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OVERVIEW

Learning from the past: a personal view on the perspectives of quantum computational chemistry

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Abstract A short exposition of activities in theoretical chemistry performed in Pisa in the past years is given here. The exposition is based on summaries of critical evaluations I did in the years. These summaries intend to show the influence Salvetti has had on my scientific formation and also testimony on the evolution of quantum and computational chemistry in Pisa and in parallel in the whole discipline. This series of evaluations have always interested Salvetti (perhaps with some influence on his activity as national coordinator of CNR research in Chemistry) and can be used now to define new research fields.

Keywords Trends of evolution in theoretical chemistry · Theoretical chemistry in Pisa · Oriano Salvetti

1 Introduction

It is a good (and recommended) practice for every scientist to periodically perform a critical evaluation of his own work, comparing it with the state of the art in his discipline and with the trends of evolution this discipline has. I adopted this practice from my first steps in theoretical chemistry and I noticed that in the progress of time these critical appraisals were requiring more and more detailed and in-depth critical analyses of the evolution of theoretical chemistry.

In the past I had several times the opportunity of expounding to Professor Salvetti the conclusions of these periodic analyses. Salvetti was professionally interested because he held for many years the public office of monitoring, promoting and supporting for CNR the national research in physical chemistry. It was a firm belief of Salvetti that physical chemistry has to play a role in all researches regarding molecular disciplines, and that quantum chemistry (which has to be considered as a part of physical chemistry) has an enormous potential, spurred by computers, with very good perspectives for the development of all molecular sciences. As I was in complete agreement with this point of view, our discussions were not debates on contrasting opinions, but exchange of information and refinements of some points.

I continued to do my critical evaluations, and it seems to me that in occasion of this special issue in honour of Oriano Salvetti I may try to renew the experience of the abovementioned expositions.

I shall make use of the material elaborated for my last evaluation, put it this time in a written form and with the addition of other information to make it understandable (and I hope of some interest) to other readers.

From these considerations some suggestions for future work are drawn.

2 Theoretical chemistry in Pisa: the beginning

The group of theoretical chemistry in Pisa was founded in 1956 by Eolo Scrocco and ruled for a very long period by Scrocco and Salvetti, with a general program envisaging a separation of tasks between the two leaders, Salvetti, called

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at Pisa a bit later, was in charge of the elaboration of ab initio computational codes, Scrocco was looking to the interpretation, as well the measurement, of molecular physical properties. Younger people were associated in the two groups [actually everybody was young, the oldest being Scrocco (40 years) followed by Salvetti (32 years)]. I was inserted in the Scrocco's group because of my preceding experience in spectroscopy (a short experience indeed: in 1956 I was 22 years old) with a view of combining IR spectroscopy and quantum mechanics. This was not a silly project because I was at that time combining measurements of the intensities of IR overtones with a formal and detailed QM treatment of the problem including the constriction of a dedicated analogue computer.

My curiosity was, however, pushing me to work on more chemical problems, the elucidation of the structure and properties of molecules isolated or interacting. At that time the results of the first ab initio calculations of molecular wave functions, regarding biatomic and the simplest triatomic molecules were published. I was confident (and Scrocco with me) that Salvetti's codes would give us within short time the possibility of extending the investigations to polyatomic molecules with methods avoiding empirical parameters and other tricks, abundant in the literature of time.

We entered so, among the firsts, in the newly established area of theoretical chemistry in the electronic computer version.

The advent of electronic computers produced in the field of theoretical chemistry a true and impressive revolution. We theoreticians were all are living in the post-revolution time, in spite of the fact that many scientists, also of eminent stature, were not fully realizing how big has been the change. Also the objectives of the discipline changed.

Theoretical research in chemistry in the old version had as main objective the interpretation of experimental findings, with the aid of simple models. Theoretical research in chemistry, in the renewed version, has as objective the description, interpretation and discovery of phenomena of chemical interest.

I stress the difference in the objectives of the two versions of theoretical chemistry; the interpretation is preserved, of course, but the description and the discovery have been added. Description means the availability of computational means able to give at the appropriate level of accuracy the information on phenomena necessary for the interpretation without to pass through experimental findings (which often give only indirect information). An appropriate level of accuracy will permit the application of the computational methods to molecular systems and to properties not yet examined with experimental methods.

