8

INTERACTIONS IN SOLVENTS AND SOLUTIONS

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8.1 SOLVENTS AND SOLUTIONS AS ASSEMBLIES OF INTERACTING MOLECULES

A convenient starting point for the exposition of the topics collected in this chapter is given by a naïve representation of liquid systems.

According to this representation a liquid at equilibrium is considered as a large assembly of molecules undergoing incessant collisions and exchanging energy among colliding partners and among internal degrees of freedom. The particles are disordered at large scale, but often there is a local order that fades away. Solutions may be enclosed within this representation.

The collection of particles contains at least two types of molecules – those having a higher molar fraction are called the solvent – the others the solute. Collisions and exchange of energy proceed as in pure liquids, local ordering may be different, being actually dependent on the properties of the molecule on which attention is focused, and on those of the nearby molecules.

Liquids at a boundary surface require more specifications to be enclosed in the representation. There is another phase to consider which can be either a solid, another liquid, or a gas. Further specifications must be added to characterize a specific boundary system (see Section 8.8), but here it is sufficient to stress that the dynamic collision picture and the occurrence of local ordering is acceptable even for the liquid portion of a boundary.

This naïve description of liquid systems actually represents a model – the basic model to describe liquids at a local scale. As it has been here formulated, it is a classical model: use has been made of physical classical concepts, as energy, collisions (and, implicitly, classical moments), spatial ordering (i.e., distribution of elements in the space).

It is clear that the model, as formulated here, is severely incomplete. Nothing has been said about another aspect that surely has a remarkable importance even at the level of naïve representations: molecules exert mutual interactions that strongly depend on their chemical composition.

To say something more about molecular interactions, one has to pass to a quantum description.

Quantum mechanics (QM) is universally acknowledged as the appropriate theory to treat material systems at the level of phenomena of interest to chemistry. Therefore quantum mechanics is the legitimate theory level at which to treat liquids.

We recall here the opening statement of a famous book on quantum chemistry:[1] "In so far as quantum mechanics is correct, chemical questions are problems in applied mathematics." Actually, the mathematics to apply to liquid systems is a hard nut to crack. Fortunately a sequence of many, but reasonable, approximations can be introduced. We shall consider and exploit them in the following section of this chapter.

It is important to stress one point before beginning. The naïve picture we have summarized can be recovered without much difficulty in the quantum formulation. This will be a semiclassical model: the identity of the constituting particle is preserved; their motions, as well as those of nuclei within each molecule, are treated as in classical mechanics: the quantum methods add the necessary details to describe interactions. This semiclassical quantum description can be extended to treat problems going beyond the possibilities of purely classical models, as, for example, to describe chemical reactions and chemical equilibria in solution. The limits between the classical and quantum parts of the model are quite flexible, and one may shift them in favor of the quantum part of the model to treat some specific phenomenon, or in favor of the classical part, to make the description of larger classes of phenomena faster.

We shall enter into more details later. It is sufficient here to underline that the choice of using a quantum approach as reference is not a caprice of theoreticians: it makes descriptions (and predictions) safer and, eventually, simpler.

We shall start with the introduction of some basic simplifications in the quantum model.

8.2 BASIC SIMPLIFICATIONS OF THE QUANTUM MODEL

The quantum mechanical description of a material system is obtained as solution of the pertinent Schrödinger equations.

The first Schrödinger equation is the famous equation everybody knows:

$$H(x)\Psi(x) = E\Psi(x) \qquad [8.1]$$

The function $\Psi(x)$ describes the "state of the system" (there are many states for each system). It explicitly depends on a set of variables, collectively called x, that are the coordinates of the particles constituting the system (electrons and nuclei). E is a number, obtained by solving the equation, which corresponds to the energy of the system in that state. H(x), called Hamiltonian, technically is an operator (i.e., a mathematical construct acting on the function placed at its right to give another function). Eq. [8.1] is an eigenvalue function: among the infinite number of possible functions depending on the variables x, only a few have the notable property of giving, when H(x) is applied to them, exactly the same function, multiplied by a number. To solve eq. [8.1] means to find such functions.

The first step in the sequence of operations necessary to reach a description of properties of the system is to give an explicit formulation of the Hamiltonian. This is not a difficult task; often its formulation is immediate. The problems of "applied mathematics" are related to the solution of the equation, not to the formulation of H.

The second Schrödinger equation adds more details. It reads:

$$i\hbar \frac{\partial}{\partial t}\Psi(x,t) = H\Psi(x,t) \qquad [8.2]$$

In practice, it expresses how the state $\Psi(x)$ of the system evolves in time (i.e., it gives $\partial\Psi(x)/\partial t$ when $\Psi(x)$ is known).

Note that in eq. [8.1] the time t was not included among the parameters defining H (and Ψ): with eq. [8.1] we are looking at stationary states, not depending on time. In spite of this, eq. [8.1] may be applied to liquids, which are characterized by a continuous dynamic exchange of energy through collisions, and by a continuous displacement of the constituting molecules. This is not a problem for the use of the time independent formulation of the Schrödinger equation for liquids: eq. [8.1] actually includes kinetic energy and all related dynamic aspects. A direct use of eq. [8.1] for liquids means to treat liquids at equilibrium. We shall not make explicit use of the second equation, even when the nonequilibrium problem is considered; the use of the semiclassical approximation permits us to treat time dependent phenomena at the classical level, simpler to use.

Let us come back to the expression of H(x). The number of parameters within (x) is exceedingly large if the system is a liquid. Fortunately, things may be simplified by using factorization techniques.

When a system contains two subsystems (say A and B) that do not interact, the Hamiltonian can be partitioned so:

$$H(x) = H_A(x_A) + H_B(x_B) \qquad [8.3]$$

This rigorously leads to a factorization of Ψ:

$$\Psi(x) = \Psi_A(x_A) + \Psi_B(x_B) \qquad [8.4]$$

and to a partition of the energy:

$$E = E_A + E_B \qquad [8.5]$$

Equation [8.1] is in consequence transformed, without simplifications, into two simpler equations:

$$H_A(x_A)\Psi_A(x_A) = E_A\Psi_A(x_A) \qquad [8.6a]$$

$$H_B(x_B)\Psi_B(x_B) = E_B\Psi_B(x_B) \qquad [8.6b]$$

In practice, there are always interactions between A and B. The Hamiltonian may always be written as:

$$H(x) = H_A(x_A) + H_B(x_B) + H_{AB}(x) \qquad [8.7]$$

The relative magnitude of the coupling term permits us to distinguish among three notable cases.

1) If the coupling term is very small, it may be neglected, coming back to equations [8.6].

2) If it is small but not negligible, it may be used to correct the solutions given by equations [8.6] with the use of appropriate mathematical tools: the factorized formulation with corrections continues to be simpler than the original one.

3) There are cases in which this factorization is profitably used, in spite of the fact that interactions between particles of A and B are of the same magnitude of interactions within both A and B.

We shall now briefly introduce two factorizations of the last type that are of paramount importance in molecular quantum chemistry, then consider other factorizations of direct interest for the description of liquid systems.

The first factorization we are introducing regards the electronic and nuclear coordinates (called r and R respectively) of the same system: $H(x) = H^e(r) + H^n(R)$. It is clear that the electrostatic interaction between two electrons (and between two nuclei) within a given molecule is of the same magnitude as that concerning a couple electron-nucleus. In spite of this, the factorization is performed, with a tremendous effect on the evolution of quantum chemistry. Its physical justification rests on the very different masses nuclei and electrons have, and therefore on their velocities. It is often called Born-Oppenheimer (BO) approximation and in the following we shall use this acronym. The BO approximation makes possible the introduction of the concept of potential energy surface (PES), a very useful model to describe the motion of nuclei (often in the semiclassical approximation) taking into account the interactions with the quantum description of the electrons.

Some more details can be useful in the following. To apply this factorization it is imperative to follow a given order. First, to solve the electronic equation with $H^e(R)$ at a fixed geometry of nuclei: the output is a wave function and an energy both parametrically dependent on the nuclear geometry R given as input: $\Psi^e(r;R)$ and $E^e(R)$ (actually there will be a set of electronic states, each with its energy). Second, to repeat the same calculations at different nuclear geometries R', many times, until a sufficiently detailed description of the function $E^e(R)$ is reached. $E^e(R)$ is the PES we have mentioned: it may be used to define the potential operator within the nuclear Hamiltonian $H^n(R)$ and then to compute vibrational and rotational states (another factorization is here introduced) or used in a semiclassical way to study the effect of nuclear motions.

The second factorization we are introducing regards the electronic part of the system (after the BO factorization). The main procedure in use leads to factorization into many separate parts, each regarding one electron only:

$$H^e(r) = \sum_i^{elec} h_i(r_i)$$

Here again the coupling terms are of the same order of magnitude as the interactions left within each one-electron Hamiltonian (that explicitly regards the electrostatic interaction of the electron with all the nuclei of the systems, placed at fixed positions). The trick allowing this factorization consists in introducing within each one-electron Hamiltonian (the symmetry of electrons makes them all equal) an averaged description of the couplings, based on the yet unknown wave functions of the other electrons. The calculation proceeds iteratively: starting from a first guess of the averaged interaction, the description is progressively refined using intermediate values of the one-electron wave functions. The final output is a $\Psi^e(r;R)$ expressed as an (anti)symmetrized product of the correct number of one-electron wave functions. Each electronic state will be described by its specific collection of such one-electron wave functions, called molecular orbitals (MO). The whole procedure is called SCF (self-consistent field), a name that reminds us of the technique in use, or HF (Hartree-Fock) to honor scientists working in its elaboration.

This partition is the second cornerstone of molecular quantum chemistry. Almost all QM molecular calculations use the SCF theory (passing then, when necessary, to a higher level of the molecular QM theory). The concepts of MOs and of orbital energies derive from this one-electron factorization.

In the following we shall make little explicit use of the two factorizations we have here examined, because we shall not enter into too technical details about how to obtain accurate molecular interaction potentials. They will be always in the background, however, and some concepts exposed here will be recalled when necessary.

The last factorization we have anticipated in the introduction regards systems composed by many molecules, as molecular crystals, clusters and liquids.

A factorization of a liquid into molecular subunits was implicit in the naïve model we have used in the introduction. The interactions within a molecule surely are larger than those among molecules; however, we cannot neglect these couplings, which are essential to describe a liquid. This is the main subject of this chapter and will be treated with due attention in the following sections.

To complete this preliminary overview, we stress that the factorization techniques are quite flexible and that they may be applied at different levels. One among them deserves mention, because it will be used in the following.

In the study of liquid systems there are several reasons to put more attention to a limited portion of the liquid, with the remainder of the liquid systems treated at a lower level of accuracy. We shall call the descriptions in which there is a portion of the whole system considered as the main component (called M) "focused models" while the remainder (called S) plays a supplementary or assisting role. In such an approximation, the Hamiltonian is partitioned in the following way:

$$H(x) = H_M(x_M) + H_S(x_S) + H_{MS}(x) \qquad [8.8]$$

Focused models are used to study local properties in pure liquids, solutions, and interfaces. The largest use is to study solvation effects and reactions in solutions. In these cases M is composed of a solute supplemented by a solvation cluster (also a single solute molecule may be used). In these models the more detailed description of M is ensured by using the BO approximation, followed by a MO-based description of the electronic structure (there are also methods that replace the QM description of the electronic structure with some simpler semiclassical model). The S components are generally described with the aid of the intermolecular potentials we shall examine in the following sections. The description of the coupling takes into account the nature of the description chosen for both M and S.

Focused models may also be used to get more detailed information on the structure of liquids, being in principle more accurate than descriptions solely based on intermolecular potentials. The computational cost is higher, of course, and this approach is now used only at the final stage of the assessment of models of the molecular interaction potential.

8.3 CLUSTER EXPANSION

The pure ab initio approach we have summarized has never been used to determine the molecular interaction potentials. Further simplifications are generally used.

We will start considering a model in which only the main component $H_M(x_M)$ of the Hamiltonian [8.8] is considered. This means to pass from a liquid to a cluster of molecules. The presence of the molecules within M is explicitly acknowledged. Adding now the further constraint of keeping each molecule at a fixed geometry, the dimensionality of the R space is severely reduced. In fact, six coordinates for each molecule will be sufficient to define the relative position of its center of mass an its orientation with respect to an arbitrary fixed reference frame. If M is composed of n molecules, the BO coordinate space will have 3n-6 coordinates.

It is convenient to consider now the whole PES $E_M(R_m)$, not limiting our attention to the minima (that correspond to equilibrium positions). For each point R_m of the hyperspace we introduce the following cluster expansion of the energy

$$E_M(R_m) = \sum_A E_A + \frac{1}{2}\sum_A \sum_B E_{AB}(R_{AB}) + \frac{1}{6}\sum_A \sum_B \sum_C E_{ABC}(R_{ABC}) + \ldots \quad [8.9]$$

In this rather artificial (but exact) decomposition the whole energy is decomposed into the sum of the energies of the separate molecules, each at the geometry they have in the gas phase, followed by the sums of two-, three-, many-body terms. For each term of eq. [8.9] we have put in parentheses the indication of the pertinent nuclear coordinate subspace to emphasize that each dimeric interaction is defined in a 6-dimensional space (R_{AB}), each trimeric interaction over a 9-dimensional space, etc., while E_M is defined over a 3n-6 space.

The total interaction energy is defined as the difference between [8.9] and the sum of the monomers's energies:

$$\Delta E(1,2,\ldots m; R_m) = \frac{1}{2}\sum_A \sum_B E_{AB}(R_{AB}) + \frac{1}{6}\sum_A \sum_B \sum_C E_{ABC}(R_{ABC}) + \ldots \quad [8.10]$$

The convergence of this expansion is relatively fast for clusters composed by neutral molecules, less fast when there are charged species. In any case, it is not possible to interrupt the expansion to the two-body terms. This contribution gives the additive terms of the interaction energy; the other terms describe non-additive effects that in principle cannot be neglected.

It is almost compulsory to proceed step by step and to study two-body interactions first. Each couple can be considered separately.

8.4 TWO-BODY INTERACTION ENERGY: THE DIMER

The definition of a two-body potential is given by:

$$\Delta E_{AB}(R) = E_{AB}(R) - [E_A + E_B] \quad [8.11]$$

We have kept the parameter $R=R_{AB}$ to underline that this potential depends both on the relative position of the two molecules and on their mutual orientation: it is a 6-dimensional function depending on these two sets of 3 parameters each, in the following indicated,

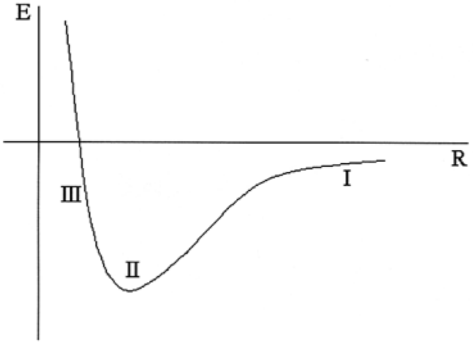

Figure 8.1. Interaction energy for a dimer with respect to the mutual approach distance at a fixed orientation.

where necessary, with r_{ab} and Ω_{ab}. $\Delta E_{AB}(R)$ has the status of a PES, with a shift in the reference energy, given here by the sum of the energies of the two monomers.

A function defined in a 6-dimensional space is hard to visualize. Many devices have been introduced to render in graphic form selected aspects of this function. Some will be used in the following: here we shall use the simplest graphical rendering, consisting in fixing an orientation (Ω_{ab}) and two coordinates in the r_{ab} set in such a way that the remaining coordinate corresponds to the mutual approach between molecule A and B, along a given straight trajectory and a fixed mutual orientation. A typical example is reported in Figure 8.1.

The energy curve may be roughly divided into three regions. Region I corresponds to large separation between interaction partners; the interaction is feeble and the curve is relatively flat. Region II corresponds to intermediate distances; the interactions are stronger compared to region I, and in the case shown in the figure, the energy (negative) reaches a minimum. This fact indicates that the interaction is binding the two molecules: we have here a dimer with stabilization energy given, in first approximation, by the minimum value of the curve. Passing at shorter distances we reach region III; here the interaction rapidly increases and there it gives origin to repulsion between the two partners. Before making more comments, a remark must be added. The shape of the interaction energy function in molecular systems is quite complex: by selecting another path of approach and/or another orientation, a completely different shape of the curve could be obtained (for example, a completely repulsive curve). This is quite easy to accept: an example will suffice. The curve of Figure 8.1 could correspond to the mutual approach of two water molecules, along a path leading to the formation of a hydrogen bond when their orientation is appropriate: by changing the orientation bringing the oxygen atoms pointing against each other, the same path will correspond to a continuously repulsive curve (see Figure 8.2 below for an even simpler example). We have to consider paths of different shape, all the paths actually, and within each path we have to consider all the three regions. To describe a liquid, we need to know weak long-range interactions as well as strong short-range repulsion at the same degree of accuracy as for the intermediate region. Studies limited to the stabilization energies of the dimers are of interest in other fields of chemical interest, such as the modeling of drugs.

The $\Delta E_{AB}(R)$ function numerically corresponds to a small fraction of the whole QM energy of the dimeric system. It would appear to be computationally safer to compute ΔE directly instead of obtaining it as a difference, as done in the formal definition [8.11]. This can be done, and indeed in some cases it is done, but experience teaches us that algorithms starting from the energies of the dimer (or of the cluster) and of the monomers are simpler and eventually more accurate. The approaches making use of this difference can be designed as variational approaches, the others directly aiming at ΔE are called perturbation approaches, because use is made of the QM perturbation theory. We shall pay more attention, here below on the variational approach, then adding the basic elements of the perturbation theory approach.

