol{r}')$, respectively. As such the problem is formulated in the so-called *strong* form: the sought-after solution u has to be at least two times continuously differentiable. Moreover, the solution is a function supported over $\mathbb{R}^3$ which poses challenges to the numerical solution of the problem. We will take a different approach and reformulate it in terms of *boundary integral operators*, *i. e.* transform the PDEs into a boundary integral equation (BIE).

► THE FIRST STEP IS TO INTRODUCE THE RELEVANT BOUNDARY INTEGRAL OPERATORS for the above mentioned transmission problem.

They are three of the four components of the Calderón projector. For any function v in the suitable function space and for $\boldsymbol{s}, \boldsymbol{s}' \in \Gamma$:

$$(\hat{\mathcal{S}}_{\star} v)(\boldsymbol{s}) = \int_{\Gamma} \mathrm{d}\boldsymbol{s}' G_{\star}(\boldsymbol{s}, \boldsymbol{s}') v(\boldsymbol{s}') \tag{2.4a}$$

$$(\hat{\mathcal{D}}_{\star} v)(\boldsymbol{s}) = \int_{\Gamma} \mathrm{d}\boldsymbol{s}' \partial_{L_{\star}, \boldsymbol{s}} G_{\star}(\boldsymbol{s}, \boldsymbol{s}') v(\boldsymbol{s}') \tag{2.4b}$$

$$(\hat{\mathcal{D}}^{\dagger}_{\star} v)(\boldsymbol{s}) = \int_{\Gamma} \mathrm{d}\boldsymbol{s}' \partial_{L_{\star}, \boldsymbol{s}'} G_{\star}(\boldsymbol{s}, \boldsymbol{s}') v(\boldsymbol{s}') \tag{2.4c}$$

where $\star$ is a placeholder for the i or e subscript. Our next step is to rewrite the u as the sum of two contributions:

$$u(\boldsymbol{r}) = \varphi(\boldsymbol{r}) + \xi(\boldsymbol{r}) = \int_{\Omega_{\mathrm{i}}} \mathrm{d}\boldsymbol{r}' \frac{\rho_{\mathrm{i}}(\boldsymbol{r}')}{|\boldsymbol{r} - \boldsymbol{r}'|} + \xi(\boldsymbol{r}) \tag{2.5}$$

the former is the electrostatic potential of ρ_{i} *in vacuo* (Newton potential), while the latter is the *reaction* potential. The reaction potential describes the polarization in the medium and it admits an integral representation as a single-layer potential:

$$\xi_{\mathrm{i}} = \hat{\mathcal{S}}_{\mathrm{i}} \sigma, \tag{2.6}$$

where σ is the apparent surface charge (ASC), the key quantity in the PCM. As shown by Cancès et al., the ASC can be computed as the *unique* solution to the following integral equation:

$$\begin{aligned} \left[\hat{\mathcal{S}}_{\mathrm{e}}\left(2\pi + \hat{\mathcal{D}}^{\dagger}_{\mathrm{i}}\right) + \left(2\pi - \hat{\mathcal{D}}_{\mathrm{e}}\right)\hat{\mathcal{S}}_{\mathrm{i}}\right]\sigma = \\ -\left[\left(2\pi - \hat{\mathcal{D}}_{\mathrm{e}}\right) - \hat{\mathcal{S}}_{\mathrm{e}}\hat{\mathcal{S}}^{-1}_{\mathrm{i}}\left(2\pi - \hat{\mathcal{D}}_{\mathrm{i}}\right)\right]\varphi \end{aligned} \tag{2.7}$$

commonly called the integral equation formalism (IEF) equation. The Green's functions for the elliptic differential operators assume a central role in the boundary integral formulation and make the IEF equation valid for a wide range of external environments: homogeneous isotropic, ionic and anisotropic liquids,[112] and systems with interfaces.[113–116]

In the special and very common case of homogeneous and isotropic environments, *i.e.* regular dielectric materials characterized by a scalar permittivity ε, the Green's functions are:

$$G_{\mathrm{e}}(\boldsymbol{r},\boldsymbol{r}') = \frac{1}{\varepsilon|\boldsymbol{r}-\boldsymbol{r}'|} = \frac{1}{\varepsilon}G_{\mathrm{i}}(\boldsymbol{r},\boldsymbol{r}'), \quad G_{\mathrm{i}}(\boldsymbol{r},\boldsymbol{r}') = \frac{1}{|\boldsymbol{r}-\boldsymbol{r}'|} \tag{2.8}$$

yielding the isotropic IEF equation:

$$\hat{\mathscr{R}}_{\varepsilon}\hat{\mathscr{S}}\sigma = -\hat{\mathscr{R}}_{\infty}\varphi \tag{2.9}$$

where the auxiliary operators:

$$\hat{\mathscr{R}}_{\varepsilon} = \left[2\pi\left(\frac{\varepsilon+1}{\varepsilon-1}\right) - \hat{\mathscr{D}}\right], \quad \hat{\mathscr{R}}_{\infty} = \lim_{\varepsilon\to\infty}\hat{\mathscr{R}}_{\varepsilon} = 2\pi - \hat{\mathscr{D}} \tag{2.10}$$

have been introduced. By letting $\varepsilon \to \infty$, one recovers the limiting case where conductor boundary conditions are imposed. This leads to the well-known conductor-like screening model (COSMO) equation:[117,118]

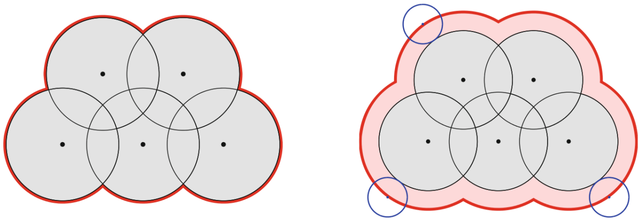
$$\hat{\mathscr{S}}\sigma = -f(\varepsilon)\varphi \tag{2.11}$$

where the factor $f(\varepsilon) = \frac{\varepsilon-1}{\varepsilon+x}$, $0 \leq x \leq 1$ has been introduced to account for the error introduced by modelling the dielectric as a perfect conductor.

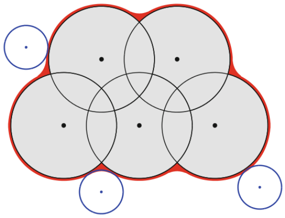
2.3 NUMERICAL APPROACHES TO BOUNDARY INTEGRAL EQUATIONS

▸ THE SOLUTION OF THE IEF-PCM BOUNDARY INTEGRAL EQUATION can only be achieved analytically for simple cavity geometries, such as single spheres and ellipsoids. When more general molecular cavities are employed one has to resort to a numerical technique: the boundary element method (BEM). This is implemented in four steps:

1. define the molecular cavity,
2. mesh the molecular surface,



(a) van der Waals surface (vdWS) **(b)** solvent-accessible surface (SAS)



(c) solvent-excluded surface (SES)

Figure 2.2 Molecular surfaces from interlocking sets of atom-centered spheres. Reproduced from ref. 121.

3. discretize the integral equation, and
4. solve the linear systems by a suitable numerical technique.

Many different approaches to these four steps have been presented, both in the field of the BEM and in the context of the PCM.

The molecular cavity is usually defined as a set of atom-centered interlocking spheres. The radii are chosen from a suitable set, usually van der Waals radii.[119,120]

If one imagines to model a solvent molecule as a rigid sphere, three types of molecular surfaces can be defined:

1. the union of the interlocking spheres surfaces is the van der Waals surface (vdWS), Figure 2.2a
2. the locus of points defined by the center of the solvent spherical probe while rolling over the vdWS is the solvent-accessible surface (SAS), Figure 2.2b

3. the locus of points defined by the contact point of the solvent spherical probe while rolling over the vdWS is the solvent-excluded surface (SES), Figure 2.2c.

Alternative definitions based on the isodensity surface of the molecular solute have also been put forth.[122]

Steps 2 and 3 are closely intertwined, in the technical BEM literature they go under the name of *finite element discretization*. Let us define a mesh of the domain Γ as an indexed collection of intervals with non-zero measure $\{I_i\}_{i=1}^{N_{\text{mesh}}}$, where N_{mesh} is the size of the mesh. Then, in a rather informal sense, a finite element is the mathematical entity formed by the vector space of functions that are piecewise regular on any given interval in the mesh.[123] Basically, given an element in the mesh, we "attach" a basis set of piecewise polynomials of a prescribed degree and use this basis to provide a representation of quantities defined on Γ within each mesh interval. Mesh generation for the molecular surfaces mentioned above is usually achieved by modified triangulation procedures. In this dissertation we used the GePol algorithm[124–129] and the mesh generators of Harbrecht and Randrianarivony especially tailored for the wavelet BEM.[121,130]

The finite element discretization is usually carried out either by the *collocation* or by the *Galerkin* approach.[110,123][*] This step transforms the original integral equation into a system of linear equations whose dimension relates to the underlying mesh size. For general integral equations and finite element discretizations, the *stiffness matrix* obtained is dense and proper linear algebra techniques need to be employed in order to avoid a detrimental impact on computational performance. In addition, finite element discretization might destroy intrinsic symmetries of the original integral operators. These can be recovered by appropriate *a posteriori* symmetrization procedures introducing, however, a degree of arbitrariness in the BEM procedure.[131]

▶ In the GePol procedure, the molecular surface is meshed by means of N_{ts} spherical polygons Π_i whose centroids define the

[*] Indeed, it is possible to show that discretization by collocation corresponds to a Galerkin method with a very specific (and asymmetric) choice of *trial* and *test* spaces.

collocation points. One-point quadrature rules are then applied at the centroid to obtain the matrix equation:

$$\boldsymbol{R}^{-1}\boldsymbol{T}\boldsymbol{q} = \boldsymbol{v}. \tag{2.12}$$

$\boldsymbol{q}$ and $\boldsymbol{v}$ are vectors of dimension N_{ts} collecting the values of the ASC and molecular electrostatic potential (MEP) at the collocation points. $\boldsymbol{R}^{-1}\boldsymbol{T}$ is the stiffness matrix. The matrices representing the boundary integral operators are:

$$\boldsymbol{T} = \left(2\pi\boldsymbol{I} - \boldsymbol{D}_{\mathrm{e}}\boldsymbol{A}\right)\boldsymbol{S}_{\mathrm{i}} + \boldsymbol{S}_{\mathrm{e}}\left(2\pi\boldsymbol{I} + \boldsymbol{A}\boldsymbol{D}_{\mathrm{i}}^{\dagger}\right) \tag{2.13}$$

$$\boldsymbol{R} = \left(2\pi\boldsymbol{I} - \boldsymbol{D}_{\mathrm{e}}\boldsymbol{A}\right) - \boldsymbol{S}_{\mathrm{e}}\boldsymbol{S}_{\mathrm{i}}^{-1}\left(2\pi\boldsymbol{I} - \boldsymbol{D}_{\mathrm{i}}\boldsymbol{A}\right) \tag{2.14}$$

$\boldsymbol{I}$ is the N_{ts}-dimensional identity matrix while the other matrices are defined as:

$$A_{ij} = a_i\delta_{ij}, \quad a_i = \mathrm{area}(\Pi_i) \tag{2.15a}$$

$$S_{ij,\mathrm{i}} = k\sqrt{\frac{4\pi}{a_i}}\delta_{ij} + \frac{1}{|\boldsymbol{s}_i - \boldsymbol{s}_j|}(1-\delta_{ij}) \tag{2.15b}$$

$$D_{ii,\mathrm{i}} = -k\sqrt{\frac{\pi}{a_i}}\frac{1}{R_i}\delta_{ij} + \frac{(\boldsymbol{s}_i - \boldsymbol{s}_j)\cdot\boldsymbol{n}_j}{|\boldsymbol{s}_i - \boldsymbol{s}_j|^3}(1-\delta_{ij}) \tag{2.15c}$$

in terms of the centroids $\boldsymbol{s}_i$, $\boldsymbol{s}_j$, the finite elements areas and their curvatures R_i. The factor $k = 1.07$ is introduced to achieve a better precision in the integration of the diagonal elements.[99] Expressions for $\boldsymbol{S}_{\mathrm{e}}$, $\boldsymbol{D}_{\mathrm{e}}$ and $\boldsymbol{D}_{\mathrm{e}}^{\dagger}$ depend on the specific outer environment and can be found in the literature.[99,113–116]

► The wavelet Galerkin BEM preserves the fundamental symmetries of the boundary integral operators and achieves sparsity in the stiffness matrix. This sparsity was leveraged in this dissertation to implement efficient algorithms with linear space and time complexity. The approach is thus superior to the traditional collocation method.

Given a hierarchical sequence of trial spaces $\{V_l\}_{l=1}^{J}$, one can decompose the l-th element in the hierarchy into the direct sum

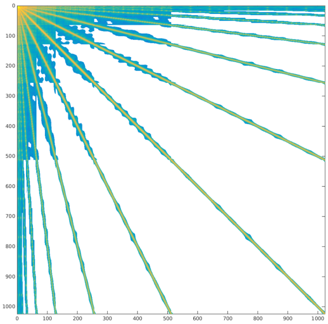


Figure 2.3 Sparsity pattern achieved by the wavelet Galerkin BEM when solving the Laplace equation on 6 patches. Reproduced from ref. 135.

$V_l = V_{l-1} \oplus W_l$. W_l is called the *wavelet space* and is the, not necessarily orthogonal, complement to V_{l-1}. Recursively applying this splitting to the trial spaces hierarchy generates the wavelet decomposition, where all complementary spaces are spanned by the wavelet basis. The fundamental insight in the wavelet BEM is to use the wavelet basis for the discretization step and employ the compression technique described by Dahmen et al. to build up the sparse system matrix.[132–134] Matrix compression is carried out in two rounds, *a priori* and *a posteriori*, resulting in a finger-like sparsity pattern for the stiffness matrix, Figure 2.3. The number of relevant matrix entries scales linearly with N_J the number of degrees of freedom for a refinement of the geometry up to level J.

CONTINUITY OF MESHES WITH RESPECT TO MOLECULAR DISTORTIONS is a central issue for stable implementations of molecular gradients and recurs frequently in the literature. Numerous schemes have been proposed to solve or alleviate this issue. We here mention the TsLess[136] and DefPol[137,138] approaches of Pomelli et al. and the FIXPVA modification[139] to the GePol algorithm put forth by Su et al. Scalmani et al. have recently proposed the continuous surface charge (CSC) scheme which uses a smooth vdWS and 3D spherical Gaussian basis functions.[140,141] Gaussian blurring was also advocated by Lange et al. in their switching/Gaussian (SWIG) method.[142,143] Both CSC and SWIG achieve continuous PESs and smooth molecular gradients. However, their convergence to the exact solution of the underlying integral equation has yet to be proved.[123] Cancès et al. took a completely different approach to the problem by employing a domain decomposition method, guaranteed to converge to the exact solution.[145] Moreover, for COSMO, the formulation is embarrassingly parallel and has been implemented in a linearly scaling fashion.[144,146–148] Very recently the method has also been extended to general dielectric environments.[149]

In the following, the PCM equations will be written in the "complete basis" meaning that we will be working with the exact integral equation and not with its discretized counterpart. As a consequence, the apparent surface charge σ and the electrostatic potential φ will have a *continuous* dependence on a cavity surface "index" $\boldsymbol{s}$. A product involving any of these quantities will have to be interpreted as the *surface integral*, *i.e.* the scalar product in the suitable, infinite-dimensional vector space on the cavity boundary Γ. The following shorthand notations will be adopted:

$$\begin{aligned}\sigma\hat{\mathscr{Y}}\sigma &= \int_{\Gamma} \mathrm{d}\boldsymbol{s}\sigma(\boldsymbol{s})\hat{\mathscr{Y}}\sigma(\boldsymbol{s}) = \left(\sigma, \hat{\mathscr{Y}}\sigma\right)_{\Gamma} \\ \sigma\varphi &= \int_{\Gamma} \mathrm{d}\boldsymbol{s}\sigma(\boldsymbol{s})\varphi(\boldsymbol{s}) = (\sigma, \varphi)_{\Gamma}\end{aligned} \tag{2.16}$$

2.4 VARIATIONAL FORMULATION OF CLASSICAL POLARIZABLE MODELS

The attentive reader will have noticed that, despite the focus of this thesis on continuum models for the quantum mechanical modelling of solvation, no mention has been made so far in this Chapter of any quantum aspect. The strategy usually adopted is to tailor a specific Hamiltonian, which includes classical contributions from the continuum and use it in the development of the quantum chemical model. Since the MEP is a linear functional of the solute charge density, the ASC itself incurs in a dependency on the solute charge density. Properly accounting for the mutual solute-solvent polarization induces a *nonlinearity* in an otherwise linear problem. Manipulating such a *nonlinear* Schrödinger equation is theoretically cumbersome,[150,151] but has been successfully done in the past.[99]

In this dissertation, we advocate a different theoretical approach: the variational formulation of classical polarizable models. In such a framework the ASC becomes an additional, independent, variationally optimizable degree of freedom. This makes the coupling to, *e.g.*, extended Lagrangian dynamics trivial.[152] It is well known that electrodynamics can be derived as the minimization of an action functional.[108] The principle of least action is however formulated in terms of *fields* and not more easily manageable quantities, such as the MEP or the ASC. A true energy functional has to fulfill the following properties:[153]

1. physical extremal points,
2. equilibrium values that are true energies, and
3. convexity (positive-definiteness)

Allen et al. and Attard pioneering attempts resulted in functionals of scalar densities violating Property 2 and could not thus be used in extended Lagrangian dynamics.[154–156]

In a seminal paper, Lipparini et al. showed how the PCM can be recast in a variational fashion yielding a true energy functional of the ASC:[40,94,157]

$$U_{\mathrm{PCM}} = \frac{1}{2}\sigma\hat{\mathscr{Y}}\sigma + \varphi\sigma, \quad \hat{\mathscr{Y}} = \hat{\mathscr{R}}_{\infty}^{-1}\hat{\mathscr{R}}_{\varepsilon}\hat{\mathscr{S}}. \tag{2.17}$$

yielding Eq. (2.9) upon minimization:

$$\frac{\partial U_{\mathrm{PCM}}}{\partial \sigma} = \hat{\mathscr{Y}}\sigma + \varphi = 0. \tag{2.18}$$

It is interesting to note how this functional follows quite immediately from the integral equation formulation and standard results in the theory of boundary integral equations.[158]

Explicit classical polarizable models can also be recast in a variational fashion allowing for their treatment on par with implicit classical polarizable models. The functional looks as follows:

$$U_{\mathrm{MM}} = \frac{1}{2}\kappa\hat{\mathscr{W}}\kappa + \kappa\zeta, \tag{2.19}$$

here κ is the variational degree of freedom representing the polarization of the explicit environment. ζ is the inducing field, *vide infra*. The reader is referred to the works of Lipparini et al. for a derivation of this functional.[35,41,159] We have made no specific reference to the particular explicit model used. The variational framework is flexible enough to encompass either the MMpol,[33] the polarizable embedding (PE),[34,160] or the fluctuating charges (FQ) models.[35,161–163]

Coupling the implicit and explicit polarizable models is straightforward in the variational framework:[35,37–39]

$$U_{\mathrm{pol}} = \frac{1}{2}\sigma\hat{\mathscr{Y}}\sigma + \sigma\varphi + \frac{1}{2}\kappa\hat{\mathscr{W}}\kappa + \kappa\zeta + \sigma\hat{\mathscr{X}}\kappa. \tag{2.20}$$

An additional term, as first derived by Steindal et al.,[37] was added to account for the mutual polarization between the implicit and explicit layers:

$$\sigma\hat{\mathscr{X}}\kappa = \kappa\hat{\mathscr{X}}^{\dagger}\sigma. \tag{2.21}$$

$\hat{\mathscr{X}}$ is the implicit/explicit interaction kernel, whose form depends on the specific explicit model chosen.

The global minimum of the convex functional is found by differentiating with respect to the variational degrees of freedom:

$$\begin{pmatrix} \hat{\mathscr{Y}} & \hat{\mathscr{X}} \\ \hat{\mathscr{X}}^{\dagger} & \hat{\mathscr{W}} \end{pmatrix} \begin{pmatrix} \sigma \\ \kappa \end{pmatrix} = - \begin{pmatrix} \varphi \\ \zeta \end{pmatrix}. \tag{2.22}$$

While φ is quite clearly the MEP, ζ can either be the molecular electric field (MMpol and PE models) or again the MEP (FQ model). In any case, both will be determined by the quantum mechanical molecular charge density and can thus be formulated as expectation values of one-electron operators. Eventually, this achieves the coupling between the classical – σ and κ – and the quantum mechanical variational degrees of freedom.

The functionals in Eqs. (2.17), (2.19) and (2.20) all have a clear physical meaning. They describe charge distributions interacting (unfavorably) with themselves and (favorably) with their respective inducing external fields and constitutes the polarization energy of the medium. The topic of variational formulations is particularly important in the field of MD simulations.[153,164–166] Our focus is however on the quantum mechanical calculations of molecular properties and the variational formulation is advantageous since it dispenses us from manipulating cumbersome nonlinear coupling terms in the Hamiltonian. Moreover, the stationarity condition Eq. 2.22 entails the existence of a classical Hellmann–Feynman theorem:

$$\frac{\mathrm{d}U_{\mathrm{pol}}}{\mathrm{d}F} = \frac{\partial U_{\mathrm{pol}}}{\partial F} + \frac{\partial U_{\mathrm{pol}}}{\partial \sigma}\frac{\partial \sigma}{\partial F} + \frac{\partial U_{\mathrm{pol}}}{\partial \kappa}\frac{\partial \kappa}{\partial F} = \frac{\partial U_{\mathrm{pol}}}{\partial F}, \quad (2.23)$$

which is paramount in the formulation of molecular properties, see Chapter 3. The variational formulation also lends itself to an implementation as a simultaneous optimization of the electronic structure and polarization degrees of freedom.[157]

Finally, let us re-express the equations above in a supermatrix formalism:

$$U_{\mathrm{pol}} = \frac{1}{2}{}^{t}\mathrm{p}\mathbb{V}\mathrm{p} + {}^{t}\mathrm{p}\mathrm{s} \quad (2.24)$$

where:

$$\mathrm{p} = \begin{pmatrix} \sigma \\ \kappa \end{pmatrix}, \quad \mathrm{s} = \begin{pmatrix} \varphi \\ \zeta \end{pmatrix}, \quad \mathbb{V} = \begin{pmatrix} \hat{\mathscr{Y}} & \hat{\mathscr{X}} \\ \hat{\mathscr{X}}^{\dagger} & \hat{\mathscr{W}} \end{pmatrix} \quad (2.25)$$

and the ${}^{t}\mathrm{p}$ symbol denotes the transposed supervector p. The scalar products are understood to be in the relevant function spaces. The supermatrix formalism will be adopted throughout the thesis.

► HOW ARE QUANTUM/CLASSICAL POLARIZABLE HAMILTONIANS IMPLEMENTED IN THIS FRAMEWORK? As shown in Chapter 1 for the

CC method, one can formulate methods in quantum chemistry as the unconstrained minimization of a Lagrangian. Due to the variational property of the classical polarizable functional one can devise an *effective* quantum/classical polarizable Lagrangian:[94]

$$\mathscr{L}_{\mathrm{eff}}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}, \mathrm{p}) = \mathscr{L}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}) + \frac{1}{2}{}^{t}\mathrm{p}\mathbb{V}\mathrm{p} + {}^{t}\mathrm{p}\mathrm{s}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}) \tag{2.26}$$

and derive the governing equations in the usual manner:

$$\frac{\partial \mathscr{L}_{\mathrm{eff}}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}, \mathrm{p})}{\partial \bar{\boldsymbol{\eta}}} = \boldsymbol{\Omega}(\boldsymbol{\eta}) + {}^{t}\mathrm{p}\frac{\partial \mathrm{s}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}})}{\partial \bar{\boldsymbol{\eta}}} = 0 \tag{2.27a}$$

$$\begin{aligned}\frac{\partial \mathscr{L}_{\mathrm{eff}}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}, \mathrm{p})}{\partial \boldsymbol{\eta}} &= \frac{\partial \mathscr{E}(\boldsymbol{\eta})}{\partial \boldsymbol{\eta}} + \left(\bar{\boldsymbol{\eta}}, \frac{\partial \boldsymbol{\Omega}(\boldsymbol{\eta})}{\partial \boldsymbol{\eta}}\right)_{W} \\ &\quad + {}^{t}\mathrm{p}\frac{\partial \mathrm{s}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}})}{\partial \boldsymbol{\eta}} = 0\end{aligned} \tag{2.27b}$$

$$\frac{\partial \mathscr{L}_{\mathrm{eff}}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}, \mathrm{p})}{\partial \mathrm{p}} = \mathbb{V}\mathrm{p} + \mathrm{s}(\boldsymbol{\eta}, \bar{\boldsymbol{\eta}}) = 0 \tag{2.27c}$$

The quantum mechanical and the classical model are thus fully coupled, due to the dependence of the source term s on the amplitudes and multipliers.