At the beginning of the activity of our group in Pisa the perspective of applying this new version of theoretical chemistry was a very long shot. It was, however, the idea of quantum chemistry Scrocco and Salvetti nurtured since several years. Suffice it to look at the joint papers they published while working in Bologna [1–10]. Such papers have all a characteristic form: the elaboration of mathematical formulas for a piece of the QM description of molecules, calculations (by hand) with these formulas and application to a chemical problem. The problems were cleverly selected and the results always illuminating but the human effort was enormous. Anyway, a small group in Pisa started to work according these lines, anxiously waiting Salvetti's results on the calculation of electron interaction integrals on an electronic computer. This was not a desperate hope because an electronic computer was actually under construction at Pisa, quite probably the first in continental Europe, surely the first in Italy. This audacious initiative was spurred by a suggestion of Enrico Fermi and vigorously supported by Scrocco and the young physicists, coming, as Scrocco, from the prestigious Roma's physical school and arrived at Pisa in those years.

The small group of younger people to which I belonged started learning from Scrocco, and also from Salvetti, still in Bologna, the techniques they used to do quantum mechanical calculations by hand, well aware that with the advent of electronic computers all the numerical methods we are using were to be reformulated. Salvetti showed remarkable attitudes in this work of reformulation and we all strongly profited of his ingenuity.

We used the computer while it was in construction, starting with the first working prototype (1,024 elements of fast memory, if I remember well). It was a very good computer with numerous ingenious devices and we used it intensively, testing all the numerous ideas on what could be done with computers in molecular quantum mechanics, simulating first by hand what the computer should be done. It has been a hectic work, I will just remember a few names, Maestro, Moccia, Arrighini, myself, Guidotti, in order of age, without entering in the detail of what was done. To give just an idea, I performed by hand (with a mechanical computer) all the sequence of steps to perform a SCF calculation on a molecule in two versions, with the diagonalization of the Fock matrix and with iteration on the first order density matrix (after having computed by hand approximate values of the two-electron integrals). I recommended on the basis of this experience the use of the density matrix technique, pioneered by Roy Mc Weeny, and we used it with satisfaction until Salvetti decided that on our computer the diagonalization of the Fock matrix was preferable.

Our interests in methodology were not limited to the calculations at the SCF level. I mention here as examples the excellent work done by Maestro, Moccia and Arrighini in the elaboration of the theory and of the computational codes for electric and magnetic properties, and my efforts of describing electron correlation with the aid of perturbation theory (Moller–Plesset and Epstein–Nesbet) combined with an original version of improved virtual orbitals (IVO), but much more was done.

3 The first evaluation

This activity I have hastily resumed required some years and at towards the end of that period I did the first critical and complete evaluation I remember. The conclusions showed lights and shades.

The lights come from the scientific performances of our group. We did a very intensive collective work, gaining experience on the elaboration of the quantum theory on computers with our own forces without external support, and reaching results of considerable interest for many aspects of the molecular QM theory.

I recall here only the work done by a small subgroup coordinated by Scrocco (Bonaccorsi, Tomasi, Scrocco, starting from the youngest) being not my intention of writing a historical report on the whole activity done at Pisa.

Scrocco was not pushing for publications; it was interested in getting a better understanding on the performances of ab initio computational chemistry. Much work was done on technical aspects: extensions of the basis set, polarization functions, unconventional bases, effect of the correlation, but more creative work was done on the methods of analysis of the molecular charge distributions.

The codes for the ab initio calculation of molecular wave functions were primarily used (with success) for more precise assessments of the molecular concepts of the preceding version of the theory, and adding others concepts not considered before. Everything was done with numerical transformations of the wave function avoiding empirical elements: transformation of the electronic density into localized orbitals, their decomposition into generalized hybrids, characterization of a large variety of substructures, as dative and bent bonds, passing then to the characterization of larger chemical groups including intergroup effects both through space and through bonds, and concluding with a general picture of the molecular distribution allowing an interpretation in terms of a semiclassical description. Analogous work was done for the interaction among molecules. The work on these themes, initiated in these first years, has been continued in the following years.