8.4.1 DECOMPOSITION OF THE INTERACTION ENERGY OF A DIMER: VARIATIONAL APPROACH

Coming back to Figure 8.1, its shape exhibiting a minimum makes it manifest that there are several types of interactions at work, with different signs and with different distance decays (at infinity all interactions go to zero). This subject has been amply studied and the main conclusions (there are details differing in the various schemes of interaction energy decomposition) are so widely known and intuitive that we feel authorized to introduce them here before giving a formal definition (that will be considered later). In Table 8.1 we report the names of these components of the interaction energy.

Table 8.1. The main components of the bimolecular interactions $\Delta E_{AB}(R)$

Component name	Acronym	Physical Meaning
Electrostatic	ES	Coulomb interactions between rigid charge distributions
Induction	IND	Mutual electrostatic deformation of the two charge distributions
Exchange	EX	Quantum effect due to the Pauli exclusion principle
Dispersion	DIS	Interactions among fluctuations in the charge distributions of the two partners
Charge transfer	CT	Transfer of electrons between partners

All components of $\Delta E_{AB}(R)$ are present in all points of the R_{AB} 6-dimensional space we have introduced. It is convenient to examine them separately. We shall make references to a single decomposition scheme[2] that we consider more convenient. Reference to other schemes will be done when necessary. Another view of methods may be found in Tomasi et al.[3]

The electrostatic term

The ES term may be positive or negative: the shape of the ES(R) function strongly depends on the electric characteristics of the partners. If both molecules are reduced to dipoles, we have the two extreme situations (see Figure 8.2) which give rise to repulsive (i.e., positive) and attractive (i.e., negative) electrostatic contributions to ΔE_{AB}, respectively. With different orientations of the two dipoles there will be different values of ES that in this simple case can be obtained with an analytical expression:

$$ES(R,\theta) = -2\mu_1\mu_2 \cos\theta / R^3 \qquad [8.12]$$

In more complex molecules, the ES(R) function has a complex shape that often determines the salient features of the whole $\Delta E_{AB}(R)$ function. This is the reason why in the studies of molecular recognition and molecular docking, great attention is paid to a proper representation of ES(R).

In the various methods for the decomposition of $\Delta E_{AB}(R)$ there are no differences in the definition of ES. This quantity can be easily computed with ab initio methods, and the following recipe is the speediest and more used way of doing it.

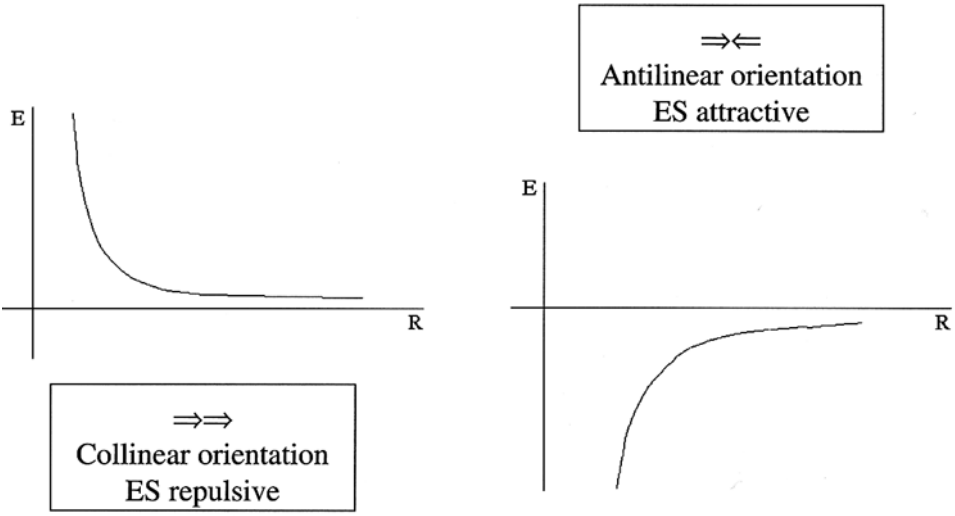

Figure 8.2. ES for two dipoles with collinear (left) and antilinear (right) orientation.

The electronic wave functions of A and B are separately computed, each with its own Hamiltonian H_A and H_B. Ab initio methods give at every level of the formulation of the theory antisymmetric electronic wave functions, satisfying the Pauli exclusion principle, on which more details will be given later.

The two antisymmetric wave functions Ψ_A and Ψ_B are then used, without modifications, in connection with the Hamiltonian of the whole system H_{AB} to get the expectation value of the energy; according to the standard notation of quantum chemistry we can write:

$$E_I = \langle \Psi_A \Psi_B | H_{AB} | \Psi_A \Psi_B \rangle \qquad [8.13]$$

It simply means the integral over the whole space of the complex conjugate of the function at the left (i.e., the function $(\Psi_A\Psi_B)^*$) multiplied by the function $H_{AB}(\Psi_A\Psi_B)$ (the application of an operator such as H_{AB} to a function always gives a function). We can neglect complex conjugates (our functions are all real); the expression given above is a compact and clear indication of a set of operations ending with an integral, and we shall use it only to speed notations.

H_{AB} differs from the sum of H_A and H_B according to the following expression

$$H_{AB} = H_A + H_B + V_{AB} \qquad [8.14]$$

V_{AB} collects terms describing electrostatic interactions between the nuclei and electrons of A with electrons and nuclei of B. The wave function Ψ_{AB} expressed as eigenfunction of H_{AB} is of course antisymmetric with respect to all the electrons, of A as well as of B, but this has not yet been introduced in the model.

The energy obtained with this recipe (the calculations are a by-product of the calculation of the dimer energy) may be so decomposed as:

$$E_I(R) = E_A + E_B + ES(R) \qquad [8.15]$$

and so:

$$ES(R) = E_I(R) - (E_A + E_B) \qquad [8.16]$$

The energies of the two monomers are already known, so the calculation of ES is immediate. Remark that in the right side of eq. [8.15] only ES depends on the geometry of the dimer, according to cluster model we are using.

The induction term

The second term of the interaction energy, IND, is always negative. IND is related to the mutual polarization of the electronic charge distributions of A and B (the nuclei are held fixed), inducing additional stabilizing effects. This induction (or polarization) energy contribution is defined in a different way in variational and perturbation theory approaches. Perturbation theory approaches are compelled to compute at the first order of the perturbation scheme only the effects due to the polarization of A with respect to the B distribution kept fixed, and in parallel the effects due to the polarization of B with A kept fixed. Mutual induction effects are introduced at higher order of the perturbation theory and have to be separated in some way from dispersion effects computed at the same time.

In the variational approach use is made of an extension of the simple technique we have used for ES.

The separation between electrons of A and B is maintained but the product $\Psi_A\Psi_B$ is now subjected to a constrained variational optimization using the Hamiltonian H_{AB}. The two wave functions are so changed, allowing the effects of mutual polarization, because of the presence of the V_{AB} term in the Hamiltonian: they will be so indicated as Ψ_A^p and Ψ_B^p.

The resulting expectation value of the energy:

$$E_{II}(R) = \left\langle \Psi_A^p \Psi_B^p \middle| H_{AB} \middle| \Psi_A^p \Psi_B^p \right\rangle \qquad [8.17]$$

may be so decomposed:

$$E_{II}(R) = E_I(R) + IND(R) \qquad [8.18]$$

and so IND(R) = E_{II}(R) - E_I(R). In this way, IND(R) contains all the mutual polarization effects.

The exchange term

The next term, EX, is positive for all the molecular systems of interest for liquids. The name makes reference to the exchange of electrons between A and B. This contribution to ΔE is sometimes called repulsion (REP) to emphasize the main effect this contribution describes. It is a true quantum mechanical effect, related to the antisymmetry of the electronic wave function of the dimer, or, if one prefers, to the Pauli exclusion principle. Actually these are two ways of expressing the same concept. Particles with a half integer value of the spin, like electrons, are subjected to the Pauli exclusion principle, which states that two particles of this type cannot be described by the same set of values of the characterizing parameters. Such particles are subjected to a special quantum version of the statistics, the Fermi-Dirac statistics, and they are called fermions. Identical fermions have to be described with an antisymmetric wave function; the opposite also holds: identical particles described by an antisymmetric wave function are fermions and satisfy the Pauli exclusion principle. Introducing these concepts in the machinery of the quantum mechanical calculations, it turns out that at each coulomb interaction between two electrons described by MOs $\phi_\mu(1)$ and $\phi_\upsilon(2)$ (the standard expression of this integral, see eq.[8.13], is: $<\phi_\mu(1)\phi_\upsilon(2)|1/r_{12}|\phi_\mu(1)\phi_\upsilon(2)>$) one has to add a second term, in which there is an exchange of the two electrons in the conjugate function: $<\phi_\upsilon(1)\phi_\mu(2)|1/r_{12}|\phi_\mu(1)\phi_\upsilon(2)>$ with a minus sign (the exchange in the label of the two electrons is a permutation of order two, bearing a sign minus in the antisymmetric case).

There are other particles, called bosons, which satisfy other quantum statistics, the Bose-Einstein statistics, and that are described by wave functions symmetric with respect to the exchange, for which the Pauli principle is not valid. We may dispense with a further consideration of bosons in this chapter.

It is clear that to consider exchange contributions to the interaction energy means to introduce the proper antisymmetrization among all the electrons of the dimer. Each monomer is independently antisymmetrized, so we only need to apply to the simple product wave functions an antisymmetrizer restricted to permutations regarding electrons of A and B at the same time: it will be called $\mathbfcal{A}_{AB}$.

By applying this operator to $\Psi_A^p\Psi_B^p$ without other changes and computing the expectation value, one obtains:

$$E_{III}(R) = \left\langle \mathbfcal{A}_{AB}\Psi_A^p\Psi_B^p \middle| H_{AB} \middle| \mathbfcal{A}_{AB}\Psi_A^p\Psi_B^p \right\rangle \quad [8.19]$$

with

$$E_{III}(R) = E_{II}(R) + EX(R) \quad [8.20]$$

and

$$EX(R) = E_{III}(R) - E_{II}(R) \quad [8.21]$$

Morokuma has done a somewhat different definition of EX: it is widely used, being inserted into the popular Kitaura-Morokuma decomposition scheme.[4] In the Morokuma definition $E_{III}(R)$ is computed as in eq. [8.19] using the original Ψ_m monomer wave functions instead of the mutually polarized Ψ_m^p ones. This means to lose, in the Morokuma definition, the coupling between polarization and antisymmetrization effects that have to be recovered later in the decomposition scheme. In addition, EX can be no longer computed as in eq. [8.20], but using E_I energy: (i.e., $EX' = E_{III}(R) - E_I(R)$). The problem of this coupling also appears in the perturbation theory schemes that are naturally inclined to use unperturbed monomeric wave functions, not including exchange of electrons between A and B: we shall come back to this subject considering the perturbation theory approach.

The charge transfer term

The charge transfer contribution CT may play an important role in some chemical processes. Intuitively, this term corresponds to the shift of some electronic charge from the occupied orbitals of a monomer to the empty orbitals of the other. In the variational decomposition schemes this effect can be separately computed by repeating the calculations on the dimer with deletion of some blocks in the Hamiltonian matrix of the system and taking then a difference of the energies (in other words: the same strategy adopted for the preceding terms, but changing the matrix blocks). In the Kitaura-Morokuma scheme CT also contains the couplings between induction and exchange effects.

We consider unnecessary to summarize the technical details; they can be found in the source paper[4] as well as in ref. [3] for the version we are resuming here.

In standard perturbation theory (PT) methods, the CT term is not considered; there are now PT methods able to evaluate it but they are rarely used in the modeling of interaction potentials for liquids.

The dispersion term

The dispersion energy contribution DIS intuitively corresponds to electrostatic interactions involving instantaneous fluctuations in the electron charge distributions of the partners: these fluctuations cancel out on the average, but their contribution to the energy is different from zero and negative for all the cases of interest for liquids. The complete theory of these stabilizing forces (by tradition, the emphasis is put on forces and not on energies, but the two quantities are related) is rather complex and based on quantum electrodynamics concepts. There is no need of using it here.

The concept of dispersion was introduced by London (1930),[5] using by far simpler arguments based on the application of the perturbation theory, as will be shown in the following subsection. A different but related interpretation puts the emphasis on the correlation in the motions of electrons.

It is worth spending some words on electron correlation.

Interactions among electrons are governed by the Coulomb law: two electrons repel each other with an energy depending on the inverse of the mutual distance: e^2/r_{ij}, where e is the charge of the electron. This means that there is correlation in the motion of electrons, each trying to be as distant as possible from the others. Using QM language, where the electron distribution is described in terms of probability functions, this means that when one electron is at position r_k in the physical space, there will be a decrease in the probability of finding a second electron near r_k, or in other words, its probability function presents a hole centered at r_k.

We have already considered similar concepts in discussing the Pauli exclusion principle and the antisymmetry of the electronic wave functions. Actually, the Pauli principle holds for particles bearing the same set of values for the characterizing quantum numbers, including spin. It says nothing about two electrons with different spin.

This fact has important consequences on the structure of the Hartree-Fock (HF) description of electrons in a molecule or in a dimer. The HF wave function and the corresponding electron distribution function take into account the correlation of motions of electrons with the same spin (there is a description of a hole in the probability, called a Fermi hole), but do not correlate motions of electrons of different spin (there is no the second component of the electron probability hole, called a Coulomb hole).

This remark is important because almost all the calculations thus far performed to get molecular interaction energies have been based on the HF procedure, which still remains the basic starting approach for all the ab initio calculations. The HF procedure gives the best definition of the molecular wave function in terms of a single antisymmetrized product of molecular orbitals (MO). To improve the HF description, one has to introduce in the calculations other antisymmetrized products obtained from the basic one by replacing one or more MOs with others (replacement of occupied MOs with virtual MOs). This is a procedure we shall see in action also in the context of the perturbation theory. At the variational level considered here, the procedure is called Configuration Interaction (CI): each configuration corresponds to one of the antisymmetrized products of MO we have introduced, including the HF one, and the coefficients in front of each component of this linear expansion of the exact (in principle) wave function are determined by applying the variational principle.

There are numerous alternative methods that introduce electron correlation in the molecular calculations at a more precise level that can be profitably used. We mention here the MC-SCF approach (the acronym means that this is a variant of HF (or SCF) procedure starting from the optimization no more of a single antisymmetric orbital product, but of many different products, or configurations), the Coupled-Cluster theory, etc., all methods based on a MO description of single-electron functions.

For readers wishing to reach a better appreciation of papers regarding the formulation of interaction potentials, we add that there is another way of introducing electron correlation effects in the calculations. It is based on the density functional theory (DFT).[6] There is a variety of DFT methods (detailed information can be found in the quoted monograph[6]); a family of these methods again makes use of MOs: they are called hybrid functional methods and give, on average, better results than other correlated methods at a lower computational cost.

The introduction of electron correlation in the description of the monomers produces changes in their charge distribution and in their propensity to be polarized. For this reason ES, IND, and EX computed with correlated wave functions are somewhat different with respect to the values obtained with the corresponding HF wave functions. The procedure sketched with equations [8.13]-[8.21] can be adapted, with some modifications, to correlated wave function using a MO basis.

The reader must be warned that here, as well as in other points of this chapter, we have simplified the discussion by omitting many details necessary for a proper handling and a fuller understanding the problem, but not essential to grasp the basic points.

What is of more practical interest here is that HF descriptions of the dimer cannot give a DIS term. This may be recovered by introducing CI descriptions of the system. The simpler CI description, now largely used in routine calculations on molecules and molecular aggregates, is called MP2. This acronym means that use has been made of a specialized version of the perturbation theory (called Møller-Plesset) limited to second order to determine the expansion coefficients.

MP2 wave functions contain elements able to give an appreciation of DIS, even if of limited accuracy. It is in fact possible to decompose MP2 values of $\Delta E_{AB}(R)$ using the strategy we have outlined for the HF case, adding to each term the appropriate MP2 correction. Each term of the decomposition is somewhat modified, because of the MP2 corrections: the remainder of the MP2 contribution can be taken as a first approximation to DIS.

There are other methods to get DIS values starting from HF wave functions, which may be more precise. Among them we quote the methods based on the response theory and on the use of dynamic polarizabilities. This powerful method has been developed during the years, and the outstanding contributions are due to McWeeny (1984) and Claverie (1986), to which reference is made for more details.[7]

The decomposition of the interaction energy through a variational approach: a summary

We have so far given a description of the elements in which $\Delta E_{AB}(R)$ may be decomposed using variational approaches. We report here the final expression:

$$\Delta E_{AB} = ES + PL + EX + CT + COUP + DIS \qquad [8.22]$$

At the HF level, all terms (but one: DIS) can be obtained with almost zero computational cost with respect to the numerical determination of ΔE_{AB}; in the HF decomposition of the interaction energy there is a small additional term (called COUP) describing further couplings between the other components, which is often left as it is obtained (i.e., as the difference between the original ΔE_{AB} value and the sum of the other four components) or subjected to further decompositions.[8] The last term, DIS, may be calculated at this level using specialistic time-dependent formulations of the HF procedure. Going beyond the HF level, the decomposition can be obtained at the MP2 level essentially using the same techniques (DIS may be appreciated by separating some of the MP2 contributions that are strictly additive).

The variational approaches we have considered are able to describe, and to decompose, the interaction energy at the level of accuracy one wishes, once the necessary computational resources are available. In fact, as we shall see later, there is no need of reaching extreme precision in the preliminary calculations to model interaction potentials for liquids, because other approximations must be introduced that will drastically reduce the accuracy of the description.