As an example, let us consider the single-reference HF and KS-DFT methods introduced in Section 1.2. First of all, we need the appropriate SCF energy functional *in vacuo*. The AO basis set expansion of the MOs lets us define the one-electron AO density matrix as:

$$\boldsymbol{D}_{\mu\nu} = \sum_{i=1}^{N_O} C_{\mu i} C^{\dagger}_{\nu i} \tag{2.28}$$

where $\boldsymbol{C}_{\alpha r}$ are the MO expansion coefficients and N_O is the total number of occupied orbitals. The SCF energy functional *in vacuo* can now be expressed as:

$$\mathscr{E}(\boldsymbol{C}) \overset{\mathrm{Tr}}{=} \boldsymbol{hD} + \frac{1}{2}\boldsymbol{G}^{\gamma}(\boldsymbol{D})\boldsymbol{D} + E_{\mathrm{xc}}[\rho(\boldsymbol{r})] + V_{\mathrm{NN}}, \tag{2.29}$$

and has to be optimized under the MO orthonormality constraint, easily introduced by means of Lagrangian multipliers:

$$\mathscr{L}(\boldsymbol{C}, \boldsymbol{\epsilon}) = \mathscr{E}(\boldsymbol{C}) - \sum_{ij} \epsilon_{ji}(\langle\phi_i|\phi_j\rangle - \delta_{ij}) \tag{2.30}$$

The various contributions are expressed in terms of AO basis integral and density matrices:

$$h_{\mu\nu} = = \int \mathrm{d}\boldsymbol{r}\chi^{\dagger}_{\mu}(\boldsymbol{r})h(\boldsymbol{r})\chi_{\nu}(\boldsymbol{r}) \tag{2.31a}$$

$$G^{\gamma}_{\mu\nu} = \sum_{\kappa\lambda} D_{\kappa\lambda}(g_{\mu\nu\kappa\lambda} - \gamma g_{\mu\lambda\kappa\nu}) \tag{2.31b}$$

$$g_{\mu\nu\kappa\lambda} = \int \mathrm{d}\boldsymbol{r} \int \mathrm{d}\boldsymbol{r}'\,\Omega_{\mu\nu}(\boldsymbol{r})g(\boldsymbol{r},\boldsymbol{r}')\Omega_{\kappa\lambda}(\boldsymbol{r}') \tag{2.31c}$$

$$E_{\mathrm{xc}}[\rho(\boldsymbol{r})] = \int \mathrm{d}\boldsymbol{r}v_{\mathrm{xc}}(\boldsymbol{r})\,(\mathrm{Tr}\boldsymbol{\Omega}(\boldsymbol{r})\boldsymbol{D}) \tag{2.31d}$$

$$\Omega_{\mu\nu}(\boldsymbol{r}) = \chi^{\dagger}_{\mu}(\boldsymbol{r})\chi_{\nu}(\boldsymbol{r}). \tag{2.31e}$$

The quantum/classical polarizable SCF functional is obtained by adding the polarization functional to Eq. (2.29):

$$\mathscr{L}_{\mathrm{eff}}(\boldsymbol{C},\boldsymbol{\epsilon},\mathrm{s}) = \mathscr{L}(\boldsymbol{C},\boldsymbol{\epsilon}) + \frac{1}{2}{}^{t}\mathrm{p}\mathbb{V}\mathrm{p} + {}^{t}\mathrm{p}(\mathrm{Tr}\mathrm{s}\boldsymbol{D}). \tag{2.32}$$

Differentiation with respect to the variational degrees of freedom yields the KS and polarization equations:

$$\boldsymbol{F}\boldsymbol{C} = \boldsymbol{S}\boldsymbol{C}\boldsymbol{\epsilon} \tag{2.33a}$$

$$\mathbb{V}\mathrm{p} + \mathrm{Tr}\mathrm{s}\boldsymbol{D} = 0 \tag{2.33b}$$

The KS matrix now includes environment contributions:

$$f_{\mu\nu} = h_{\mu\nu} + G^{\gamma}_{\mu\nu}(\boldsymbol{D}) + f_{\mathrm{xc};\mu\nu} + {}^{t}\mathrm{p}\mathrm{s}_{\mu\nu}. \tag{2.34}$$

With respect to the coupling described in abstract terms above, the SCF case is formally simpler. In fact, whereas in the general case the source term depends on *both* primal (amplitudes) and dual (multipliers) variational degrees of freedom, here only the dependence on the primal parameters (MO coefficients) needs to be considered.[157]

3

Response Theory and Molecular Properties

White light goin' messin' up my brain
White light it's gonna drive me insane

— THE VELVET UNDERGROUND

What's the frequency, Kenneth?
I never understood the frequency

— R.E.M.

Response theory provides an *ab initio* framework for the formulation and computation of molecular properties and thus a connection between *ab initio* and experimental methods based on spectroscopy. The response treatment of molecular properties has its roots in time-dependent perturbation theory[44] and has been continually developed in quantum chemistry for the past 30 years.[14,74,167–171]

Section 3.1 will give a brief introduction to response theory for isolated molecules. The concepts of quasienergy,[169] variational perturbation theory[74] and pole-and-residue analysis of response functions[167] will be introduced. The exposition closely follows that given by Saue in ref. 172. I will explicitly derive the SCF response function for a quantum/classical polarizable Hamiltonian in Section 3.2. The derivation will employ the density matrix-based, AO formalism introduced by Thorvaldsen et al. in ref. 173.

3.1 RESPONSE THEORY IN A NUTSHELL

► LET US CONSIDER THE EXPERIMENTALLY RELEVANT SITUATION where a molecular system is subject to an external source of electromagnetic radiation, Figure 3.1. Here and in the following, ”external” will be used to mean an electromagnetic field which is ”weak” when compared to the electron–electron and electron–nuclei interactions in the molecule.

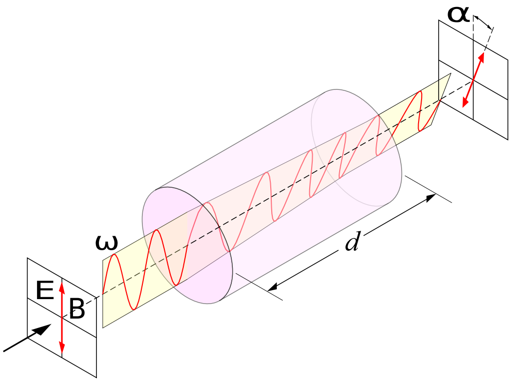


Figure 3.1 When a molecular system is subject to an external electromagnetic radiation of frequency ω, a macroscopic, experimentally measurable response can be detected. Intensity and position of the signal can be related to the microscopic detail of the molecular system, as described by quantum mechanics. The picture depicts an optical rotation experiment where the linear polarization of the incident electromagnetic field is rotated by an angle α upon traversing a chiral material. Reproduced, with modifications, from Wikipedia.

The system can then be described by means of a combined matter–field Hamiltonian:

$$H = H_{\text{matter}} + H_{\text{field}} + H_{\text{int}}, \tag{3.1}$$

where the three terms describe the molecular sample, the electromagnetic field and their interaction, respectively. Since our focus is on the molecular system, one can neglect the quantized description of the field and treat the interaction term in a semiclassical fashion.[174]

The time-dependent Schrödinger equation is now the appropriate equation of motion:

$$H\psi(t) = \mathrm{i}\frac{\partial\psi(t)}{\partial t}, \tag{3.2}$$

where the time-dependent, semiclassical matter–field Hamiltonian is used:

$$H = H_0 + V(t). \tag{3.3}$$

The perturbation is a one-electron operator. We will further assume that it is periodic in time $V(t) = V(t+T)$ and admits a discrete Fourier decomposition:

$$\begin{aligned} V(t) = \sum_{k=-N}^{N} \mathrm{e}^{-\mathrm{i}\omega_k t} V(\omega_k) &= \sum_{k=-N}^{N} \mathrm{e}^{-\mathrm{i}\omega_k t} \sum_{X} \epsilon_X(\omega_k) V_X \\ &= \sum_{x} \mathrm{e}^{-\mathrm{i}\omega_x t} \epsilon_x V_X, \end{aligned} \tag{3.4}$$

where all the frequencies are integer multiples, $\omega_k = n_k\omega$, of a fundamental frequency $\omega = \frac{2\pi}{T}$.[167] Frequencies and amplitudes in the Fourier decomposition obey the following relations:

$$\omega_{-k} = \omega_k, \quad \epsilon_x = \epsilon_X^*(\omega_k) = \epsilon_X(\omega_{-k}) = \epsilon_{-x}^*, \tag{3.5}$$

since the $V(t)$ is required to be Hermitian. For notational convenience, the perturbation operator (X) and frequency (k) indices have been collapsed into the common index x.

▶ Under the assumption that the external field is weak with respect to the molecular field, time-dependent perturbation theory is an appropriate tool to approximately solve Eq. (3.2).[*] The response theory route to molecular properties introduces a phase-separated ansatz for the time-dependent wave function:

$$\psi(t) = \mathrm{e}^{-\mathrm{i}F(t)}\bar{\psi}(t), \tag{3.6}$$

[*] *Real-time* methods, where the time-dependent Schrödinger equation is integrated directly in a set time interval, offer an alternative approach to perturbation theory.[44,175,176]

where the time-derivative of the phase factor defines the time-dependent *quasienergy*:

$$Q(t) = \dot{F}(t) = \left\langle \bar{\psi}(t) \middle| H_0 + V(t) - \mathrm{i}\frac{\partial}{\partial t} \middle| \bar{\psi}(t) \right\rangle . \tag{3.7}$$

The time-dependent quasienergy is variational, but the corresponding time-dependent Hellmann–Feynman theorem cannot straightforwardly be applied to the calculation of molecular properties.[169,171] Fortunately, we can exploit the periodicity of the perturbation operator to introduce the time-averaged quasienergy:

$$\{Q(t)\}_T = \frac{1}{T}\int_0^T \mathrm{d}t Q(t) = Q_0 + \sum_x \epsilon_x E_x \tag{3.8}$$

where:

$$\begin{aligned} Q_0 &= \left\{\langle \bar{\psi}(t) \,|\, H_0 \,|\, \bar{\psi}(t)\rangle\right\}_T - \left\{\left\langle \bar{\psi}(t) \middle| \mathrm{i}\frac{\partial}{\partial t} \middle| \bar{\psi}(t) \right\rangle\right\}_T \\ &= E_0(0) - S \end{aligned} \tag{3.9a}$$

$$E_x = \left\{\langle \bar{\psi}(t) \,|\, V_X \,|\, \bar{\psi}(t)\rangle \exp(-\mathrm{i}\omega_k t)\right\}_T \tag{3.9b}$$

Differentiating the time-averaged quasienergy yields the time-averaged Hellmann–Feynman theorem:

$$\frac{\mathrm{d}\,\{Q(t)\}_T}{\mathrm{d}\epsilon_X(\omega_k)} = \left\{\left\langle \bar{\psi}(t) \middle| \frac{\partial H}{\partial \epsilon_x} \middle| \bar{\psi}(t) \right\rangle\right\}_T = E_x, \tag{3.10}$$

which can be used to connect response functions to molecular properties. Letting $|0\rangle$ represent the unperturbed reference state, we can develop the Kubo expansion at zero perturbation strength of the expectation value of the observable H_X:[177]

$$\begin{aligned} \langle \bar{\psi}(t) | V_X | \bar{\psi}(t)\rangle \simeq{}& \langle 0 \,|\, V_X \,|\, 0\rangle \\ &+ \sum_{k=-N}^{N} \langle\langle V_X; V(\omega_k)\rangle\rangle_{\omega_k} \mathrm{e}^{-\mathrm{i}\omega_k t} \\ &+ \frac{1}{2}\sum_{k,l=-N}^{N} \langle\langle V_X; V(\omega_k), V(\omega_l)\rangle\rangle_{\omega_k,\omega_l} \mathrm{e}^{-\mathrm{i}(\omega_k+\omega_l)t} \end{aligned} \tag{3.11}$$

response functions may be identified as the Fourier coefficients in the expansion. These are none other but higher order derivatives of the time-averaged quasienergy, as a comparison with the same expansion for the right-hand side of Eq. (3.10) will confirm:

$$\begin{aligned}\frac{\mathrm{d}\,\{Q(t)\}_T}{\mathrm{d}\epsilon_x} \simeq \langle 0 \,|\, V_X \,|\, 0\rangle\, \delta_{\omega_x} \\ + \sum_y \langle\langle V_X; V_Y\rangle\rangle_{\omega_y}\, \epsilon_y \delta_{\omega_x+\omega_y} \\ + \frac{1}{2}\sum_{y,z} \langle\langle V_X; V_Y, V_Z\rangle\rangle_{\omega_y,\omega_z}\, \epsilon_y\epsilon_z\delta_{\omega_x+\omega_y+\omega_z}.\end{aligned} \tag{3.12}$$

First and higher order molecular properties can now be identified from the response functions appearing as Fourier coefficients in the Kubo expansion by taking the appropriate perturbation-strength derivatives at zero field strength:

$$\begin{aligned}\left.\frac{\mathrm{d}^n\,\{Q(t)\}_T}{\mathrm{d}\epsilon_{x_1}\,\mathrm{d}\epsilon_{x_2}\cdots\mathrm{d}\epsilon_{x_n}}\right|_{\epsilon=0} = \\ \langle\langle V_{X_1}; V_{X_2}, \dots, V_{X_n}\rangle\rangle_{\omega_{x_2},\dots,\omega_{x_n}} \delta_{\omega_{x_1}+\dots+\omega_{x_n}},\end{aligned} \tag{3.13}$$

the $\delta_{\omega_{x_1}+\dots+\omega_{x_n}}$ notation is used to enforce the sum rule on the probing and response frequencies involved in the expansion:

$$\sum_{i=1}^{n} \omega_{x_i} = 0 \tag{3.14}$$

Response functions quantify how, to a certain order in the perturbing field tuples, the expectation value of a given observable is modified. The semicolon appearing in the response functions separates the operator V_X, whose response is measured, from the external perturbations V_Y, V_Z, … causing it. From the perturbation expansion Eq. (3.12), it is clear that permutation symmetry exists between the external perturbations provided that the corresponding frequencies are permuted concomitantly.

HAVING INTRODUCED RESPONSE FUNCTIONS AS A USEFUL TOOL to quantify the effect of external perturbations on molecular properties, it is now time to consider how to compute them. In this Section, we are concerned with exact wave functions that can be variationally parametrized by a set of parameters $\boldsymbol{\eta}$: $|0\rangle = |0(\boldsymbol{\eta})\rangle$. We recall that the Lagrangian method outlined in Section 1.3 can be employed also in this case.[169–171] The optimal parameter set is determined upon minimization of the time-averaged quasienergy:

$$\frac{\mathrm{d}\,\{Q(t)\}_T}{\mathrm{d}\boldsymbol{\eta}} = 0. \tag{3.15}$$

In variational perturbation theory,[74,172] we assume the variational parameters to be functions of the perturbation strength parameters: $\boldsymbol{\eta} = \boldsymbol{\eta}(\boldsymbol{\epsilon})$. Furthermore, we require the stationarity condition to hold at *all* perturbation strengths, with $\eta(0) = 0$, for convenience.

The perturbation-strength total derivative at zero perturbation strength of the time-averaged quasi energy is:

$$\begin{aligned}
\left[\prod_{i=1}^{n}\frac{\mathrm{d}}{\mathrm{d}\epsilon_{x_i}}\right]\{Q(t)\}_T &= Q^{[n]}_{x_1\dots x_n} \\
&= Q^{[n]}_{0;x_1\dots x_n} + \sum_{j=1}^{n} E^{[n-1]}_{x_j;x_1\dots x_{j-1}x_{j+1}\dots x_n} \\
&= \left[\prod_{i=1}^{n}\frac{\mathrm{d}}{\mathrm{d}\epsilon_{x_i}}\right] Q_0 + \sum_{j=1}^{n}\left[\prod_{i\neq j}^{n-1}\frac{\mathrm{d}}{\mathrm{d}\epsilon_{x_i}}\right] E_{x_j}
\end{aligned} \tag{3.16}$$

Notice that this is just an alternative and more verbose notation for Eq. (3.13), which allows to express response functions in terms of wave function perturbed parameters. Application of the chain rule to the total derivatives in fact yields:

$$Q^{[1]}_{a} = \sum_{\sigma}\left[Q^{[1]}_{0;\sigma}\eta^{[1]}_{\sigma;a} + E_a\right]\delta_{\omega_a} \tag{3.17a}$$

$$\begin{aligned}
Q^{[2]}_{ab} = \sum_{\sigma\tau}\bigl[&\eta^{[1]}_{\sigma;a}Q^{[2]}_{0;\sigma\tau}\eta^{[1]}_{\tau;b} + Q^{[1]}_{0;\sigma}\eta^{[2]}_{\sigma;a} \\
&+ E^{[1]}_{a;\sigma}\eta^{[1]}_{\sigma;b} + E^{[1]}_{b;\sigma}\eta^{[1]}_{\sigma;a}\bigr]\delta_{\omega_a+\omega_b}
\end{aligned} \tag{3.17b}$$

where the following tensors were introduced:

$$Q^{[n]}_{0;\sigma_1\cdots\sigma_n} = \frac{\partial^n Q_0}{\partial\eta_{\sigma_1}\cdots\partial\eta_{\sigma_n}} \tag{3.18a}$$

$$E^{[n]}_{x;\sigma_1\cdots\sigma_n} = \frac{\partial^n E_x}{\partial\eta_{\sigma_1}\cdots\partial\eta_{\sigma_n}} \tag{3.18b}$$

$$\eta^{[n]}_{\sigma;x_1\ldots x_n} = \frac{\partial^n \eta_\sigma}{\partial\epsilon_{x_1}\cdots\partial\epsilon_{x_n}} \tag{3.18c}$$

The response equations, determining the tensor of perturbed wave function parameters $\boldsymbol{\eta}^{[n]}$, are obtained by differentiating the time-averaged quasienergy variational condition Eq. (3.15) with respect to the perturbation parameters:[74,167,169]

$$R^{[n]}_{\sigma;x_1\cdots x_n} = \left[\prod_{i=1}^{n}\frac{\mathrm{d}}{\mathrm{d}\epsilon_{x_i}}\right]\left.\frac{\mathrm{d}\,\{Q(t)\}_T}{\mathrm{d}\eta_\sigma}\right|_{\epsilon=0} = 0, \tag{3.19}$$

followed by evaluation at zero perturbation strength. The first order response of the wave function $\boldsymbol{\eta}^{[1]}$, needed for the determination of second order properties $Q^{[2]}_{ab}$, can be computed by solving the corresponding response equation:

$$R^{[0]}_\sigma = Q^{[1]}_{0;\sigma} = 0 \tag{3.20a}$$

$$R^{[1]}_{\sigma;a} = \sum_\tau Q^{[2]}_{0;\sigma\tau}\eta^{[1]}_{\tau;a} + E^{[1]}_{a;\sigma} = 0. \tag{3.20b}$$

The time-averaged quasienergy formalism allows to formulate response properties to static and dynamic fields on an equal footing as perturbation-strength derivatives. Moreover, variational perturbation theory achieves a transparent derivation of the necessary response equations.[74]

► LET US CONSIDER IN MORE DETAIL THE FORM OF THE LINEAR RESPONSE FUNCTION EQ. (3.17b). The formal solution to the response equation Eq. (3.20b) can be obtained by inverting the *Hessian*, $\boldsymbol{Q}^{[2]}_0$. Eq. (3.17b) can then be rewritten as:

$$\langle\langle V_A; V_B\rangle\rangle_{\omega_b} = -\sum_{\sigma\tau} E^{[1]}_{a;\sigma}\left[\boldsymbol{Q}^{[2]}_0\right]^{-1}_{\sigma\tau} E^{[1]}_{b;\tau}. \tag{3.21}$$

Expansion into the exact eigenbasis of H_0 yields the sum-over-states (SOS) expression for the linear response function:

$$\begin{aligned}\langle\langle V_A; V_B\rangle\rangle_{\omega_b} = -\sum_{n>0}\Bigg[&\frac{\langle 0|V_A|n\rangle\langle n|V_B|0\rangle}{\omega_{n0}-\omega_b} \\ &+\frac{\langle 0|V_B|n\rangle\langle n|V_A|0\rangle}{\omega_{n0}-\omega_a}\Bigg]\delta_{\omega_a+\omega_b}.\end{aligned} \tag{3.22}$$

The excitation energies of the system appear in the denominators $\omega_{n0} = E_n - E_0$ and can thus be identified as the *poles* of the response function. Moreover, the *residues* at the poles are the transition moments determining the intensity of the spectroscopic transitions:

$$\lim_{\omega_b\to\omega_{n0}} \langle\langle V_A; V_B\rangle\rangle_{\omega_b} = \langle 0|V_A|n\rangle\langle n|V_B|0\rangle\,. \tag{3.23}$$

A similar analysis holds also for higher order response functions. The pole structure of the higher order quantities also conveys information about the excited states *via* single and double residues.[167,169,170]

THE DERIVATION ABOVE HOLDS FOR AN EXACT STATE, a situation that is never realized in common practice. However, response theory is also applicable to approximate states. As noted by Norman, a response theory treatment of molecular properties can be summarized into the following four steps:[14]

1. Single out a quantity of interest that can be connected to molecular properties. In our case, the time-averaged quasienergy;
2. Introduce a suitable parametrization of the time-dependent, phase-separated wave function;
3. Devise the appropriate equation of motion, based on the time-dependent Schrödinger equation, for the time-dependent wave function parameters;
4. Identify response functions and response equations.

Thus, one can formulate and compute molecular properties based on the approximate state ansätze of quantum chemistry. An interesting formulation of SCF response theory is the open-ended AO density matrix-based approach presented by Thorvaldsen et al.[173] By formulating the perturbation-strength derivative of the time-averaged quasienergy Lagrangian in terms of the AO density matrix, the authors were able to formulate arbitrary order response functions in the AO basis. The density matrix is the variational degree of freedom and the response equations can be obtained by differentiation of the time-dependent SCF (TDSCF) equation. The approach lends itself to an efficient AO-based implementation,[178,179] can fully leverage different response parameters elimination schemes[173,180] and is amenable to an open-ended, recursive implementation.[181–183] We will base our derivation of SCF response theory for quantum/classical polarizable Hamiltonians of this framework.

3.2 SCF RESPONSE THEORY FOR QUANTUM/CLASSICAL POLARIZABLE HAMILTONIANS

The development of response theory for quantum/classical polarizable Hamiltonians has moved almost at the same pace as the models themselves. An ample literature exists in the context of the PCM,[184–190] polarizable MM models,[34,191–193] and general QM/MM/Continuum models.[37–39]

► SOLVENT RELAXATION IS AN IMPORTANT POINT WHEN FORMULATING RESPONSE PROPERTIES. Solvation dynamics occurs on timescales and through relaxation modes that are typical of the solvent molecular structure and of the peculiar solute-solvent interactions. This is clearly difficult to model with continuum models, since the entire frequency spectrum of the permittivity $\varepsilon(\omega)$ would be required.[194–198] However, if one considers the initial steps of an electronic excitation process, a Franck–Condon-like response of the solvent can be assumed. Nuclear motions of the solute and solvent molecules alike will not be able to follow the fast rearrangement of the electronic density, therefore the corresponding part of the response will remain frozen in the state immediately preceding the change. Such an assumption, albeit approximate, leads to the following partition of the polarization vector:

$$\boldsymbol{P} \simeq \boldsymbol{P}_{\mathrm{fast}} + \boldsymbol{P}_{\mathrm{slow}}. \tag{3.24}$$

This is equivalent to considering only the asymptotic limits of the solvent dielectric spectrum, *i. e.* the static ε_{s} and optical dielectric constants ε_{∞}.[29,30,199,200]

The variational setting introduced in Section 2.4, offers a series of advantages also in the formulation of response theory. As already noted, a classical counterpart to the Hellmann–Feynman theorem holds:

$$\frac{\mathrm{d}U_{\mathrm{pol}}}{\mathrm{d}F} = \frac{\partial U_{\mathrm{pol}}}{\partial F} + \frac{\partial U_{\mathrm{pol}}}{\partial \mathrm{s}}\frac{\partial \mathrm{s}}{\partial F} = \frac{\partial U_{\mathrm{pol}}}{\partial F}, \quad \text{(2.23 from Chapter 2)}$$

which forms the basis for our formal development in **Paper V**.[201] There we show how the variational polarization functional can successfully achieve a transparent derivation of arbitrary order response functions, when the fixed-cavity approximation for the PCM is assumed. Here we report a summary of our findings in **Paper V** employing the supermatrix form of the classical functional as given in Eq. (2.24). In the notation of Thorvaldsen et al., we introduce the generalized free energy:

$$\begin{aligned}\tilde{\mathscr{G}} &= \tilde{\mathscr{E}} + \frac{1}{2}{}^{t}\tilde{\mathrm{p}}\mathbb{V}\tilde{\mathrm{p}} + {}^{t}\tilde{\mathrm{p}}\mathrm{Tr}(\tilde{\mathbf{s}}\tilde{\boldsymbol{D}}) \\ &\overset{\mathrm{Tr}}{=} \left[\tilde{\boldsymbol{h}} + \tilde{\boldsymbol{V}}^{t} + \frac{1}{2}\tilde{\boldsymbol{G}}^{\gamma}(\tilde{\boldsymbol{D}}) - \frac{\mathrm{i}}{2}\tilde{\boldsymbol{T}}\right]\tilde{\boldsymbol{D}} + \tilde{E}_{\mathrm{xc}}[\tilde{\rho}(\tilde{\boldsymbol{D}})] + h_{\mathrm{nuc}} \\ &+ \frac{1}{2}{}^{t}\tilde{\mathrm{p}}\mathbb{V}\tilde{\mathrm{p}} + {}^{t}\tilde{\mathrm{p}}\tilde{\mathbf{s}}\tilde{\boldsymbol{D}},\end{aligned} \tag{3.25}$$

whose perturbation-strength derivatives at zero perturbation strength will yield the desired response functions.