The most evident shade was that we do not arrive to establish our ab initio code as a reference in the scientific literature, in spite of the fact that with this code were obtained the first ab initio descriptions of molecules with real chemical complexity (I cite as example the study of a large set of three-membered ring molecules [11, 12]), accompanied by many features (orbital localization with decomposition into atomic hybrids, electrostatic molecular potential, inner shell ionization potential, protonation effects) which had in the following years a large use.

There were several reasons for this lack of success, some specific of the case (we did in Pisa codes for Slater orbitals following the lack of confidence of Salvetti and Scrocco on Gaussian expansions) others more in general in character evidencing weaknesses of our group. The codes were in fact scarcely commented and distributed ad personam perhaps to keep control of their use. No advertising was done in congresses or in other similar occasions. No reviews or accounts were written.

Similar remarks hold for the other aspects of our activity. We have lived more than 10 years in almost complete isolation. Few guests, only for very short visits, no stays of members of our group to work in other laboratories, no use of international computing centers (they were beginning to be active in those years).

This was a situation which was rapidly deteriorating. I convinced Scrocco (and Salvetti) that there was an urgent need of changing attitude and I took a more important role in this change. The two leaders were not fluent in foreign languages (save Scrocco for French) and I began to travel for congresses, international schools, workshops and stays in other laboratories, as well as to write reviews on the subjects on which our experience was larger.

Seeing in retrospection these efforts paid well. I will not given here an account of them and I just recall an aspect related to what said above. I imported from Paris the first and fresh version of the first edition of the Gaussian code and we start to use it, after the elimination of some bugs still present in the version Hehre was elaborating. The shift from Slater to Gauss basis functions was criticized by members of our group, but the performances of Gaussian 70 were better than those of our codes, and my guess of the future success of the Gaussian code (which turned out to be right) was making it interesting for the insertion of our routines.

Our perspectives of work changed. A larger group within the Pisa team took shape, it was composed by the three already mentioned members, Scrocco, myself and Bonaccorsi, and by new entries, Petrongolo, Alagona, Ghio, Cimiraglia. This group focussed his work on a more limited number of lines of research, defining for each line a specific strategy, but with all lines (and strategies) converging on a single theme: the description and interpretation of interactions among molecules and molecular subunits subjected to physical or chemical perturbation of different nature.

The work along two lines of research, molecules and chemical interactions, including reaction mechanisms with application to biological systems, and interactions of molecules with light (photochemistry), progressed well, and after some years they were subjected to another general evaluation

4 Another evaluation

There were again lights and shades in this evaluation.

We profited of Gaussian-based codes (we used Gaussian, IBMOL, GAMESS, Monstergauss) and of the set of IBM computers replacing the home-made one and allowing so the extension of our studies over a larger variety of molecules. For the first theme we did an extensive work, starting with the introduction in the computational literature of the molecular electrostatic potential (MEP) and of his companion molecular polarization potential (MPP), combining them with partition of the molecular charge distribution into subunits based on localized orbitals. We used these concepts and the related tools to better defining other more complex chemical concepts, as polarity of the bonds, through-space and through-bonds polarizations, transferability of chemical groups (with a description of the modifications induced by a change of molecular contest), decomposition of the non-covalent molecular interactions of polar type into contributions with a clear physical meaning, directly derived from the variational description without resorting to perturbation theory approximations. The description of excited states (computed at a low quantum level) was analyzed with the same tools, giving a rationale both for the single molecule and the non-covalent interaction perfectly fitting in the scheme defined for ground-state molecules. All the elements of the analysis were inserted into a general computational context.