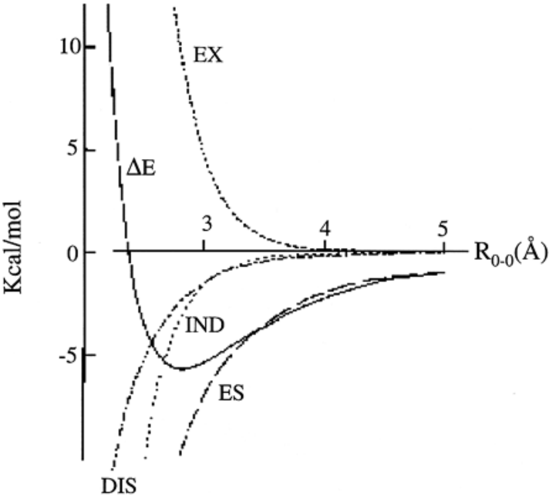

Figure 8.3. Decomposition of the interaction energy ΔE in $H_2O\cdots HOH$.

We report in Figure 8.3 as an example the decomposition of the interaction energy of the water dimer, in the same orientation Ω used in Figure 8.1.

At large distances the interaction is dominated by ES; this contribution also gives a reasonable approximation to ΔE at the equilibrium distance. The IND decays with the distance more rapidly than ES; this contribution is particularly sensitive to the quality of the expansion basis set $\{\chi\}$. Old calculations of IND using restricted basis sets are not reliable. EX is a short ranged term: its contribution is however essential to fix the position of the minimum (and to describe portion III of the PES). CT and DIS terms have both a short-range character.

This schematic analysis is valid for almost all the dimeric interactions where at least one partner has a dipolar character. The presence of a hydrogen bond (as is the case for the example given in the figure) only introduces quantitative modifications, sufficient however to show by simple visual inspection if there is a hydrogen bond or not.

Analogous trends in the decomposition of ΔE are present in the interactions involving charged-neutral species (also in the case of apolar molecules). A special case is given by the interaction of a molecule with the bare proton: in this case there is no EX contribution.

If the partners have no permanent charge, or dipole, the interaction at large-medium distances is dominated by DIS, and by EX at small values of R.

8.4.2 BASIS SET SUPERPOSITION ERROR AND COUNTERPOISE CORRECTIONS

Calculations of the interaction energies are affected by a formal error that may have important consequences on the final value of the energy and on its decomposition. We shall consider here the case of variational calculations for dimers, but the basic considerations can be extended to larger clusters and to other computational methods. The origin of the error is a non-perfect balance in the quality of the calculation of dimer energy, E_{AB} and of energies of the two monomers, E_A and E_B. In fact, there are more computational degrees of freedom available for the dimer than for each monomer separately. The number of degrees of freedom corresponds to the number of basis functions available for the optimization of the electronic structure of the molecule, and hence for the minimization of the energy. Let us consider, to clarify the concept, the case of two water molecules giving origin to a dimer; each water molecule has ten electrons, while the quality and number of expansion functions is selected at the beginning of the calculation. This is called the expansion basis set (just basis set, or BS, for brevity) and it will be indicated for the molecule A with $\{\chi_A\}$. The number of these basis functions is fixed, for example, 30 functions. The second molecule will be described by a similar basis set $\{\chi_B\}$ containing in this example expansion functions of the same quality and number as for molecule A (the two molecules are in this example of the same chemical nature). The wave function of the dimer AB and its energy will be determined in terms of the union of the two basis sets, namely $\{\chi_{AB}\} = \{\chi_A \oplus \chi_B\}$, composed of 60 functions. It is evident that it is easier to describe 20 electrons with 60 parameters than 10 electrons with 30 only. The conclusion is that the dimer is better described than the two monomers, and so the dimer energy is relatively lower than the sum of the energies of the two monomers.

This is called the basis set superposition (BSS) error. Why superposition error? When the two components of the dimer are at large distance, $\{\chi_A\}$ and $\{\chi_B\}$ are well separated, i.e., they have small superposition (or overlap), and so the relative error we are considering is modest, zero at infinity. When the two monomers are at shorter distances the superposition of the two basis sets increases (the basis functions are always centered on the pertinent nuclei) as well as the error.

There is a simple recipe to correct this error: it consists of performing all the necessary calculations with the same basis set, the dimeric basis $\{\chi_{AB}\}$ which depends on the geometry of the dimer.[9] This means that the energy of the monomers must be repeated for each position in the $\{R^6\}$ configuration space (see Section 8.4 for its definition). We add a superscript CP (counterpoise) to denote quantities modified in such a way and we also add the specification of the basis set. We replace eq. [8.11] with the following one:

$$\Delta E_{AB}^{CP}(\chi_{AB};R) = E_{AB}(\chi_{AB};R) - \left[E_A^{CP}(\chi_{AB};R) + E_B^{CP}(\chi_{AB};R)\right] \qquad [8.23]$$

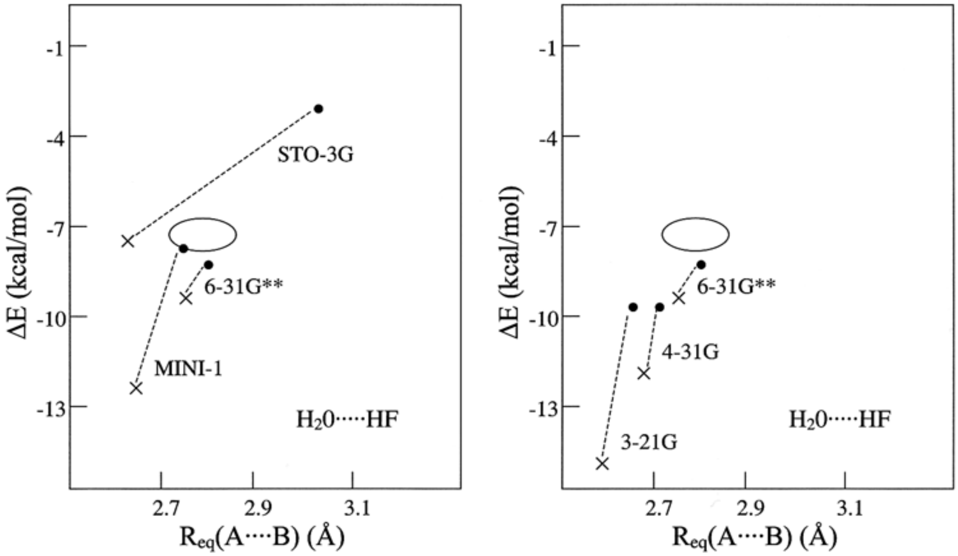

Figure 8.4. Location of the minimum energy for $H_2O\cdots HF$ dimer according to the various basis sets and the various methods. Crosses (×) refer to SCF calculations without CP corrections, full circles (●) to CP corrected calculations. The ovoidal area refer to an estimate of the location of the minimum at the HF limit (including an estimate of the error). Left side: minimal basis sets; right side: double valence-shell basis sets.

ΔE^{CP} is by far more corresponding to the exact potential energy functions in calculations performed at the HF level with a basis set of a small-medium size. Passing to calculations with larger basis sets, the BSS error is obviously smaller, but the CP correction is always beneficial.

We give in Figure 8.4 a graphical view of how CP corrections modify the equilibrium position of the dimer and, at the same time, its stabilization energy.

The same holds for calculations performed at higher levels of the QM theory, beyond the HF approximation, with decreasing effects of the CP corrections, however. We may leave this last subject to the attention of the specialists because for the determination of interaction potential for liquids, the HF approximation is in general sufficient; in some cases it may be supplemented by applying simple levels of description for electron correlation, as we have already said.

The CP corrected interaction energy may be decomposed into terms each having a definite physical meaning, in analogy with what we have exposed in the preceding subsection for ΔE without CP corrections. There are slightly different ways of doing it. We summarize here the strategy that more closely follows the physics of the problem.[10] When this correction is applied, the various terms better satisfy chemical intuition in passing from one dimer to another of different chemical composition. Each term of the ΔE decomposition is corrected with an additive term Δ^X (X stays for one of the components of the interaction energy) which is expressed as a difference in the monomers' energies computed with the opportune basis set.

Let us consider again the decomposition we have done in eq. [8.19].

The physical definition of ES (electrostatic interactions among rigid partners) clearly indicates that there is no room here for CP corrections, which would involve some shift of the monomer's charge on the ghost basis functions of the partner. This physical observation corresponds to the structure of the blocks of the Hamiltonian matrix used to compute ES: no elements regarding the BS of the partner are present in conclusion and thus no corrections to ES are possible.

In analogy, IND must be left unmodified. Physical analysis of the contribution and the structure of the blocks used for the calculation agree in suggesting it.

CP corrections must be performed on the other elements of ΔE, but here again physical considerations and the formal structure of the block partition suggest using different CP corrections for each term.

Let us introduce a partition into the BS space of each monomer and of the dimer. This partition can be introduced after the calculation of the wave function of the two monomers. At this point we know, for each monomer M (M stays for A or for B), how the complete monomer's BS is partitioned into occupied and virtual orbitals ϕ_M:

$$\{\chi_{\mathrm{M}}\}=\{\phi_M^0 \oplus \phi_M^v\} \qquad [8.24]$$

For the exchange term we proceed in the following way. The CP corrected term is expressed as the sum of the EX contribution determined as detailed above, plus a CP correction term called Δ^{EX}:

$$EX^{CP} = EX + \Delta^{EX} \qquad [8.25]$$

Δ^{EX} in turn is decomposed into two contributions:

$$\Delta^{EX} = \Delta_{\mathrm{A}}^{EX} + \Delta_B^{EX} \qquad [8.26]$$

with

$$\Delta_A^{EX} = \left[E_A(\chi_A) - E_A\left(\chi_A^{EX}\right)\right] \qquad [8.27]$$

and a similar expression for the other partner. The CP correction to EX is so related to the calculation of another energy for the monomers, performed on a basis set containing occupied MOs of A as well as of B:

$$\{\chi_A^{EX}\}=\{\phi_A^0 \oplus \phi_B^0\} \qquad [8.28]$$

We have used here as ghost basis the occupied orbitals of the second monomer, following the suggestions given by the physics of the interaction.

The other components of the interaction energy are changed in a similar way. The Δ^{X} corrections are all positive and computed with different extensions of the BS for the monomers, as detailed in Table 8.2.

Table 8.2 Explicit expressions of the Δ^X counterpoise corrections to the interaction energy components

$$\Delta_A^{EX} = \left[E_A(\chi_A) - E_A\left(\phi_A^0 \oplus \phi_B^0\right)\right]$$

$$\Delta_B^{EX} = \left[E_B(\chi_B) - E_B\left(\phi_A^0 \oplus \phi_B^0\right)\right]$$

$$\Delta_A^{CT} = \left[E_A(\chi_A) - E_A\left(\phi_A^0 \oplus \phi_B\right)\right]$$

$$\Delta_B^{CT} = \left[E_B(\chi_B) - E_B\left(\phi_B^0 \oplus \phi_A\right)\right]$$

$$\Delta_A^{TOT} = \left[E_A(\chi_A) - E_A\left(\chi_A \oplus \chi_B\right)\right]$$

$$\Delta_B^{TOT} = \left[E_B(\chi_B) - E_B\left(\chi_A \oplus \chi_B\right)\right]$$

The correction Δ^{TOT} permits to recover the full CP correction. It may be used to define the Δ^{COUP} correction:

$$\Delta^{COUP} = \Delta^{TOT} - \left(\Delta^{EX} + \Delta^{CT}\right) \qquad [8.29]$$

or the correction to the remainder, if COUP is further decomposed.[8b] This last step is of little utility for solvent-solvent interactions, but useful for stronger chemical interactions. There is no need of analyzing here these refinements of the method.

The performances of the CP corrections to the interaction energy decomposition can be appreciated in a systematic study on representative hydrogen-bond dimers.[11] A general review on the CP theory has been done by van Dujneveldt et al.[12] (who prefer to use a different decomposition).

8.4.3 PERTURBATION THEORY APPROACH

The perturbation theory (PT) approach aims at exploiting a consideration we have already expressed, namely, that ΔE is by far smaller than the sum of the energies of the separate monomers. It would be safer (and hopefully easier) to compute ΔE directly instead of getting it as difference between two large numbers. The formulation of the perturbation theory for this problem that we shall give here below has all the basic premises to satisfy this program. In practice, things are different: the introduction of other aspects in this formulation of PT, made necessary by the physics of the problem, and the examination and correction of finer details, put in evidence by the analysis of the results, make the PT approach more costly than variational calculations of comparable accuracy. Modern PT methods are competitive in accuracy with variational procedures but are rarely used at accurate levels to model potentials for liquids, the main reason being the computational cost.

In spite of this we dedicate a subsection to PT methods, because this theoretical approach shows here, as in many other problems, its unique capability of giving an interpretation of the problem. To model interactions, we need, in fact, to have a clear vision of the physical elements giving origin to the interaction, and some information about the basic mathematical behavior of such elements (behavior at large distances, etc.).

The formal perturbation theory is simple to summarize.

The theory addresses the problem of giving an approximate solution for a target system hard to solve directly, by exploiting the knowledge of a simpler (but similar) system. The target system is represented by its Hamiltonian H and by the corresponding wave function Ψ defined as solution of the corresponding Schrödinger equation (see eq. [8.1])

$$H\Psi = E\Psi \qquad [8.30]$$

The simpler unperturbed system is described in terms of a similar equation

$$H^0\Phi_0 = E_0\Phi_0 \qquad [8.31]$$

The following partition of H is then introduced

$$H = H^0 + \lambda V \qquad [8.32]$$

as well as the following expansion of the unknown wave function and energy as powers of the parameter λ:

$$\Psi = \Phi_0 + \lambda\Phi^{(1)} + \lambda^2\Phi^{(2)} + \lambda^3\Phi^{(3)} + \ldots \qquad [8.33]$$

$$E = E_0 + \lambda E^{(1)} + \lambda^2 E^{(2)} + \lambda^3 E^{(3)} + \cdots \qquad [8.34]$$

The corrections to the wave function and to the energy are obtained introducing the formal expressions [8.32]-[8.34] in the equation [8.30] and separating the terms according to their order in the power of λ. In this way one obtains a set of integro-differential equations to be separately solved. The first equation is merely the Schrödinger equation [8.31] of the simple system, supposed to be completely known. The others give, order by order, the corrections $\Phi^{(n)}$ to the wave function, and $E^{(n)}$ to the energy. These equations may be solved by exploiting the other solutions, $\Phi_1, \Phi_2, \Phi_3, \ldots, \Phi_K$, of the simpler problem [8.31], that constitute a complete basis set and are supposed to be completely known. With this approach every correction to Ψ is given as linear combination

$$\Phi^{(n)} = \sum_K C_K^n \Phi_k \qquad [8.35]$$

The coefficients are immediately defined in terms of the integrals $V_{LK} = <\Phi_L|V|\Phi_K>$ where the indexes L and K span the whole set of the eigenfunctions of the unperturbed system (including Φ_0 where necessary). The corrections to the energy follow immediately, order by order. They only depend on the V_{LK} integrals and on the energies E_1, E_2, ..., E_K, ... of the simple (unperturbed) system. The problem is so reduced to a simple summation of elements, all derived from the simpler system with the addition of a matrix containing the V_{LK} integrals.

This formulation exactly corresponds to the original problem, provided that the expansions [8.33] and [8.34] of Ψ and E converge and that these expansions are computed until convergence.

We are not interested here in examining other aspects of this theory, such as the convergence criteria, the definitions to introduce in the case of interrupted (and so approximate) expansions, or the problems of practical implementation of the method.

The MP2 wave functions we have introduced in a preceding subsection are just the application of this method to another problem, that of the electronic correlation. In this case, the simpler unperturbed system is the HF approximation, the corrections are limited to the second order, and the corresponding contributions to the energy are expressed as a simple summation of elements. The MP2 method is currently used in the PT description of the intermolecular potential:[13] in such cases, two different applications of PT are used at the same time.

We pass now to apply PT to the calculation of $\Delta E_{AB}(R)$. The most reasonable choice consists of defining the unperturbed system as the sum of the two non-interacting monomers. We thus have:

$$H^0 = H_A + H_B \qquad [8.36]$$

$$\Phi_0 = |\Psi_0^A \Psi_0^B > \qquad [8.37]$$

$$E_0 = E_0^A + E_0^B \qquad [8.38]$$

Φ_0 is the simple product of the two monomers' wave functions. The perturbation operator is the difference of the two Hamiltonians, that of the dimer and H^0. The perturbation parameter λ may be set equal to 1:

$$V = H - H^0 = V_{AB} \qquad [8.39]$$

The set $\Phi_1, \Phi_2, \Phi_3, \ldots, \Phi_K$ of the solutions of the unperturbed system can be obtained by replacing within each monomer wave function, one, two or more occupied MO with vacant MOs belonging to the same monomer. The perturbation operator V only contains one- and two-body interactions, and so, being the MOs orthonormal, the only V_{LK} integrals different from zero are those in which L and K differ at the maximum by two MOs.

The formulation is quite appealing: there is no need for repeated calculations, the decomposition of the interaction energy can be immediately obtained by separately collecting contributions corresponding to different ways of replacing occupied with virtual orbitals.