To keep track of the number of chain rule applications, we will denote higher-order derivatives of the KS generalized free energy with the composite $mn, abc \dots$ superscript:

$$\begin{aligned} \mathscr{G}^{mn,abc} &= \frac{\partial^{m+n+3}\mathscr{G}}{\partial(\boldsymbol{D}^T)^m \partial \mathrm{p}^n \partial\epsilon_a \partial\epsilon_b \partial\epsilon_c} \\ &= \mathscr{E}^{m,abc} + \frac{\partial^{m+n+3} U_{\mathrm{pol}}}{\partial(\boldsymbol{D}^T)^m \partial \mathrm{p}^n \partial\epsilon_a \partial\epsilon_b \partial\epsilon_c}. \end{aligned} \tag{3.26}$$

In this notation, the $abc \dots$ indices denote the perturbations with respect to which differentiation occurs. The index m denotes the order of differentiation with respect to the density matrix. n denotes the order of differentiation with respect to the polarization. The classical interaction kernel $\mathbb{V}$ might, in the most general scenario, depend on the molecular geometry. In **Paper V** and in the following we ignore this possibility and work under the simplifying assumption that $\mathbb{V}$ is independent of the nuclear positions. This goes under the name of *fixed-cavity approximation* in the context of the PCM.[184] Under this simplifying assumption, the perturbation-strength derivative of the classical functional will only include terms stemming from the linear interaction term:

$$\frac{\mathrm{d}}{\mathrm{d}\epsilon_a} \left\{ U_{\mathrm{pol}} \right\}_T \overset{\{\mathrm{Tr}\}_T}{=} {}^t\tilde{\mathrm{p}}\tilde{\mathbf{s}}^a \tilde{\boldsymbol{D}}, \tag{3.27}$$

where the second term only involves derivatives of the source integrals. Moreover, in the general expression for the perturbation-strength derivative of the polarization functional in Eq. (3.26), the m and n indices can only assume the values 0 or 1. In fact, the density matrix dependence is at most linear in the polarization functional, while the classical Hellmann–Feynman theorem ensures that the polarization appears at most linearly in $\tilde{\mathscr{G}}^{00,a}$:

$$\begin{aligned} \tilde{\mathscr{G}}^{00,a}(\tilde{\boldsymbol{D}}, \tilde{\sigma}, t) &= \tilde{\mathscr{E}}^{0,a} + {}^t\tilde{\mathrm{p}}\mathrm{Tr}(\tilde{\mathbf{s}}^a \tilde{\boldsymbol{D}}) \\ &\overset{\mathrm{Tr}}{=} (\tilde{\boldsymbol{h}}^a + \tilde{\boldsymbol{V}}^{t,a} + \frac{1}{2}\tilde{\boldsymbol{G}}^{\gamma,a}(\tilde{\boldsymbol{D}}) + \tilde{\boldsymbol{F}}_{\mathrm{xc}}^{\Omega_a} - \frac{\mathrm{i}}{2}\tilde{\boldsymbol{T}}^a)\tilde{\boldsymbol{D}} \\ &\qquad + h_{\mathrm{nuc}}^a + {}^t\tilde{\mathrm{p}}\tilde{\mathbf{s}}^a \tilde{\boldsymbol{D}}. \end{aligned} \tag{3.28}$$

The integral derivative matrices involved in the previous expression were introduced in ref. 173. Further perturbation-strength differentiations and evaluation at zero perturbation strength will yield the desired response functions:

$$L^{a} \overset{\{\mathrm{Tr}\}_T}{=} \mathscr{G}^{00,a} - \boldsymbol{S}^{a}\boldsymbol{W} \tag{3.29a}$$

$$\begin{aligned} L^{ab} \overset{\{\mathrm{Tr}\}_T}{=} & \mathscr{G}^{00,ab} + \mathscr{G}^{10,a}\boldsymbol{D}^{b} + \mathscr{G}^{01,a}\mathrm{p}^{b} \\ & - \boldsymbol{S}^{ab}\boldsymbol{W} - \boldsymbol{S}^{a}\boldsymbol{W}^{b} \end{aligned} \tag{3.29b}$$

$$\begin{aligned} L^{abc} \overset{\{\mathrm{Tr}\}_T}{=} & \mathscr{G}^{00,abc} + \mathscr{G}^{10,ac}\boldsymbol{D}^{b} + \mathscr{G}^{10,ab}\boldsymbol{D}^{c} + \mathscr{G}^{20,a}\boldsymbol{D}^{b}\boldsymbol{D}^{c} \\ & + \mathscr{G}^{10,a}\boldsymbol{D}^{bc} + \mathscr{G}^{11,a}\boldsymbol{D}^{b}\mathrm{p}^{c} \\ & + \mathscr{G}^{01,ac}\mathrm{p}^{b} + \mathscr{G}^{01,ab}\mathrm{p}^{c} + \mathscr{G}^{01,a}\mathrm{p}^{bc} + \mathscr{G}^{11,a}\mathrm{p}^{b}\boldsymbol{D}^{c} \\ & - \boldsymbol{S}^{abc}\boldsymbol{W} - \boldsymbol{S}^{ab}\boldsymbol{W}^{c} - \boldsymbol{S}^{ac}\boldsymbol{W}^{b} - \boldsymbol{S}^{a}\boldsymbol{W}^{bc} \end{aligned} \tag{3.29c}$$

and similarly for higher orders.

The governing equations for the perturbed polarization densities are obtained in complete analogy with the handling of pertubed density matrices described in ref. 173. Denoting by the superscript b_N a tuple of simultaneous perturbations, the polarization can be decomposed into frequency components $\mathrm{p}_{\omega}^{b_N}$. Similarly to the treatment of the perturbed density matrices, we introduce a partition of the frequency components of the polarization into homogeneous (H) and particular (P) terms:

$$\mathrm{p}_{\omega}^{b_N} = \mathrm{p}_{\mathrm{P}}^{b_N} + \mathrm{p}_{\mathrm{H}}^{b_N}, \tag{3.30}$$

and we thus get the following system of equations:

$$\begin{cases} \mathbb{V}\mathrm{p}_{\mathrm{H}}^{b_N} + \mathrm{Trs}\boldsymbol{D}_{\mathrm{H}}^{b_N} = 0 & (3.31\mathrm{a}) \\ \mathbb{V}\mathrm{p}_{\mathrm{P}}^{b_N} + \mathrm{Trs}\boldsymbol{D}_{\mathrm{P}}^{b_N} = \mathbb{S}_{\omega}^{(n-1)}. & (3.31\mathrm{b}) \end{cases}$$

$\mathbb{S}_{\omega}^{(n-1)}$ contains all terms that depend on lower order density matrices and differentiated source integrals. The term $\mathbb{S}_{\omega}^{(n-1)}$ always contains at least a first derivative of the source integrals and is thus zero if the basis set is independent of the perturbation tuple under consideration.

Consequently, the particular term of the polarization is nonzero if and only if the basis set depends on the external perturbation.

Response equations can be obtained by differentiating the TDSCF equation with respect to the perturbation tuple b_N:[173,181]

$$\left[\boldsymbol{E}^{[2]} - \omega_{b_N}\boldsymbol{S}^{[2]}\right]\boldsymbol{X}^{b_N} = \boldsymbol{M}^{b_N}_{\mathrm{RHS}}, \tag{3.32}$$

where the generalized Hessian $\boldsymbol{E}^{[2]}$ and metric $\boldsymbol{S}^{[2]}$ matrices were introduced and are defined by the transformations of the response parameters $\boldsymbol{X}^{b_N}$ they induce:[178,179]

$$\begin{aligned}\boldsymbol{E}^{[2]}\boldsymbol{X}^{b_N} = {} & \boldsymbol{G}^{\mathrm{KS}}([\boldsymbol{X}^{b_N}, \boldsymbol{D}]_{\boldsymbol{S}})\boldsymbol{D}\boldsymbol{S} - \boldsymbol{S}\boldsymbol{D}\boldsymbol{G}^{\mathrm{KS}}([\boldsymbol{X}^{b_N}, \boldsymbol{D}]_{\boldsymbol{S}}) \\ & + \boldsymbol{F}[\boldsymbol{X}^{b_N}, \boldsymbol{D}]_{\boldsymbol{S}}\boldsymbol{S} - \boldsymbol{S}[\boldsymbol{X}^{b_N}, \boldsymbol{D}]_{\boldsymbol{S}}\boldsymbol{F} \\ & + \sigma_{\mathrm{H}}^{b_N}\boldsymbol{\varphi}\boldsymbol{D}\boldsymbol{S} - \boldsymbol{S}\boldsymbol{D}\boldsymbol{\varphi}\sigma_{\mathrm{H}}^{b_N}\end{aligned} \tag{3.33a}$$

$$\boldsymbol{S}^{[2]}\boldsymbol{X}^{b_N} = \boldsymbol{S}[\boldsymbol{X}^{b_N}, \boldsymbol{D}]_{\boldsymbol{S}}\boldsymbol{S}. \tag{3.33b}$$

The generalized Hessian matrix $\boldsymbol{E}^{[2]}$ includes two types of classical terms: implicit and explicit. *Implicit* terms are those included in the zeroth-order Fock matrix, $\boldsymbol{F}$. The last two terms in Eq. 3.33a are *explicit* terms, as they explicitly involve the N-th order homogeneous polarization variational density. The nonequilibrium response framework needed in continuum models when dealing with frequency-dependent properties,[99,187] will affect the explicit terms in Eq. (3.33a). These are evaluated by making use of the optical permittivity ε_∞ in the polarization equations (3.31a) and (3.31b). The right-hand side in the response equation only includes terms that depend on particular contributions up to the desired order or lower-order perturbed variational densities:[181]

$$\boldsymbol{M}^{b_N}_{\mathrm{RHS}} = \left[\left(\tilde{\boldsymbol{\mathscr{F}}} - \frac{\mathrm{i}}{2}\tilde{\boldsymbol{S}}\frac{\mathrm{d}}{\mathrm{d}t}\right)\tilde{\boldsymbol{D}}\tilde{\boldsymbol{S}}\right]^{\ominus, b_N}_{\mathrm{P}}, \tag{3.34}$$

where $\boldsymbol{\mathscr{F}}$ is the generalized KS matrix, see ref. 173 for details.

A direct solution of the response equation (3.32) by inversion is not feasible due to the size of the $\left[\boldsymbol{E}^{[2]} - \omega_{b_N}\boldsymbol{S}^{[2]}\right]$ matrix. *Subspace iteration* methods are usually employed and the solution is achieved iteratively by enlarging a projection subspace of trial vectors.[202–205]

These methods can be implemented efficiently and in matrix-free form since the linear transformations $\boldsymbol{E}^{[2]}\boldsymbol{X}^{b_N}$ and $\boldsymbol{S}^{[2]}\boldsymbol{X}^{b_N}$ have known forms only involving integral and (perturbed) density matrices. Moreover, Jacobi precondinioting of the iterations is usually sufficiently robust and efficient, due to the diagonal dominance of the generalized Hessian.

4

Electron Correlation and Solvation

> Potius sero quam numquam
>
> — Titus Livius, *Ab Urbe Condita*

I will present results on the formulation of quantum/classical polarizable models when the quantum part of the system includes a many-body description of electron correlation either by a MBPT, CC or hybrid approach. The contents of this Chapter are the result of an ongoing collaboration with prof. T. Daniel Crawford (Virginia Tech) and Dr. Andrew C. Simmonett (NIH).

I will leverage the variational formulation of quantum/classical polarizable Hamiltonians described in Section 2.4. This is an element of novelty with respect to the existing literature. I will show how a fully variational framework enables transparent derivations of MBPT and CC theory, encompassing previous work[206–223] and solving some inconsistencies in the formulation of MBPT noted by Ángyán.[224,225]

Sections 4.1 and 4.2 will introduce the effective CC Lagrangian and the relevant notation for the source terms in the classical energy functional, respectively. In Section 4.3 I will derive the governing equation for the effective Lagrangian, showing how previous work on continuum[206,207,209] and explicit models[220,222] can easily be derived in the variational framework.

The second part of this Chapter will be devoted to the derivation of MBPT for quantum/classical polarizable Hamiltonians. I will exploit the CC ansatz for the wave function and formulate MBPT in terms of the effective CC Lagrangian, an approach guaranteeing term-by-term size-extensivity.

Iterative and noniterative approximations to the CCSD and CCSDT models will be the subject of Section 4.5 where the equations governing the CC2 and CC3 models will be derived. Eventually, I will describe schemes for the noniterative inclusion of the effect of connected triples excitations on top of the CCSD wave function. The symmetric and asymmetric (T) corrections will be derived.

Notation

For ease of reference, I will repeat some of the notational conventions introduced in Chapter 1 here. The cluster operator at truncation level $\mathscr{M}$ is:

$$T = \sum_{u=1}^{\mathscr{M}} T_u = \sum_{u=1}^{\mathscr{M}} \sum_{\mu_u} t_{\mu_u} \tau_{\mu_u}, \qquad \text{(1.24 from Chapter 1)}$$

where t_{μ_u} and τ_{μ_u} are the cluster amplitudes and cluster operators for the μ_u-th excited determinant at the u-th excitation level, respectively. The similarity transformed counterpart of the operator O is denoted by $\overline{O}$:

$$\overline{O} = \mathrm{e}^{-T} O \mathrm{e}^{T}. \qquad \text{(1.27 from Chapter 1)}$$

We recall that hermiticity of O is not preserved by the similarity transformation. Manipulation of similarity transformed operators involves the use of their Baker–Campbell–Hausdorff expansions:

$$\begin{aligned} \overline{O} &= O + \tilde{O} \\ &= O + [O,T] + \frac{1}{2}[[O,T],T] + \dots \end{aligned} \qquad \text{(1.28 from Chapter 1)}$$

since we are concerned with one- and two-electron operators only, such expansions will truncate after the third and fifth terms, respectively.[53] The similarity transformation by means of the singles cluster operator only, *i. e.* the T_1-transformation, will be denoted by a ”check” on top of the operator:

$$\check{O} = \mathrm{e}^{-T_1} O \mathrm{e}^{T_1}. \qquad \text{(1.43 from Chapter 1)}$$

The T_1-transformation preserves the particle rank of the operator O, see Appendix A for details. Finally, the u-th excited component of the coupled cluster left state will be denoted as:

$$\langle \bar{t}_u | = \sum_{\mu_u} \bar{t}_{\mu_u} \langle \mu_u | , \qquad \text{(1.35 from Chapter 1)}$$

where $\bar{t}_{\mu_u}$ are Lagrange multipliers.

4.1 EFFECTIVE COUPLED CLUSTER LAGRANGIAN

Our purpose in this Section is to derive an *effective* CC Lagrangian that takes into account the coupling of the correlated electronic state with the classical polarizable environment. This can be readily obtained[94] by coupling the usual Lagrangian in Eq. (1.34) with the classical polarization functional in Eq. (2.20). Care must however be taken in the definition of the classical variational degrees of freedom as to not erroneously include contributions from the reference state in the subsequent correlated treatment.

Once again, let us assume that the reference state is a closed-shell HF determinant. Further, we assume that the reference determinant was optimized in the presence of the classical polarizable environment. Then the polarization degree of freedom corresponding to the environment satisfies:

$$\mathbb{V}\mathrm{p}_{\mathrm{HF}} + \mathrm{s}_{\mathrm{HF}} = 0 \tag{4.1}$$

and corresponds to the *reference reaction field*. In the subsequent correlated treatment one can separate the reaction field into reference and correlated components:

$$\mathrm{p}^{\mathrm{tot}} = \mathrm{p}_{\mathrm{HF}} + \mathrm{p} \tag{4.2}$$

and similarly for the source term:

$$\begin{aligned}\mathrm{s}(t,\bar{t})_{\mathscr{M}} &= \mathrm{s}_{\mathrm{HF}} + \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathscr{M}} \\ &= \langle \mathrm{HF}|\mathrm{s}|\mathrm{HF}\rangle + \langle \mathrm{HF}|\tilde{\mathrm{s}}|\mathrm{HF}\rangle + \sum_{u=1}^{\mathscr{M}} \langle \bar{t}_u|\tilde{\mathrm{s}}|\mathrm{HF}\rangle .\end{aligned} \tag{4.3}$$

The BCH expansions of the source term has been rewritten as:

$$\bar{\mathrm{s}} = \mathrm{s} + \tilde{\mathrm{s}} = \mathrm{s} + [\mathrm{s}, T] + \frac{1}{2}[[\mathrm{s}, T], T], \tag{4.4}$$

taking advantage of the fact that s is a nondiagonal, one-electron operators and hence its commutator expansion truncates at the third term. Moreover, normal-ordering of the operators has been introduced.[54,65] This is equivalent to applying a shift to the correlation part of the source term one-electron operators to remove the reference source terms:

$$\begin{aligned} \mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}} &= \langle \mathrm{HF}|\tilde{\mathrm{s}}|\mathrm{HF}\rangle + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}_u|\bar{\mathrm{s}}|\mathrm{HF}\rangle \\ &= \langle \mathrm{HF}|\bar{\mathrm{s}} - \mathrm{s}_{\mathrm{HF}}|\mathrm{HF}\rangle + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}_u|\bar{\mathrm{s}} - \mathrm{s}_{\mathrm{HF}}|\mathrm{HF}\rangle\,. \end{aligned} \tag{4.5}$$

Eventually, the polarization functional can be rewritten as:

$$\begin{aligned} U_{\mathrm{pol}} &= \frac{1}{2}({}^t\mathrm{p}_{\mathrm{HF}} + {}^t\mathrm{p})\mathbb{V}(\mathrm{p}_{\mathrm{HF}} + \mathrm{p}) \\ &+ ({}^t\mathrm{p}_{\mathrm{HF}} + {}^t\mathrm{p})(\mathrm{s}_{\mathrm{HF}} + \mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}}) \\ &= \frac{1}{2}{}^t\mathrm{p}_{\mathrm{HF}}\mathbb{V}\mathrm{p}_{\mathrm{HF}} + {}^t\mathrm{p}_{\mathrm{HF}}\mathrm{s}_{\mathrm{HF}} + \frac{1}{2}{}^t\mathrm{p}_{\mathrm{HF}}\mathbb{V}\mathrm{p} + \frac{1}{2}{}^t\mathrm{p}\mathbb{V}\mathrm{p}_{\mathrm{HF}} \\ &+ {}^t\mathrm{p}_{\mathrm{HF}}\mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}} + {}^t\mathrm{p}\mathrm{s}_{\mathrm{HF}} + \frac{1}{2}{}^t\mathrm{p}\mathbb{V}\mathrm{p} + {}^t\mathrm{p}\mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}} \\ &= U_{\mathrm{pol}}^{\mathrm{ref}} + \frac{1}{2}{}^t\mathrm{p}\mathbb{V}\mathrm{p} + {}^t\mathrm{p}\mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}} + {}^t\mathrm{p}_{\mathrm{HF}}\mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}}. \end{aligned} \tag{4.6}$$

The reference polarization energy $U_{\mathrm{pol}}^{\mathrm{ref}}$ still appears among the terms in the functional but will obviously not enter in the optimization of the CC wave function. One can then write the effective Lagrangian as:

$$\begin{aligned} \mathscr{L}_{\mathrm{eff}}(t, \bar{t}, \mathrm{p})_{\mathcal{M}} = \langle \mathrm{HF}|\overline{H_0}|\mathrm{HF}\rangle &+ \sum_{u=1}^{\mathcal{M}} \langle t_u|\overline{H_0}|\mathrm{HF}\rangle \\ &+ \frac{1}{2}{}^t\mathrm{p}\mathbb{V}\mathrm{p} + {}^t\mathrm{p}\mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}} \\ &+ {}^t\mathrm{p}_{\mathrm{HF}}\mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathcal{M}} + U_{\mathrm{pol}}^{\mathrm{ref}} \end{aligned} \tag{4.7}$$

In accordance with previous work,[207,209] the Hamiltonian H_0 is augmented with the ${}^{t}\mathrm{p}_{\mathrm{HF}}\mathrm{s}_{\mathrm{N}}(t,\bar{t})$ term to yield the perturbation-to-the-energy (PTE) Hamiltonian – H – and eventually the perturbation-to-the-energy-and-the-density (PTED) Lagrangian:[210–214,225]

$$\mathscr{L}_{\mathrm{eff}}(t,\bar{t},\mathrm{p})_{\mathscr{M}} = {}^{\mathrm{PTE}}\mathscr{L}_{\mathrm{eff}}(t,\bar{t})_{\mathscr{M}} + \frac{1}{2}{}^{t}\mathrm{p}\mathbb{V}\mathrm{p} + {}^{t}\mathrm{p}\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathscr{M}}, \quad (4.8)$$

where the PTE Lagrangian has been introduced:

$${}^{\mathrm{PTE}}\mathscr{L}_{\mathrm{eff}}(t,\bar{t})_{\mathscr{M}} = \langle\mathrm{HF}|\overline{H}|\mathrm{HF}\rangle + \sum_{u=1}^{\mathscr{M}}\langle\bar{t}_u|\overline{H}|\mathrm{HF}\rangle + U_{\mathrm{pol}}^{\mathrm{ref}}. \quad (4.9)$$

As noted by Cammi for the implicit PCM model, the PTE Hamiltonian is computed in MP-partitioned form by employing the “solvated” orbitals and Fock matrix:

$$H = F + \Phi. \quad (4.10)$$

F is a diagonal one-electron operator and Φ is the fluctuation potential. The simple nature of the Fock operator lets us re-express the PTE Lagrangian as follows:

$$\begin{aligned}{}^{\mathrm{PTE}}\mathscr{L}_{\mathrm{eff}}(t,\bar{t})_{\mathscr{M}} = G_0 &+ \sum_{u=1}^{\mathscr{M}}\bar{t}_{\mu_u}\epsilon_{\mu_u}t_{\mu_u} + \langle\mathrm{HF}|\overline{\Phi}|\mathrm{HF}\rangle \\ &+ \sum_{u=1}^{\mathscr{M}}\langle\bar{t}_u|\overline{\Phi}|\mathrm{HF}\rangle\end{aligned} \quad (4.11)$$

where $G_0 = E_0 + U_{\mathrm{pol}}^{\mathrm{ref}}$ is the reference free energy.

4.2 SOURCE TERMS IN THE CLASSICAL ENERGY FUNCTIONAL

Let us take a closer look at the source term in the classical energy functional. It is important to single out which terms contribute in the various expectation values where the similarity-transformed sources Eq. (4.4) are involved. This analysis is carried out in detail in Appendix A.2 and we report here the final results for the coupled cluster with single substitutions (CCS), CCSD and CCSDT models.

For the CCS model ($\mathscr{M} = 1$) one has:

$$
\begin{aligned}
\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCS}} &= \langle \mathrm{HF}|[\mathrm{s}, T_1]|\mathrm{HF}\rangle + \langle \bar{t}_1|\check{\mathrm{s}}|\mathrm{HF}\rangle \\
&= \langle \mathrm{HF}|[\mathrm{s}, T_1]|\mathrm{HF}\rangle + \langle \bar{t}_1|\mathrm{s}|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_1|[\mathrm{s}, T_1]|\mathrm{HF}\rangle + \frac{1}{2}\langle \bar{t}_1|[[\mathrm{s}, T_1], T_1]|\mathrm{HF}\rangle
\end{aligned}
\tag{4.12}
$$

while for the CCSD model ($\mathscr{M} = 2$):

$$
\begin{aligned}
\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCSD}} = \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCS}} &+ \langle \bar{t}_1|[\mathrm{s}, T_2]|\mathrm{HF}\rangle \\
+ \langle \bar{t}_2|[\mathrm{s}, T_2]|\mathrm{HF}\rangle &+ \langle \bar{t}_2|[[\mathrm{s}, T_1], T_2]|\mathrm{HF}\rangle
\end{aligned}
\tag{4.13}
$$

Eventually, within the CCSDT model ($\mathscr{M} = 3$) four more terms are added:

$$
\begin{aligned}
\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCSDT}} &= \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCSD}} + \langle \bar{t}_2|[\mathrm{s}, T_3]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_3|[\mathrm{s}, T_3]|\mathrm{HF}\rangle \\
&+ \frac{1}{2}\langle \bar{t}_3|[[\mathrm{s}, T_2], T_2]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_3|[[\mathrm{s}, T_1], T_3]|\mathrm{HF}\rangle
\end{aligned}
\tag{4.14}
$$

4.3 GOVERNING EQUATIONS AND THEIR APPROXIMATIONS

► Differentiation of the effective Lagrangian in Eq. (4.8) with respect to the variational parameters t_{μ_i}, $\bar{t}_{\mu_i}$ and p yields the PTED-CC equations:

$$
\Omega_{\mu_q}(t,\bar{t},\mathrm{p}) = \epsilon_{\mu_q} t_{\mu_q} + \langle \mu_q|\overline{\Phi}|\mathrm{HF}\rangle + {}^{t}\mathrm{p}\,\langle \mu_q|\bar{\mathrm{s}}|\mathrm{HF}\rangle = 0 \tag{4.15a}
$$

$$
\begin{aligned}
\bar{\Omega}_{\mu_q}(t,\bar{t},\mathrm{p}) = \epsilon_{\mu_q} \bar{t}_{\mu_q} + \langle \mathrm{HF}|[\overline{\Phi}, \tau_{\mu_q}]|\mathrm{HF}\rangle &+ \sum_{u=1}^{\mathscr{M}} \langle \bar{t}_u|[\overline{\Phi}, \tau_{\mu_q}]|\mathrm{HF}\rangle \\
+ {}^{t}\mathrm{p}\,\langle \mathrm{HF}|[\mathrm{s}, \tau_{\mu_q}]|\mathrm{HF}\rangle\, \delta_{\mu_q\mu_1} &+ {}^{t}\mathrm{p} \sum_{u=1}^{\mathscr{M}} \langle \bar{t}_u|[\mathrm{s}, \tau_{\mu_q}]|\mathrm{HF}\rangle \\
+ {}^{t}\mathrm{p} \sum_{u=1}^{\mathscr{M}} \langle \bar{t}_u|[[\mathrm{s}, T], \tau_{\mu_q}]|\mathrm{HF}\rangle &= 0
\end{aligned}
\tag{4.15b}
$$

$$
\Omega_{\mathrm{p}}(t,\bar{t},\mathrm{p}) = \mathbb{V}\mathrm{p} + \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathscr{M}} = 0 \tag{4.15c}
$$

A coupling of the amplitudes and multipliers equations is introduced by the presence of the $\mathrm{s_N}(t,\bar{t})_{\mathscr{M}}$ expectation value in the polarization equation. This requires a proper macroiteration/microiteration self-consistency scheme for its implementation.[207,208] As a consequence, a single-point PTED-CC will suffer from a 2× prefactor in its computational cost with respect to an *in vacuo* CC calculation.