Surprisingly, our codes turned out to be less rewarding in terms of citations than expected, in spite of having put them in two computational platforms (Monstergauss and GAMESS) and having made freely available the Gaussian and IBMOL versions of the subroutines. Actually there has been interest in the scientific community and many of our ideas permeated in the panoply of used computational tools, especially in the field of biological chemistry where the basic concepts of so-called semiclassical approximation were widely adopted. There are in fact several important basic mechanisms in biological chemistry (as for example the molecular recognition) which are ruled in a first good approximation by the simple electrostatic interactions, the leading term being the rigid Coulomb interaction, easy to compute without approximations making use of the electrostatic molecular potential. The MEP was considered to be the most important single advance in 40 years of molecular biology [13]. The reason of this relative lack of success was due in my opinion to the fact of having not produced an all-containing program, well-documented and allowing an immediate use of these computational features; the subroutines amply spread were used by others, generally without mentioning the source. There were also other reasons; one was obviated by the intervention of Salvetti who after a discussion about a my evaluation bought us the at that time most up-to-date graphical station (Evans–Sutherland) which was amply later used by our subgroup and by others in Pisa working on biological and organic problems.

The solution would have been to write this all-containing program but this was presenting other problems. The evolution of quantum chemistry was leading to give more emphasis on the description of electron correlation effects while our programs were conceived, documented and tested to the Hartree–Fock level. Almost nobody in our group wish to repeat the efforts spent in the preceding years in assessing the model (with the perspective of having troubles to do it, without acquiring much new insight).

The result of the discussions about this appraisal was that our group was divided into sub-groups: Cimiraglia and Persico working most on excited states and electron correlation; Petrongolo first on bio-organic problems keeping in charge the collaboration in act with Clementi on Monte Carlo description of solvation effects, and later, independently, on the spectroscopic properties of small molecules; Alagona and Ghio on organic and bio-organic problems; Bonaccorsi helping me in the development of the continuum solvation model. Scrocco was coordinating all the activities until his premature retirement.

It was not a strict partition, much work was done joining forces of different groups, and I kept a say in each group.

Almost all members spent longer periods in laboratories abroad. We strengthened collaborations with several laboratories abroad, in Europe and in the USA.

We had a considerable number of post-doc or graduate students, mainly from abroad (especially Spain and France, but also Germany, Denmark, Portugal, Greece); we had a number of professors spending a sabbatical year in Pisa (USA, Canada, Spain, France, SSRR) working on joint projects. Something was learned from the past.

The continuum solvation method I have just mentioned (it is now called PCM) was a natural outcome of the part of the semiclassical model regarding molecular interactions. The initial steps of the formulation of the model required several years, but with the elaboration of the first paper the perspectives of continuation were clear. Much work has been done in the following years, there is no need of resuming it here (readers are addressed to references [14] and [15, see chapter 1] for the last general presentations) but among the large number of topics for which we formulated at the beginning a preliminary working scheme there are a few for which the real work has not yet initiated (and nobody in other laboratories has done them in the meantime).

In the years following the reorganization of our group I have described, I was more and more engaged in modeling solvation effects (or, better, medium effects, because our approach applies also to other media) progressively losing the contact with the other members of the original group (who continue their work at our department in other institutions; apparently the organization we devised was robust enough).

New forces to work on the continuum model were searched. The most important contributions came from Cammi (now professor at Parma), by Mennucci (who is now in charge of the whole project) and from Barone (who at Naples built, starting from PCM, the most active group of computational chemistry in Italy), but I am obliged to many others. I cite the names of a few: Miertuš, who wrote the first PCM code [16] on the basis of the formulation jointly given by Scrocco and myself, and that gave me an essential support few years later in a critical moment: Silla in Valencia who after a long stay sent us two good students (his older coworker, Pascual-Auhir, greatly helped to get a very efficient code for the definition of the solute containing cavity [17]), Olivares del Valle in Badajoz who spent a year in Pisa as visitor doing an excellent work on some PCM topics (as electron correlation [18, 19] and molecular vibrations [20, 21], both in solution) and who introduced all his group to PCM initiating a collaboration which continues today (his older coworker, Aguilar, did an important contribution to the definition of non-equilibrium solvation effects [22]), Luque and Orozco in Barcelona who greatly extended the use of PCM mainly in the field of organic and bio-organic systems [23] and sent us a very brilliant student, Curutchet, who recently spent a few years in Pisa giving us an important contribution to the elaboration of the PCM models for the electronic energy transfer [24–26]: Ruud in Trömso with collaborations on a variety of subjects involving molecular response theories.