Interrupting the expansion at the second order, one obtains the following result:

$$\begin{aligned}
&\Delta E \approx E^{(1)} + E^{(2)} = \\
&\langle \Psi_A \Psi_B | V \Psi_A \Psi_B \rangle + && \text{I order: electrostatic term} \\
&-\sum_K \frac{|\langle \Psi_0^A \Psi_0^B | V \Psi_K^A \Psi_0^B \rangle|^2}{E_K^A - E_0^A} + && \text{II order: polarization of A} \\
&-\sum_K \frac{|\langle \Psi_0^A \Psi_0^B | V \Psi_0^A \Psi_K^B \rangle|^2}{E_K^B - E_0^B} + && \text{II order: polarization of B} \qquad [8.40] \\
&-\sum_K \sum_L \frac{|\langle \Psi_0^A \Psi_0^B | V \Psi_K^A \Psi_L^B \rangle|^2}{(E_K^A + E_L^B) - (E_0^A + E_0^B)} + && \text{II order: dispersion A-B + higher order terms}
\end{aligned}$$

We have here explicitly written the monomer wave functions, with a generic indication of their electronic definition: Ψ_0^A is the starting wave function of A, already indicated with Ψ_A, Ψ_K^A is another configuration for A with one or two occupied one-electron orbitals replaced by virtual MOs.

The first order contribution exactly corresponds to the definition we have done of ES with equation [8.16]: it is the Coulomb interaction between the charge distributions of A and B.

The second term of the expansion, i.e., the first element of the second order contributions, corresponds to the polarization of A, due to the fixed unperturbed charge distribution of B; the next term gives the polarization of B, due to the fixed charge distribution of A. The two terms, summed together, approximate IND. We have already commented that perturbation theory in a standard formulation cannot give IND with a unique term: further refinements regarding mutual polarization effects have to be searched at higher order of the PT expansion.

The last term of the second order contribution is interpreted as a dispersion energy contribution. The manifold of excited monomer states is limited here at single MO replacements within each monomer; the resulting energy contribution should correspond to a preliminary evaluation of DIS, with refinements coming from higher orders in the PT expansion.

Remark that in PT methods, the final value of ΔE is not available. It is not possible here to get a numerical appraisal of correction to the values obtained at a low level of the expansion. All contributions are computed separately and added together to give ΔE.

In conclusion, this PT formulation, which has different names, among which "standard" PT and RS (Rayleigh-Schrödinger) PT, gives us the same ES as in the variational methods, a uncompleted value of IND and a uncompleted appraisal of DIS: higher order PT contributions should refine both terms. One advantage with respect to the variational approach is evident: DIS appears in PT as one of the leading terms, while in variational treatments one has to do ad hoc additional calculations.

Conversely, in the RS-PT formulation CT and EX terms are not present. The absence of CT contributions is quickly explained: RS-PT works on separated monomers and CT contributions should be described by replacements of an occupied MO of A with an empty MO of B (or by an occupied MO of B with an empty MO of A), and these electronic configurations do not belong to the set of state on which the theory is based. For many years the lack of CT terms has not been considered important. The attention focused on the examination of the interaction energy of very simple systems, such as two rare gas atoms, in which CT effects are in fact of very limited importance.

The absence of EX terms, on the contrary, indicates a serious deficiency of the RS formulation, to which we have to pay more attention.

The wave function Φ_K used in the RS formulation does not fully reflect the electron permutational symmetry of the dimer: the permutations among electrons of A and B are neglected. This leads to severe inconsistencies and large errors when RS PT is applied over the whole range of distances. One has to rework the perturbation theory in the search of other approaches. The simplest way would simply replace $\Phi_0 = |\Psi_A^0 \Psi_B^0>$ with $|\boldsymbol{\mathcal{A}}_{AB}\Phi_0>$ where $\boldsymbol{\mathcal{A}}_{AB}$ is the additional antisymmetry operator we have already introduced. Unfortunately $|\boldsymbol{\mathcal{A}}_{AB}\Phi_0>$ is not an eigenfunction of H^0 as asked by the PT. Two ways of overcoming this difficulty are possible. One could abandon the natural partitioning [8.36] and define another unperturbed Hamiltonian having $|\mathcal{A}_{AB}\,\Phi_0>$ as eigenfunction. Changes in the definition of the unperturbed Hamiltonian are no rare events in the field of application of the perturbation theory and there are also other reasons suggesting a change in the definition of it in the study of dimeric interactions. This strategy has been explored with mixed success: some improvements are accompanied by the lack of well-defined meaning of the energy components when the expansion basis set grows toward completeness. A second way consists in keeping the original, and natural, definition of H^0 and in changing the PT. This is the way currently used at present: the various versions of the theory can be collected under the acronym SAPT (symmetry adapted perturbation theory)

It is worth remarking that in the first theoretical paper on the interaction between two atoms (or molecules) (Eisenschitz and London, 1930[14]) use was made of a SAPT; the problem was forgotten for about 40 years (rich, however, in activities for the PT study of weak interactions using the standard RS formulation). A renewed intense activity started at the end of the sixties, which eventually led to a unifying view of the different ways in which SAPT may be formulated. The first complete monograph is due to Arrighini[15] (1981), and now the theory can be found in many other monographs or review articles. We quote here our favorites: Claverie[16] (1976), a monumental monograph not yet giving a complete formal elaboration but rich in suggestions; Jeziorski and Kolos[17] (1982), short, clear and critical; Jeziorski et al.[13] (1994), clear and centered on the most used versions of SAPT.

SAPT theories are continuously refined and extended. Readers of this chapter surely are not interested to find here a synopsis of a very intricate subject that could be condensed into compact and elegant formulations, hard to decode, or expanded into long and complex sequences of formulas. This subject can be left to specialists, or to curious people, for which the above given references represent a good starting point.

The essential points can be summarized as follows. The introduction of the intra-monomer antisymmetry can be done at different levels of the theory. The simplest formulation is just to use $|\mathcal{A}_{AB}\Phi_0>$ as unperturbed wave function, introducing a truncated expansion of the antisymmetry operator. This means to pass from rigorous to approximate formulations.

One advantage is that the perturbation energies (see eq. [8.30]), at each order, may be written as the sum of the original RS value and of a second term related to the introduction of the exchange:

$$E^{(n)} = E^{(n)}_{RS} + E^{(n)}_{exc} \qquad [8.41]$$

The results at the lower orders can be so summarized:

$$\Delta E = \left\{ E^{(1)}_{RS} + E^{(1)}_{exc} \right\} + \left\{ E^{(2)}_{RS} + E^{(2)}_{exc} \right\} + \cdots \qquad [8.42]$$

$E^{(1)}_{exc}$ does not fully correspond to EX obtained with the variational approach. The main reason is that use has been made of an approximation of the antisymmetrizer: other contributions are shifted to higher order of the PT series. A second reason is that use has been here made of the original MOs φ_i to be contrasted with the polarized ones φ_i^p, see Section 8.4.1: for this reason there will be in the next orders contributions mixing exchange and polarization effects.

At the second order we have:

$$E^{(2)}_{exc} = E^{(2)}_{exc-dis} + E^{(2)}_{exc-ind} \qquad [8.43]$$

The partition of this second order contribution into two terms is based on the nature of the MO replacements occurring in each configuration Ψ^m_K appearing in the sums of eq. [8.40]. These two terms give a mixing of exchange and dispersion (or induction) contributions.

Passing to higher orders $E^{(n)}$ the formulas are more complex. In the RS part it is possible to define pure terms, as $E^{(3)}_{RSdis}$, but in general they are of mixed nature. The same happens for the $E^{(n)}_{exc}$ contributions.

The examination of these high order contributions is addressed in the studies of the mathematical behavior of the separate components of the PT series. Little use has so far been made of them in the actual determination of molecular interaction potentials.

8.4.4 MODELING OF THE SEPARATE COMPONENTS OF ΔE

The numerical output of variational decompositions of ΔE (supplemented by some PT decompositions) nowadays represents the main source of information to model molecular interaction potentials. In the past, this modeling was largely based on experimental data (supported by PT arguments), but the difficulty of adding new experimental data, combined with the difficulty of giving an interpretation and a decoupling of them in the cases of complex molecules, has shifted the emphasis to theoretically computed values.

The recipes for the decomposition we have done in the preceding sections are too complex to be used to study liquid systems, where there is the need of repeating the calculation of $\Delta E(r,\Omega)$ for a very large set of the six variables and for a large number of dimers. There is thus the need of extracting simpler mathematical expressions from the data on model systems. We shall examine separately the different contributions to the dimer interaction energy. As will be shown in the following pages, the basic elements for the modeling are to a good extent drawn from the PT approach.

The electrostatic term

ES may be written in the following form, completely equivalent to eq. [8.16]

$$ES = \int\int \rho^T_A(r_1)\frac{1}{r_{12}}\rho^T_B(r_2)dr_1dr_2 \qquad [8.44]$$

we have here introduced the total charge density function for the two separate monomers. The density function $\rho^T_M(r)$ is a one-electron function, which describes the distribution in the space of both electrons and nuclei. Formula [8.44] is symmetric both in A and B, as well as in r_1 and r_2.

It is often convenient to decompose the double integration given in eq. [8.44] in the following way

$$ES = \int \rho^T_A(r_1)V_B(r_1)dr_1 \qquad [8.45]$$

where

$$V_B(r_1) = \int \rho^T_B(r_2)\frac{1}{r_{12}}dr_2 \qquad [8.46]$$

$V_B(r_1)$ is the electrostatic potential of molecule B (often called MEP or MESP, according to the authors[3,18,19]). This a true molecular quantity, not depending on interactions, and it is often used to look at local details of the electrostatic interactions between molecules as required, for example, in chemical reactivity and molecular docking problems.

To model simplified expressions of the intermolecular potential the direct use of eq. [8.45] does not introduce significant improvements. The MEP, however, may be used in two ways. We consider here the first, consisting of defining, and using, a multipolar expansion of it. The theory of multipolar expansion is reported in all the textbooks on electrostatics and on molecular interactions, as well as in many papers, using widely different formalisms. It can be used to separately expand ρ_A, ρ_B, and $1/r_{12}$ of eq. [8.44] or V_B and ρ_A of eq. [8.45]. We adopt here the second choice. The multipolar expansion of $V_B(r_1)$ may be so expressed:

$$V_B(r_1) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} M_{l,m}^{B} R^{-(l+1)} Y_l^m(\theta, \varphi) \qquad [8.47]$$

It is a Taylor expansion in powers of the distance R from the expansion center. There are negative powers of R only, because this expansion is conceived for points lying outside a sphere containing all the elements of the charge distribution.

The other elements of [8.47] are the harmonic spherical functions Y_l^m and the multipole elements $M_{l,m}^B$ which have values specific for the molecule:

$$M_{l,m}^{B} = \left(\frac{4\pi}{2l+1}\right) \int r^l Y_l^m(\theta, \varphi) \rho_B(r) d^3r = \left\langle \Psi_B \middle| M_l^m \Psi_B \right\rangle \qquad [8.48]$$

The spherical harmonics are quite appropriate to express the explicit orientational dependence of the interaction, but in the chemical practice it is customary to introduce a linear transformation of the complex spherical functions Y_l^m into real functions expressed over Cartesian coordinates, which are easier to visualize. In Table 8.3 we report the expressions of the multipole moments.

Table 8.3. Multipole moments expressed with the aid of real Cartesian harmonics

M_0	1 element	Charge	Q
M_1^m	3 elements	Dipole	μ_x, μ_y, μ_z
M_2^m	5 elements	Quadrupole	θ_{xy}, θ_{xz}, θ_{yz}, $\theta_{x^2-y^2}$, θ_{z^2}
M_3^m	7 elements	Octupole	ω_{xxy}, etc.

The leading parameter is l, which defines the 2^l poles. They are, in order, the monopole (l=0, a single element corresponding to the net molecular charge), the dipole (l=1, three elements, corresponding to the 3 components of this vector), the quadrupole (l=2, five components, corresponding to the 5 distinct elements of this first rank tensor), the octupole, etc. We have replaced the potential given by the diffuse and detailed charge distribution ρ_B with that of a point charge, plus a point dipole, plus a point quadrupole, etc., placed all at the expansion center. Note that the potential of the 2^l pole is proportional to $r^{-(l+1)}$. This means that the potential of the dipole decreases faster than that of the monopole, the quadrupole faster than that of the dipole, and so on.

To get the electrostatic interaction energy, the multipolar expansion of the potential $V_B(r)$ is multiplied by a multipolar expansion of $\rho_A(r)$. The result is:

$$ES \approx \sum_{l=0}^{\infty} \sum_{l'=0}^{\infty} D_{ll'} R^{-(l+l'+1)} \quad [8.49]$$

where

$$D_{ll'} = \sum_{m=-l}^{l} C_{ll'}^{m} M_{lm}^{A} M_{l'm}^{B} \quad [8.50]$$

is the interaction energy of the permanent dipole l of A with the permanent dipole l' of B ($C_{ll'}^{m}$ is a numerical coefficient depending only on l, l', and m).

The calculation of ES via eq. [8.49] is much faster than through eq. [8.44]: the integrations are done once, to fix the M_{lm}^{X} molecular multipole values and then used to define the whole ES(R) surface.

For small size and almost spherical molecules, the convergence is fast and the expansion may be interrupted at a low order: it is thus possible to use experimental values of the net charge and of the dipole moment (better if supplemented by the quadrupole, if available) to get a reasonable description of ES at low computational cost and without QM calculations.

We have, however, put a $\approx$ symbol instead of $=$ in eq. [8.49] to highlight a limitation of this expansion. To analyze this problem, it is convenient to go back to the MEP.

Expansion [8.47] has the correct asymptotic behavior: when the number of terms of a truncated expression is kept fixed, the description improves at large distances from the expansion center. The expansion is also convergent at large values of R: this remark is not a pleonasm, because for multipole expansions of other terms of the interaction energy (as for example the dispersion and induction terms), the convergence is not ensured.

Convergence and asymptoticity are not sufficient, because the expansion theorem holds (as we have already remarked) for points r lying outside a sphere containing all the elements of the charge distribution. At the QM level this condition is never fulfilled because each $\rho(r)$ fades exponentially to zero when $r \to \infty$. This is not a serious problem for the use of multipole expansions if the two molecules are far apart, and it simply reduces a little the quality of the results if almost spherical molecules are at close contact. More important are the expansion limitations when one, or both, molecules have a large and irregular shape. At strict contact a part of one molecule may be inserted into a crevice of the partner, within its nominal expansion sphere. For large molecules at close contact a systematic enlargement of the truncated expression may lead to use high value multipoles (apparent indication of slow convergence) with disastrously unphysical results (real demonstration of the lack of convergence).

The introduction of correction terms to the multipolar expansions of V_B or of ES, acting at short distances and called “penetration terms”, has been done for formal studies of this problem but it is not used in practical applications.

For larger molecules it is necessary to pass to many-center multipole expansions. The formalism is the same as above, but now the expansion regards a portion of the molecule, for which the radius of the encircling sphere is smaller than that of the whole molecule. Here it is no longer possible to use experimental multipoles. One has to pass to QM calculations supplemented by a suitable procedure of partition of the molecule into fragments (this operation is necessary to define the fragmental definition of multipoles with an analog of eq. [8.42]). There are many approaches to define such partitions of the molecular charge distribution and the ensuing multipole expansions: for a review see, e.g., Tomasi et al.[20]

It is important to remark here that such local expansions may have a charge term even if the molecule has no net charge (with these expansions the sum of the local charges must be equal to the total charge of the molecule).

There is freedom in selecting the centers of these local expansions as well as their number.

A formal solution to this problem is available for the molecular wave functions expressed in terms of Gaussian functions (as is the general rule). Each elementary electron distribution entering in the definition of Ψ, is described by a couple of basic functions $\chi_s^*\chi_t$ centered at positions r_s and r_t. This distribution may be replaced by a single Gaussian function centered at the well defined position of the overlap center: χ_u at r_u. The new Gaussian function may be exactly decomposed into a finite local multipole expansion. It is possible to decompose the spherical function Y into a finite (but large) number of local multipole expansions each with a limited number of components. This method works (the penetration terms have been shown to be reasonably small) but the number of expansion centers is exceedingly large.

Some expedient approximations may be devised, introducing a balance between the number of expansion centers and the level of truncation of each expansion. This work has been done for years on empirical bases. One strategy is to keep each expansion at the lowest possible order (i.e., local charges) and to optimize number and location of such charges.

The modern use of this approach has been pioneered by Alagona et al.,[21] using a number of sites larger than the number of atoms, with values of the charges selected by minimization of the difference of the potential they generate with respect to the MEP function $V_B(r)$ (eq. [8.40]). This is the second application of the MEP function we have mentioned.

Alagona's approach has been reformulated by Momany in a simpler way, by reducing the number of sites to that of the nuclei present in the molecule.[22] This strategy has gained wide popularity: almost all the potentials in use for relative large molecules reduce the electrostatic contributions to Coulomb contributions between atomic charges. A relatively larger number of sites are in use for the intermolecular potentials of some simple molecules, as, for example, water, for which more accuracy is sought.

Momany's idea has led to a new definition of atomic charges. It would be possible to write volumes about atomic charges (AC), a concept that has no a precise definition in QM formalism, but is of extreme utility in practical applications. Many definitions of AC are based on manipulations of the molecular wave function, as, for example, the famous Mulliken charges.[23] Other definitions are based on different analyses of the QM definition of the charge density, as for example Bader's charges.[24] There are also charges derived from other theoretical approaches, such as the electronegativity equalization, or from experimental values, such as from the vibrational polar tensors.

The charges obtained using Momamy's idea of fitting the MEP with atomic charges are sometimes called PDAC (potential derived atomic charges). It has been realized that a fitting of MEP on the whole space was not convenient. It is better to reduce this fitting to the portion of space of close contact between molecules, i.e., near the van der Waals surface. This is the main technique now in use to define PDAC values.