It is thus convenient to devise approximations that are able to simplify the Lagrangian and the governing equations by breaking or weakening the coupling. While Eq. (4.15c) is *directly* coupled to the multipliers equation, since the source terms directly depends on amplitudes and multipliers, it is only *indirectly* coupled to the amplitudes equation, where only the polarization enters. Moreover, the leading terms in the correlated source operator expectation value prominently involve the singles cluster operator and the singles multiplier state. Three approximations have currently been proposed: perturbation-to-the-energy with singles substitutions (PTES), perturbation-to-the-energy with approximate singles substitutions (PTE(S)) and perturbation-to-the-energy (PTE).

PTES Scheme

The first approximate scheme* truncates the source term to its CCS expectation value, yielding the effective Lagrangian:[209,226]

$$
\begin{aligned}
{}^{\mathrm{PTES}}\mathscr{L}_{\mathrm{eff}}(t,\bar{t},\mathrm{p})_{\mathscr{M}} = {}&{}^{\mathrm{PTE}}\mathscr{L}_{\mathrm{eff}}(t,\bar{t})_{\mathscr{M}} \\
&+ \frac{1}{2}{}^{t}\mathrm{p}\mathbb{V}\mathrm{p} + {}^{t}\mathrm{p}\mathrm{s_N}(t,\bar{t})_{\mathrm{CCS}}
\end{aligned}
\tag{4.16}
$$

[*] Thanks to prof. Marco Caricato (University of Kansas) for clarifying some details of his original derivation of the PTES scheme.

and the corresponding governing equations:

$$\begin{aligned} \Omega_{\mu_q}(t,\bar{t},\mathrm{p}) &= \epsilon_{\mu_q} t_{\mu_q} + \langle \mu_q | \bar{\Phi} | \mathrm{HF} \rangle \\ &\quad + {}^t\mathrm{p}\, \langle \mu_q | \check{\mathrm{s}} | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} = 0 \end{aligned} \tag{4.17a}$$

$$\begin{aligned} \bar{\Omega}_{\mu_q}(t,\bar{t},\mathrm{p}) &= \epsilon_{\mu_q} \bar{t}_{\mu_q} + \langle \mathrm{HF} | [\bar{\Phi}, \tau_{\mu_q}] | \mathrm{HF} \rangle + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}_u | [\bar{\Phi}, \tau_{\mu_q}] | \mathrm{HF} \rangle \\ &\quad + {}^t\mathrm{p}\, \langle \mathrm{HF} | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} + {}^t\mathrm{p}\, \langle \bar{t}_1 | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} \\ &\quad + {}^t\mathrm{p}\, \langle \bar{t}_1 | [[\mathrm{s}, T_1], \tau_{\mu_q}] | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} = 0 \end{aligned} \tag{4.17b}$$

$$\Omega_{\mathrm{p}}(t,\bar{t},\mathrm{p}) = \mathbb{V}\mathrm{p} + \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCS}} = 0 \tag{4.17c}$$

These equations are, however, still coupled due to the presence of the multipliers in the CCS source term in the polarization equation. To break the coupling, we split the system of equations (4.17) into *two* systems of equations, one for the amplitudes:

$$\begin{aligned} {}^{\mathrm{PTES}}\Omega_{\mu_q}(t,\bar{t},\mathrm{p}) &= \epsilon_{\mu_q} t_{\mu_q} + \langle \mu_q | \bar{\Phi} | \mathrm{HF} \rangle \\ &\quad + {}^t\mathrm{p}\, \langle \mu_q | \check{\mathrm{s}} | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} = 0 \end{aligned} \tag{4.18a}$$

$${}^{\mathrm{PTES}}\Omega_{\mathrm{p}}(t,\mathrm{p}) = \mathbb{V}\mathrm{p} + \langle \mathrm{HF} | \check{\mathrm{s}}_{\mathrm{N}} | \mathrm{HF} \rangle = 0 \tag{4.18b}$$

where we further approximate the source term $\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCS}}$ with its multiplier-independent part:

$$\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCS}} \simeq \langle \mathrm{HF} | [\mathrm{s}, T_1] | \mathrm{HF} \rangle = \langle \mathrm{HF} | \check{\mathrm{s}}_{\mathrm{N}} | \mathrm{HF} \rangle\,, \tag{4.19}$$

and one for the multipliers:

$$\begin{aligned} {}^{\mathrm{PTES}}\bar{\Omega}_{\mu_q}(t,\bar{t},\mathrm{p}) &= \epsilon_{\mu_q} \bar{t}_{\mu_q} + \langle \mathrm{HF} | [\bar{\Phi}, \tau_{\mu_q}] | \mathrm{HF} \rangle + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}_u | [\bar{\Phi}, \tau_{\mu_q}] | \mathrm{HF} \rangle \\ &\quad + {}^t\mathrm{p}\, \langle \mathrm{HF} | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} + {}^t\mathrm{p}\, \langle \bar{t}_1 | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} \\ &\quad + {}^t\mathrm{p}\, \langle \bar{t}_1 | [[\mathrm{s}, T_1], \tau_{\mu_q}] | \mathrm{HF} \rangle\, \delta_{\mu_q \mu_1} = 0 \end{aligned} \tag{4.20a}$$

$${}^{\mathrm{PTES}}\Omega_{\mathrm{p}}(t,\bar{t},\mathrm{p}) = \mathbb{V}\mathrm{p} + \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CCS}} = 0 \tag{4.20b}$$

where no truncation for the source term is introduced.

BOTH THE AMPLITUDES AND MULTIPLIERS EQUATIONS are formally identical to the PTED equations (4.15) but are coupled to approximate polarization equations. For the amplitudes equation (4.18a), one computes the polarization from a modified CCS expectation value of the source term. This adds a negligible $O(N^5)$ term to the iterative solution of the equations. The amplitudes equations are instead coupled to the polarization obtained using the full CCS expectation value of the source term. This adds another $O(N^5)$ step to the iterative procedure, which is, overall, negligible. Let us notice that this scheme is not consistent with electrostatics, as the amplitudes and multipliers are optimized in the presence of two different polarizations.

PTE(S) Scheme

The PTES approximation can be brought one step further, by truncating the CCS expectation value to its multiplier-independent term already in the effective Lagrangian. The coupling between the amplitudes and multipliers is broken, while still improving upon the reference reaction field with correlated contributions.[209] The effective Lagrangian would then read as:

$$\begin{aligned} {}^{\mathrm{PTE(S)}}\mathscr{L}_{\mathrm{eff}}(t,\bar{t},\mathrm{p})_{\mathscr{M}} &= {}^{\mathrm{PTE}}\mathscr{L}_{\mathrm{eff}}(t,\bar{t})_{\mathscr{M}} \\ &\quad + \frac{1}{2}{}^{t}\mathrm{p}\mathbb{V}\mathrm{p} + {}^{t}\mathrm{p}\,\langle\mathrm{HF}|\check{\mathrm{s}}_{\mathrm{N}}|\mathrm{HF}\rangle \end{aligned} \tag{4.21}$$

which uncouples all equations:

$$ {}^{\mathrm{PTE(S)}}\Omega_{\mu_q}(t,\bar{t}) = \epsilon_{\mu_q} t_{\mu_q} + \langle\mu_q|\overline{\Phi}|\mathrm{HF}\rangle = 0 \tag{4.22a}$$

$$\begin{aligned} {}^{\mathrm{PTE(S)}}\bar{\Omega}_{\mu_q}(t,\bar{t},\mathrm{p}) &= \epsilon_{\mu_q}\bar{t}_{\mu_q} + \langle\mathrm{HF}|[\overline{\Phi},\tau_{\mu_q}]|\mathrm{HF}\rangle \\ &\quad + \sum_{u=1}^{\mathscr{M}} \langle\bar{t}_u|[\overline{\Phi},\tau_{\mu_q}]|\mathrm{HF}\rangle \\ &\quad + {}^{t}\mathrm{p}\,\langle\mathrm{HF}|[\mathrm{s},\tau_{\mu_q}]|\mathrm{HF}\rangle\,\delta_{\mu_q\mu_1} = 0 \end{aligned} \tag{4.22b}$$

$$ {}^{\mathrm{PTE(S)}}\Omega_{\mathrm{p}}(t,\bar{t},\mathrm{p}) = \mathbb{V}\mathrm{p} + \langle\mathrm{HF}|\check{\mathrm{s}}_{\mathrm{N}}|\mathrm{HF}\rangle = 0 \tag{4.22c}$$

The amplitude equations are formally equivalent to those derived in the PTE scheme, *vide infra*. The equations for the multipliers are also formally equivalent to the PTE equations, apart from the equation determining the singles multipliers which features an additional term involving the polarization: ${}^{t}\mathrm{p}\,\langle \mathrm{HF}|[\mathrm{s}, \tau_{\mu_q}]|\mathrm{HF}\rangle\,\delta_{\mu_q\mu_1}$. This term is not, however, coupled to the other equations given that p is fixed once the singles amplitudes have been determined.

Practical implementation of the PTE(S) scheme will solve the PTE-like amplitude equation, form the source term $\langle \mathrm{HF}|\check{\mathrm{s}}_{\mathrm{N}}|\mathrm{HF}\rangle$, solve for the polarization degrees of freedom and calculate the polarization energy as a correction to the CC energy. Only when a first-order molecular property, such as the molecular gradient, is needed, will the multipliers equations need to be solved. In other words, only the T_1-dependent part of the CC density is used to define the classical sources.

PTE Scheme

Complete neglect of the polarization functional leads to the most drastic approximation to the full quantum/classical polarizable effective Lagrangian, the PTE scheme. This is equivalent to differentiating the polarization-independent PTE effective Lagrangian:

$$^{\mathrm{PTE}}\Omega_{\mu_q}(t, \bar{t}, \mathrm{p}) = \epsilon_{\mu_q} t_{\mu_q} + \langle \mu_q|\overline{\Phi}|\mathrm{HF}\rangle = 0 \tag{4.23a}$$

$$^{\mathrm{PTE}}\bar{\Omega}_{\mu_q}(t, \bar{t}, \mathrm{p}) = \epsilon_{\mu_q} \bar{t}_{\mu_q} + \langle \mathrm{HF}|[\overline{\Phi}, \tau_{\mu_q}]|\mathrm{HF}\rangle + \sum_{u=1}^{\mathscr{M}} \langle \bar{t}_u|[\overline{\Phi}, \tau_{\mu_q}]|\mathrm{HF}\rangle = 0 \tag{4.23b}$$

The PTE scheme naturally preserves the scaling of the underlying CC method, since no coupling between the CC amplitudes and multipliers equations is introduced. The scheme only requires access to a reference state optimized in the presence of the classical medium and is thus readily implemented. The PTE model offers an efficient approximation to the full PTED model with a computational cost comparable to that of *in vacuo* CC theory.[210,227,228]

However, the polarization included in the correlation treatment is the same as for the reference determinant, an approximation which appears questionable from the point of view of classical electrostatics.

There is, in fact, no relaxation of the reference reaction field due to the correlated description of the electronic density.

4.4 MBPT FOR QUANTUM/CLASSICAL POLARIZABLE HAMILTONIANS

We will now develop a perturbative many-body expansion of the effective PTED-CC Lagrangian. The use of a CC ansatz for the wave function ensures term-by-term size-extensivity of the energy at all orders.[53] The fluctuation potential $\boldsymbol{\Phi}$ is assumed as the perturbation, hence it will be considered of order 1: $\boldsymbol{\Phi} = O(1)$. We still assume a closed-shell HF reference function and perturbation orders will be counted accordingly. A superscript index in square brackets - $[i]$ - will denote an i-th order contribution. We further assume that real wave functions are used.

The structure of the stationarity conditions, Eqs. (4.15a) and (4.15b), already shows that $t_{\mu_u}^{[0]} = 0,\ \forall u$ and $\bar{t}_{\mu_u}^{[0]} = 0,\ \forall u$. Thus cluster operators can be of order 1 and higher. We introduce the following notation for the i-th order cluster operators and multipliers states:

$$T_u^{[i]} = \sum_{\mu_u} t_{\mu_u}^{[i]} \tau_{\mu_u}, \quad \langle \bar{t}_u^{[i]} | = \sum_{\mu_u} \bar{t}_{\mu_u}^{[i]} \langle \mu_u | \tag{4.24}$$

The PTED-CC equations are expanded in orders of the perturbation and terms are collected order by order. The use of an effective, variational Lagrangian implies the validity of the $2n+1$ rule for the amplitudes t_{μ_u} and polarization p and of the $2n+2$ rule for the multipliers $\bar{t}_{\mu_u}$. We can thus derive energy corrections up to fifth order by means of the amplitudes and polarization up to and including second order terms and the multipliers up to and including second order.

The polarization equation couples to the multipliers and amplitudes equations *via* the source term. Its perturbative expansion will be given as:

$$\mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathscr{M}} = \mathrm{s}_{\mathrm{N}}^{[0]} + \mathrm{s}_{\mathrm{N}}^{[1]} + \mathrm{s}_{\mathrm{N}}^{[2]} + \dots \tag{4.25}$$

and correspondingly for the polarization:

$$\mathbb{V}\mathrm{p}^{[i]} + \mathrm{s}_{\mathrm{N}}^{[i]} = 0 \tag{4.26}$$

The source operator s will be considered as *zeroth-order* in the perturbation. The order of the contributions to $\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathscr{M}}$ will be solely determined by the amplitudes and multipliers. From the structure of (4.15c), it is already clear that $\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathscr{M}}$ is at least first order in the fluctuation potential:

$$\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathscr{M}} = \mathrm{s}_{\mathrm{N}}^{[1]} + \mathrm{s}_{\mathrm{N}}^{[2]} + \ldots \tag{4.27}$$

which also implies:

$$\mathbb{V}\mathrm{p}^{[0]} + \mathrm{s}_{\mathrm{N}}^{[0]} = 0 \Rightarrow \mathrm{p}^{[0]} = 0 \tag{4.28}$$

4.4.1 *First order equations*

AMPLITUDES

$$\Omega_{\mu_q}^{[1]} = \epsilon_{\mu_q} t_{\mu_q}^{[1]} + \langle \mu_q | \Phi | \mathrm{HF} \rangle + {}^{t}\mathrm{p}^{[1]} \langle \mu_q | \mathrm{s} | \mathrm{HF} \rangle \, \delta_{\mu_q \mu_1} = 0 \tag{4.29}$$

Explicitly considering the singles, doubles and triples excitation manifolds:

$$\Omega_{\mu_1}^{[1]} = \epsilon_{\mu_1} t_{\mu_1}^{[1]} + {}^{t}\mathrm{p}^{[1]} \langle \mu_1 | \mathrm{s} | \mathrm{HF} \rangle = 0 \tag{4.30a}$$

$$\Omega_{\mu_2}^{[1]} = \epsilon_{\mu_2} t_{\mu_2}^{[1]} + \langle \mu_2 | \Phi | \mathrm{HF} \rangle = 0 \tag{4.30b}$$

$$\Omega_{\mu_3}^{[1]} = \epsilon_{\mu_3} t_{\mu_3}^{[1]} = 0 \tag{4.30c}$$

Having chosen a closed-shell HF as reference, the term $\langle \mu_1 | \Phi | \mathrm{HF} \rangle$ is zero in the first-order singles equation. However, due to the quantum/classical coupling, there will still be nonzero first-order singles amplitudes.

MULTIPLIERS

$$\begin{aligned}\bar{\Omega}_{\mu_q}^{[1]} = \epsilon_{\mu_q} \bar{t}_{\mu_q}^{[1]} &+ \langle \mathrm{HF} | [\Phi, \tau_{\mu_q}] | \mathrm{HF} \rangle \\ &+ {}^{t}\mathrm{p}^{[1]} \langle \mathrm{HF} | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle \, \delta_{\mu_q \mu_1} = 0\end{aligned}$$

and expanding the commutators:

$$\bar{\Omega}_{\mu_q}^{[1]} = \epsilon_{\mu_q} \bar{t}_{\mu_q}^{[1]} + \langle \mathrm{HF} | \Phi | \mu_q \rangle + {}^{t}\mathrm{p}^{[1]} \langle \mathrm{HF} | \mathrm{s} | \mu_q \rangle \, \delta_{\mu_q \mu_1} = 0 \tag{4.31}$$

This clearly shows that Eq. (4.29) and Eq. (4.31) are complex conjugates. Under the assumption of real wave functions we can also conclude that:

$$t_{\mu_u}^{[1]} = \bar{t}_{\mu_u}^{[1]}, \ \forall u \tag{4.32}$$

Thus, as for the amplitudes, despite the closed-shell HF reference, the singles multipliers will already appear in first order, due to the quantum/classical coupling. Moreover, as is the case *in vacuo*, there are neither triples amplitudes nor multipliers to first order: $t_{\mu_3}^{[1]} = \bar{t}_{\mu_3}^{[1]} = 0$.

POLARIZATION

$$\mathbb{V}\mathrm{p}^{[1]} + \langle \mathrm{HF}|[\mathrm{s}, T_1^{[1]}]|\mathrm{HF}\rangle + \langle \bar{t}_1^{[1]}|\mathrm{s}|\mathrm{HF}\rangle = 0 \tag{4.33}$$

Under the assumption of real wave functions, the equivalence of first order amplitudes and multipliers yields:

$$\langle \mathrm{HF}|[\mathrm{s}, T_1^{[1]}]|\mathrm{HF}\rangle = \langle \bar{t}_1^{[1]}|\mathrm{s}|\mathrm{HF}\rangle \tag{4.34}$$

so that the first order polarization equation becomes:

$$\mathbb{V}\mathrm{p}^{[1]} + 2\,\langle \mathrm{HF}|[\mathrm{s}, T_1^{[1]}]|\mathrm{HF}\rangle = 0 \tag{4.35}$$

4.4.2 *Second order equations*

AMPLITUDES

$$\begin{aligned}\Omega_{\mu_q}^{[2]} &= \epsilon_{\mu_q} t_{\mu_q}^{[2]} + \langle \mu_q|[\Phi, T^{[1]}]|\mathrm{HF}\rangle \\ &\quad + {}^t\mathrm{p}^{[2]}\,\langle \mu_q|\mathrm{s}|\mathrm{HF}\rangle\,\delta_{\mu_q\mu_1} \\ &\quad + {}^t\mathrm{p}^{[1]}\,\langle \mu_q|[\mathrm{s}, T^{[1]}]|\mathrm{HF}\rangle = 0\end{aligned} \tag{4.36}$$

As already noted elsewhere,[53,73] the second term in Eq. (4.36) can involve no higher than triple excitations. Moreover, the triples first appear to second order and are not *directly* affected by the quantum/classical coupling, as can be seen by explicitly considering the singles, doubles and triples excitation manifolds:

$$\begin{aligned} \Omega^{[2]}_{\mu_1} &= \epsilon_{\mu_1} t^{[2]}_{\mu_1} + \langle \mu_1 | [\boldsymbol{\Phi}, T^{[1]}] | \mathrm{HF} \rangle + {}^{t}\mathrm{p}^{[2]} \langle \mu_1 | \mathrm{s} | \mathrm{HF} \rangle \\ &\quad + {}^{t}\mathrm{p}^{[1]} \langle \mu_1 | [\mathrm{s}, T^{[1]}] | \mathrm{HF} \rangle = 0 \end{aligned} \tag{4.37a}$$

$$\begin{aligned} \Omega^{[2]}_{\mu_2} &= \epsilon_{\mu_2} t^{[2]}_{\mu_2} + \langle \mu_2 | [\boldsymbol{\Phi}, T^{[1]}] | \mathrm{HF} \rangle \\ &\quad + {}^{t}\mathrm{p}^{[1]} \langle \mu_2 | [\mathrm{s}, T^{[1]}_2] | \mathrm{HF} \rangle = 0 \end{aligned} \tag{4.37b}$$

$$\Omega^{[2]}_{\mu_3} = \epsilon_{\mu_3} t^{[2]}_{\mu_3} + \langle \mu_3 | [\boldsymbol{\Phi}, T^{[1]}_2] | \mathrm{HF} \rangle = 0 \tag{4.37c}$$

MULTIPLIERS

$$\begin{aligned} \bar{\Omega}^{[2]}_{\mu_q} &= \epsilon_{\mu_q} \bar{t}^{[2]}_{\mu_q} + \langle \mathrm{HF} | [[\boldsymbol{\Phi}, T^{[1]}], \tau_{\mu_q}] | \mathrm{HF} \rangle + \sum_{u=1}^{\mathscr{M}} \langle \bar{t}^{[1]}_u | [\boldsymbol{\Phi}, \tau_{\mu_q}] | \mathrm{HF} \rangle \\ &+ {}^{t}\mathrm{p}^{[2]} \langle \mathrm{HF} | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle \, \delta_{\mu_q \mu_1} \\ &+ {}^{t}\mathrm{p}^{[1]} \sum_{u=1}^{\mathscr{M}} \langle \bar{t}^{[1]}_u | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle = 0 \end{aligned}$$

Since first-order singles amplitudes are now nonzero, the double commutator term will contribute to the singles multipliers equation. This is markedly in contrast with the derivation *in vacuo*, see Section

1.4.[53,73] For the singles, doubles and triples manifolds the multipliers equations to second order are given as:

$$
\begin{aligned}
\bar{\Omega}^{[2]}_{\mu_1} = {} & \epsilon_{\mu_1}\bar{t}^{[2]}_{\mu_1} + \langle \mathrm{HF}|[[\boldsymbol{\Phi}, T^{[1]}_1], \tau_{\mu_1}]|\mathrm{HF}\rangle + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}^{[1]}_u|[\boldsymbol{\Phi}, \tau_{\mu_1}]|\mathrm{HF}\rangle \\
& + {}^{t}\mathrm{p}^{[2]} \langle \mathrm{HF}|[\mathrm{s}, \tau_{\mu_1}]|\mathrm{HF}\rangle \\
& + {}^{t}\mathrm{p}^{[1]} \langle \bar{t}^{[1]}_1|[\mathrm{s}, \tau_{\mu_1}]|\mathrm{HF}\rangle = 0 \qquad (4.38\mathrm{a})
\end{aligned}
$$

$$
\begin{aligned}
\bar{\Omega}^{[2]}_{\mu_2} = {} & \epsilon_{\mu_2}\bar{t}^{[2]}_{\mu_2} + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}^{[1]}_u|[\boldsymbol{\Phi}, \tau_{\mu_2}]|\mathrm{HF}\rangle \\
& + {}^{t}\mathrm{p}^{[1]} \sum_{u=1}^{\mathcal{M}} \langle \bar{t}^{[1]}_u|[\mathrm{s}, \tau_{\mu_2}]|\mathrm{HF}\rangle = 0 \qquad (4.38\mathrm{b})
\end{aligned}
$$

$$
\bar{\Omega}^{[2]}_{\mu_3} = \epsilon_{\mu_3}\bar{t}^{[2]}_{\mu_3} + \sum_{u=1}^{\mathcal{M}} \langle \bar{t}^{[1]}_u|[\boldsymbol{\Phi}, \tau_{\mu_3}]|\mathrm{HF}\rangle = 0 \qquad (4.38\mathrm{c})
$$

Koch et al. showed that, assuming real wave functions, the *in vacuo* second order amplitudes and multipliers equations are the complex conjugates of each other for the singles, doubles and triples manifolds.[53,54,73] This symmetry is a consequence of choosing a closed-shell HF determinant as reference function[54] and is *broken* by the quantum/classical coupling. As an example, consider the triples multipliers equation. *In vacuo* one has:

$$
\begin{aligned}
\epsilon_{\mu_3} t^{[2]}_{\mu_3} &= -\langle \mu_i|[\boldsymbol{\Phi}, T^{[1]}_2]|\mathrm{HF}\rangle \\
&= -\langle \bar{t}^{[1]}_2|[\boldsymbol{\Phi}, \tau_{\mu_3}]|\mathrm{HF}\rangle = \epsilon_{\mu_3}\bar{t}^{[2]}_{\mu_3},
\end{aligned}
\qquad (1.40 \text{ from Chapter } 1)
$$

whereas now the first-order singles multiplier state also contributes to the second-order triples multipliers.

POLARIZATION

$$
\begin{aligned}
\mathbb{V}\mathrm{p}^{[2]} + \langle \mathrm{HF}|[\mathrm{s}, T^{[2]}_1]|\mathrm{HF}\rangle + \langle \bar{t}^{[2]}_1|\mathrm{s}|\mathrm{HF}\rangle & \\
+ \langle \bar{t}^{[1]}_1|[\mathrm{s}, T^{[1]}]|\mathrm{HF}\rangle + \langle \bar{t}^{[1]}_2|[\mathrm{s}, T^{[1]}_2]|\mathrm{HF}\rangle = 0 &
\end{aligned}
\qquad (4.39)
$$

There are no explicit contributions from the triples and thus the CCSD polarization is correct through fourth order in the fluctuation potential.

4.4.3 *Free energies up to fifth order*

From the expansion of the effective Lagrangian we can obtain free energy corrections up to the desired order. Given the variational nature of the Lagrangian, only terms fulfilling the $2n+1$ and $2n+2$ rules will appear in the free energy corrections. To zeroth-order all variational parameters are zero. To first order we thus have:

$$G^{[1]} = \langle \mathrm{HF}|\varPhi|\mathrm{HF}\rangle \,. \tag{4.40}$$

The reference energy can thus be recovered as usual:

$$G_{\mathrm{HF}} = G^{[0]} + G^{[1]}, \tag{4.41}$$

where $G^{[0]}$ includes the quantum/classical coupling.