I have mentioned leaders of groups which have shown a permanent interest for our groups, with collaboration extended up to now. This short enumeration of people is closed with the names of some students who continues to work on this field after having acquired a position in other institutions: Cossi (Alessandria), Corni (Modena), Frediani (Tromsö), Caricato (USA).

The listing is far from being complete, but it is sufficient to show the our activity has at a good extent lost the parochial character I considered a negative factor in my preceding appraisals.

Another important contribution to reduce parochialism has been the collaboration with Gaussian. I think that my active participation to a couple of congresses and to a Gordon conference in 1996 has been at the origin of the contact with Mike Frisch and the Gaussian team. Deals were made in 1997 and the almost complete set of our programs was available in the 1998 version of Gaussian. We arrived for solvation to insert the codes on a general program of large use: the goal we failed 20 years before for the semiclassical description. The effects were immediate; among the numerous requests of help in using the program we received (which we satisfied at our best), I like to recall here that with Clarissa da Silva, who came from Brazil to make her PhD thesis in Pisa, starting a collaboration (and a friendship) which continues today [27, 28].

Our work was organized in a different way; we in Pisa (and Naples and Parma) continued our methodological work, exploring other aspects of the solvation problem according to plans suggested by our evaluation of the interest of the various problems, without bothering about commercial motivations, and sending to Gaussian the results to see if there was interest to put them in the official releases of the program.

5 A third evaluation: the evolution of theoretical chemistry

By 1996, I did another evaluation of our activities deserving a mention here. In doing it I primarily paid attention to the evaluation of theoretical chemistry at large over a long period, and comparing it with the evolution of experimental chemistry. Also in the preceding appraisals I have mentioned attention was paid to the evolution of theoretical chemistry, but in the present case this analysis suggested possible changes in my perspectives of scientific activity.

The evolution of theoretical chemistry may be described in terms of a sequence of steps, each corresponding to some appreciable changes in methods, motivations and perspectives, and also in the vocabulary. Changes that may be assimilated to the revolutions introduced by Kuhn in its analysis of the evolution of scientific disciplines [29].

The first steps in this sequence of changes (or “revolutions”) which have modulated theoretical chemistry since the beginning of the past century are well known, amply accepted and are here simply recalled.

The first revolution is related to the acknowledgment of the structure of atoms (electrons and nuclei) from which the extension to molecules was formally simple, even if not clear in the details.

The second revolution, 30 years later, is related to the advent of the QM descriptions of microscopic systems with important applications to the chemistry.

The third revolution is related to the introduction of electronic computers which opened the way to QM calculations on molecular systems.

After recalling these three revolutions, I observed the almost constant delay among them (1900, 1930, 1960) and asked if there was in 1996 a fourth revolution in act.

There was in fact evidence of changes in methods and related perspectives, in my opinion, to the success of ab initio QM methods in giving accurate descriptions of a large variety of phenomena related to isolated and interacting molecules. These successes have given origin to a sense of confidence in calculations which has spread from the community of theoreticians to the larger community of chemists involved in the actual manipulation of chemical systems. After 60 years of hard work, quantum mechanics and calculations have been accepted by the whole chemical community.

These successes have put in evidence and empirically demonstrated another aspects of ab initio calculations: their congruence. With the term congruence, I indicate the characteristics ab initio methods of improving the results by improving the parameters of the calculation without sudden and random jumps.

The congruence opened a new perspective for molecular calculations: layered, combined, hierarchical approaches, extrapolations procedures, there is a large variety of methods ultimately based on the concept of congruence, and of confidence. The success several of such methods indicates that people who plan and use these procedures are confident of keeping under control the disturbances introduced by the use of different levels in performing a given computational task.

It may be also mentioned the introduction into these combined procedures the molecular mechanics description of molecular subsystems. MM was in use since longtime as a non-QM substitute of too expensive ab initio methods, but in this stage of the evolution of computational chemistry it was legitimated as a component of complex calculations, MM descriptions make also easy the use of tools not widely used in precedence, among them I recall the even larger use of molecular graphics, also in the animated version describing nuclear motions. Computational chemistry has surely gained much in efficiency.