The induction term

It is possible to define a molecular index P_A for the induction term to be used in combination with the MEP V_A to get a detailed description of the spatial propensity of the molecule to develop electrostatic interactions of classical type. Both functions are used under the form of an interaction with a unit point charge q placed at position r. In the case of V_A this means a simple multiplication; in the case of P_A there is the need of making additional calculations (to polarize the charge distribution of A). There are fast methods to do it, both at the variational level[25a] and at the PT level.[25b] The analysis of P_A has not yet extensively been used to model IND contributions to ΔE, and it shall not be used here. This remark has been added to signal that when one needs to develop interactions potentials for molecular not yet studied interactions including, e.g., complex solutes, the use of this approach could be of considerable help.

The multipole expansion of IND may be expressed in the following way:

$$IND = IND(A \leftarrow B) + IND(B \leftarrow A) \qquad [8.51]$$

with

$$IND(A \leftarrow B) \approx -\frac{1}{2}\sum_{ll'=1}^{\infty}\sum_{kk'=1}^{\infty} R^{-(l+l'+k+k'+2)} \sum_{m=-l<}^{l<} \sum_{m'=-k<}^{k<} C_{ll'}^{m} C_{kk'}^{m'} \times \pi_{lk}^{A}(m,m') M_{l',-m}^{B} M_{k',-m}^{B} \qquad [8.52]$$

and a similar expression for IND(B←A) with A and B labels exchanged.

We have here introduced the static polarizability tensor elements $\pi_{lk}^{X}(m,m')$: these tensors are response properties of the molecule with respect to external electric fields F (with components F_α), electric field gradients ∇F (with elements $\nabla F_{\alpha\beta}$) and higher field derivatives, such as $\nabla^2 F$ (with elements $\nabla^2 F_{\alpha\beta\gamma}$), etc. It is possible to compute these quantities with the aid of PT techniques, but variational procedures are more powerful and more exact.

The polarizability tensors are defined as the coefficients of the expansion of one molecular property (the energy, the dipole, etc.) with respect to an external field and its derivatives.

Among these response properties the most known are the dipole polarizability tensors α, β, and γ, that give the first three components of the expansion of a dipole moment μ subjected to an external homogeneous field F:

$$\mu_\alpha = -\frac{\partial E}{\partial F_\alpha} = \mu_\alpha^{(0)} + \alpha_{\alpha\beta} F_\beta + \beta_{\alpha\beta\gamma} F_\beta F_\gamma + \gamma_{\alpha\beta\gamma} F_\beta F_\gamma F_\delta + \ldots \qquad [8.53]$$

the convention of summation over the repeated indexes (which are the Cartesian coordinates) is applied here.

Other polarizabilities that may have practical importance are the quadrupole polarizability tensors A, B, etc. whose elements can be defined in terms of the expansion of a molecular quadrupole θ subjected to a uniform electric field:

$$\theta_{\alpha\beta} = -3\frac{\partial E}{\partial F_{\alpha\beta}} = \theta_{\alpha\beta}^{(0)} + A_{\gamma,\alpha\beta}F_{\gamma} + \frac{1}{2}B_{\gamma\delta,\alpha\beta}F_{\gamma}F_{\delta} + \ldots \qquad [8.54]$$

The A, B, ... terms are also present in the expansion series of the dipole when the molecule is subjected to higher derivatives of F. For example, the tensor A determines both the quadrupole induced by a uniform field and the dipole induced by a field gradient.

The electrical influence of a molecule on a second molecule cannot be reduced to a constant field F or to the combination of it with a gradient ∇F. So an appropriate handling of the formal expansion [8.52] may turn out to be a delicate task. In addition, the formal analysis of convergence of the series gives negative answers: there are only demonstrations that in special simple cases there is divergence. It is advisable not to push the higher limit of truncated expansions much with the hope of making the result better.

The use of several expansion centers surely improves the situation. The averaged value of dipole first polarizability α can be satisfactorily expressed as a sum of transferable group contributions, but the calculations of IND with distributed polarizabilities are rather unstable, probably divergent, and it is convenient to limit the calculation to the first term alone, as is actually done in almost all the practical implementations. Instability and lack of convergence are factors suggesting an accurate examination of the function to fit the opportune values for these distributed α polarizabilities.

The dispersion term

The dispersion term DIS can be formally treated as IND. Asymptotically (at large R), DIS can be expressed in terms of the dynamic multipole polarizabilities of the monomers.

$$DIS \approx -\frac{1}{2\pi}\sum_{l,l'=1}^{\infty}\sum_{k,k'=1}^{\infty} R^{-(l+l'+k+k'+2)} \sum_{m=-l<}^{l<}\sum_{m'=-k<}^{k<} C_{ll'}^{m}C_{kk'}^{m'} \times \int_{0}^{\infty} \pi_{lk}^{A}(m,m';i\omega)\pi_{l'k'}^{B}(-m,-m';i\omega)d\omega \qquad [8.55]$$

The dynamic polarizabilities are similar to the static ones, but they are dependent on the frequency of the applied field, and they have to be computed at the imaginary frequency iω

Here again the standard PT techniques are not accurate enough, and one has to employ others techniques. It is worth remarking that at short or intermediate distances the dynamic multipole polarizabilities give an appreciation of DIS of poor quality, unless computed on the dimer basis set. This is a consequence of the BSS errors: the PT theory has thus to abandon the objective of computing everything solely relying on monomers properties.

At the variational level there are no formal problems to use the dynamic polarizabilities, for which there are efficient variational procedures.

The expansion is often truncated to the first term (dipole contributions only), giving origin to a single term with distance dependence equal to R^{-6}. From eq. [8.49] it turns out that all the members of this expansion have an even negative dependence on R. For accurate studies, especially for simple systems in the gas phase, the next terms, C_8R^{-8}, $C_{10}R^{-10}$, ... are often considered. To have an odd term, one has to consider third order elements in the PT theory, which generally are rarely used.

Limitations due to the non-convergence of these expansion series are reduced by the use of multicenter expansions: in such a way it is possible to reach a satisfactory representation even for polyatomic molecules at short distances using the first expansion term only.

In general, the expansion sites are the (heavy) atoms of the dimer, using a simpler formulation due to London. The London formulation uses the averaged (isotropic) value of the static dipole polarizabilities, $\overline{\alpha}_j$, of the atoms and their first ionization potentials I_i and I_j:

$$DIS(6) \approx C_6(AB)R^{-6} = \sum_i^A \sum_j^B C_6(i,j)R_{ij}^{-6} \qquad [8.56]$$

with

$$C_6(i,j) = \frac{3}{2}\frac{\langle\alpha_i\rangle\langle\alpha_j\rangle I_i I_j}{I_i + I_j} \qquad [8.57]$$

This formula derives from the standard RS-PT with the expansion over the excited state truncated at the first term. For isolated atoms i and j, the coefficients $C_6(i,j)$ can be drawn from experimental data, while for atomic fragments of molecules only from computations.

The exchange (or repulsion) term

The exchange terms are related to the introduction of the intermonomer antisymmetrizer $\boldsymbol{A}_{AB}$ in the expression giving the electrostatic contribution. The correction factors introduced in the SAPT methods[15] may be related to a renormalization factor that may be written in the following form when $\boldsymbol{A}_{AB}$ is replaced with 1+P for simplicity:

$$\frac{1}{\langle\Phi_0|P\Phi_0\rangle} = \frac{1}{\langle\Psi_A\Psi_B|P\Psi_A\Psi_B\rangle} = \frac{1}{\left(1+\langle P\rangle\right)} \qquad [8.58]$$

This factor is different from 1, because <P> contains all the multiple overlap values between MOs of A and B. <P> may be then expanded into terms containing an increasing number of multiple overlaps (or exchanges of orbitals):

$$\langle P\rangle = \langle P_1\rangle + \langle P_2\rangle + \langle P_3\rangle + \langle P_4\rangle + \ldots \qquad [8.59]$$

The exchange energy may be expanded into increasing powers of MO overlap integrals S:

$$EX = EX(S_2) + EX(S_3) + EX(S_4) + \ldots \qquad [8.60]$$

with

$$EX(S_2) = \langle VP_2\rangle - \langle P_2\rangle \qquad [8.61]$$

This first term is sufficient for modeling intermolecular potentials. The overlaps depend on the monomer separation roughly as exp(-αR) so the following terms give small contribution at large-medium distances. At short distances the positive exchange term rapidly increases. Reasons of uniformity with the other terms of the interaction potential suggest replacing the exp(-αR) dependence with a highly negative power of R: R^{-12} in most cases. The exchange terms describe what is often called the steric repulsion between molecules (actually there are other short range repulsive contributions, as the electrostatic penetration components not described by the multipole expansion).

The other terms

Charge transfer contributions (CT) have been rarely introduced in the modeling of interaction potentials for liquids. Some attempts at modeling have been done for the study of interactions leading to chemical reactions, but in such cases, direct calculations of the interaction term are usually employed.

For curious readers, we add that the tentative modeling was based on an alternative formulation of the PT (rarely used for complete studies on the intermolecular interaction, because it presents several problems) in which the promotion of electrons of a partner on the virtual orbital of the second is admitted. The formal expressions are similar to those shown in eq. [8.40]. For the second order contributions we have

$$-\sum_{K} \frac{\left|\left\langle \Psi_0^a \Psi_0^b \middle| V \Psi_K^a \Psi_0^b \right\rangle\right|^2}{E_K^a - E_0^a}$$

The sum over K is strongly reduced (often to just one term, the HOMO-LUMO interaction), with K corresponding to the replacement of the occupied MO ϕ_r^0 of A with the virtual MO ϕ_t^v of B (A is the donor, B the acceptor). The expression is then simplified: the numerator is reduced to a combination of two-electron Coulomb integrals multiplied by the opportune overlap. The CT contribution rapidly decays with increasing R.

COUP contributions, obtained as a remainder in the variational decomposition of ΔE, are not modeled. The contributions are small and of short-range character.

A conclusive view

In this long analysis of the modeling of the separate components we have learned the following:

- All terms of the decomposition may be partitioned into short- and long-range contributions.
- The long-range contributions present problems of convergence, but these problems may be reduced by resorting to multicenter distributions based on suitable partitions of the molecular systems.
- The short-range contributions are in general of repulsive character and are dominated by the EX terms. The effect of the other short-range contributions is strongly reduced when multicenter expansions are used.

Adapting these remarks, one may write a tentative analytical expression for ΔE(R):

$$\Delta E \approx \sum_{r} \sum_{t} \sum_{n} C_{rt}^{(n)} R_{rt}^{-n} \qquad [8.62]$$

The expansion centers (called "sites") are indicated by the indexes r and t for the molecule A and B respectively. The index n indicates the behavior of the specific term with respect to the intersite distance R_{rt}; each couple r-t of sites has a specific set of allowed n values.

In such a way it is possible to combine sites corresponding only to a point charge with sites having more terms in the expansion. For two sites r-t both described by a point charge the only interaction term is $C_{rt}^{(1)}R_{rt}^{-1}$, while for a couple r-t described by a point charge and a dipole, the contribution to the interaction is limited to the R^{-2} term, and, if it is described by two dipoles, to the R^{-3} term. The last example shows that eq. [8.62] is cryptic or not well developed. In fact, if we examine eq. [8.12], which reports the interaction energy between two dipoles, it turns out that the dependence on the orientation angle θ apparently is missing in eq. [8.62]. The coefficients $C_{rt}^{(n)}$ must be specified in more detail as given in equations [8.50] and [8.52] by adding the opportune l, l' and m indexes (or the corresponding combination of Cartesian coordinates), or must be reduced to the isotropic form. This means to replace the three components of a dipole, and the five components of a quadrupole, and so on, by an average over all the orientations (i.e., over the m values). There is a loss of accuracy, very large in the case of two dipoles, and of decreasing importance in passing to higher multipoles. The loss in accuracy is greatly decreased when a multi-site development is employed. Many analytical expressions of interaction potentials use this choice. In such cases the $C_{rt}^{(n)}$ coefficients are just numbers.

The coefficients $C_{rt}^{(n)}$ can be drawn from experimental values (but this is limited to the cases in which there is one site only for both A and B), from ad hoc calculations, or by a fitting of ΔE values. In the past, large use has been made of "experimental" ΔE values, derived, e.g., from crystal packing energies, but now the main sources are the variationally computed QM values, followed by a fit.

The use of expression [8.62] for the fitting of QM values represents a remarkable improvement with respect to the past strategy of reaching a good fitting with complete freedom of the analytical form of the expression. There are in the literature interaction potentials using, e.g., non-integer values of n and/or other analytical expressions without physical meaning. This strategy leads to potentials that cannot be extended to similar systems, and that cannot be compared with the potential obtained by others for the same system.

Expression [8.62] has several merits, but also several defects. Among the latter we note that given powers of R may collect terms of different origin. For example, the term R^{-6} describes both the induction dipole-induced dipole interaction and the dispersion dipole-dipole interaction: two contributions with a different sensitivity with respect to changes in the molecular system. Theory and computational methods both permit getting two separate $C_{rt}^{(6)}$ coefficients for the two contributions. This is done in a limited number of potentials (the most important cases are the NEMOn[26] and the ASP-Wn[27] families of models). The most popular choice of a unique term for contributions of different origin is motivated by the need of reducing computational efforts, both in the derivation and in the use of the potential. To fit a unique $C_{rt}^{(6)}$ coefficient means to use ΔE values only: for two coefficients there is the need of separately fitting IND and DIS contributions.

8.4.5 THE RELAXATION OF THE RIGID MONOMER CONSTRAINT

We have so far examined decompositions of two-body interaction potentials, keeping fixed the internal geometry of both partners. This constraint is clearly unphysical, and does not correspond to the naïve model we have considered in the introduction, because molecules always exhibit internal motions, even when isolated, and because molecular collisions in a liquid (as well as in a cluster) lead to exchanges of energy between internal as well as external degrees of freedom.

It may be convenient to introduce a loose classification of the origin of changes in the internal geometry of molecules in clusters and liquids, and to use it for the dimer case we are considering here:

1) permanent or semipermanent molecular interactions;
2) internal dynamism of the molecule;
3) molecular collisions.

In the variety of liquid systems there are quite abundant cases in which relatively strong interactions among partners induce changes in the internal geometry. The formation of hydrogen-bonded adducts is an example of general occurrence (e.g., in water solutions). The interactions of a metal cations and their first solvation shells is a second outstanding example but the variety of cases is very large. It is not easy to give general rules on the distinction between permanent and semipermanent interactions of this type. In general it depends on the time scale of the phenomenon being studied, but it is clear that the long residence time of water molecule (in some cases, on the order of years[28]) in the first solvation shell around a cation leads us to consider this effect as permanent.

In such cases, it is convenient to reconsider the definition of the cluster expansion and to introduce some extra variables in the nuclear coordinate subspace to span for the analysis. For example, in the case of a dimer $M^{n+}\cdot H_2O$, it is convenient to add three coordinates corresponding to the internal coordinates of the water molecule (the total number of degrees of freedom in such case is again 6, because of the spherical symmetry of the metal cation). There is no need of repeating, for this model, the variational decomposition of the energy (the PT approaches have more difficulties to treat changes in the internal geometry). The conclusions do not change qualitatively, but the quantitative results can be sensibly modified.

Another important case of permanent interactions is related to chemical equilibria with molecular components of the liquid. The outstanding example is the prototropic equilibrium, especially the case $AH + B \rightarrow A^- + HB^+$. There are water-water potentials, including the possibility of describing the ionic dissociation of H_2O.

The semipermanent interactions are generally neglected in the modeling of the potentials for liquids. Things are different when one looks at problems requiring a detailed local description of the interactions. Molecular docking problems are a typical example. In such cases, use is made of variational QM calculations, or especially for docking, where one molecule at least has a large size, use is made of molecular mechanics (MM) algorithms, allowing local modification of the systems.

The second category corresponds to molecular vibrations; rotations of a molecule as a whole have been already considered in, or definition of, the $\Delta E(R)$ potential. The third category, molecular collisions, gives rise to exchange of energy among molecules that can be expressed as changes in the translational and rotational energies of the rigid molecule and changes in the internal vibrational energy distributions. In conclusion, all the cases of non-rigidity we have to consider here can be limited to molecular vibrations considered in a broad sense (couplings among vibrations and rotations are generally neglected in intermolecular potentials for liquids).

The vibrations are generally treated at the classical level, in terms of local deformation coordinates. The local deformation functions are of the same type of those used in molecular mechanics (MM) methods. Nowadays, MM treats geometry changes for molecules of any dimension and chemical composition.

In the MM approach, the energy of the system is decomposed as follows:

$$E_{tot} = [E_{str} + E_{ben} + E_{tor} + E_{other}] + E_{elec} + E_{vdW} \qquad [8.63]$$

the terms within square brackets regard contributions due to the bond stretching, to the angle bending, and to torsional interactions, supplemented by other contributions due to more specific deformations and by couplings among different internal coordinates. The E_{elec} terms regard Coulomb and inductions terms between fragments not chemically bound: among them there are the interactions between solute and solvent molecules. The same holds for the van der Waals interactions (i.e., repulsion and dispersion) collected in the last term of the equation.

It must be remarked that E_{tot} is actually a difference of energy with respect to a state of the system in which the internal geometry of each bonded component of the system is at equilibrium.

The versions of MM potentials (generally called force fields) for solvent molecules may be simpler, and in fact limited libraries of MM parameters are used to describe internal geometry change effects in liquid systems. We report in Table 8.4 the definitions of the basic, and simpler, expressions used for liquids.