We introduce the following notation:

$$\mathrm{s}_{\mathrm{N}}^{[m]}(t^{[p]}, \bar{t}^{[q]}), \tag{4.42}$$

for a source term of m-th order formed by amplitudes up to and including p-th order and by multipliers up to and including q-th order. Red boxes will appear around quantum/classical coupling terms that involve the triples manifold.

► THE SECOND ORDER ENERGY CORRECTION WILL BE FORMED including first order amplitudes and polarization, while using zeroth order multipliers:

$$\begin{aligned}
G^{[2]} &= \langle \mathrm{HF}|[\varPhi, T^{[1]}]|\mathrm{HF}\rangle \\
&\quad + \frac{1}{2}{}^{t}\mathrm{p}^{[1]}\mathbb{V}\mathrm{p}^{[1]} + {}^{t}\mathrm{p}^{[1]}\mathrm{s}_{\mathrm{N}}^{[1]}(t^{[1]}, \bar{t}^{[0]}) \\
&= E^{[2]} + \frac{1}{2}{}^{t}\mathrm{p}^{[1]}\mathbb{V}\mathrm{p}^{[1]} + {}^{t}\mathrm{p}^{[1]}\,\langle \mathrm{HF}|[\mathrm{s}, T_1^{[1]}]|\mathrm{HF}\rangle \\
&= E^{[2]}
\end{aligned} \tag{4.43}$$

The polarization terms were eliminated by virtue of Eq. (4.35). Thus, at least formally, $G^{[2]}$ has the same expression as *in vacuo* and is consistent with *both* electrostatics and perturbation theory. We remark that this would not be the case if one had based the development of MBPT on the use of a nonlinear Hamiltonian.[224]

► THE THIRD ORDER ENERGY CORRECTION WILL BE FORMED including first order amplitudes, multipliers and polarization:

$$\begin{aligned} G^{[3]} &= \sum_{u=1}^{2} \langle \bar{t}_u^{[1]} | [\boldsymbol{\Phi}, T^{[1]}] | \mathrm{HF} \rangle + {}^t\mathrm{p}^{[1]} \mathrm{s}_\mathrm{N}^{[2]}(t^{[1]}, \bar{t}^{[1]}) \\ &= E^{[3]} + {}^t\mathrm{p}^{[1]} \langle \bar{t}_1^{[1]} | [\mathrm{s}, T^{[1]}] | \mathrm{HF} \rangle \\ &+ {}^t\mathrm{p}^{[1]} \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_2^{[1]}] | \mathrm{HF} \rangle \end{aligned} \tag{4.44}$$

► THE FOURTH ORDER ENERGY CORRECTIONS WILL BE FORMED including second order amplitudes and polarization, while using first order multipliers:

$$\begin{aligned} G^{[4]} &= \sum_{u=1}^{2} \langle \bar{t}_u^{[1]} | [\boldsymbol{\Phi}, T^{[2]}] | \mathrm{HF} \rangle \\ &+ \sum_{u=1}^{2} \langle \bar{t}_u^{[1]} | \frac{1}{2} [[\boldsymbol{\Phi}, T^{[1]}], T^{[1]}] | \mathrm{HF} \rangle + \frac{1}{2} {}^t\mathrm{p}^{[2]} \mathbb{V} \mathrm{p}^{[2]} \\ &+ {}^t\mathrm{p}^{[2]} \mathrm{s}_\mathrm{N}^{[2]}(t^{[2]}, \bar{t}^{[1]}) + {}^t\mathrm{p}^{[1]} \mathrm{s}_\mathrm{N}^{[3]}(t^{[2]}, \bar{t}^{[1]}) \end{aligned} \tag{4.45}$$

The first two terms are recognized to be equal to $E^{[4]}$, so that:

$$\begin{aligned} G^{[4]} &= E^{[4]} + \frac{1}{2} {}^t\mathrm{p}^{[2]} \mathbb{V} \mathrm{p}^{[2]} + {}^t\mathrm{p}^{[2]} \langle \mathrm{HF} | [\mathrm{s}, T_1^{[2]}] | \mathrm{HF} \rangle \\ &+ {}^t\mathrm{p}^{[2]} \langle \bar{t}_1^{[1]} | [\mathrm{s}, T^{[1]}] | \mathrm{HF} \rangle + {}^t\mathrm{p}^{[2]} \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_2^{[1]}] | \mathrm{HF} \rangle \\ &+ {}^t\mathrm{p}^{[1]} \langle \bar{t}_1^{[1]} | [\mathrm{s}, T_1^{[2]} + T_2^{[2]}] | \mathrm{HF} \rangle \\ &+ {}^t\mathrm{p}^{[1]} \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_2^{[2]} + T_3^{[2]}] | \mathrm{HF} \rangle \\ &+ {}^t\mathrm{p}^{[1]} \langle \bar{t}_1^{[1]} | \frac{1}{2} [[\mathrm{s}, T_1^{[1]}], T_1^{[1]}] | \mathrm{HF} \rangle \\ &+ {}^t\mathrm{p}^{[1]} \langle \bar{t}_2^{[1]} | [[\mathrm{s}, T_1^{[1]}], T_2^{[1]}] | \mathrm{HF} \rangle \end{aligned} \tag{4.46}$$

Employing Eq. (4.39), the terms involving the second order polarization can be simplified further:

$$
\begin{aligned}
G^{[4]} = E^{[4]} &+ \frac{1}{2}{}^{t}\mathrm{p}^{[2]}\,\langle \mathrm{HF}|[\mathrm{s}, T_1^{[2]}]|\mathrm{HF}\rangle \\
&+ \frac{1}{2}{}^{t}\mathrm{p}^{[2]}\left(\langle \bar{t}_1^{[1]}|[\mathrm{s}, T^{[1]}]|\mathrm{HF}\rangle + \langle \bar{t}_2^{[1]}|[\mathrm{s}, T_2^{[1]}]|\mathrm{HF}\rangle\right) \\
&+ \frac{1}{2}{}^{t}\mathrm{p}^{[2]}\left(\langle \bar{t}_1^{[1]}|[\mathrm{s}, T^{[1]}]|\mathrm{HF}\rangle + \langle \bar{t}_2^{[1]}|[\mathrm{s}, T_2^{[1]}]|\mathrm{HF}\rangle\right) \\
&+ {}^{t}\mathrm{p}^{[1]}\,\langle \bar{t}_1^{[1]}|[\mathrm{s}, T_1^{[2]} + T_2^{[2]}]|\mathrm{HF}\rangle \\
&+ {}^{t}\mathrm{p}^{[1]}\,\langle \bar{t}_2^{[1]}|[\mathrm{s}, T_2^{[2]} + T_3^{[2]}]|\mathrm{HF}\rangle \\
&+ {}^{t}\mathrm{p}^{[1]}\,\langle \bar{t}_1^{[1]}|\frac{1}{2}[[\mathrm{s}, T_1^{[1]}], T_1^{[1]}]|\mathrm{HF}\rangle \\
&+ {}^{t}\mathrm{p}^{[1]}\,\langle \bar{t}_2^{[1]}|[[\mathrm{s}, T_1^{[1]}], T_2^{[1]}]|\mathrm{HF}\rangle
\end{aligned}
\tag{4.47}
$$

Notice that the term $\frac{1}{2}{}^{t}\mathrm{p}^{[2]}\,\langle \bar{t}_1^{[2]}|\mathrm{s}|\mathrm{HF}\rangle$ has not been included, since it would violate the $2n+2$ rule for the multipliers. Moreover, there is only one term that involves both the triples amplitudes and the polarization.

► EVENTUALLY, THE FIFTH ORDER ENERGY CORRECTION IS FORMED including second order amplitudes, multipliers and polarization:

$$
\begin{aligned}
G^{[5]} = &\ \langle \mathrm{HF}|\frac{1}{2}[[\Phi, T^{[2]}], T^{[2]}]|\mathrm{HF}\rangle \\
&+ \sum_{u=1}^{2} \langle \bar{t}_u^{[1]}|[[\Phi, T^{[2]}], T^{[1]}]|\mathrm{HF}\rangle \\
&+ \sum_{u=1}^{3} \langle \bar{t}_u^{[2]}|[\Phi, T^{[2]}]|\mathrm{HF}\rangle \\
&+ \sum_{u=1}^{3} \langle \bar{t}_u^{[2]}|\frac{1}{2}[[\Phi, T^{[1]}], T^{[1]}]|\mathrm{HF}\rangle \\
&+ {}^{t}\mathrm{p}^{[2]}\mathrm{s}_{\mathrm{N}}^{[3]}(t^{[2]}, \bar{t}^{[2]}) + {}^{t}\mathrm{p}^{[1]}\mathrm{s}_{\mathrm{N}}^{[4]}(t^{[2]}, \bar{t}^{[2]})
\end{aligned}
\tag{4.48}
$$

This can be rewritten in terms of $E^{[5]}$ and a number of polarization terms:

$$
\begin{aligned}
G^{[5]} = E^{[5]} + {}^{t}\mathrm{p}^{[2]}\Bigg(& \sum_{u=1}^{2} \langle \bar{t}_u^{[1]} | [\mathrm{s}, T^{[2]}] | \mathrm{HF} \rangle \\
& + \sum_{u=1}^{2} \langle \bar{t}_u^{[1]} | \frac{1}{2} [[\mathrm{s}, T^{[1]}], T^{[1]}] | \mathrm{HF} \rangle \\
& + \sum_{u=1}^{3} \langle \bar{t}_u^{[2]} | [\mathrm{s}, T^{[1]}] | \mathrm{HF} \rangle \Bigg) \\
& + {}^{t}\mathrm{p}^{[1]}\Bigg(\sum_{u=1}^{3} \langle \bar{t}_u^{[2]} [\mathrm{s}, T^{[2]}] | \mathrm{HF} \rangle \\
& + \sum_{u=1}^{3} \langle \bar{t}_u^{[2]} \frac{1}{2} [[\mathrm{s}, T^{[1]}], T^{[1]}] | \mathrm{HF} \rangle \\
& + \sum_{u=1}^{2} \langle \bar{t}_u^{[1]} | [[\mathrm{s}, T^{[1]}], T^{[2]}] | \mathrm{HF} \rangle \Bigg)
\end{aligned}
\tag{4.49}
$$

Finally, consideration of the excitation ranks involved in the quantum/classical coupling terms yields

$$
\begin{aligned}
G^{[5]} = E^{[5]} + {}^{t}\mathrm{p}^{[2]} \Big(& \langle \bar{t}_1^{[1]} | [\mathrm{s}, T_1^{[2]} + T_2^{[2]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_2^{[2]} + T_3^{[2]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_1^{[2]} | [\mathrm{s}, T^{[1]}] | \mathrm{HF} \rangle + \langle \bar{t}_1^{[1]} | \frac{1}{2} [[\mathrm{s}, T_1^{[1]}], T_1^{[1]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_2^{[1]} | [[\mathrm{s}, T_1^{[1]}], T_2^{[1]}] | \mathrm{HF} \rangle \\
& + {}^{t}\mathrm{p}^{[1]} \Big(\langle \bar{t}_1^{[2]} | [\mathrm{s}, T_1^{[2]} + T_2^{[2]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_2^{[2]} | [\mathrm{s}, T_2^{[2]} + T_3^{[2]}] | \mathrm{HF} \rangle + \langle \bar{t}_3^{[2]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_1^{[2]} | \frac{1}{2} [[\mathrm{s}, T_1^{[1]}], T_1^{[1]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_2^{[2]} | [[\mathrm{s}, T_1^{[1]}], T_2^{[1]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_3^{[2]} | \frac{1}{2} [[\mathrm{s}, T_2^{[1]}], T_2^{[1]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_1^{[1]} | [[\mathrm{s}, T_1^{[1]}], T_1^{[2]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_2^{[1]} | [[\mathrm{s}, T_1^{[1]}], T_2^{[2]}] | \mathrm{HF} \rangle \\
& + \langle \bar{t}_2^{[1]} | [[\mathrm{s}, T_2^{[1]}], T_1^{[2]}] | \mathrm{HF} \rangle \Big)
\end{aligned}
\tag{4.50}
$$

Similarly to the exposition in Chapter 1, these expressions will form the basis for the development of approximations beyond CCSD including connected triples.

The PTED-CCSD scheme for the quantum/classical coupling only includes singles and doubles in its excitation manifold and is thus correct up to third order in perturbation theory. Already in fourth order connected triples make their appearance and any model going beyond third order must then take their effect into account. The fourth and fifth order contributions to the energy due to connected triples given in Eqs. (1.42a) and (1.42b) will be augmented by additional terms due to the nonzero first order singles and the quantum/classical polarizable coupling. To fourth order these are:

$$\begin{aligned} G_T^{[4]} = {} & \langle \bar{t}_1^{[1]} | [\boldsymbol{\Phi}, T_3^{[2]}] | \mathrm{HF} \rangle + \langle \bar{t}_2^{[1]} | [\boldsymbol{\Phi}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + {}^t\mathrm{p}^{[1]} \, \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle \,, \end{aligned} \tag{4.51}$$

while the fifth order contributions are:

$$\begin{aligned} G_T^{[5]} = {} & \langle \bar{t}_2^{[1]} | [[\boldsymbol{\Phi}, T_3^{[2]}], T_1^{[1]}] | \mathrm{HF} \rangle + \langle \bar{t}_1^{[2]} | [\boldsymbol{\Phi}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + \langle \bar{t}_2^{[2]} | [\boldsymbol{\Phi}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + \langle \bar{t}_3^{[2]} | [\boldsymbol{\Phi}, T_2^{[2]}] | \mathrm{HF} \rangle + \langle \bar{t}_3^{[2]} | [\boldsymbol{\Phi}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + \frac{1}{2} \langle \bar{t}_3^{[2]} | [[\boldsymbol{\Phi}, T_2^{[1]}], T_2^{[1]}] | \mathrm{HF} \rangle \\ & + \langle \bar{t}_3^{[2]} | [[\boldsymbol{\Phi}, T_1^{[1]}], T_2^{[1]}] | \mathrm{HF} \rangle \\ & + {}^t\mathrm{p}^{[2]} \, \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle + {}^t\mathrm{p}^{[1]} \, \langle \bar{t}_2^{[2]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + {}^t\mathrm{p}^{[1]} \, \langle \bar{t}_3^{[2]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + {}^t\mathrm{p}^{[1]} \, \langle \bar{t}_3^{[2]} | \frac{1}{2} [[\mathrm{s}, T_2^{[1]}], T_2^{[1]}] | \mathrm{HF} \rangle \end{aligned} \tag{4.52}$$

We have highlighted the vacuum-like terms that appear due to the nonzero first order singles amplitudes and multipliers in yellow.

4.4.4 *Approximations to PTED*

Perturbative expansions can also be developed starting from the approximations to PTED presented in Section 4.3. For the PTE scheme, the only change with respect to the *in vacuo* theory as presented in Section 1.4 is the use of the solvated Fock matrix.[210,224,225]

► IN THE PTE(S) SCHEME, the amplitudes equations are uncoupled from the multipliers and polarization equations. MBPT for this approximate model can be developed similarly to that in the PTE scheme. The first and second order parameters are determined by:

$$\epsilon_{\mu_2} t^{[1]}_{\mu_2} = -\langle \mu_2 | \boldsymbol{\Phi} | \mathrm{HF} \rangle = -\langle \mathrm{HF} | [\boldsymbol{\Phi}, \tau_{\mu_2}] | \mathrm{HF} \rangle = \epsilon_{\mu_2} \bar{t}^{[1]}_{\mu_2} \tag{4.53a}$$

$$\epsilon_{\mu_q} t^{[2]}_{\mu_q} = -\langle \mu_q | [\boldsymbol{\Phi}, T^{[1]}_2] | \mathrm{HF} \rangle \tag{4.53b}$$

$$\epsilon_{\mu_q} \bar{t}^{[2]}_{\mu_q} = -\langle \bar{t}^{[1]}_2 | [\boldsymbol{\Phi}, \tau_{\mu_q}] | \mathrm{HF} \rangle \tag{4.53c}$$

$$- {}^t\mathrm{p}^{[2]} \langle \mathrm{HF} | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle \, \delta_{\mu_q \mu_1} = 0 \tag{4.53d}$$

$$\mathbb{V}\mathrm{p}^{[2]} + \langle \mathrm{HF} | [\mathrm{s}, T^{[2]}_1] | \mathrm{HF} \rangle = 0 \tag{4.53e}$$

Notice that the first order singles amplitudes and multipliers are now zero, as is the first order polarization. The second order singles multipliers are coupled to the second order polarization. Notice however that $\mathrm{p}^{[2]}$ only depends on $T^{[2]}_1$ and can thus be computed on-the-fly, without iterating between Eqs. (4.53d) and (4.53e) Starting from Eqs. (1.41a)–(1.41e), the free energy corrections in the PTE(S) scheme are:

$$G^{[1]} = E^{[1]} \tag{4.54a}$$

$$G^{[2]} = E^{[2]} \tag{4.54b}$$

$$G^{[3]} = E^{[3]} \tag{4.54c}$$

$$G^{[4]} = E^{[4]} + \frac{1}{2} {}^t\mathrm{p}^{[2]} \langle \mathrm{HF} | [\mathrm{s}, T^{[2]}_1] | \mathrm{HF} \rangle \tag{4.54d}$$

$$G^{[5]} = E^{[5]} \tag{4.54e}$$

► In the PTES scheme, two different polarizations are introduced to achieve an approximate decoupling of the governing equations. MBPT can be developed by considering the Lagrangian (4.16) to form the energy corrections, Eq. (4.18) for the order analysis of the amplitudes, Eq. (4.20) for the order analysis of the multipliers. The order analysis of the polarization will be developed based on Eq.

(4.20b), *i. e.* the polarization coupled to the multipliers. To first order:

$$\epsilon_{\mu_2} t^{[1]}_{\mu_2} = -\langle \mu_2 | \Phi | \mathrm{HF} \rangle = -\langle \mathrm{HF} | [\Phi, \tau_{\mu_2}] | \mathrm{HF} \rangle = \epsilon_{\mu_2} \bar{t}^{[1]}_{\mu_2} \tag{4.55a}$$

$$\epsilon_{\mu_1} \bar{t}^{[1]}_{\mu_1} = -{}^{t}\mathrm{p}^{[1]} \langle \mathrm{HF} | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle \, \delta_{\mu_q \mu_1} \tag{4.55b}$$

$$\mathbb{V}\mathrm{p}^{[1]} + \langle \bar{t}^{[1]}_1 | \mathrm{s} | \mathrm{HF} \rangle = 0 \tag{4.55c}$$

while to second order:

$$\epsilon_{\mu_q} t^{[2]}_{\mu_q} = -\langle \mu_q | [\Phi, T^{[1]}_2] | \mathrm{HF} \rangle \tag{4.56a}$$

$$\epsilon_{\mu_q} \bar{t}^{[2]}_{\mu_q} = -\langle \bar{t}^{[1]}_2 | [\Phi, \tau_{\mu_q}] | \mathrm{HF} \rangle \tag{4.56b}$$

$$- {}^{t}\mathrm{p}^{[2]} \langle \mathrm{HF} | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle \, \delta_{\mu_q \mu_1}$$

$$- {}^{t}\mathrm{p}^{[1]} \langle \bar{t}^{[1]}_1 | [\mathrm{s}, \tau_{\mu_q}] | \mathrm{HF} \rangle = 0 \tag{4.56c}$$

$$\mathbb{V}\mathrm{p}^{[2]} + \langle \mathrm{HF} | [\mathrm{s}, T^{[2]}_1] | \mathrm{HF} \rangle + \langle \bar{t}^{[2]}_1 | \mathrm{s} | \mathrm{HF} \rangle = 0 \tag{4.56d}$$

We can now develop the free energy corrections in the PTES scheme based on Eqs. (1.41a)–(1.41e)

$$G^{[1]} = E^{[1]} \tag{4.57a}$$

$$G^{[2]} = E^{[2]} \tag{4.57b}$$

$$G^{[3]} = E^{[3]} \tag{4.57c}$$

$$G^{[4]} = E^{[4]} + \frac{1}{2} {}^{t}\mathrm{p}^{[2]} \langle \mathrm{HF} | [\mathrm{s}, T^{[2]}_1] | \mathrm{HF} \rangle \tag{4.57d}$$

$$G^{[5]} = E^{[5]} + {}^{t}\mathrm{p}^{[2]} \langle \bar{t}^{[1]}_1 | [\mathrm{s}, T^{[2]}_1] | \mathrm{HF} \rangle \tag{4.57e}$$

4.5 APPROXIMATE COUPLED CLUSTER METHODS WITH QUANTUM/CLASSICAL POLARIZABLE HAMILTONIANS

In complete analogy to the discussion in Section 1.5, we can derive iterative and noniterative schemes for the approximate inclusion of higher order excitations in the CC hierarchy. Starting from the CC2

Lagrangian, Eq. (1.46), we can write down the corresponding PTED effective Lagrangian:[222,223]

$$
\begin{aligned}
\mathscr{L}_{\mathrm{eff}}(t,\bar{t},\mathrm{p})_{\mathrm{CC2}} = E_0 &+ \sum_{u=1}^{2} \bar{t}_{\mu_u}\epsilon_{\mu_u}t_{\mu_u} \\
&+ \langle \mathrm{HF}|\check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, Q_2]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_1|\check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, Q_2]|\mathrm{HF}\rangle + \langle \bar{t}_2|\check{\boldsymbol{\Phi}}|\mathrm{HF}\rangle \\
&+ \frac{1}{2}{}^{t}\mathrm{p}\mathbb{V}\mathrm{p} + {}^{t}\mathrm{p}\mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CC2}}
\end{aligned}
\tag{4.58}
$$

where the source term is formed according to Eq. (1.48) The amplitudes equations now become:

$$
\begin{aligned}
\epsilon_{\mu_1}t_{\mu_1} &+ \langle \mu_1|\check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, Q_2]|\mathrm{HF}\rangle & (4.59a) \\
&+ {}^{t}\mathrm{p}\,\langle \mu_1|\check{\mathrm{s}} + [\check{\mathrm{s}}, Q_2]|\mathrm{HF}\rangle = 0 & (4.59b) \\
\epsilon_{\mu_2}t_{\mu_2} &+ \langle \mu_2|\check{\boldsymbol{\Phi}}|\mathrm{HF}\rangle + {}^{t}\mathrm{p}\,\langle \mu_2|[\check{\mathrm{s}}, Q_2]|\mathrm{HF}\rangle = 0 & (4.59c)
\end{aligned}
$$

while for the multipliers one has:

$$
\begin{aligned}
\epsilon_{\mu_1}\bar{t}_{\mu_1} &+ \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], Q_2]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + {}^{t}\mathrm{p}\,\langle \mathrm{HF}|[\check{\mathrm{s}}_{\mathrm{N}}, \tau_{\mu_1}]|\mathrm{HF}\rangle \\
&+ {}^{t}\mathrm{p}\,\langle \bar{t}_1|[\check{\mathrm{s}}, \tau_{\mu_1}]|\mathrm{HF}\rangle \\
&+ {}^{t}\mathrm{p}\,\langle \bar{t}_2|[[\check{\mathrm{s}}, \tau_{\mu_1}], Q_2]|\mathrm{HF}\rangle = 0 & (4.60a) \\
\epsilon_{\mu_2}\bar{t}_{\mu_2} &+ \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle \\
&+ {}^{t}\mathrm{p}\,\langle \bar{t}_1|[\check{\mathrm{s}}, \tau_{\mu_2}]|\mathrm{HF}\rangle + {}^{t}\mathrm{p}\,\langle \bar{t}_2|[\check{\mathrm{s}}, \tau_{\mu_2}]|\mathrm{HF}\rangle = 0 & (4.60b)
\end{aligned}
$$

Finally, the polarization is obtained by solving:

$$
\mathbb{V}\mathrm{p} + \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\mathrm{CC2}} = 0 \tag{4.61}
$$

The PTED-CC3 model is obtained similarly. The source term is formed according to Eq. (1.53). Thus, adding the polarization functional to the Lagrangian (1.51), we obtain the effective Lagrangian:

$$\begin{aligned}\mathscr{L}_{\text{eff}}(t,\bar{t},\mathrm{p})_{\text{CC3}} = E_0 &+ \sum_{u=1}^{3} \bar{t}_{\mu_u} \epsilon_{\mu_u} t_{\mu_u} \\ &+ \langle \mathrm{HF} | \check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, T_2] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_1 | \check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, T_2] + [\check{\boldsymbol{\Phi}}, Q_3] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_2 | \check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, T_2] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_2 | \frac{1}{2} [[\check{\boldsymbol{\Phi}}, T_2], T_2] + [\check{\boldsymbol{\Phi}}, Q_3] | \mathrm{HF} \rangle \\ &+ \langle \bar{t}_3 | [\check{\boldsymbol{\Phi}}, T_2] | \mathrm{HF} \rangle \\ &+ \frac{1}{2} {}^{t}\mathrm{p} \mathbb{V} \mathrm{p} + {}^{t}\mathrm{p} \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\text{CC3}}\end{aligned} \tag{4.62}$$

The polarization equation is straightforwardly:

$$\mathbb{V}\mathrm{p} + \mathrm{s}_{\mathrm{N}}(t,\bar{t})_{\text{CC3}} = 0 \tag{4.63}$$