The changes I have here remarked regard the computational aspects of our discipline. There were also changes in the main aspect of theoretical chemistry in the preceding stages: the elaboration of more powerful theories and computational codes for the calculation of molecular wave functions, but it is evident that the drive in advances greatly reduced with the years.

The most important contribution to the molecular QM theory, the density functional theory (DFT) required more than a decade to be accepted by our community (I remark, in passing, the important contribution to the practical use of this theory given by Salvetti and his group starting from 1975 [30–33]) and even more time to arrive to stable and robust computational set-up (further efforts and new ideas were however still necessary).

Another important computational advance, the coupled cluster theory (CCT), which is less innovative in nature than DFT, required analogous times to reach maturity. DFT and CCT were becoming the standard levels for molecular calculations of higher quality, but other methods more powerful and eventually reaching at a lower computational effort the full accuracy required in these calculations were not in sight.

I inserted the considerations reported in the preceding sentences at the end of an essay written in honour of S.F. Boys, centered on the analysis of the very important contribution he gave to the rise and development of our discipline [34]. After the presentation of this essay at an electronic conference there was a large discussion by mail (65 contributions, if I remember well) on what are the elements indicating a new revolution.

At the conclusion of this open forum I remarked that a new revolution is not easy to be recognized at its very beginning, but that the most promising elements of novelty were the development of purely computational methods an the increasing attention paid to complex systems and to the use of simulations.

My personal conclusion, not explicitly said in that occasion, was that we were already working on complex systems, and that there were no reasons of changing our strategy.

6 The last evaluation

I may pass now to consider the last evaluation of our activity, done about 3 years ago. Also in this case, I paid attention to the evolution of theoretical chemistry at large. The remarks expressed in 1996 were confirmed, with new elements added to the evaluation.

The progresses in computational studies have produced a change in the main motivation of these activities. In computational chemistry, we are passed in more systematic way from studies addressing the interpretation of phenomena involving molecules to studies simulating such phenomena.

Simulations are nowadays performed in almost all types of application of computational chemistry.

Also in studies addressing the basic properties of a single molecule, the type of application which has characterized quantum chemistry for a long time, the calculations have now an implicit character of simulation; the main goal is to get a description of properties, whatever they are, equilibrium geometry, electronic transitions, molecular vibrations, etc. This remark holds also for the interactions among molecules, from the non-covalent interactions to the chemical reaction mechanisms.

In other fields the use of simulations is explicitly declared. In general these simulations regard complex systems: solutions, biopolymers and more recently complex synthetic systems. We shall later consider more in detail simulations of liquid systems, but I have to stress here the increasing importance of the study of complex systems.

In conclusion, simulations are pervading computational chemistry. This is an important change of perspective. Simulations are justified by the “confidence” on calculations I have already signaled and formal analogies with the experimental measurements performed on the real material systems. In both cases there is at the end of the study of a piece of evidence (experimental or computational) on some properties of the system which have to be later interpreted, and in both cases the methodology of interpretation is not rooted in the methods used to get such evidence. In the case of computational simulations we are losing the original motivation giving to theoretical chemists the strength to endure for decades in the effort of giving a definitive description and interpretation of phenomena occurring at the submolecular levels. It may be said that in passing to simulations theoretical chemistry has lost in rigor.

To give an interpretation of phenomena occurring in complex systems actually is a hard task and the difficulties are (partly) rooted in the original formulation of quantum mechanics. QM was defined on the basis of the analysis of isolated systems. Interactions of the system with the external world were of course considered; they are fundamental for the Copenhagen interpretation of the theory. The idealized interactions giving origin to the measurement of the property are however transient and weak, and after this interaction the systems recover itself, perhaps in another state. In the real world this is an exceptional situation: molecules are always interacting.

In computational chemistry the concept of supermolecule is often used. With a supermolecule we are again on safer formal grounds, but the problem is just shifted; we are unable to rigorously compute the properties of a single molecule within a supermolecular cluster, in other words we are formally unable to get a really accurate evaluation of the quantities for which the computational work was done. There are of course ways of partly overcome this problem, but it is not necessary to enter here into such details.