To describe internal geometry effects in the dimeric interaction, these MM parameters are in general used in combination with a partitioning of the interaction potential into atomic sites. The coupling terms are neglected and the numerical values of the parameters of the site (e.g., the local charges) are left unchanged when there is a change of internal geometry produced by these local deformations. Only the relative position of the sites changes. We stress that interaction potential only regards interaction among sites of different molecules, while the local deformation affects the internal energy of the molecule.

Table 8.4

STRETCH	$E_{str} = k_s(1 - l_0)^2$
BEND	$E_{ben} = k_b(\theta - \theta_0)^2$
TORSION	$E_{tor} = k_t[1 \pm \cos(n\omega)]$

k_s	stretch force constant
k_b	bend force constant
k_t	torsion force constant
l_0	reference bond length
θ_0	reference bond angle

8.5 THREE- AND MANY-BODY INTERACTIONS

The tree-body component of the interaction energy of a trimer ABC is defined as:

$$\Delta E(ABC;R_{ABC}) = E_{ABC}(R_{ABC}) - \frac{1}{2}\sum_{A}\sum_{B} E_{AB}(R_{AB}) - \sum_{K} E_{K} \qquad [8.64]$$

This function may be computed, point-by-point, over the appropriate R_{ABC} space, either with variational and PT methods, as the dimeric interactions. The results are again affected by BSS errors, and they can be corrected with the appropriate extension of the CP procedure. A complete span of the surface is, of course, by far more demanding than for a dimer, and actually extensive scans of the decomposition of the E_{ABC} potential energy surface have thus far been done for a very limited number of systems.

Analogous remarks hold for the four-body component $\Delta E(ABCD; R_{ABCD})$ of the cluster expansion energy, as well as for the five- and six- body components, the definition of which can be easily extracted from the eq. [8.9]. The computational task becomes more and more exacting in increasing the number of bodies, as well as the dimensions which rise to 18 with fixed geometries of the components, and there are no reasonable perspectives of having in the future such a systematic scan as that available for dimers.

The studies have been so far centered on four types of systems that represent four different (and typical) situations:

1) clusters composed of rare gas atoms or by small almost spherical molecules (e.g., methane);
2) clusters composed of polar and protic molecules (especially water);
3) clusters composed of a single non-polar molecule (e.g., an alkane) and a number of water molecules;
4) clusters composed of a single charged species (typically atomic ions) and a number of water molecules.

Inside the four categories, attention has mostly been paid to clusters with a uniform chemical composition (e.g., trimers AAA more than A_2B or ABC for cases 1 and 2).

Clearly the types of many-body analyses are not sufficient to cover all cases of chemical relevance for liquids; for example, the mixed polar solvents (belonging to type 2) and the water solutions containing a cation in presence of some ligand (type 4) are poorly considered.

In spite of these deficiencies the available data are sufficient to draw some general trends that in general confirm what physical intuition suggests. We combine here below conclusions drawn from the formal analysis and from the examination of numerical cases.

ES contributions are strictly additive: there are no three- or many body terms for ES. The term “many-body correction” to ES introduced in some reviews actually regards two other effects. The first is the electron correlation effects which come out when the starting point is the HF description of the monomer. We have already considered this topic that does not belong, strictly speaking, to the many-body effects related to the cluster expansion [8.9]. The second regards a screening effect that we shall discuss later.

The other contributions are all non-additive. The cluster expansion [8.9] applies to these terms too:

$$TERM(ABCDE\ldots) = \frac{1}{2}\sum_{A}\sum_{B} TERM_{AB}(R_{AB}) + \frac{1}{6}\sum_{A}\sum_{B}\sum_{C} TERM_{ABC}(R_{ABC}) + \ldots \qquad [8.65]$$

The most important are the IND and DIS terms. CT is active for some special systems (long range electron transfer) but of scarce importance for normal liquids. EX many-body contributions rapidly fade away with the number of bodies: the three-body terms have been studied with some details,[29] but they are not yet used extensively to model interaction potentials for liquids.

The IND many-body contributions are dominated by the first dipole polarizability α contributions. The field F produced by the charge distribution of the other molecules and acting on the units for which α is defined, at a first (and good) approximation, as additive. The non-linearity derives from the fact that the contribution to the interaction energy is related to the square of the electric field. So in modeling many body effects for IND the attention is limited to molecular contributions of the type

$$E_{ind}(M) = -\frac{1}{2}\sum_{m=1}^{M}\mu_m^{ind}F(r_m) \qquad [8.66]$$

the index m runs over all the sites of the molecule M. The dipole moment of site m is decomposed into a static and an induction dipole:

$$\mu_m = \mu_m^0 + \mu_m^{ind} \qquad [8.67]$$

with the induction term α_m depending on the polarizability and on the total electric field F^{tot}. The latter comes from the other permanent charges and dipoles, as well as from the induced dipoles present in the system:

$$\mu_m^{ind} = \alpha_m F^{tot} = \alpha_m \sum_{s=1}^{S} F_s(r_m) \qquad [8.68]$$

Generally, the calculation of F is not limited to three-body contributions but includes higher order terms; for example, in simulation methods the contributions coming from all the molecules included in the simulation box, which may be of the order of hundreds. These contributions are not computed separately, but just used to have a collective value of F.

The sum of three- and higher body contributions to IND thus may be written and computed in the following way:

$$IND(many-body) \approx \sum_{m} E_{ind}\left(m;F^{tot}\right) \qquad [8.69]$$

When the system contains molecules of large size it is advisable to use a many-site description of the molecular polarizability α. This of course means to increase the computational effort, which is not negligible, especially in computer simulations.

The many-body contribution to IND may be negative as well as positive. In general, it reinforces with a negative contribution minima on the PES.

The non-additive DIS contributions are described in terms of the first dipole dynamic polarizability or by the corresponding approximate expression we have introduced for the dimeric case.

DIS contributions are already present and are quite important for the liquid aggregation of spherical systems. Even spherical monomers exhibit dynamical dipoles and the related two- and many-body contributions to DIS.

The most important term is known as the Axilrod-Teller term and describes the interaction of three instantaneous dipoles. The sign of the Axilrod-Teller term strongly depends on the geometry. It is negative for almost linear geometries and positive in triangular arrangements. Four body contributions of the same nature are generally of opposite sign and thus they reduce the effect of these terms on the PES shape.

The potentials for polar liquids generally neglect many-body dispersion contributions.

Screening many-body effects

When the material condensed system contains mobile charges, the electrostatic interactions, which are strong and with the slowest decay with the distance, are severely damped. Every charged component of the system tends to attract mobile components bearing the opposite charge. Typical examples are the counterion charge cloud surrounding each ion in salt solutions, and the counterion condensation effects acting on immobile charged species as DNA or other polyelectrolytes in salt solutions. In both cases, at large distance the electrostatic effect of the charge is screened by the similar electrostatic effect, but with an opposite sign, of the counterion distribution.

A similar screening effect is present for dipolar liquids: each molecule bearing a permanent dipole tends to organize around itself other dipolar molecules with the orientation which optimizes stabilization energy and screens the field produced by the singled out molecule.

The organization of the orientation of molecular dipoles around a singled-out charged component is even more effective. The interaction at long distance between two point charges screened by the solvent dipoles is $Q_1Q_2/\varepsilon R_{12}$ where ε is the dielectric constant of the liquid. When the two charges are placed in a salt solution the value of the electrostatic energy is even lower, being screened by counterions as well as by oriented dipoles.

For the dispersion contributions there is no screening. We arrive to the apparently paradoxical situation that for relatively large bodies, even when bearing net charges, the interactions at large distances are governed by the dispersion forces, weak in comparison with others, and having a more rapid decrease with the distance.

Effective interaction potentials

In the last sentences we have changed view with respect to the beginning of Section 8.4, where we introduced the cluster expansion of the interaction potentials. Still keeping a microscopic view, we passed from the examination of the properties of PES of increasing dimensions to a view that takes into consideration very limited portions of such surfaces selected on the basis of energetic effects, or, in other words, on the basis of probabilistic considerations. The screening effects we have mentioned are due to an averaged distribution of the other components around a single partner of the system, and its average is based on the relative energies of all the conformations of the system, spanning the whole pertinent PES.

This view based on averaged distributions is related to the "focused" model we introduced in Section 8.2.

If we suppose that the assisting part S of the system described by the Hamiltonian [8.8] with coordinates X_S is in equilibrium with the main part M at every coordinate X_M, we may repeat the cluster decomposition analyses given in Section 8.3, starting again from the dimer and proceeding to the trimers, etc. The potential function $\Delta E_{AB}(R)$ we have called potential energy surface (PES) now assumes a different name, potential of mean force (MFP), emphasizing the fact that it regards no more interactions between A and B but also the mean effects of the other bodies present in the system. It must be remarked that the approach is not limited to equilibrium distributions of S: it may be extended to distributions of S displaced from the equilibrium. The non-equilibrium description has an important role, and the implementation of non-equilibrium methods today represents one of the frontiers of the theory of liquids.

An important aspect of this revisited analysis of the dissection of ΔE_{AB} into separate components is that all terms, including ES, are now described in terms of monomer distributions which feel the effects of S. The analyses we have done suggest that these changes can be expressed in terms of a monomer's MO basis $\{\phi_i^p\}$ "polarized" in a way similar to that we have used to describe IND. Actually, this "polarization" or deformation of the monomer is not due to classical polarization effects only, but to all the components of the interaction of S with A-B, namely dispersion, exchange, etc.

The results of the decomposition of the intermolecular interaction energy of cluster M are not qualitatively different from those found for the same cluster M in vacuo. There are quantitative changes, often of not negligible entity and that correspond, in general, to a damping of the effects.

The use of this approach requires us to consider the availability of efficient and accurate models and procedures to evaluate the effects of S on M, and at the same time, of M on S. The basic premises of this approach have been laid many years ago, essentially with the introduction of the concept of solvent reaction field made by Onsager in 1936,[30] but only recently have they been satisfactory formulated. There are good reasons to expect that their use on the formulation of "effective" intermolecular potentials will increase in the next few years.

Actually, the decomposition of the $\Delta E_M(R)$ interaction energy is preceded by a step not present for isolated systems.

There is the need of defining and analyzing the interactions of each monomer A, B, etc. with the solvent alone. The focused model is reduced to a single molecule alone, let us say A, which may be a solute molecule but also a component of the dominant mole fraction, the solvent, or a molecular component of the pure liquid.

This subject is treated in detail in other chapters of this book and something more will be added in the remainder of this chapter. Here, we shall be concise.

There are two main approaches, the first based on discrete (i.e., molecular) descriptions of S, the second on a continuous description of the assisting portion of the medium, via appropriate integral equations based on the density distribution of the medium and on appropriate integral kernels describing the various interactions (classical electrostatic, dispersion, exchange-repulsion). Both approaches aim at an equilibration of S with M: there is the need of repeating calculations until the desired convergence is reached. More details on both approaches will be given in the specific sections; here we shall limit ourselves to quoting some aspects related to interaction potentials, which constitute the main topic of this section.

The approach based on discrete descriptions of the solvent makes explicit use of the molecular interaction potentials which may be those defined without consideration of S; the calculations are rather demanding of computation time, and this is the main reason explaining why much effort has been spent to have simple analytical expressions of such potentials.

The second continuous approach is often called Effective Hamiltonian Approach (EHA) and more recently Implicit Solvation Method (ISM).[31] It is based on the use of continuous response functions not requiring explicit solvent-solvent and solute-solvent interaction potentials, and it is by far less computer-demanding than the simulation approach.

As we shall show in the section devoted to these methods, there are several possible versions; here it is worth quoting the Polarizable Continuum Model (PCM) for calculations at the ab initio QM level.[32]

PCM it is the only method used so far to get effective two body A-B potentials over the whole range of distances R (three-body corrections have been introduced in Ref. [33]).

Until now, the EHA approach has been mostly used to study solvent effects on a solute molecule. In such studies, M is composed of just a single solute molecule (M = A) or of a solute molecule accompanied by a few solvent molecules ($M = AS_n$). These alternative choices make the results indirectly relevant to the question of the difference between traditional and effective intermolecular potential energies. However, some hints can be extracted from the available data. The experience thus far collected shows that when both M and S have a polar nature, the classical electrostatic contributions are dominant with an exchange-repulsion term, giving an important contribution to the energy but a small effect on the charge distribution of M and, as a consequence, on the molecular properties on which the interaction potential depends (e.g., multipole distribution of the charge density, static and dynamic polarizabilities). Dispersion effects play a role when M is not polar and they become the dominant component of the solvation effects when both M and S are not polar.

The calculation of effective PCM interaction potentials has been so far limited to the cases in which the solvent effects are more sizeable, namely the interactions of metal cations with water. They have been used in computer simulations of models of very dilute ionic solutions (a single ion in water), noticeably improving the results with respect to similar studies using traditional potentials.[34]

8.6 THE VARIETY OF INTERACTION POTENTIALS

In the preceding sections we have examined the definition of the components of the intermolecular potential, paying attention mostly to rigorous methods and to some approximations based on these methods.

The beginning of qualitative and semi-quantitative computational studies on the properties of liquids dates back at least to the 1950s, and in the early years of these studies, the computational resources were not so powerful as they are today. For this reason, for many years, the potentials used have been simple, discarding what our understanding of the dimeric interactions suggested. There is no reason, however, to neglect here these simplified versions of the potential, because very simple and naïve expressions have given excellent results and are still in use. The struggle for better and more detailed potentials is justified, of course, because chemistry always tends to have more and more accurate estimates of the properties of interest, and there are many problems in which a semi-quantitative assessment is not sufficient.

We shall try to give a cursory view of the variety of intermolecular potentials in use for liquid systems, paying more attention to the simplest ones. We shall almost completely neglect potentials used in other fields, such as the scattering of two isolated molecules, the determination of spectroscopic properties of dimers and trimers, and the accurate study of local chemical interactions, which all require more sophisticated potentials.

The main criterion to judge the quality of a potential is *a posteriori*, namely, based on the examination of the performance of that potential in describing properties of the liquid system. In fact, the performances of a potential are to a good extent based on subtle factors expressing the equilibrium reached in the definition of its various components. The experience gained in using this criterion has unfortunately shown that there is no definite answer. Typically, a potential, or a family of potentials, better describe some properties of the liquid, while a second one is more proper for other properties. For this reason there are many potentials in use for the same liquid and there are in the literature continuous comparisons among different potentials. A second criterion is based on the computational cost, an aspect of direct interest for people planning to make numerical studies but of little interest for people only interested in the results.

Our exposition will not try to classify potentials according to such criteria, but simply show the variety of potentials in use. We shall pay attention to the description adopted for a single molecule, that must then be combined with that adopted for the interaction partners. In particular, we shall consider the number of sites and the shape of the molecule used in each description.

The number of sites reflects the possibility we have examined, and advocated, of using many-center expansions to improve the representation. Each expansion center will be a site. There are models with one, two, and more sites. This sequence of increasing complexity reaches the number of heavy atoms of the molecule and then the whole number of atoms, including hydrogens. It is not limited to the nuclei as expansion sites. There are potentials introducing other locations of sites, in substitution or in addition to the nuclei. For example potentials widely used in simulations adopt for water a four-site model; other potentials (rarely used in simulations) prefer to use the middle of the bonds instead of (or in addition to) nuclei. Each site of the molecule must be combined with the sites of the second (and other) molecule to give the potential.

The shape of the molecule reflects the effect of the exchange-repulsion interaction. For almost all many-site models the shape is not given, but it implicitly results to be that of the union of the spheres centered on the expansion sites provided by a source of exchange-repulsion potential. There are some simple models in which the shape is explicitly stated. There will be spheres, ellipsoids, cylinders and more complex shapes, as fused spheres, spherocylinders, etc. Some typical examples are reported in Table 8.5.

Table 8.5. Single site-based potentials

#	Shape	Interaction	Name
1	Sphere	hard	HS
2	Sphere	soft	SS
3	Sphere	hard with charge	CHS
4	Sphere	soft with charge	CSS
5	Sphere	hard with rigid dipole	DHS
6	Sphere	soft with dipole	DSS
7	Disc	hard	HD
8	Disc	hard with dipole	SD
9	Ellipsoid	hard	
10	Ellipsoid		Gay-Berne[35]
11	Quadrupolar shape		Zewdie[36]
12	Sphere	repulsion dispersion	Lennard Jones (LJ)
13	Sphere	repulsion dispersion	Buckingham
14	Sphere	LJ + charge	LJ+q
15	Sphere	LJ + dipole	Stockmayer
16	Sphere	LJ + dipole+ soft sticky	SSD[37]

Potential 1 is extremely simple: the only parameter is the radius of the sphere. In spite of this simplicity, an impressive number of physical results have been obtained using the HS potential on the whole range of densities and aggregations. Also, mixtures of liquids have been successfully treated, introducing in the computational machinery the desired number of spheres with appropriate radii. The HS model is at the basis of the Scaled Particle Theory (SPT),[38] which still constitutes a basic element of modern solvation methods (see later for more details).

Of course, HS cannot give many details. A step toward realism is given by potential 2, in which the hard potential is replaced by a steep but smoothly repulsive potential. It is worth reminding readers that the shift from HS to SS in computer simulations required the availability of a new generation of computers. Simulations had in the past, and still have at present, to face the problem that an increase in the complexity of the potential leads to a large increment of the computational demand.

Potentials 3 and 4 have been introduced to study ionic solutions and similar fluids containing mobile electric charges (as, for example, molten salts). In ionic solutions the appropriate mixture of charged and uncharged spheres is used. These potentials are the first examples of potentials in our list, in which the two-body characteristics become explicit. The interaction between two charged spheres is in fact described in terms of the charge values of a couple of spheres: Q_kQ_l/r_{lk} (or $Q_kQ_l/\varepsilon r_{lk}$).