The amplitudes are determined by:

$$\begin{aligned}\epsilon_{\mu_1} t_{\mu_1} &+ \langle \mu_1 | \check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, T_2] + [\check{\boldsymbol{\Phi}}, Q_3] | \mathrm{HF} \rangle \\ &+ {}^{t}\mathrm{p} \, \langle \mu_1 | \check{\mathrm{s}} + [\check{\mathrm{s}}, T_2] | \mathrm{HF} \rangle = 0\end{aligned} \tag{4.64a}$$

$$\begin{aligned}\epsilon_{\mu_2} t_{\mu_2} &+ \langle \mu_2 | \check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, T_2] + \frac{1}{2} [[\check{\boldsymbol{\Phi}}, T_2], T_2] + [\check{\boldsymbol{\Phi}}, Q_3] | \mathrm{HF} \rangle \\ &+ {}^{t}\mathrm{p} \, \langle \mu_2 | [\check{\mathrm{s}}, T_2] + [\check{\mathrm{s}}, Q_3] | \mathrm{HF} \rangle = 0\end{aligned} \tag{4.64b}$$

$$\epsilon_{\mu_3} t_{\mu_3} + \langle \mu_3 | [\check{\boldsymbol{\Phi}}, T_2] | \mathrm{HF} \rangle \tag{4.64c}$$

$$+ {}^{t}\mathrm{p} \, \langle \mu_3 | [\check{\mathrm{s}}, Q_3] + \frac{1}{2} [[\check{\mathrm{s}}, T_2], T_2] | \mathrm{HF} \rangle = 0 \tag{4.64d}$$

and finally the multipliers obey:

$$
\begin{aligned}
\epsilon_{\mu_1}\bar{t}_{\mu_1} &+ \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], Q_3]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_3|[[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2]|\mathrm{HF}\rangle + {}^t\mathrm{p}\,\langle \mathrm{HF}|[\check{\mathrm{s}}_{\mathrm{N}}, \tau_{\mu_1}]|\mathrm{HF}\rangle \\
&+ {}^t\mathrm{p}\,\langle \bar{t}_1|[\check{\mathrm{s}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + {}^t\mathrm{p}\,\langle \bar{t}_2|[[\check{\mathrm{s}}, \tau_{\mu_1}], Q_2]|\mathrm{HF}\rangle \\
&+ {}^t\mathrm{p}\,\langle \bar{t}_3|[[\check{\mathrm{s}}, \tau_{\mu_1}], Q_3]|\mathrm{HF}\rangle = 0 \qquad (4.65\mathrm{a}) \\
\epsilon_{\mu_2}\bar{t}_{\mu_2} &+ \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle \\
&+ \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}], T_2]|\mathrm{HF}\rangle + \langle \bar{t}_3|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle \\
&+ {}^t\mathrm{p}\,\langle \bar{t}_1|[\check{\mathrm{s}}, \tau_{\mu_2}]|\mathrm{HF}\rangle + {}^t\mathrm{p}\,\langle \bar{t}_2|[\check{\mathrm{s}}, \tau_{\mu_2}]|\mathrm{HF}\rangle \\
&+ {}^t\mathrm{p}\,\langle \bar{t}_3|[[\check{\mathrm{s}}, \tau_{\mu_2}], T_2]|\mathrm{HF}\rangle = 0 \qquad (4.65\mathrm{b}) \\
\epsilon_{\mu_3}\bar{t}_{\mu_3} &+ \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_3}]|\mathrm{HF}\rangle + \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_3}]|\mathrm{HF}\rangle \\
&+ {}^t\mathrm{p}\,\langle \bar{t}_2|[\check{\mathrm{s}}, \tau_{\mu_3}]|\mathrm{HF}\rangle + {}^t\mathrm{p}\,\langle \bar{t}_3|[\check{\mathrm{s}}, \tau_{\mu_3}]|\mathrm{HF}\rangle = 0 \qquad (4.65\mathrm{c})
\end{aligned}
$$

► We can construct the *noniterative* ΛCCSD(T)[83–85] and CCSD(T)[80] methods as shown in Chapter 1. We propose to include all the fourth order terms in Eq. (4.51) and the following two terms from the fifth order connected triples corrections in Eq. (4.52):

$$
\langle \bar{t}_1^{[2]}|[\boldsymbol{\Phi}, T_3^{[2]}]|\mathrm{HF}\rangle\,, \quad {}^t\mathrm{p}^{[1]}\,\langle \bar{t}_2^{[2]}|[\mathrm{s}, T_3^{[2]}]|\mathrm{HF}\rangle \qquad (4.66)
$$

Inserting the converged CCSD parameters, denoted with a $*$ superscript, yields the following expressions:

$$
G_{\Lambda(\mathrm{T})} = \sum_{u=1}^{2} \langle \bar{t}_u^*|[\boldsymbol{\Phi}, T_3^*]|\mathrm{HF}\rangle + {}^t\mathrm{p}^*\,\langle \bar{t}_2^*|[\mathrm{s}, T_3^*]|\mathrm{HF}\rangle \quad (4.67\mathrm{a})
$$

$$
G_{(\mathrm{T})} = \sum_{u=1}^{2} \langle t_u^*|[\boldsymbol{\Phi}, T_3^*]|\mathrm{HF}\rangle + {}^t\mathrm{p}^*\,\langle t_2^*|[\mathrm{s}, T_3^*]|\mathrm{HF}\rangle \quad (4.67\mathrm{b})
$$

We recall that both the left and right state are used in the ΛCCSD(T) method, while CCSD(T) uses the right state only, replacing the multipliers with the amplitudes. Further insight into the proposed correction can be gained by inserting the MBPT expansion of the converged CCSD parameters.[73,88–91] First of all, we notice that $T_3^* =$

$T_3^{[2]} + \tilde{T}_3 + O(3)$ contains higher than second order contributions. In particular, $\tilde{T}_3$ is a third order contributions to the connected triples arising from second order connected doubles:

$$\begin{aligned} \epsilon_{\mu_3} t^*_{\mu_3} = & -\langle \mu_3 | [\Phi, T_2^{[1]}] | \mathrm{HF} \rangle \\ & - \langle \mu_3 | [\Phi, T_2^{[2]}] | \mathrm{HF} \rangle + O(3) \end{aligned} \tag{4.68}$$

such that the third order $\tilde{T}_3$ can re rewritten as:

$$\tilde{T}_3 = \sum_{\mu_3} \left(-\epsilon_{\mu_3}^{-1} \langle \mu_3 | [\Phi, T_2^{[2]}] | \mathrm{HF} \rangle \right) \tau_{\mu_3} \tag{4.69}$$

The converged PTED-CCSD parameters are correct up to second order in the fluctuation potential:

$$t^*_{\mu_i} = t^{[1]}_{\mu_i} + t^{[2]}_{\mu_i} + O(3) \tag{4.70a}$$

$$\bar{t}^*_{\mu_i} = \bar{t}^{[1]}_{\mu_i} + \bar{t}^{[2]}_{\mu_i} + O(3) \tag{4.70b}$$

$$\mathrm{p}^* = \mathrm{p}^{[1]} + \mathrm{p}^{[2]} + O(3) \tag{4.70c}$$

Using the equations above one can expand the energy correction as follows:

$$\begin{aligned} G_{\Lambda(\mathrm{T})} = & \sum_{u=1}^{2} \langle \bar{t}_u^{[1]} | [\Phi, T_3^{[2]}] | \mathrm{HF} \rangle + \langle \bar{t}_3^{[2]} | [\Phi, T_2^{[2]}] | \mathrm{HF} \rangle \\ & + \sum_{u=1}^{2} \langle \bar{t}_u^{[2]} | [\Phi, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + {}^t\mathrm{p}^{[1]} \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle + {}^t\mathrm{p}^{[1]} \langle \bar{t}_2^{[2]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + {}^t\mathrm{p}^{[1]} \langle \bar{t}_2^{[1]} | [\mathrm{s}, \tilde{T}_3] | \mathrm{HF} \rangle + {}^t\mathrm{p}^{[2]} \langle \bar{t}_2^{[1]} | [\mathrm{s}, T_3^{[2]}] | \mathrm{HF} \rangle \\ & + O(6) \end{aligned} \tag{4.71}$$

4.6 APPROXIMATE COUPLED CLUSTER METHODS AND APPROXIMATE QUANTUM/CLASSICAL COUPLING SCHEMES

The iterative CC2 and CC3 and the noniterative ΛCCSD(T) and CCSD(T) methods can be formulated, *mutatis mutandis*, also within the approximate quantum/classical coupling schemes mentioned previously.[209,223,226]

Let us first consider the noniterative models for the inclusion of connected triples. The PTE scheme is particularly simple: the equations are unchanged with respect to vacuum theory, the only change being in the definition of the MOs and the Fock matrix.[207,227,228] Comparing the fourth and fifth order MBPT energy corrections in the PTE(S), Eqs. (4.54a)–(4.54e), and PTES, Eqs. (4.57a)–(4.57e), schemes to those obtained for the PTED scheme, Eqs. (4.40)–(4.50), we can see that there are no contributions from the triples to the quantum/classical terms involving the polarization. Thus, also for PTE(S) and PTES the asymmetric and symmetric triples corrections are formally identical to the vacuum expression given in equations (1.55) The converged CCSD parameters are optimized in the presence of an approximate polarization and are used to form the triples free energy corrections. Thus, despite the absence of explicit polarization terms in the PTE(S) and PTES triples free energy corrections, the effect of the polarization on the approximate triples amplitudes is implicitly included.

► The theory and implementation for iterative CC methods with quantum/classical polarizable Hamiltonians has already been presented in the context of the multipolar continuum and polarizable embedding models.[222,223,229,230] Once again, the PTE scheme can be trivially derived from the PTED effective Lagrangians (4.58) and (4.62) by neglecting the polarization components. In the PTE(S) scheme, we replace the expectation value of the source with its CCS counterpart and further neglect the multiplier-dependent part, Eq. (4.19). For CC2, the amplitudes equations are the same as *in vacuo*, Eqs. (1.44) The multipliers are instead determined by:

$$\begin{aligned}\epsilon_{\mu_1}\bar{t}_{\mu_1} + \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], Q_2]|\mathrm{HF}\rangle \\ + \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + {}^t\mathrm{p}\,\langle \mathrm{HF}|[\check{\mathrm{s}}_{\mathrm{N}}, \tau_{\mu_1}]|\mathrm{HF}\rangle = 0 \qquad (4.72\mathrm{a})\end{aligned}$$

$$\epsilon_{\mu_2}\bar{t}_{\mu_2} + \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle = 0 \qquad (4.72\mathrm{b})$$

The CC3 amplitudes are once again the same as *in vacuo*, Eqs. (1.49) The multipliers equations are:

$$\begin{aligned}\epsilon_{\mu_1}\bar{t}_{\mu_1} &+ \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], Q_3]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_3|[[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2]|\mathrm{HF}\rangle \\ &+ {}^{t}\mathrm{p}\,\langle \mathrm{HF}|[\check{\mathrm{s}}_{\mathrm{N}}, \tau_{\mu_1}]|\mathrm{HF}\rangle = 0\end{aligned} \tag{4.73a}$$

$$\begin{aligned}\epsilon_{\mu_2}\bar{t}_{\mu_2} &+ \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}], T_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_3|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle = 0\end{aligned} \tag{4.73b}$$

$$\epsilon_{\mu_3}\bar{t}_{\mu_3} + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_3}]|\mathrm{HF}\rangle + \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_3}]|\mathrm{HF}\rangle = 0 \tag{4.73c}$$

In both coupled cluster models, the polarization is still determined by Eq. (4.22c) and only the singles multipliers equation is modified.

In the PTES scheme, we replace the expectation value of the source with its CCS counterpart. The singles amplitudes equation thus contains a quantum/classical coupling term. However, to avoid the coupling with the multipliers equations, an additional approximation is introduced in the polarization equation, where the source term is truncated to its multiplier-independent part. As already noted, this leads to the use of *two* different polarization equations when solving for the amplitudes and the multipliers. Within the CC2 model we have the following amplitudes equations:

$$\epsilon_{\mu_1}t_{\mu_1} + \langle \mu_1|\check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, Q_2]|\mathrm{HF}\rangle + {}^{t}\mathrm{p}\,\langle \mu_1|\check{\mathrm{s}}|\mathrm{HF}\rangle = 0 \tag{4.74a}$$

$$\epsilon_{\mu_2}t_{\mu_2} + \langle \mu_2|\check{\boldsymbol{\Phi}}|\mathrm{HF}\rangle = 0 \tag{4.74b}$$

$$\mathbb{V}\mathrm{p} + \langle \mathrm{HF}|\check{\mathrm{s}}_{\mathrm{N}}|\mathrm{HF}\rangle = 0 \tag{4.74c}$$

For the CC2 multipliers one has:

$$\begin{aligned}\epsilon_{\mu_1}\bar{t}_{\mu_1} &+ \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], Q_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}]|\mathrm{HF}\rangle \\ &+ {}^{t}\mathrm{p}\,\langle \mathrm{HF}|[\check{\mathrm{s}}_{\mathrm{N}}, \tau_{\mu_1}]|\mathrm{HF}\rangle + {}^{t}\mathrm{p}\,\langle \bar{t}_1|[\check{\mathrm{s}}, \tau_{\mu_1}]|\mathrm{HF}\rangle = 0\end{aligned} \tag{4.75a}$$

$$\epsilon_{\mu_2}\bar{t}_{\mu_2} + \langle \mathrm{HF}|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}]|\mathrm{HF}\rangle = 0 \tag{4.75b}$$

$$\mathbb{V}\mathrm{p} + \mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathrm{CCS}} = 0 \tag{4.75c}$$

We note that the PTES approximation is crucial in the implementation of PE-CC2 presented by Schwabe et al. in ref. 223 The resolution of the identity can in fact still be applied when assuming the PTES approximation. Moreover, the simplified PE-CC (sPECC) Lagrangian of Krause et al. is essentially the PTE(S) approximation for PE-CC.[226]

Finally, for the CC3 model the amplitudes are determined by:

$$\begin{aligned}
\epsilon_{\mu_1} t_{\mu_1} &+ \langle \mu_1 | \check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, T_2] + [\check{\boldsymbol{\Phi}}, Q_3] | \mathrm{HF} \rangle \\
&+ {}^{t}\mathrm{p} \, \langle \mu_1 | \check{\mathrm{s}} | \mathrm{HF} \rangle = 0 \qquad \text{(4.76a)} \\
\epsilon_{\mu_2} t_{\mu_2} &+ \langle \mu_2 | \check{\boldsymbol{\Phi}} + [\check{\boldsymbol{\Phi}}, T_2] | \mathrm{HF} \rangle \\
&+ \langle \mu_2 | + \frac{1}{2} [[\check{\boldsymbol{\Phi}}, T_2], T_2] + [\check{\boldsymbol{\Phi}}, Q_3] | \mathrm{HF} \rangle = 0 \qquad \text{(4.76b)} \\
\epsilon_{\mu_3} t_{\mu_3} &+ \langle \mu_3 | [\check{\boldsymbol{\Phi}}, T_2] | \mathrm{HF} \rangle = 0 \qquad \text{(4.76c)} \\
\mathbb{V}\mathrm{p} &+ \langle \mathrm{HF} | \check{\mathrm{s}}_{\mathrm{N}} | \mathrm{HF} \rangle = 0 \qquad \text{(4.76d)}
\end{aligned}$$

and the multipliers by:

$$\begin{aligned}
\epsilon_{\mu_1} \bar{t}_{\mu_1} &+ \langle \mathrm{HF} | [\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] | \mathrm{HF} \rangle + \langle \bar{t}_1 | [\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_2 | [\check{\boldsymbol{\Phi}}, \tau_{\mu_1}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], Q_3] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_3 | [[\check{\boldsymbol{\Phi}}, \tau_{\mu_1}], T_2] | \mathrm{HF} \rangle + {}^{t}\mathrm{p} \, \langle \mathrm{HF} | [\check{\mathrm{s}}_{\mathrm{N}}, \tau_{\mu_1}] | \mathrm{HF} \rangle \\
&+ {}^{t}\mathrm{p} \, \langle \bar{t}_1 | [\check{\mathrm{s}}, \tau_{\mu_1}] | \mathrm{HF} \rangle = 0 \qquad \text{(4.77a)} \\
\epsilon_{\mu_2} \bar{t}_{\mu_2} &+ \langle \mathrm{HF} | [\check{\boldsymbol{\Phi}}, \tau_{\mu_2}] | \mathrm{HF} \rangle + \langle \bar{t}_1 | [\check{\boldsymbol{\Phi}}, \tau_{\mu_2}] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_2 | [\check{\boldsymbol{\Phi}}, \tau_{\mu_2}] + [[\check{\boldsymbol{\Phi}}, \tau_{\mu_2}], T_2] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_3 | [\check{\boldsymbol{\Phi}}, \tau_{\mu_2}] | \mathrm{HF} \rangle = 0 \qquad \text{(4.77b)} \\
\epsilon_{\mu_3} \bar{t}_{\mu_3} &+ \langle \bar{t}_1 | [\check{\boldsymbol{\Phi}}, \tau_{\mu_3}] | \mathrm{HF} \rangle + \langle \bar{t}_2 | [\check{\boldsymbol{\Phi}}, \tau_{\mu_3}] | \mathrm{HF} \rangle = 0 \qquad \text{(4.77c)} \\
\mathbb{V}\mathrm{p} &+ \mathrm{s}_{\mathrm{N}}(t, \bar{t})_{\mathrm{CCS}} = 0 \qquad \text{(4.77d)}
\end{aligned}$$

5

Summary of Contributions

> ½ research and ½ Τέχνη
> ½ observation, ½ Τέχνη
> ½ training, ½ Τέχνη
> — Ezra Pound, *Canto LXXXV*

This final Chapter provides a brief overview of the motivations, results and conclusions of the papers this dissertation is based on. All publications included in this dissertation have involved some programming effort. In Section 5.1 I will describe the principles we have striven to follow in developing our PCM software library and its management philosophy. I will also give some details on the interfaces we have developed to different quantum chemistry codes. A shorter version of the material in Section 5.1 has been published in the proceedings of the *Producing High Performance and Sustainable Software for Molecular Simulation* workshop held at the 2015 Supercomputing Conference.[231] Sections 5.2–5.6 contain very short summaries of the papers and a list of my contributions. My coauthors have all read and approved the description of contributions.

5.1 SOFTWARE

The growing complexity of quantum chemical program packages requires that an appropriate strategy be devised to implement new features. Scalability is of paramount importance, but it has become clear that maintainability and extensibility of the code play an equally important role in managing software complexity[232–237] and ensuring scientific reproducibility.[238–243]

► THE IDEA OF A *MODULAR PROGRAMMING PARADIGM* CAN BE TRACED BACK TO THE DAWN OF COMPUTER SCIENCE. Dijkstra successfully used it in the development of the THE operating system in 1968,[244] while Parnas advocated it as a best practice already in 1972.[245] Modularity is nothing more than a *divide et impera* strategy applied to programming and it has been recognized as beneficial in many other scientific computing contexts. New features are isolated into libraries that can be accessed by host programs through a well-defined application programming interface (API).

In this paradigm, computational tasks are implemented into separate, independent and interchangeable modules. Modules are to be thought as computational black boxes *developed*, *tested*, *packaged* and *distributed* independently of the particular host program in which they will be used. A well-defined API clearly delimits the boundaries of the functionality offered, effectively enforcing a programming style and standardisation of the functionality, eventually.[246]

Recently, a debate over *open-source* licensing[247] and *open data* practices has sparked in the quantum chemistry community.[248–250] Open-source licensing enables an open code review process that is, in our opinion, essential in guaranteeing scientific reproducibility.[248] The points raised *against* wholesale adoption of open-source licensing models,[249] especially the concerns about code quality and maintenance, do partially resonate with us. However, we still think that a modular approach to programming can only have significant impact, in terms of improved reproducibility and overall code quality, when an open-source licensing model is adopted. Open-source development can fully leverage the benefits of widespread, cloud-based, free, code development services, such as hosted distributed version control systems (DVCSs),[*] continuous integration,[†] code coverage analysis,[‡] static and dynamic code analyses,[§] nightly regression testing, public issue tracking, code review and so forth: adoption of a modern code development workflow is easily within reach.

It is, of course, true that the above mentioned services are not exclusive prerogatives of open-source projects. However, an open review

[*] https://github.com/
https://gitlab.com/

[†] https://travis-ci.org/
https://www.appveyor.com/
https://magnum-ci.com

[‡] https://coveralls.io/

[§] https://scan.coverity.com/

process of scientific software can often help to establish reproducibility, extensibility and sustainability of the software ecosystem. Open-source software, modular development of new functionalities and full-fledged exploitation of DVCSs ensure a much larger scientific impact. Third-parties can easily contribute to the project: by improving the documentation, by reporting bugs or by actively extending the codebase with new functionality.

► The PCM is an ideal candidate for the creation of a solvation API. Consider for example the schematic representation of a PCM-SCF algorithm given in Figure 5.1. The input to and from the PCM library is limited and well-defined, as are the components that host quantum chemistry codes need to implement. This provides a natural API design: the API functions can be compared *vis-à-vis* with the working equations derived for the different quantum chemical methods.

The PCMSolver library has been developed to fulfill these requirements and offer the community an easy-to-use implementation of the PCM.[251] PCMSolver is written in C++ with Fortran, C and Python components. Architectural and conceptual organization of the code is provided by the C++ layer. To ensure the largest possible impact, the code is C++03 ISO standard compliant, with external dependencies kept to a minimum. Tuples, container algorithms and functional programming tools are not part of the standard we chose to comply to. Parts of the Boost C++ libraries are used to alleviate these shortcomings.[252] Linear algebra operations are managed through the Eigen C++ template library.[253] The Python layer provides input reading and parsing facilities, as implemented by the GetKw library.[254] Cavity construction and discretization is handled either by the Fortan or by the C layer, depending on which computational *backend* is needed. Evaluation of the Green's functions, needed to set up the representation of the boundary integral operators, leverages automatic differentiation (AD). We use the Taylor library, a template C++ implementation of AD.[255,256] The adoption of git[*] as DVCS, CMake[†] for cross-platform builds and automatic documentation deployment on ReadTheDocs[‡] simplify extensibility of the module and promote third-party contributions to the code base. Continuous inte-

[*] `https://git-scm.com/`

[†] `https://cmake.org/`

[‡] `https://readthedocs.org/`

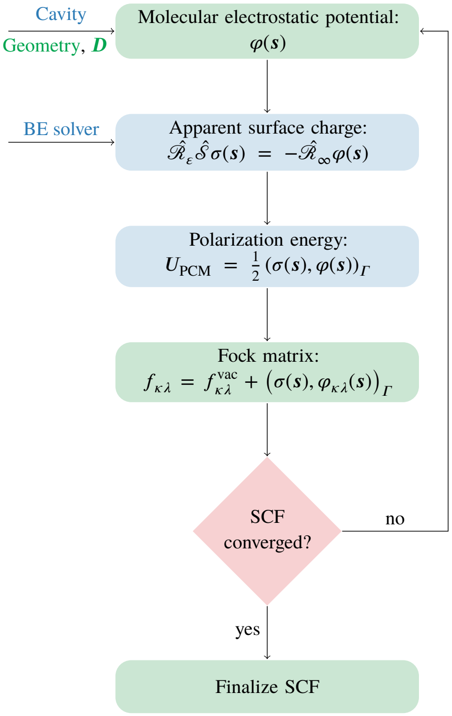


Figure 5.1 Schematic view of a PCM-SCF algorithm. Computations/data in blue are implemented by the PCM API. Computations/data in green are implemented by the host quantum chemistry code.

gration and nightly testing offer an invaluable level of confidence in the code.

Judicious usage of the C++ object-oriented paradigm is the key to this wide spectrum of functionalities. The library is in itself made of modules, communicating by means of composition at the outermost level of design. This is an indispensable feature to achieve frictionless language mixing. Library internal classes balance the dynamic polymorphism offered by inheritance and the static polymorphism offered by template programming.[257–259] Preeminent use of composition over inheritance keeps the coupling between different submodules as low as possible.[260]

The library is released under the terms of the version 3 GNU Lesser General Public License (LGPL), a standard open-source license.[261] We strongly believe that open-source software is the key to a larger impact for scientific software and a standard license means lower thresholds to adoption and third-party contributions.[261] The library serves as our development platform for the PCM. The interfaces to different quantum chemistry codes allow us to explore new methodologies, significantly cutting down development times. Use of our API *significantly* limits coding effort on the side of the host: continuum solvation at the SCF level of theory can be implemented in the host program almost out-of-the-box.

The library was designed to allow host-API communication through *pure* functions, *i. e.* free from side-effects. Such an implementation hinges on the theoretical realization that the PCM layer is independent of the AO or MO spaces defined in the quantum chemical layer. Passing and modifying large data structures, such as the Fock and density matrices, can be completely avoided. As schematically depicted in Figure 5.1, computation of the ASC only depends on the electrostatic potential sampled at the cavity boundary:

$$\varphi(\boldsymbol{s}) = \sum_A \frac{Z_A}{|\boldsymbol{R}_A - \boldsymbol{s}|} + \sum_{\kappa\lambda} D_{\lambda\kappa} \left[\int \mathrm{d}\boldsymbol{r} \frac{-\Omega_{\kappa\lambda}(\boldsymbol{r})}{|\boldsymbol{r} - \boldsymbol{s}|} \right], \tag{5.1}$$

which is the contraction of charge attraction integrals with a, possibly perturbed, density matrix, a task handled by the host program. Formation of the solvent contribution to the Fock matrix requires the computation of the scalar product $\left(\sigma(\boldsymbol{s}), \varphi_{\kappa\lambda}(\boldsymbol{s})\right)_\Gamma$ between the ASC and the charge attraction integral matrix, again a task easily accomplished by the host program. As shown in Figure 5.2, data transfer between PCMSolver and the host is limited to the communication of $\varphi(\boldsymbol{s})$ and $\sigma(\boldsymbol{s})$ and can be implemented *without* storing any quantity to disk, avoiding possibly costly I/O operations.