The case of the properties of a single molecule was presented here as an example, perhaps the simplest, of situations not easy to deal with standard QM.

These situations are found in all the complex systems and we pass now to examine a case of complex systems amply studied in the last years: the solutions.

There are two approaches in use for solutions: the discrete and the continuum solvent model. Both started several decades ago as a simple model: a single solute molecule surrounded by the solvent. This is a model which stems from the isolated molecule model traditionally used in quantum chemistry (with a big additional step, of course). Both approaches have largely advanced in the last decade in the definition of the condensed phase, now covering almost all the possible structures (interfaces, membranes vesicles, capillary pores, etc.) as well as of the solutes, largely extended in size and complexity.

The methods deriving from the two approaches range among the most important achievements of computational chemistry of the past years.

I will focus now my attention on the continuum approach to study solutions on which our work was done.

In the continuum model the discrete representation of the solvent molecules is replaced by a continuum distribution, and the interaction between this medium and the solute (described at the QM level) has been recently [15, see chapter 1] recast in a form based on a set of operators, symbolically indicated with $\widehat{Q}_{\mathrm{X}}(\vec{r},\vec{r}\prime)$, where the $\vec{r}$ ’s are position vectors and X stays for a specific interaction.

A large variety of interactions can be described in such a way. In the basic theory of solvation (a single solute molecule in a homogeneous medium) four $\widehat{Q}_{\mathrm{X}}$ operators are used, corresponding to the four components of the free energy interaction: cavity formation free energy, electrostatic, dispersion, repulsion solute–solvent interactions. Many other operators of this kind have been defined and used, all with a clear physical meaning, and all corresponding to the kernel of an appropriate integral equation.

The formal aspect which characterizes this approach is that with these operators we have established connections between two density distributions which can be used for the calculations without passing from the wave function. The approach is quite flexible and can be tuned in different ways; changing the nature of the two distributions, changing their spatial extent, extending the formulation in several ways (static vs. dynamic, two bodies vs. many bodies). Of particular interest is the combination of two densities obeying different statistics (fermions and bosons, fermions and classical particles). The flexibility of the approach has been thus far only partly exploited, and new applications which have been presented in two already cited publications [14, 15] have been elaborated. More will follow, but this is in the future.

We have a strong feeling of having detected a methodological approach that may be applied not only to solvation problems, but also to problems of different physical nature involving condensed phases and complex systems.

This is not the answer to the problems of applying QM to complex systems we have mentioned, but perhaps it may be of some help.

These considerations were expressed, as I have already said, 3 years ago in performing an evaluation of our activity. This activity, essentially based on solvation studies, has had thus far indisputable success; the range of applications of the method has been considerably enlarged, their use has shed new light on complex phenomena, our work has been appreciated by the chemical community. The perspectives for the immediate future are bright, with new applications under elaboration.

There was no reason for us of abandoning this approach to pass to another field, without guarantee of success.

7 The definition of a new research field

The perspective of using in other fields the integral equation techniques we elaborated and used with success for the solvation was indeed strong, and was accompanied by another consideration. We learned from our past experience that it is possible to rejuvenate old models, elaborated before the advent of quantum mechanics and since then used with minor changes. We learned that a convenient way of doing it is to start from an accurate examination of the basis of the theory and to start with some specific problems treated with new methods, not available at the time of the initial definition of the model. Generalizations and enlargements are to be defined in the progression of the work.

The field to select must be of broad interest and permitting the use of a combined variety of computational approaches to study the selected properties from the microscopic to the meso- or macroscopic level. Good candidates can be found in the family of transport phenomena, which are of very disparate physical origin bur sharing some formal (or substantial) affinities. This is not the place for an elaboration of these rather generic considerations. They will be presented in another occasion.

The only remark on this subject I would like to add is that I have strongly missed the occasion of expounding my last considerations to Salvetti and of opening a discussion with him on my future proposals. Surely he would have listened me in his usual attentive and relaxed way, giving suggestions drawn from his large experience and good sense.

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