Potentials 5 and 6 are the first examples in our lists of anisotropic potentials. The interaction here depends on the mutual orientations of the two dipoles. Other versions of the dipole-into-a-sphere potentials (not reported in Table 8.5) include induced dipoles and actually belong to a higher level of complexity in the models, because for their use there is the need of an iterative loop to fix the local value of F. There are also other similar models simulating liquids in which the location of the dipoles is held fixed at nodes of a regular 3D grid, the hard sphere potential is discarded, and the optimization only regard orientation and strength of the local dipoles. This last type of model is used in combination with solutes M described in another, more detailed way.

Potentials 7-11 add more realism in the description of molecular shape. Among them, the Gay-Berne[35] potential (10) has gained a large popularity in the description of liquid crystals. The quite recent potential (11)[36] aims at replacing Gay-Berne potential. It has been added here to show that even in the field of simple potentials there is space for innovation.

Potentials 12 and 13 are very important for chemical studies on liquids and solutions.

The Lennard-Jones potential (12) includes dispersion and repulsion interactions in the form:

$$\text{LJ:} \qquad E_{AB}^{LJ} = \varepsilon\left[\left(\frac{\sigma}{R}\right)^{12} - \left(\frac{\sigma}{R}\right)^{6}\right] \qquad [8.70]$$

The dependence of the potential on the couple of molecules is here explicit, because the parameters ε and σ depend on the couple. In the original version, ε is defined as the depth of the attractive well and σ as the distance at which the steep repulsive wall begins.

More recently, the LJ expression has been adopted as an analytical template to fit numerical values of the interaction, using independently the two parameters.:

LJ with 2 parameters: $$E_{AB}^{LJ}(R) = A_{AB}\left(\frac{1}{R}\right)^{12} - C_{AB}\left(\frac{1}{R}\right)^{6} \qquad [8.71]$$

LJ expressions are of extensive use in MM to model non-covalent interactions among molecular sites, often with the addition of local charges (potential 14)

LJ with charge: $$E_{ms}(r_{ms}) = A_{ms}\left(\frac{1}{r_{ms}}\right)^{12} - C_{ms}\left(\frac{1}{r_{ms}}\right)^{6} + \frac{q_m q_s}{r_{ms}} \qquad [8.72]$$

Some potentials add an effective dielectric constant in the denominator of the Coulomb term to mimic polarization effects.

The Buckhingam potential is similar to LJ with a more physical description of the repulsion term given in terms of a decaying exponential function:

$$E_{AB}^{(BU)} = \varepsilon\left\{\frac{6}{\alpha-6}\exp\left[-\alpha\left(\frac{r}{r^*}\right)-1\right] - \frac{\alpha}{\alpha-6}\left(\frac{r}{r^*}\right)^{-6}\right\} \qquad [8.73]$$

where:

ε	depth of the attractive well
r	R_{AB}
r*	distance of the minimum
α	numerical parameter

The difference in the computational costs of LJ and Buckingham potentials is related to the difference between computing the square of a value already available (R^{-12} from R^{-6}) and that of computing an exponential. Here again the increment in computational costs of simulations due to small changes in the potential plays a significant role. Also, the Buckingham + charge potential is used to describe liquids.

The last potential of Table 8.5 is specialized for water. It has been enclosed in the table to document the progress in one-site potentials; in this case, the LJ + dipole is supplemented by a short-range "sticky" tetrahedral interaction.

The listing of one-center potentials is not exhausted by the examples given in Table 8.5. We have, for example, neglected all the potentials in use for rare gases systems in which much attention is paid to using higher terms to describe the dispersion contribution. Our aim was just to show with a few examples how it is possible to define a large variety of potentials remaining within the constraints of using a single center.

The problem of giving a cursory but significant enough view of potentials becomes harder when one passes to many-site potentials. In Table 8.6 we report some analogues of HS with a more complex shape.

They consist of fused regular forms (spheres or combination of spheres with other regular solids). The hard version of these potentials is accompanied by soft modifications and by versions including dipole, charges, as in Table 8.5.

A step further along this way is given by a potential composed by spheres linked by 'spacers' with a constant length but allowing changes of conformation with appropriate torsion potentials. These potentials are used for polymers or for molecules having long hydrocarbon chains. This is not, however, the main trend in the evolution of potentials.

Table 8.6. Many-site simple potentials

#	Shape	Interaction	Name
1	three fused spheres	hard	hard dumbbell HD
2	two half spheres + cylinder	hard	hard spherocylinder HSC
3	general convex shape	hard	hard convex core HCC

The largest number of solvents are composed by polyatomic molecules of small-medium size, exhibiting a variable (but in general not excessive) degree of flexibility. In solutions, the interactions involve these solvents and molecules having the same characteristics as solvent or with more complex chemical composition. In all cases (pure liquids, solutions with solute of variable complexity), one has to take into account interactions having a remarkable degree of specificity. The chemical approach to the problem addresses this specificity on which the whole chemistry is based. This is the real field of application of the definition and analysis of molecular interactions on which we have spent the first sections of this chapter.

It is clear that we are entering here into a very complex realm, hard to summarize. A whole book would be necessary.

It is possible to make a rough distinction between potential of general applicability and potentials conceived for specific couples (or collections) of molecules.

In both cases, the many-site expansions are used, but for general potentials, in which transferability is asked, the description is obviously less detailed. The LJ+charge (potential 14 in Table 8.5) is a popular choice for these potentials; the sites are in general limited to the heavy atoms of the molecule. There are, however, many other versions with a variety of changes to this standard setting.

The potentials elaborated for specific cases are often more detailed and they adapt a larger number of devices to increase the accuracy. Many have been developed for pure liquids, but the number of potentials regarding specific combinations of solute and solvent is not negligible.

The number of solvents in chemistry is quite large. The number of available specific potentials is by far more limited, but too large to be summarized here. In addition, a simple list of names and references, not accompanied by critical remarks about the performances of such potentials in describing liquid systems would have little utility.

The numerous textbooks on intermolecular potentials are of little help, because outdated or paying little attention to the analytical exposition of computational models. More useful are monographs and reviews regarding computer simulations of liquids[39] or original papers making comparisons among different potentials.

These last are more abundant for water. This solvent, because of its importance and its molecular simplicity, has been the benchmark for many ideas about the description and modeling of intermolecular interactions. Almost all potentials that have been thus far proposed for not extremely flexible molecular component of liquid systems may be found in the literature regarding water. Alternative strategies in the defining number and position of sites, use diffuse instead of point charges, different approaches to model the many-body corrections, flexible potentials, dissociation of the molecule are some features that can be examined by looking at the water potential literature.

There is a large critical literature, but two recent reviews (Floris and Tani[40] and Wallqvist and Mountain,[41] both published in 1999) are here recommended as an excellent guide to this subject. The two reviews consider and analyze about 100 potentials for pure water. WM review starts from historical models, FM review pays attention to recent models (about 70 models, supplemented by ion-water potentials). The two reviews partly overlap, but they are to a good extent complementary, especially in the analysis of the performances of such models.

There are, to the best of our knowledge, no reviews of comparable accuracy for the potentials regarding other liquid systems.

8.7 THEORETICAL AND COMPUTING MODELING OF PURE LIQUIDS AND SOLUTIONS

8.7.1 PHYSICAL MODELS

In this chapter we shall present a necessarily partial review of the main theoretical approaches so far developed to treat liquid systems in terms of physical functions. We shall restrict ourselves to two basic theories, integral equation and perturbation theories, to keep the chapter within reasonable bounds. In addition, only the basic theoretical principles underlying the original methods will be discussed, because the progress has been less rapid for theory than for numerical applications. The latter are in fact developing so fast that it is an impossible task to try to give an exhaustive view in a few pages.

A fundamental approach to liquids is provided by the integral equation methods[42-44] (sometimes called distribution function methods), initiated by Kirkwood and Yvon in the 1930s. As we shall show below, one starts by writing down an exact equation for the molecular distribution function of interest, usually the pair function, and then introduces one or more approximations to solve the problem. These approximations are often motivated by considerations of mathematical simplicity, so that their validity depends on *a posteriori* agreement with computer simulation or experiment. The theories in question, called YBG (Yvon-Born-Green), PY (Percus-Yevick), and the HNC (hypernetted chain) approximation, provide the distribution functions directly, and are thus applicable to a wide variety of properties.

An alternative, and particularly successful, approach to liquids is provided by the thermodynamic perturbation theories.[42,44] In this approach, the properties of the fluid of interest are related to those of a reference fluid through a suitable expansion. One attempts to choose a reference system that is in some sense close to the real system, and whose properties are well known (e.g., through computer simulation studies or an integral equation theory).

As a last physical approach we mention, but do not further consider, the scaled-particle-theory (SPT)[38,45] which was developed about the same time as the Percus-Yevick theory. It gives good results for the thermodynamic properties of hard molecules (spheres or convex molecules). It is not a complete theory (in contrast to the integral equation and perturbation theories) since it does not yield the molecular distribution functions (although they can be obtained for some finite range of intermolecular separations).

Early work on the theory of dense fluids dealt almost exclusively with simple atomic fluids, in which the intermolecular forces are between the centers of spherical molecules and depend only on the separation distance r. However, in real fluids the intermolecular forces depend on the molecular orientations, vibrational coordinates, etc., in addition to r.

The complexity of the problem thus requires the assumption of some approximations; most of the formulated theories, for example, assume

(a) a rigid molecule approximation,

(b) a classical treatment of the traslational and rotational motions, and

(c) a pairwise additivity of the intermolecular forces.

In the rigid molecule approximation it is assumed that the intermolecular potential energy $V(\mathbf{r}^N,\omega^N)$ depends only on the positions of the centers of mass $\mathbf{r}^N=r_1r_2...r_N$ for the N molecules and on their orientations $\omega^N = \omega_1\omega_2\ldots\omega_N$. This implies that the vibrational coordinates of the molecules are dynamically and statistically independent on the center of mass and orientation coordinates, and that the internal rotations are either absent, or independent of the $\mathbf{r}^N$ and ω^N coordinates. The molecules are also assumed to be in their ground electronic states.

At the bases of the second basic assumption made, e.g., that the fluids behave classically, there is the knowledge that the quantum effects in the thermodynamic properties are usually small, and can be calculated readily to the first approximation. For the structural properties (e.g., pair correlation function, structure factors), no detailed estimates are available for molecular liquids, while for atomic liquids the relevant theoretical expressions for the quantum corrections are available in the literature.

The third basic approximation usually introduced is that the total intermolecular potential energy $V(\mathbf{r}^N,\omega^N)$ is simply the sum of the intermolecular potentials for isolated pairs ij of molecules, i.e.,

$$V\left(\boldsymbol{r}^N, \omega^N\right) = \sum_{i<j} V\left(r_{ij}, \omega_i, \omega_j\right) \qquad [8.74]$$

In the sum i is kept less than j in order to avoid counting any pair interaction twice.

Eq. [8.74] is exact in the low-density gas limit, since interactions involving three or more molecules can be ignored. It is not exact for dense fluids or solids, however, because the presence of additional molecules nearby distorts the electron charge distributions in molecules i and j, and thus changes the intermolecular interaction between this pair from the isolated pair value. In order to get a more reliable description, three-body (and higher multi-body) correction terms should be introduced.

The influence of three-body terms on the physical properties has been studied in detail for atomic fluids,[46,47] while much less is known about molecular fluids. In the latter case, the accurate potentials are few and statistical mechanical calculations are usually done with model potentials. A particular model may be purely empirical (e.g., atom-atom), or semiempirical (e.g., generalized Stockmayer), where some of the terms have a theoretical basis. The so-called generalized Stockmayer model consists of central and non-central terms. For the central part, one assumes a two-parameter central form (the classical example is the Lennard-Jones, LJ, form introduced in the previous sections). The long-range, non-central part in general contains a truncated sum of multipolar, induction and dispersion terms. In addition, a short-range, angle-dependent overlap part, representing the shape or core of the potential, is usually introduced. The multipolar interactions are pair-wise additive, but the induction, dispersion and overlap interactions contain three-body (and higher multi-body) terms. Hence, three-body interactions are strongly suspected to be of large importance also for molecular liquids.

This review will be mainly restricted to a discussion of small rigid molecules in their ground electronic states. However, one can generalize in a number of directions by extending the pair potential $v(r_{ij},\omega_i,\omega_j)$ of eq. [8.74] so as to treat:

(a) non-rigid molecules,
(b) molecules with internal rotation,
(c) large (e.g., long chain) molecules which may be flexible,
(d) electronic excited state molecules.

In addition, the inclusion of covalence and charge transfer effects are also possible. The first two generalizations are straightforward in principle; one lets v depend on coordinates describing the additional degrees of freedom involved. As for (c), for very large molecules the site-site plus charge-charge model is the only viable one. Under (d) we can quote the so-called long-range 'resonance' interactions.

As the last note, we anticipate that in the following only equilibrium properties will be considered; however, it is fundamental to recall from the beginning that dynamical (e.g., non-equilibrium) analyses are an important and active field of research in the theory of physical models.[42,48,49]

Before entering into more details of each theory, it is worth introducing some basic definitions of statistical mechanics. All equilibrium properties of a system can be calculated if both the intermolecular potential energy and the distribution functions are known. In considering fluids in equilibrium, we can distinguish three principal cases:

(a) isotropic, homogeneous fluids, (e.g., liquid or compressed gas in the absence of an external field),
(b) anisotropic, homogeneous fluids (e.g., a polyatomic fluid in the presence of a uniform electric field, nematic liquid crystals), and
(c) inhomogeneous fluids (e.g., the interfacial region).

These fluid states have been listed in order of increasing complexity; thus, more independent variables are involved in cases (b) and (c), and consequently the evaluation of the necessary distribution functions is more difficult.

For molecular fluids, it is convenient to define different types of distribution functions, correlation functions and related quantities. In particular, in the pair-wise additive theory of homogeneous fluids (see eq. [8.74]), a central role is played by the angular pair correlation function $g(\mathbf{r}_{12}\omega_1\omega_2)$ proportional to the probability density of finding two molecules with position $\mathbf{r}_1$ and $\mathbf{r}_2$ and orientations ω_1 and ω_2 (a schematic representation of such function is reported in Figure 8.5).

In fact, one is frequently interested in some observable property <B>, which is (experimentally) a time average of a function of the phase variables $B(\mathbf{r}^N,\omega^N)$; the latter is often a sum of pair terms $b(\mathbf{r}_{ij},\omega_i,\omega_j)$ so that <B> is given by

$$\langle B\rangle = \int d\boldsymbol{r}^N d\omega^N P\left(\boldsymbol{r}^N\omega^N\right)B\left(\boldsymbol{r}^N\omega^N\right) = \frac{1}{2}\rho N\int d r\left\langle g(\boldsymbol{r}\omega_1\omega_2)b\left(\boldsymbol{r}\omega_1\omega_2\right)\right\rangle_{\omega_1\omega_2} \qquad [8.75]$$

i.e., in terms of the pair correlation function g(12). Examples of such properties are the configurational contribution to energy, pressure, mean squared torque, and the mean squared force. In eq. [8.75] $\langle g(\mathbf{r}\omega_1\omega_2)b(\mathbf{r}\omega_1\omega_2)\rangle_{\omega_1\omega_2}$ means the unweighted average over orientations.

In addition to g(12), it is also useful to define:

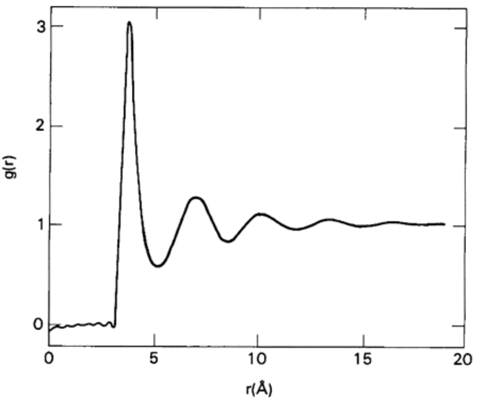

Figure 8.5. Example of the radial distribution function g(r) of a typical monoatomic liquid.

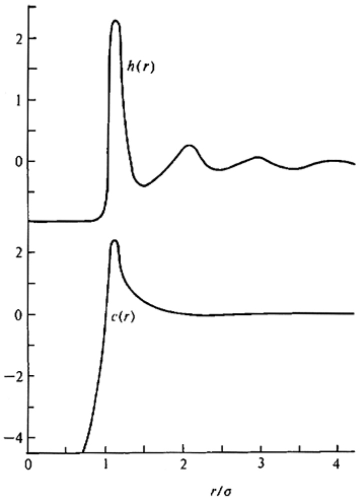

Figure 8.6. Examples of h(r) and c(r) functions for a typical monoatomic liquid.

a) the site-site correlation function $g_{\alpha\beta}(r_{\alpha\beta})$ proportional to the probability density that sites α and β on different molecules are separated by distance r, regardless of molecular orientations;
b) the total correlation function $h(r_{12}\omega_1\omega_2) = g(r_{12}\omega_1\omega_2) - 1$;
c) the direct correlation function $c(r_{12}\omega_1\omega_2)$.

Simple examples of h and c functions are reported in Figure 8.6.

In the list above, item (a) implies definite sites within molecules; these sites may be the nuclei themselves or sites at arbitrary locations within the molecules.