The API is implemented in ISO C99 as a *context-aware* set of functions.[262]* Upon initialization of the library, a *context* object containing the state of the PCM API is constructed and an opaque handle to it (a pointer in C++ parlance) is returned to the host program. Further transactions between PCMSolver and the host program proceed

* `https://github.com/bast/context-api-example`

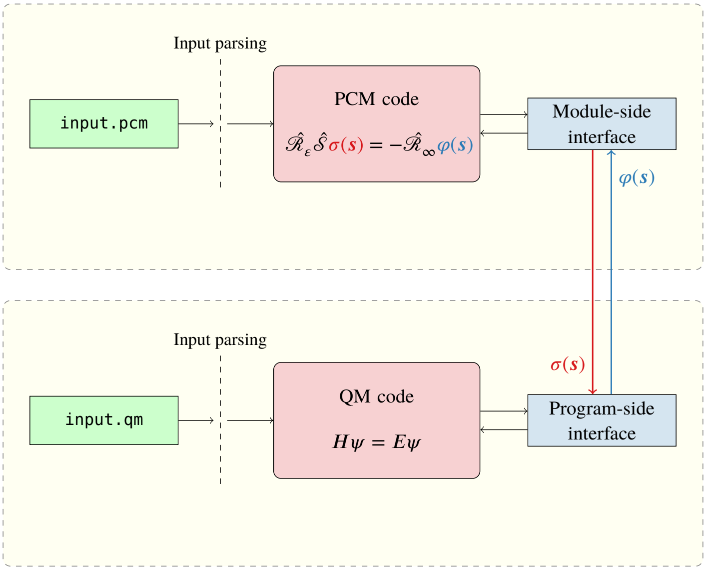


Figure 5.2 Schematic view of the relationship between a host quantum chemistry program and the PCMSolver library.

through manipulations of the context object. A context-aware API offers a simple strategy for parallelization. The host program could spawn contexts on a per-process basis, limiting ownership and access to a context just to its parent process. Race conditions are trivially avoided in such a scenario.

PCMSolver introduces the concept of surface functions: labelled instances of any quantity defined on the cavity surface. Bookkeeping of a possibly arbitrary number of such quantities is managed through a map storing labels and pointers to the contents of the functions. Listings 5.1 and 5.2 show how calls to PCMSolver API functions might look like in an actual C or Fortran host program, respectively.

Listing 5.1 Relevant calls to PCMSolver in a C host program. Ellipses in the functions' argument list stand for omitted parameters. For the full, functional example visit `http://pcmsolver.readthedocs.io/en/v1.1.6/users/C-example.html`

```c
// Include API functions and data structures definitions
#include "pcmsolver.h"
#include "PCMInput.h"
```

```
// Initialize API context
pcmsolver_context_t * pcm_context = pcmsolver_new(...);
// Register surface function from host program to API context
pcmsolver_set_surface_function(pcm_context, ...);
// Compute the ASC from a MEP surface function
pcmsolver_compute_asc(pcm_context, ...);
// Retrieve surface function to host from API context
pcmsolver_get_surface_function(pcm_context, ...);
// Compute polarization energy from surface functions
double energy = pcmsolver_compute_polarization_energy(pcm_context, ...);
// Clean up API context
pcmsolver_delete(pcm_context);
```

Listing 5.2 Relevant calls to PCMSolver in a Fortran host program. Notice the use of the standard Fortan ISO C bindings. Ellipses in the functions' argument list stand for omitted parameters. For the full, functional example visit `http://pcmsolver.readthedocs.io/en/v1.1.6/users/fortran-example.html`

```
! Use standard ISO C bindings
use, intrinsic :: iso_c_binding
! Use API functions and data structures
use pcmsolver
! Declare handle to API context as C pointer
type(c_ptr) :: pcm_context
! Declare polarization energy as a C-interoperable real number
real(c_double) :: energy
! Initialize API context
pcm_context = pcmsolver_new(...)
! Register surface function from host program to API context
call pcmsolver_set_surface_function(pcm_context, ...)
! Compute the ASC from a MEP surface function
call pcmsolver_compute_asc(pcm_context, ...)
! Retrieve surface function to host from API context
call pcmsolver_get_surface_function(pcm_context, ...)
! Compute polarization energy from surface functions
energy = pcmsolver_compute_polarization_energy(pcm_context, ...)
! Clean up API context
call pcmsolver_delete(pcm_context)
```

PCMSolver currently offers an implementation of the traditional collocation solvers for isotropic media,[99] together with some unique functionalities: the wavelet Galerkin solvers on smooth molecular surfaces,[135,263] the Green's functions for spherical diffuse interfaces[116] and the delayed solvers for real-time time-dependent SCF simulations.[198]

► PROGRAMMING EFFORT IN THIS DISSERTATION has not only been directed at the creation of the PCMSOLVER library, but also at interfacing it with a number of quantum chemistry codes. The first interface was implemented and released within the DIRAC code and is described in **Paper I**.[264,265]. Interfaces to the LSDALTON[266,267] and DALTON[266,267] codes have followed, as described in **Paper II** and **Paper V**, respectively.[135,201] Details about the interface to RESPECT[268] can be found in **Paper IV**.[269] Coupling with PSI4[270] has allowed us to implement the PCM-CC developments described in this dissertation. Finally, development of an interface with the KOALA code is underway.[271,272]

5.2 CONTINUUM SOLVATION IN THE RELATIVISTIC REGIME

Four-Component Relativistic Calculations in Solution with the Polarizable Continuum Model of Solvation: Theory, Implementation, and Application to the Group 16 Dihydrides H_2X (X = O, S, Se, Te, Po)
R. Di Remigio, R. Bast, L. Frediani, and T. Saue
J. Phys. Chem. A, 2015, **119**, 5061–5077
DOI: `10.1063/1.4943782`

Systems containing heavy elements are notoriously challenging for quantum chemistry. One has to properly include the effect of special relativity in the quantum chemical description in order to achieve at least qualitative agreement with experiment. Additional complications arise if one needs to also include environment effects. Continuum models arguably represent a cost-effective strategy to achieve a first approximation of these effects. In **Paper I** we presented the first derivation and implementation of the PCM coupled to a SCF description of the solute in the fully relativistic, four-component regime. Our preliminary calculations on the group 16 dihydrides H_2X (X = O, S, Se, Te, Po) have shown that the method predicts a noticeable interplay of relativistic and solvent effects when heavier elements are involved. The main point of **Paper I** was, however, the adoption of a fully modular programming strategy. We showed that it is entirely possible to adopt the same PCM code and implementation "checkpoints" across altogether different problem domains, Fig. 5.1.

As a by-product of the four-component implementation, we were able to obtain and visualize MEP maps from four-component SCF wave functions. These add yet another interpretive tool to the toolbox available in the four-component relativistic regime. The interface to DIRAC was first released in the 2014 version, providing PCM capabilities to the software package.

I contributed the theoretical derivation of the quantum/classical polarizable terms in a four-component SCF framework, for energies and linear response properties. I devised the coupling of the four-component program DIRAC with PCMSolver by providing the implementation and testing of:

1. MEP integrals for four-component wave functions,
2. the additional Fock matrix contributions, and
3. the additional terms in the response equations.

I performed all the calculations and large part of the data analysis for the results reported in the paper. Finally, I wrote the first draft of the paper and coordinated editing of all subsequent versions.

5.3 THE WAVELET GALERKIN BOUNDARY ELEMENT METHOD FOR PCM

Wavelet Formulation of the Polarizable Continuum Model. II. Use of Piecewise Bilinear Boundary Elements
M. Bugeanu, **R. Di Remigio**, K. Mozgawa, S. S. Reine, H. Harbrecht, and L. Frediani
Phys. Chem. Chem. Phys., 2015, **17**, 31566–31581
DOI: `10.1039/C5CP03410H`

Continuum solvation models are inherently parametrized. Apart from solvent permittivities, the atomic radii and molecular surface definition play a crucial role in determining the performance of the models. However, the numerical accuracy of the BEM procedure used to numerically solve the underlying BIE is a not-so-often studied aspect of these models. Traditionally, collocation methods have been used, but these require parametrization of some of the necessary surface integrals. Galerkin methods do not suffer from such a limitation and additionally preserve symmetry of the underlying boundary integral operators. The use of biorthogonal wavelet bases as finite elements achieves sparsity in the BEM procedure, due to the intrinsical hierarchy and the existence of *a priori* and *a posteriori* matrix compression estimates. Thus, wavelet Galerkin BEM represents a valid alternative to traditional collocation methods, both to achieve a better computational scaling and to provide accurate, benchmark results.[132–134]

Already Weijo et al. had shown that using piecewise constant (PWC) wavelet bases can lead to superior accuracy and convergence in the calculation of quantum mechanical molecular solvation energies. In this work we showed that even faster convergence can be achieved when piecewise linear (PWL) wavelet bases are used instead. Moreover, the same holds for the calculation of static electric properties. Notably, the traditional collocation solver cannot guarantee the same accuracy, even for very large finite element bases. This suggests that, in some cases, BEM collocation methodologies might slow down or even prevent the convergence of the quantum mechanical response equations solvers.

For **Paper II**, I provided template interface and test sets for the cavity generator[121,130] and wavelet Galerkin BEM solver[133,134] with PCMSolver. These were used to interface with the new C++ implementation of the wavelet Galerkin solvers of Monica Bugeanu. I implemented the interface between the LSDalton quantum chemistry software package and the PCMSolver software library. The interface allows to run HF and KS-DFT single-point and linear response calculations. Together with coauthor Krzysztof Mozgawa, I performed the benchmark quantum chemical calculations presented in the paper. Finally, I coordinated the editing of all manuscript drafts. In particular, I wrote the first draft of Sections 2.1 and 2.3. The first draft of Sections 3 and 4 was co-written with the first author, Monica

Bugeanu. I performed most of the data analysis and produced tables and graphs.

Finally, the interface to LSDALTON was later released in the 2016 version, providing PCM capabilities to the software package.

5.4 NON HOMOGENEOUS ENVIRONMENTS

A Polarizable Continuum Model for Molecules at Spherical Diffuse Interfaces
R. Di Remigio, K. Mozgawa, H. Cao, V. Weijo, and L. Frediani
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Continuum solvation models offer a simple route to the treatment of non homogeneous environments. The general integral equation formulation is in fact transparent with respect to the definition of the Green's function for the space portion exterior to the cavity. As outlined in Chapter 2, the boundary integral operators in the IEF equation:

$$\begin{aligned}\left[\hat{\mathcal{S}}_\mathrm{e}\left(2\pi + \hat{\mathcal{D}}_\mathrm{i}^\dagger\right) + \left(2\pi - \hat{\mathcal{D}}_\mathrm{e}\right)\hat{\mathcal{S}}_\mathrm{i}\right]\sigma &= \\ -\left[\left(2\pi - \hat{\mathcal{D}}_\mathrm{e}\right) - \hat{\mathcal{S}}_\mathrm{e}\hat{\mathcal{S}}_\mathrm{i}^{-1}\left(2\pi - \hat{\mathcal{D}}_\mathrm{i}\right)\right]\varphi,\end{aligned}$$

(2.7 from Chapter 2)

can be set up once the Green's functions $G_\mathrm{i}(\boldsymbol{r}, \boldsymbol{r}')$ and $G_\mathrm{e}(\boldsymbol{r}, \boldsymbol{r}')$ are known.[112] Frediani et al. showed that a numerical representation of the Green's function is sufficient to obtain the boundary integral operators in the PCM integral equation. The authors introduced a numerical integration procedure to calculate the Green's function for an environment characterized by spatially varying, yet cilindrically symmetric, permittivity functions: a model for planar diffuse interfaces.

In this work, a similar procedure was introduced to tackle diffuse interfaces in spherical symmetry. In contrast to previously existing work, our implementation offers a more robust treatment of thin interfaces, with a rather generic functional form for the permittivity profile. We thoroughly analyzed the necessity for the *a posteriori* removal of the Coulomb singularity from the computed Green's function and its efficient implementation. Interface width and curvature influence the transfer of ions and molecules across spherically symmetric interfaces and peculiar properties may arise. In this work, we analyzed both effects on the water-vapor and oil-water transfer of Li^+, Br^-, acetone, *para*-nitroaniline and the Lo dye. Nonelectrostatic interactions were not included in our implementation, although they have been proved to be crucial for non homogeneous environments.[103] Nevertheless our implementation represents a first significant step in the continuum treatment of such nontrivial environments.

I contributed the theoretical work for **Paper III**, based on earlier drafts from coauthors Ville Weijo and Hui Cao. In particular, I derived the separation of the Coulomb singularity in its final form.* Moreover, I contributed the implementation and testing of the Green's function code. The interface to the LSDALTON program package, developed within **Paper II**, was also used for this paper. I wrote the first draft of the paper and coordinated all subsequent editing stages.

5.5 RELATIVISTIC CALCULATION OF EPR AND PNMR PARAMETERS IN SOLUTION

Four-Component Relativistic Density Functional Theory with the Polarizable Continuum Model: Application to EPR Parameters and Paramagnetic NMR Shifts
R. Di Remigio, M. Repisky, S. Komorovsky, P. Hrobarik, L. Frediani, and K. Ruud
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Paper IV is a step further in our exploration of the interplay between relativistic and solvent effects initiated with **Paper I**. Whereas **Paper I** presented the essential framework for the coupling of four-component SCF wave functions with a classical polarizable contin-

*Equation (40) for $G_{\mathrm{img}}(\boldsymbol{r}, \boldsymbol{r}')$ in the final published version of the paper contains a misprint. The parentheses should not appear.

uum, in this paper we explored the calculation of first-order magnetic properties: electron paramagnetic resonance (EPR) and paramagnetic nuclear magnetic resonance (pNMR) parameters.[273–276] The two works are thus complementary since they explore two different classes of properties and present implementations in two algorithmically different relativistic quantum chemistry codes. In the relativistic framework, spin-orbit interactions are included from the outset in the variational optimization of the wave function. Hence, EPR and pNMR parameters are formulated as expectation values, by virtue of the Hellmann–Feynman theorem.[44,53] Moreover, the ReSpect code can exploit the *Kramers unrestricted* formalism, allowing for spin polarization and thus granting facile access to the computation of spin-dependent properties.[50] The same modular programming strategy was adopted in crafting an interface between the relativistic four-component code ReSpect[268] and PCMSolver.

My contributions to this paper include prototyping the interface between the PCMSolver library and the ReSpect quantum chemistry code. The interface is maintained in collaboration with coauthor Michal Repisky, who also refined the implementation to achieve better computational performance. I tested the interface against one-component and four-component results obtained with the LSDalton and DIRAC codes, respectively. I helped coauthors Michal Repisky, Stanislav Komorovsky and Peter Hrobarik with setting up the PCM calculations described in the paper. Finally, I provided the first draft for Section 2 of the paper and took part in all editing stages. The interface to ReSpect will be released in the next public version of the software package, providing PCM and COSMO capabilities.

5.6 OPEN-ENDED SELF-CONSISTENT FIELD RESPONSE THEORY IN SOLUTION

Open-Ended Formulation of Self-Consistent Field Response Theory with the Polarizable Continuum Model for Solvation
R. Di Remigio, M. T. P. Beerepoot, Y. Cornaton, M. Ringholm, A. H. S. Steindal, K. Ruud, and L. Frediani
Submitted to *Phys. Chem. Chem. Phys.*

In recent years, the availability of strong lasers has allowed to design and carry out experiments where the high-order response of molecular materials can be routinely probed. The more intense the light source, the more complicated the interpretation of the measured signal. Our group has recently developed an open-ended methodology for the computation of SCF response functions[173,181] and their single residues.[182] These developments offer a route towards a synergistic experimental and theoretical approach to high-order absorption spectroscopies. **Paper V** grafts a classical polarizable continuum approach to solvation on top of the open-ended methodology of Thorvaldsen et al. Still nowadays, continuum models represent a cost-effective methodology for the approximate inclusion of solvent effects, albeit their known limitations with respect to specific solute-solvent interactions.

I developed the theoretical framework for the open-ended SCF formulation of molecular response properties when a quantum/classical polarizable continuum Hamiltonian is used.[40,173] I provided its implementation within the DALTON code, by interfacing the PCMSOLVER library and the open-ended SCF response code of Ringholm et al.[181,182] I performed extensive testing of the code by comparing with previously published implementations of the PCM-SCF response functions within DALTON.[188–190] Together with coauthors Maarten T. P. Beerepoot and Yann Cornaton, I carried out the multiphoton absorption calculations presented in the paper. I contributed to data collection and data analysis. I drafted the initial versions of Sections 2 and 3 of the manuscript and coordinated all editing stages with coauthor Maarten T. P. Beerepoot.

A

Some Mathematical Results

For brevity's sake, some results and derivations have been omitted from the main body of the thesis. I collect the ones I judge most relevant in this Appendix. Section A.1 presents the T_1-transformed form of the CCS, CCSD and CCSDT Lagrangians, the corresponding amplitudes and multipliers equations and the one-electron operators expectation values.

Basic results in the fields of functional analysis and boundary integral equations that were omitted from Chapter 2 are presented here. No proofs or examples are given, the interested reader is referred to the monographs by Ern et al.,[123] Hsiao et al.[158] and Sauter et al.[111]

A.1 THE T_1-TRANSFORMATION

Carrying out a similarity transformation of an operator O by means of the T_1 cluster operator will preserve the particle rank of O, since T_1 is a one-electron operator.[75] Starting from the arbitrary order Lagrangian (1.34), we want to derive their T_1-transformed expressions.

▶ FOR THE CCS MODEL, THIS IS STRAIGHTFORWARD. The Lagrangian is:

$$\mathscr{L}(t,\bar{t})_{\mathrm{CCS}} = E_0 + \bar{t}_{\mu_1}\epsilon_{\mu_1}t_{\mu_1} + \langle \mathrm{HF}|\check{\Phi}|\mathrm{HF}\rangle + \langle \bar{t}_1|\check{\Phi}|\mathrm{HF}\rangle \quad \text{(A.1)}$$

the governing equations:

$$\epsilon_{\mu_1} t_{\mu_1} + \langle \mu_1 | \check{\Phi} | \mathrm{HF} \rangle = 0 \tag{A.2a}$$

$$\epsilon_{\mu_1} \bar{t}_{\mu_1} + \langle \mathrm{HF} | [\check{\Phi}, \tau_{\mu_1}] | \mathrm{HF} \rangle + \langle \bar{t}_1 | [\check{\Phi}, \tau_{\mu_1}] | \mathrm{HF} \rangle = 0 \tag{A.2b}$$

When including higher order excitations we will seek simplifications in the commutator expansions by employing the following result:[53]

Lemma 1 (Excitation ranks manifold). *The k-fold nested commutator of a particle rank m_O operator O with cluster operators T_{n_i} of rank n_i acting on the reference determinant:*

$$[[[O, T_{n_1}], \ldots], T_{n_k}] \, |\mathrm{HF}\rangle \tag{A.3}$$

generates a linear combination of determinants with excitation ranks v in the range:

$$\sum_{i=1}^{k} n_i - m_O \leq v \leq \sum_{i=1}^{k} n_i + m_O - k \tag{A.4}$$

Corollary (Excited states overlaps). *The overlap of a determinant μ_n with excitation rank n onto the linear combination of determinants generated by the k-fold nested commutator of an operator O with particle rank m_O with cluster operators T_{n_i} of rank n_i is nonzero if and only if the sum of cluster operator ranks satisfies:*

$$n - m_O + k \leq \sum_{i=1}^{k} n_i \leq n + m_O \tag{A.5}$$

In compact form:

$$\begin{gathered} \langle \mu_n | [[[O, T_{n_1}], \ldots], T_{n_k}] | \mathrm{HF} \rangle \neq 0 \iff \\ n - m_O + k \leq \sum_{i=1}^{k} n_i \leq n + m_O \end{gathered} \tag{A.6}$$

- THE CCSD LAGRANGIAN IS THEN:

$$\begin{aligned}\mathscr{L}(t,\bar{t})_{\text{CCSD}} = E_0 &+ \sum_{u=1}^{2} \bar{t}_{\mu_u}\epsilon_{\mu_u}t_{\mu_u} \\ &+ \langle \text{HF}|\check{\Phi} + [\check{\Phi}, T_2]|\text{HF}\rangle \\ &+ \langle \bar{t}_1|\check{\Phi} + [\check{\Phi}, T_2]|\text{HF}\rangle \\ &+ \langle \bar{t}_2|\check{\Phi} + [\check{\Phi}, T_2]|\text{HF}\rangle \\ &+ \langle \bar{t}_2|\frac{1}{2}[[\check{\Phi}, T_2], T_2]|\text{HF}\rangle\end{aligned} \tag{A.7}$$

with the governing equations:

$$\epsilon_{\mu_1}t_{\mu_1} + \langle \mu_1|\check{\Phi} + [\check{\Phi}, T_2]|\text{HF}\rangle = 0 \tag{A.8a}$$

$$\epsilon_{\mu_2}t_{\mu_2} + \langle \mu_2|\check{\Phi} + [\check{\Phi}, T_2] + \frac{1}{2}[[\check{\Phi}, T_2], T_2]|\text{HF}\rangle = 0 \tag{A.8b}$$

$$\begin{aligned}\epsilon_{\mu_1}\bar{t}_{\mu_1} &+ \langle \text{HF}|[\check{\Phi}, \tau_{\mu_1}]|\text{HF}\rangle + \langle \bar{t}_1|[\check{\Phi}, \tau_{\mu_1}] + [[\check{\Phi}, \tau_{\mu_1}], T_2]|\text{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{\Phi}, \tau_{\mu_1}] + [[\check{\Phi}, \tau_{\mu_1}], T_2]|\text{HF}\rangle = 0\end{aligned} \tag{A.8c}$$

$$\begin{aligned}\epsilon_{\mu_2}\bar{t}_{\mu_2} &+ \langle \text{HF}|[\check{\Phi}, \tau_{\mu_2}]|\text{HF}\rangle + \langle \bar{t}_1|[\check{\Phi}, \tau_{\mu_2}]|\text{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{\Phi}, \tau_{\mu_2}] + [[\check{\Phi}, \tau_{\mu_2}], T_2]|\text{HF}\rangle = 0\end{aligned} \tag{A.8d}$$

Equations (A.8b), (A.8c) and (A.8d) can be compared with the corresponding CC2 equations (1.44b), (1.47a) and (1.47b), respectively, to highlight which terms were neglected in constructing the iterative method for the approximate inclusion of double excitations.

- The CCSDT Lagrangian is built in the same exact manner:

$$
\begin{aligned}
\mathscr{L}(t,\bar{t})_{\mathrm{CCSDT}} = E_0 &+ \sum_{u=1}^{3} \bar{t}_{\mu_u} \epsilon_{\mu_u} t_{\mu_u} \\
&+ \langle \mathrm{HF} | \check{\Phi} + [\check{\Phi}, T_2] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_1 | \check{\Phi} + [\check{\Phi}, T_2] + [\check{\Phi}, T_3] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_2 | \check{\Phi} + [\check{\Phi}, T_2] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_2 | \frac{1}{2}[[\check{\Phi}, T_2], T_2] + [\check{\Phi}, T_3] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_3 | [\check{\Phi}, T_2] + \frac{1}{2}[[\check{\Phi}, T_2], T_2] | \mathrm{HF} \rangle \\
&+ \langle \bar{t}_3 | [\check{\Phi}, T_3] + [[\check{\Phi}, T_2], T_3] | \mathrm{HF} \rangle
\end{aligned}
\tag{A.9}
$$

Notice that the reference expectation value of the similarity transformed fluctuation potential $\overline{\Phi}$ is unchanged with respect to the expression in the CCSD Lagrangian. This is a consequence of the well-known fact that the CC energy can be expressed purely in terms of T_1 and T_2:

$$
E_{\mathrm{CC}} = \langle \mathrm{HF} | \overline{H} | \mathrm{HF} \rangle = \langle \mathrm{HF} | H(1 + T_1 + T_2 + T_1^2) | \mathrm{HF} \rangle \tag{A.10}
$$

The CCSDT amplitude equations are:

$$
\epsilon_{\mu_1} t_{\mu_1} + \langle \mu_1 | \check{\Phi} + [\check{\Phi}, T_2] + [\check{\Phi}, T_3] | \mathrm{HF} \rangle = 0 \tag{A.11a}
$$

$$
\begin{aligned}
\epsilon_{\mu_2} t_{\mu_2} &+ \langle \mu_2 | \check{\Phi} + [\check{\Phi}, T_2] | \mathrm{HF} \rangle \\
&+ \langle \mu_2 | \frac{1}{2}[[\check{\Phi}, T_2], T_2] + [\check{\Phi}, T_3] | \mathrm{HF} \rangle = 0
\end{aligned}
\tag{A.11b}
$$

$$
\begin{aligned}
\epsilon_{\mu_3} t_{\mu_3} &+ \langle \mu_3 | [\check{\Phi}, T_2] + \frac{1}{2}[[\check{\Phi}, T_2], T_2] | \mathrm{HF} \rangle \\
&+ \langle \mu_3 | [\check{\Phi}, T_3] + [[\check{\Phi}, T_2], T_3] | \mathrm{HF} \rangle = 0
\end{aligned}
\tag{A.11c}
$$

while the multipliers are determined by solving the following:

$$\begin{aligned}
&\epsilon_{\mu_1}\bar{t}_{\mu_1} + \langle \mathrm{HF}|[\check{\Phi}, \tau_{\mu_1}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\Phi}, \tau_{\mu_1}] + [[\check{\Phi}, \tau_{\mu_1}], T_2]|\mathrm{HF}\rangle \\
&\qquad + \langle \bar{t}_2|[\check{\Phi}, \tau_{\mu_1}] + [[\check{\Phi}, \tau_{\mu_1}], T_2] + [[\check{\Phi}, \tau_{\mu_1}], T_3]|\mathrm{HF}\rangle \\
&\qquad + \langle \bar{t}_3|[[\check{\Phi}, \tau_{\mu_1}], T_2] + \frac{1}{2}[[[\check{\Phi}, \tau_{\mu_1}], T_2], T_2]|\mathrm{HF}\rangle \\
&\qquad + \langle \bar{t}_3|[[\check{\Phi}, \tau_{\mu_1}], T_3]|\mathrm{HF}\rangle = 0 \qquad \text{(A.12a)} \\
&\epsilon_{\mu_2}\bar{t}_{\mu_2} + \langle \mathrm{HF}|[\check{\Phi}, \tau_{\mu_2}]|\mathrm{HF}\rangle + \langle \bar{t}_1|[\check{\Phi}, \tau_{\mu_2}]|\mathrm{HF}\rangle \\
&\qquad + \langle \bar{t}_2|[\check{\Phi}, \tau_{\mu_2}] + [[\check{\Phi}, \tau_{\mu_2}], T_2]|\mathrm{HF}\rangle \\
&\qquad + \langle \bar{t}_3|[\check{\Phi}, \tau_{\mu_2}] + [[\check{\Phi}, \tau_{\mu_2}], T_2]|\mathrm{HF}\rangle \\
&\qquad + \langle \bar{t}_3|[[\check{\Phi}, \tau_{\mu_2}], T_3]|\mathrm{HF}\rangle = 0 \qquad \text{(A.12b)} \\
&\epsilon_{\mu_3}\bar{t}_{\mu_3} + \langle \bar{t}_1|[\check{\Phi}, \tau_{\mu_3}]|\mathrm{HF}\rangle + \langle \bar{t}_2|[\check{\Phi}, \tau_{\mu_3}]|\mathrm{HF}\rangle \\
&\qquad + \langle \bar{t}_3|[\check{\Phi}, \tau_{\mu_3}] + [[\check{\Phi}, \tau_{\mu_3}], T_2]|\mathrm{HF}\rangle = 0 \qquad \text{(A.12c)}
\end{aligned}$$

A comparison of equations (A.11c), (A.12a), (A.12b) and (A.12c) with equations (1.49c), (1.52a), (1.52b) and (1.52c), respectively, serves to highlight which terms were neglected in constructing the CC3 method.

A.2 COUPLED CLUSTER EXPECTATION VALUES

A similar analysis in terms of T_1-transformed operators can be given for the expectation value of one-electron operators, Eq. (1.37). First of all, by virtue of the cluster commutation condition,[53] the commutator expansion of the similarity transformation of a general one-electron operator truncates after the twofold nested commutator:

$$\overline{O} = O + [O, T] + \frac{1}{2}[[O, T], T] \qquad \text{(A.13)}$$

where T is the complete cluster operator. However, due to Lemma 1, some of the cluster operators will not contribute to the expectation value.

For a general truncation level $\mathscr{M}$ one has:

$$\begin{aligned} O(t,\bar{t}) &= \langle \mathrm{HF}| O + [O,T] + \frac{1}{2}[[O,T],T]|\mathrm{HF}\rangle \\ &+ \sum_{u=1}^{\mathscr{M}} \langle \bar{t}_u| O + [O,T] + \frac{1}{2}[[O,T],T]|\mathrm{HF}\rangle \,, \end{aligned} \tag{A.14}$$

and by virtue of Lemma 1 and its Corollary:

$$\begin{aligned} O(t,\bar{t}) &= \langle \mathrm{HF}| O + [O,T_1]|\mathrm{HF}\rangle + \langle \bar{t}_1|O|\mathrm{HF}\rangle \\ &+ \sum_{u=1}^{\mathscr{M}} \langle \bar{t}_u|[O,T] + \frac{1}{2}[[O,T],T]|\mathrm{HF}\rangle \end{aligned} \tag{A.15}$$

Note that the singles amplitudes assume a unique role in the CC expectation value. In the following, we give explicit expressions for the CCS, CCSD and CCSDT models. These results are at the basis of our developments in Chapter 4. We will refer to the T_1-transformed expressions as *dressed*, in contrast to the *bare* expressions, where the operator O appears untransformed.

► FOR THE CCS MODEL, THE EXPECTATION VALUE OF A ONE-ELECTRON OPERATOR IS SIMPLY:

$$\begin{aligned} O(t,\bar{t})_{\mathrm{CCS}} &= \langle \mathrm{HF}|\check{O}|\mathrm{HF}\rangle + \langle \bar{t}_1|\check{O}|\mathrm{HF}\rangle \\ &= \langle \mathrm{HF}|O + [O,T_1]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_1|O + [O,T_1] + \frac{1}{2}[[O,T_1],T_1]|\mathrm{HF}\rangle \end{aligned} \tag{A.16}$$

Adding double excitations to the manifold yields:

$$\begin{aligned} O(t,\bar{t})_{\mathrm{CCSD}} &= O(t,\bar{t})_{\mathrm{CCS}} + \langle \bar{t}_1|[\check{O},T_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_2|[\check{O},T_2]|\mathrm{HF}\rangle \\ &= O(t,\bar{t})_{\mathrm{CCS}} + \langle \bar{t}_1|[O,T_2]|\mathrm{HF}\rangle \\ &+ \langle \bar{t}_2|[O,T_2] + [[O,T_1],T_2]|\mathrm{HF}\rangle \,, \end{aligned} \tag{A.17}$$

where a number of terms was dropped thanks to Lemma 1 and its Corollary. Eventually, including triples one obtains:

$$\begin{aligned} O(t,\bar{t})_{\text{CCSDT}} &= O(t,\bar{t})_{\text{CCSD}} + \langle \bar{t}_2 | [\check{O}, T_3] | \text{HF} \rangle \\ &+ \langle \bar{t}_3 | [\check{O}, T_3] + \frac{1}{2}[[\check{O}, T_2], T_2] | \text{HF} \rangle \\ &= O(t,\bar{t})_{\text{CCSD}} + \langle \bar{t}_2 | [O, T_3] | \text{HF} \rangle \\ &+ \langle \bar{t}_3 | [O, T_3] + [[O, T_1], T_3] | \text{HF} \rangle \\ &+ \langle \bar{t}_3 | \frac{1}{2}[[O, T_2], T_2] | \text{HF} \rangle \end{aligned} \tag{A.18}$$

where Lemma 1 and its corollary were again extensively employed.

The use of normal-ordered operators is common in coupled cluster theory. Both for the dressed and bare representations, the expectation values of such operators can be formed by simply replacing the operator with its normal-ordered counterpart, $\check{O}_{\text{N}}$ or O, respectively. This achieves elimination of the reference expectation value from the first term in equation (A.16).

A.3 SELECTED RESULTS IN FUNCTIONAL ANALYSIS

Definition 1 (Continuity). A bilinear form on a normed vector space V is *bounded*, or *continuous*, if there is a constant C such that $\forall u, v \in V$:

$$a(u, v) \leq C \|u\| \|v\|$$

Definition 2 (Coercivity). A bilinear form on a normed vector space V is *coercive*, or *elliptic*, if there is a constant $\alpha > 0$ such that $\forall u \in V$:

$$a(u, u) \geq \alpha \|u\|^2$$

Coercivity implies that no eigenvalue of the linear operator associated to the bilinear form can be zero, hence its invertibility.[123]

Definition 3 (Sobolev spaces). Let s and p be two integers with $s \geq 0$ and $1 \leq p \leq +\infty$. The so-called *Sobolev space* $W^{s,p}(\Omega)$ is defined as

$$W^{s,p}(\Omega) = \left\{u \in \mathscr{D}'(\Omega) | \partial^\alpha u \in L^p(\Omega), |\alpha| \leq s\right\} \qquad \text{(A.19)}$$

where $\mathscr{D}'(\Omega)$ is the space of Schwartz distributions and the derivatives $\partial^\alpha u$ are understood in a distributional sense.

Lemma 2 (Hilbert Sobolev spaces). *Let $s \geq 0$. The space $H^s(\Omega) = W^{s,2}(\Omega)$ is a Hilbert space when equipped with the scalar product*

$$(u, v)_{s,\Omega} = \sum_{|\alpha| \leq s} \int_\Omega \partial^\alpha u \partial^\alpha v. \qquad \text{(A.20)}$$

The associated norm is denoted by $\| \cdot \|_{s,\Omega}$.

Definition 4 (Fractional Sobolev spaces). For $0 < s < 1$ and $1 \leq p < +\infty$, the so-called *Sobolev space with fractional exponent* is defined as

$$W^{s,p}(\Omega) = \left\{ u \in L^p(\Omega) \left| \frac{u(\boldsymbol{r}) - u(\boldsymbol{r}')}{\|\boldsymbol{r} - \boldsymbol{r}'\|^{s+\frac{d}{p}}} \in L^p(\Omega \times \Omega) \right. \right\}. \qquad \text{(A.21)}$$

Furthermore, when $s > 1$ is not integer, letting $\sigma = s - [s]$, where $[s]$ is the integer part of s, $W^{s,p}(\Omega)$ is defined as

$$W^{s,p}(\Omega) = \left\{u \in W^{[s],p}(\Omega) | \partial^\alpha u \in W^{\sigma,p}(\Omega) \, \forall \alpha, \, |\alpha| = [s]\right\}.$$

When $p = 2$, we denote $H^s(\Omega) = W^{s,2}(\Omega)$.

Definition 5 (Abstract weak problem). An abstract weak problem is posed as follows:

$$\left\{ \begin{array}{l} \text{Seek } u \in W \text{ such that:} \\ \forall v \in V \quad a(u, v) = b(v) \end{array} \right. \qquad \text{(A.22)}$$

where:

- W and V are normed vector spaces. W is the *solution space*, V the *test space*.
- a is a *continuous* bilinear form on $W \times V$.
- b is a *continous* linear form on V.

Definition 6 (Well-posedness). The abstract weak problem in Definition 5 is *well-posed* if it admits one and only one solution and the solution is bounded by the *a priori* estimate:

$$\exists c > 0, \forall f \in V', \|u\|_W \leq c\|f\|_{V'} \tag{A.23}$$

where V' is the dual space of V.

Definition 7 (Transmission problem). We assume Euclidean space $\mathbb{R}^3$ to be partitioned into two subdomains $\mathit{\Omega}_\mathrm{i}$ and $\mathit{\Omega}_\mathrm{e}$ sharing a boundary $\mathit{\Gamma}$. We further assume that $\mathit{\Omega}_\mathrm{i}$ is a closed domain, entirely contained inside $\mathit{\Omega}_\mathrm{e}$. The transmission problem is posed as follows:

$$\begin{cases} L_\mathrm{i} u = f_\mathrm{i} \text{ in } \mathit{\Omega}_\mathrm{i} & \text{(A.24a)} \\ L_\mathrm{e} u = f_\mathrm{e} \text{ in } \mathit{\Omega}_\mathrm{e} & \text{(A.24b)} \\ [u] = u_\mathrm{e} - u_\mathrm{i} = g_\mathrm{D} \text{ on } \mathit{\Gamma} & \text{(A.24c)} \\ [\partial_L u] = \partial_{L_\mathrm{e}} u - \partial_{L_\mathrm{i}} u = g_\mathrm{N} \text{ on } \mathit{\Gamma} & \text{(A.24d)} \\ |u(\boldsymbol{r})| \leq C\|\boldsymbol{r}\|^{-1} \text{ for } \|\boldsymbol{r}\| \to \infty & \text{(A.24e)} \end{cases}$$

where the differential operators are assumed elliptic and the jump conditions are given in terms of Dirichlet g_D and Neumann g_N data.

A.4 DERIVATION OF THE IEF EQUATION

I will show a detailed derivation of the IEF equation for the PCM transmission problem Eq. (2.3):

$$\begin{cases} L_\mathrm{i}u = \nabla^2 u = -4\pi\rho_\mathrm{i} \text{ in } \Omega_\mathrm{i} & \text{(A.25a)} \\ L_\mathrm{e}u = 0 \text{ in } \Omega_\mathrm{e} & \text{(A.25b)} \\ [u] = u_\mathrm{e} - u_\mathrm{i} = 0 \text{ on } \Gamma & \text{(A.25c)} \\ [\partial_L u] = \partial_{L_\mathrm{e}}u - \partial_{L_\mathrm{i}}u = 0 \text{ on } \Gamma & \text{(A.25d)} \\ |u(\boldsymbol{r})| \leq C\|\boldsymbol{r}\|^{-1} \text{ for } \|\boldsymbol{r}\| \to \infty & \text{(A.25e)} \end{cases}$$

We first state two important results in the theory of boundary integral equations.

Lemma 3 (Properties of the boundary integral operators). *The integral operators introduced in Eqs.* (2.4a)–(2.4c) *enjoy the following properties*[111,158]*:*

1. *on* $L^2(\Gamma)$, $\hat{\mathcal{S}}_\star$ *is self-adjoint,* $\hat{\mathcal{D}}_\star^\dagger$ *is the adjoint operator of* $\hat{\mathcal{D}}_\star$.

2. *The commutation relations hold:*

$$\hat{\mathcal{D}}_\star\hat{\mathcal{S}}_\star = \hat{\mathcal{S}}_\star\hat{\mathcal{D}}_\star^\dagger, \quad \hat{\mathcal{S}}_\star\hat{\mathcal{D}}_\star = \hat{\mathcal{D}}_\star^\dagger\hat{\mathcal{S}}_\star \tag{A.26}$$

3. *The boundary integral operators are continuous mappings between Sobolev spaces of fractional order:*

$$\hat{\mathcal{S}}_\star : H^{-\frac{1}{2}}(\Gamma) \to H^{\frac{1}{2}}(\Gamma) \tag{A.27a}$$

$$\hat{\mathcal{D}}_\star : H^{\frac{1}{2}}(\Gamma) \to H^{\frac{1}{2}}(\Gamma) \tag{A.27b}$$

$$\hat{\mathcal{D}}_\star^\dagger : H^{-\frac{1}{2}}(\Gamma) \to H^{-\frac{1}{2}}(\Gamma) \tag{A.27c}$$

4. *The operator* $\hat{\mathcal{S}}_\star$ *is coervice and admits a continuous inverse in the aforementioned Sobolev spaces.*

5. *The operators* $\lambda - \hat{\mathcal{D}}_\star$ *and* $\lambda - \hat{\mathcal{D}}_\star^\dagger$ *with* $\lambda \in (-2\pi, +\infty)$ *admit a continuous inverse in the aforementioned Sobolev spaces.*

LEMMA 4 (INTEGRAL REPRESENTATION). *For the transmission problem A.24 there holds:*

1. $\forall \boldsymbol{r} \in \Omega_{\mathrm{i}}$

$$u = \hat{\mathscr{S}}_{\mathrm{i}}(\partial_{L_{\mathrm{i}}} u) - \hat{\mathscr{D}}_{\mathrm{i}}(u_{\mathrm{i}}) + \int\limits_{\Omega_{\mathrm{i}}} \mathrm{d}\boldsymbol{r}' G_{\mathrm{i}}(\boldsymbol{r}, \boldsymbol{r}') f_{\mathrm{i}} \tag{A.28}$$

2. $\forall \boldsymbol{r} \in \Omega_{\mathrm{e}}$

$$u = -\hat{\mathscr{S}}_{\mathrm{e}}(\partial_{L_{\mathrm{e}}} u) + \hat{\mathscr{D}}_{\mathrm{e}}(u_{\mathrm{e}}) + \int\limits_{\Omega_{\mathrm{e}}} \mathrm{d}\boldsymbol{r}' G_{\mathrm{e}}(\boldsymbol{r}, \boldsymbol{r}') f_{\mathrm{e}} \tag{A.29}$$

3. $\forall \boldsymbol{r} \in \Gamma$

$$\frac{1}{2} u_{\mathrm{i}} = \hat{\mathscr{S}}_{\mathrm{i}}(\partial_{L_{\mathrm{i}}} u) - \hat{\mathscr{D}}_{\mathrm{i}}(u_{\mathrm{i}}) + \int\limits_{\Omega_{\mathrm{i}}} \mathrm{d}\boldsymbol{r}' G_{\mathrm{i}}(\boldsymbol{r}, \boldsymbol{r}') f_{\mathrm{i}} \tag{A.30}$$

4. $\forall \boldsymbol{r} \in \Gamma$

$$\frac{1}{2} u_{\mathrm{e}} = -\hat{\mathscr{S}}_{\mathrm{e}}(\partial_{L_{\mathrm{e}}} u) + \hat{\mathscr{D}}_{\mathrm{e}}(u_{\mathrm{e}}) + \int\limits_{\Omega_{\mathrm{e}}} \mathrm{d}\boldsymbol{r}' G_{\mathrm{e}}(\boldsymbol{r}, \boldsymbol{r}') f_{\mathrm{e}} \tag{A.31}$$

We introduce the following auxiliary potential:

$$h(\boldsymbol{r}) = \begin{cases} \int\limits_{\mathbb{R}^3} \mathrm{d}\boldsymbol{r}' G_{\mathrm{i}}(\boldsymbol{r}, \boldsymbol{r}') \rho_{\mathrm{i}}(\boldsymbol{r}') \quad \boldsymbol{r} \in \Omega_{\mathrm{i}} & \text{(A.32a)} \\ \int\limits_{\mathbb{R}^3} \mathrm{d}\boldsymbol{r}' G_{\mathrm{e}}(\boldsymbol{r}, \boldsymbol{r}') \rho_{\mathrm{i}}(\boldsymbol{r}') \quad \boldsymbol{r} \in \Omega_{\mathrm{e}} & \text{(A.32b)} \end{cases}$$

for which we have:

$$\begin{cases} \nabla^2 h = \rho_{\mathrm{i}} \text{ in } \Omega_{\mathrm{i}} & \text{(A.33a)} \\ L_{\mathrm{e}} h = 0 \text{ in } \Omega_{\mathrm{e}} & \text{(A.33b)} \end{cases}$$

We then define the *reaction potential* as:

$$\xi = u - h \tag{A.34}$$

such that:

$$\begin{cases} \nabla^2 \xi = 0 \text{ in } \Omega_\mathrm{i} & \text{(A.35a)} \\ L_\mathrm{e}\xi = 0 \text{ in } \Omega_\mathrm{e} & \text{(A.35b)} \\ -[\xi] = [h] \text{ on } \Gamma & \text{(A.35c)} \\ -[\partial_L \xi] = [\partial_L h] \text{ on } \Gamma & \text{(A.35d)} \end{cases}$$

inside the cavity, the reaction potential can be represented by a *single layer potential*:

$$\xi_\mathrm{i} = \hat{\mathscr{S}}_\mathrm{i}\sigma \tag{A.36}$$

where the function σ is the, yet unknown, apparent surface charge.

To derive an equation for σ, we set up a system of equations containing the jump conditions and the integral representations of the reaction and auxiliary potentials:

$$\begin{cases} \hat{\mathscr{S}}_\mathrm{i}(\partial_{L_\mathrm{i}}\xi) - \hat{\mathscr{D}}_\mathrm{i}(\xi_\mathrm{i}) = \frac{1}{2}\xi_\mathrm{i} & \text{(A.37a)} \\ \hat{\mathscr{S}}_\mathrm{e}(\partial_{L_\mathrm{e}}\xi) - \hat{\mathscr{D}}_\mathrm{e}(\xi_\mathrm{e}) = -\frac{1}{2}\xi_\mathrm{e} & \text{(A.37b)} \\ \hat{\mathscr{S}}_\mathrm{e}(\partial_{L_\mathrm{e}}h) - \hat{\mathscr{D}}_\mathrm{e}(h_\mathrm{e}) = -\frac{1}{2}h_\mathrm{e} & \text{(A.37c)} \\ \xi_\mathrm{i} - \xi_\mathrm{e} = h_\mathrm{e} - h_\mathrm{i} & \text{(A.37d)} \\ \partial_{L_\mathrm{i}}\xi - \partial_{L_\mathrm{e}}\xi = \partial_{L_\mathrm{e}}h - \partial_{L_\mathrm{i}}h & \text{(A.37e)} \end{cases}$$

The final ingredient is the Dirichlet-to-Neumann (DtN) map, which can be derived by employing Eq. (A.30) to the Newton potential:

$$\phi(\boldsymbol{r}) = (\hat{\mathscr{N}}\rho_\mathrm{i})(\boldsymbol{r}) = \int_{\mathbb{R}^3} \mathrm{d}\boldsymbol{r}' G_\mathrm{i}(\boldsymbol{r},\boldsymbol{r}')\rho_\mathrm{i}(\boldsymbol{r}') = h(\boldsymbol{r})|_{\Omega_\mathrm{i}} \tag{A.38}$$

which is equal, in Ω_i, to the auxiliary potential $h(\boldsymbol{r})$. The DtN map is thus given as:

$$\left(\frac{1}{2} - \hat{\mathscr{D}}_\mathrm{i}\right)\phi_\mathrm{i} + \hat{\mathscr{S}}_\mathrm{i}(\partial_{L_\mathrm{i}}\phi) = 0 \tag{A.39}$$

With this last ingredient at hand, algebraic manipulations lead to the IEF equation:

$$\begin{aligned}\left[\hat{\mathscr{S}}_\mathrm{e}\left(2\pi + \hat{\mathscr{D}}_\mathrm{i}^\dagger\right) + \left(2\pi - \hat{\mathscr{D}}_\mathrm{e}\right)\hat{\mathscr{S}}_\mathrm{i}\right]\sigma = \\ -\left[\left(2\pi - \hat{\mathscr{D}}_\mathrm{e}\right) - \hat{\mathscr{S}}_\mathrm{e}\hat{\mathscr{S}}_\mathrm{i}^{-1}\left(2\pi - \hat{\mathscr{D}}_\mathrm{i}\right)\right]\varphi,\end{aligned}$$

(2.7 from Chapter 2)

A.5 WEAK FORMULATION OF PARTIAL DIFFERENTIAL EQUATIONS

The transmission problem can be reformulated in a variational fashion. Such a formulation allows for a larger vector space, with weaker regularity conditions, to be explored as solution space for the problem. We will follow the exposition of Ern et al. quite closely in introducing the *weak* formulation of PDE. For simplicity, we assume Dirichlet boundary conditions for a conductor, *i. e.* the basic assumption behind COSMO. The *strong* formulation of the electrostatic problem then reads:

$$\nabla^2\varphi = -4\pi\rho, \quad \varphi \in \mathscr{C}_0^2(\Omega_\mathrm{i}), \tag{A.40}$$

where $\mathscr{C}_0^2(\Omega_\mathrm{i})$ is the vector space of twice continuously differentiable functions in Ω_i with null trace on Γ. We can relax this regularity requirement on Ψ by introducing the *Hilbert Sobolev space* of test functions $H_0^1(\Omega_\mathrm{i})$:

$$H_0^1(\Omega_\mathrm{i}) = \{f : \Omega_\mathrm{i} \to \mathbb{R} | f, \nabla f \in L^2(\Omega_\mathrm{i}), f_\Gamma = 0\}. \tag{A.41}$$

Projecting the differential problem onto this space and using the $\eta\nabla^2\gamma = \nabla\cdot(\eta\nabla\gamma) - \nabla\eta\cdot\nabla\gamma$ identity one obtains the *weak* formulation of the differential problem:

$$\begin{cases}\text{Seek } \Psi \in H_0^1(\Omega_\mathrm{i}) \text{ such that:} \\ (\nabla\zeta, \nabla\Psi) = -4\pi(\zeta, \rho) \quad \forall\zeta \in H_0^1(\Omega_\mathrm{i})\end{cases} \tag{A.42}$$

The form $(\nabla\cdot, \nabla\cdot)$ is *bilinear* and continuous in $H_0^1(\Omega_\mathrm{i}) \times H_0^1(\Omega_\mathrm{i})$, while $-4\pi(\cdot, \rho)$ is *linear* and continuous in $H_0^1(\Omega_\mathrm{i})$. We rewrite Eq. (A.42) in the abstract form:

$$\begin{cases} \text{Seek } u \in V \text{ such that:} \\ \forall v \in V \quad a(u, v) = b(v) \end{cases} \tag{A.22}$$

and state the following fundamental results:

Lemma 5 (Lax–Milgram). *If the bilinear form a is continous and coercive in V, then, for any continuous linear form b, Problem* (A.22) *is well-posed.*

Corollary (Variational property). *If the bilinear form is symmetric and positive the unique solution to Problem* (A.22) *is the unique minimum on V of the functional:*

$$\mathscr{F}(u) = \frac{1}{2} a(u, u) - b(u)$$

It is important to note how BIEs can also be reformulated in a variational framework, as shown in ref. 158

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Paper I

Four-Component Relativistic Calculations in Solution with the Polarizable Continuum Model of Solvation: Theory, Implementation, and Application to the Group 16 Dihydrides H_2X (X = O, S, Se, Te, Po)

R. Di Remigio, R. Bast, L. Frediani, and T. Saue

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Paper II

Wavelet Formulation of the Polarizable Continuum Model. II. Use of Piecewise Bilinear Boundary Elements
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Paper III

A Polarizable Continuum Model for Molecules at Spherical Diffuse Interfaces

R. Di Remigio, K. Mozgawa, H. Cao, V. Weijo, and L. Frediani

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Paper IV

Four-Component Relativistic Density Functional Theory with the Polarizable Continuum Model: Application to EPR Parameters and Paramagnetic NMR Shifts

R. Di Remigio, M. Repisky, S. Komorovsky, P. Hrobarik, L. Frediani, and K. Ruud

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Paper V

Open-Ended Formulation of Self-Consistent Field Response Theory with the Polarizable Continuum Model for Solvation

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