In addition, the total correlation, h, between molecules 1 and 2 can be separated into two parts: (i) a direct effect of 1 on 2 which is short-ranged and is characterized by c, and (ii) and indirect effect in which 1 influences other molecules, 3, 4, etc., which in turn affect 2. The indirect effect is the sum of all contributions from other molecules averaged over their configurations. For an isotropic and homogeneous fluid formed by non-spherical molecules, we have

$$h(\boldsymbol{r}_{12}\omega_1\omega_2) = c(\boldsymbol{r}_{12}\omega_1\omega_2) + \rho\int d\boldsymbol{r}_3 \left\langle c(\boldsymbol{r}_{13}\omega_1\omega_3)h(\boldsymbol{r}_{32}\omega_3\omega_2)\right\rangle_{\omega_3} \qquad [8.76]$$

which is the generalization of the Ornstein-Zernike (OZ) equation[50] to non-spherical molecules. The OZ equation is the starting point for many theories of the pair correlation function (PY, HNC, etc.); however, numerical solutions starting from [8.76] are complicated by the large number of variables involved. By expanding the direct and total correlation functions in spherical harmonics, one obtains a set of algebraically coupled equations relating the harmonic coefficients of h and c. These equations involve only one variable in the place of many in the original OZ equation. In addition, the theories we shall describe below truncate the infinite set of coupled equations into a finite set, thereby enabling a reasonably simple solution to be carried out.

8.7.1.1 Integral equation methods

The structure of the integral equation approach for calculating the angular pair correlation function $g(r_{12}\omega_1\omega_2)$ starts with the OZ integral equation [8.76] between the total (h) and the direct (c) correlation function, which is here schematically rewritten as h=h[c] where h[c] denotes a functional of c. Coupled to that a second relation, the so-called closure relation c=c[h], is introduced. While the former is exact, the latter relation is approximated; the form of this approximation is the main distinction among the various integral equation theories to be described below.

In the OZ equation, h depends on c, and in the closure relation, c depends on h; thus the unknown h depends on itself and must be determined self-consistently. This (self-consistency requiring, or integral equation) structure is characteristic of all many body problems.

Two of the classic integral equation approximations for atomic liquids are the PY (Percus-Yevick)[51] and the HNC (hypernetted chain)[52] approximations that use the following closures

$$h - c = y - 1 \qquad \text{(PY)} \qquad [8.77]$$

$$h - c = \ln y \qquad \text{(HNC)} \qquad [8.78]$$

where y is the direct correlation function defined by $g(12)=\exp(-\beta\, v(12))y(12)$ with v(12) the pair potential and $\beta=1/kT$.

The closures [8.77-8.78] can be also written in the form

$$c = g\left(1 - e^{\beta v(12)}\right) \qquad \text{(PY)} \qquad [8.79]$$

$$c = h - \beta v(12) - \ln g \qquad \text{(HNC)} \qquad [8.80]$$

For atomic liquids the PY theory is better for steep repulsive pair potentials, e.g., hard spheres, whereas the HNC theory is better when attractive forces are present, e.g., Lennard-Jones, and Coulomb potentials. No stated tests are available for molecular liquids; more details are given below.

As said before, in practice the integral equations for molecular liquids are almost always solved using spherical harmonic expansions. This is because the basic form [8.76] of the OZ relation contains too many variables to be handled efficiently. In addition, harmonic expansions are necessarily truncated after a finite number of terms. The validity of the truncations rests on the rate of convergence of the harmonic series that depends in turn on the degree of anisotropy in the intermolecular potential.

We recall that the solution to the PY approximation for the hard sphere atomic fluid is analytical and it also forms a basis for other theories, e.g., in molecular fluids the MSA and RISM theories to be discussed below.

The mean spherical approximation (MSA)[52] theory for fluids originated as the extension to continuum fluids of the spherical model for lattice gases. In practice it is usually applied to potentials with spherical hard cores, although extensions to soft core and non-spherical core potentials have been discussed.

The MSA is based on the OZ relation together with the closure

$$h = -1 \qquad r < \sigma \qquad [8.81]$$

$$c = -\beta v(12) \qquad r < \sigma \qquad [8.82]$$

where σ is the diameter of the spherical hard core part of the pair potential v(12).

The condition [8.81] is exact for hard core potentials since g(12)=0 for $r < \sigma$, while the condition [8.82] is the approximation, being correct only asymptotically (large r). We thus expect the approximation to be worst near the hard core; we also note that the theory is not exact at low density (except for a pure hard sphere potential, where MSA=PY), but this is not too important since good theories exist for low densities, and we are therefore mainly interested in high densities. Once again the solution of the MSA problem is most easily accomplished using the spherical harmonic component of h and c.

In the list of the various correlation functions we have introduced at item (b) the so-called site-site pair correlation functions $g_{\alpha\beta}(r_{\alpha\beta})$; since they depend only on the radial variables $r_{\alpha\beta}$ (between sites), they are naturally simpler than $g(r_{12};\omega_1\omega_2)$ but, at the same time, they contain less information. The theories for $g_{\alpha\beta}$ fall into two categories based on site-site or particle-particle OZ equations, respectively. Various closures can be used with either category.

As concerns the site-site approach the most important theory is the 'reference interaction site model', or RISM.[53,54] This method applies to an intermolecular pair potential modeled by a site-site form, i.e., $V(r\omega_1\omega_2) = \Sigma_{\alpha\beta} v_{\alpha\beta}(r_{\alpha\beta})$ and its original intuitive derivation is based on exploring the possibility of decomposing $g(r;\omega_1\omega_2)$ also in the same form, i.e., as a sum of site-site $g_{\alpha\beta}(r)$s.

The RISM theory consists of (i) an OZ-like relation between the set $\{h_{\alpha\beta}\}$ (where $h_{\alpha\beta}(r)=g_{\alpha\beta}(r)-1$) and corresponding set $\{c_{\alpha\beta}\}$ of direct correlation functions, and (ii) a PY-type or other type of closure. The OZ-like relation is here a matrix one.

Although successful in many applications, the RISM approximation suffers from a number of major defects. First, it is not the best choice to calculate the equation of state, and the results that are obtained are thermodynamically inconsistent. Secondly, calculated structural properties show an unphysical dependence on the presence of 'auxiliary' sites, i.e., on sites that label points in a molecule but contribute nothing to the intermolecular potential. Thirdly, use of the RISM approximation leads to trivial and incorrect results for certain quantities descriptive of angular correlations in the fluid.[48]

Attempts to develop a more satisfactory theory within the interaction-site picture have developed along two different lines. The first relies on treating the RISM-OZ relation as providing the definition of the site-site direct correlation functions, $c_{\alpha\beta}$. In this way the usual RISM closures can be modified by adding terms to $c_{\alpha\beta}$ such that the asymptotic result is satisfied.

In the alternative approach, the basic observation is that the RISM-OZ relation, though plausible, does not provide an adequate basis for a complete theory of the structure of molecular fluids. Accordingly, it is there rather than in the closure relation that improvement must be sought.[55]

Despite the defects we have underlined, in the last years the RISM method has received much more attention than other integral equation methods; promising developments in this area are represented by the inclusion of polarizable media in RISM[56] and the coupling of the RISM equations to a quantum mechanical description.[57]

8.7.1.2 Perturbation theories

In perturbation theories[44,58] one relates the properties (e.g., the distribution functions or free energy) of the real system, for which the intermolecular potential energy is E, to those of a reference system where the potential is E_0, usually by an expansion in powers of the perturbation potential $E_1=E - E_0$.

The methods used are conveniently classified according to whether the reference system potential is spherically symmetric or anisotropic. Theories of the first type are most appropriate when the anisotropy in the full potential is weak and long ranged; those of the second type have a greater physical appeal and a wider range of possible application, but they are more difficult to implement because the calculation of the reference-system properties poses greater problems.

In considering perturbation theory for liquids it is convenient first to discuss the historical development for atomic liquids.

In many cases the intermolecular pair potential can be separated in a natural way into a sharp, short-range repulsion and a smoothly varying, long range attraction. A separation of this type is an explicit ingredient of many empirical representations of the intermolecular forces including, for example, the Lennard-Jones potential. It is now generally accepted that the structure of simple liquids, at least of high density, is largely determined by geometric factors associated with the packing of the molecular hard cores. By contrast, the attractive interactions may, in the first approximation, be regarded as giving rise to a uniform background potential that provides the cohesive energy of the liquid but has little effect on its structure. A further plausible approximation consists of modeling the short-range forces by the infinitely steep repulsion of the hard-sphere potential. In this way, the properties of a given liquid can be related to those of a hard-sphere reference system, the attractive part of the potential being treated as a perturbation. The choice of the hard-sphere fluid as a reference system is an obvious one, since its thermodynamic and structural properties are well known.

The idea of representing a liquid as a system of hard spheres moving in a uniform, attractive potential well is an old one; suffice here to recall the van der Waals equation. Roughly one can thus regard perturbation methods as attempts to improve the theory of van der Waals in a systematic fashion.

The basis of all the perturbation theories we shall consider is a division of the pair potential of the form

$$v(12) = v_0(12) + w(12) \qquad [8.83]$$

where v_0 is the pair potential of the reference system and w(12) is the perturbation. The following step is to compute the effect of the perturbation on the thermodynamic properties and pair distribution function of the reference system. This can be done systematically via an expansion in powers either of inverse temperature (the "λ expansion") or of a parameter that measures the range of the perturbation (the "γ expansion").

In spite of the fact that hard spheres are a natural choice of the reference system, for the reasons discussed above, realistic intermolecular potentials do not have an infinitely steep hard core, and there is no natural separation into a hard-sphere part and a weak perturbation. A possible improvement is that to take proper account of the "softness"' of the repulsive part of the intermolecular potential. A method of doing this was proposed by Rowlinson,[59] who used an expansion in powers of a softness parameter, n^{-1}, about $n^{-1}=0$ (corresponding to a hard sphere fluid). This method gives good results for the repulsive, but not for the attractive, part of the potential. Subsequently several researchers attempted to combine the advantages of both approaches. The first successful method was that of Barker and Henderson (BH),[60] who showed that a second-order theory gave quantitative results for the thermodynamic properties of a Lennard-Jones liquid. Even more rapidly convergent results were later obtained by Weeks, Chandler and Andersen (WCA)[61] using a somewhat different reference system.

Given the great success of perturbation theories in treating the properties of atomic liquids, a large effort has been devoted to extending the methods to deal with molecular systems. The first rigorous application of these theories to molecular fluids seems to have been made in 1951 by Barker,[62] who expanded the partition function for a polar fluid about that for a fluid of isotropic molecules.

Roughly, the basic problem is the same as in the atomic case, but the practical difficulties are much more severe. A possible approach is to choose a reference-system potential $v_0(r)$ spherically symmetric so that the integrations over the orientations (absent in atomic fluids) involve only the perturbation. The real system can be thus studied by a straightforward generalization of the λ-expansion developed for atomic fluids.

Perturbation theories based on spherically symmetric reference potentials, however, cannot be expected to work well when (as in the most real molecules) the short-range repulsive forces are strongly anisotropic. The natural approach in such cases is to include the strongly varying interactions in the specification of an isotropic reference potential to relate the properties of the reference system to those of hard molecules having the same shape.[63] Calculation of this type have been made by Tildesley,[64] exploiting a generalization of the WBA approach quoted above. In a similar way also, the BH perturbation theory has been generalized with good results.[65] The main disadvantage of these methods is the large computational effort that their implementation requires.

8.7.2 COMPUTER SIMULATIONS

In this section we will give a brief review of methodologies to perform computer simulations. These approaches nowadays have a major role in the study of liquid-state physics: they are developing so fast that it is impossible to give a complete view of all the different methodologies used and of the overwhelmingly large number of applications. Therefore we will only give a brief account of the basic principles of such methodologies, of how a computer simulation can be carried out, and we will briefly discuss limitations and advantages of the methods. The literature in the field is enormous: here we will refer interested readers to some of the basic textbooks on this subject.[42,66,67]

The microscopic state of a system may be specified in terms of the positions and momenta of the set of particles (atoms or molecules). Making the approximation that a classical description is adequate, the Hamiltonian H of a system of N particles can be written as a sum of a kinetic K and a potential V energy functions of the set of coordinates q_i and momenta p_i of each particle i, i.e.:

$$H(q,p)=K(p)+V(q) \tag{8.84}$$

In the equation the coordinates q can simply be the set of Cartesian coordinates of each atom in the system, but in this case we treat the molecules as rigid bodies (as is usually done in most simulations); q will consist of the Cartesian coordinates of each molecular center of mass together with a set of other parameters specifying the molecular orientation. In any case p is the set of conjugate momenta.

Usually the kinetic energy K takes the form:

$$K = \sum_{i=1}^{N} \sum_{\mu} \frac{p_{i\mu}^{2}}{2m_{i}} \qquad [8.85]$$

where the index μ runs over the components (x, y, z) of the momentum of molecule i and m_i is the molecular mass.

The potential energy V contains the interesting information regarding intermolecular interactions. A detailed analysis on this subject has been given in the previous sections; here we shall recall only some basic aspects.

It is possible to construct from H an equation of motion that governs the time-evolution of the system, as well as to state the equilibrium distribution function for positions and momenta. Thus H (or better V) is the basic input to a computer simulation program. Almost universally, in computer simulation the potential energy is broken up into terms involving pairs, triplets, etc. of molecules, i.e.:

$$V = \sum_{i} v_1(r_i) + \sum_{i} \sum_{j>i} v_2(r_i, r_j) + \sum_{i} \sum_{j>i} \sum_{k>j>i} v_3(r_i, r_j, r_k) + \ldots \qquad [8.86]$$

The notation indicates that the summation runs over all distinct pairs i and j or triplets i, j and k, without counting any pair or triplet twice. In eq. [8.86], the first term represents the effect of an external field on the system, while the remaining terms represent interactions between the particles of the system. Among them, the second one, the pair potential, is the most important. As said in the previous section, in the case of molecular systems the interaction between nuclei and electronic charge clouds of a pair of molecules i and j is generally a complicated function of the relative positions r_i and r_j, and orientations Ω_i and Ω_j (for atomic systems this term depends only on the pair separation, so that it may written as $v_2(r_{ij})$).

In the simplest approximation the total interaction is viewed as a sum of pair-wise contributions from distinct sites a in molecule i, at position r_{ia}, and b in molecule j, at position r_{jb}, i.e.:

$$v(r_{ij}, \Omega_i, \Omega_j) = \sum \sum v_{ab}(r_{ab}) \qquad [8.87]$$

In the equation, v_{ab} is the potential acting between sites a and b, whose inter-separation is r_{ab}.

The pair potential shows the typical features of intermolecular interactions as shown in Figure 8.1: there is an attractive tail at large separation, due to correlation between the electron clouds surrounding the atoms ('van der Waals' or 'London' dispersion), a negative well, responsible for cohesion in condensed phases, and a steeply rising repulsive wall at short distances, due to overlap between electron clouds.

Turning the attention to terms in eq. [8.86] involving triplets, they are usually significant at liquid densities, while four-body and higher are expected to be small in comparison with v_2 and v_3. Despite of their significance, only rarely triplet terms are included in computer simulations: that is due to the fact that the calculation of quantities related to a sum over triplets of molecules are very time-consuming. On the other hand, the average three-body effects can be partially included in a pair-wise approximation, leading it to give a good description of liquid properties. This can be achieved by defining an "effective" pair potential, able to represent all the many-body effects. To do this, eq. [8.86] can be re-written as:

$$V \approx \sum_i v_1(r_i) + \sum_i \sum_{j>i} v_2^{eff}(r_{ij}) \qquad [8.88]$$

The most widely used effective potential in computer simulations is the simple Lennard-Jones 12-6 potential (see eq. [8.70]), but other possibilities are also available; see Section 8.6 for discussion on these choices.

8.7.2.1 Car-Parrinello direct QM simulation

Until now we have focused the attention to the most usual way of determining a potential interaction to be used in simulations. It is worth mentioning a different approach to the problem, in which the distribution of electrons is not treated by means of an "effective" interaction potential, but is treated *ab initio* by density functional theory (DFT). The most popular method is the Car-Parrinello (CP) approach,[68,69] in which the electronic degrees of freedom are explicitly included in the description and the electrons (to which a fictitious mass is assigned) are allowed to relax during the course of the simulation by a process called "simulated-annealing". In that way, any division of V into pair-wise and higher terms is avoided and the interatomic forces are generated in a consistent and accurate way as the simulation proceeds. This point constitutes the main difference between a CP simulation and a conventional MD simulation, which is preceded by the determination of the potential and in which the process leading to the potential is completely separated from the actual simulation. The forces are computed using electronic structure calculations based on DFT, so that the interatomic potential is parameter-free and derived from first principles, with no experimental input.

Let us consider a system for which the BO approximation holds and for which the motion of the nuclei can be described by classical mechanics. The interaction potential is given by:

$$V(R) = \left\langle \psi_0 | \hat{H} | \psi_0 \right\rangle \qquad [8.89]$$

where H is the Hamiltonian of the system at fixed R positions and ψ_0 is the corresponding instantaneous ground state. Eq. [8.89] permits to define the interaction potential from first principles.

In order to use eq. [8.89] in a MD simulation, calculations of ψ_0 for a number of configurations of the order of 10^4 are needed. Obviously this is computationally very demanding, so that the use of certain very accurate QM methods (for example, the configuration interaction (CI)) is precluded. A practical alternative is the use of DFT. Following Kohn and Sham,[70] the electron density ρ(r) can be written in terms of occupied single-particle orthonormal orbitals:

$$\rho(r) = \sum_i \left|\psi_i(r)\right|^2 \qquad [8.90]$$

A point on the BO potential energy surface (PES) is then given by the minimum with respect to the ψ_i of the energy functional:

$$V[\{\psi_i\},\{R_I\},\{\alpha_v\}] = \sum_i \int_\Omega d^3r \psi_i^*(r)\left[-\frac{h^2}{2m}\nabla^2\right]\psi_i(r) + U[\rho(r),\{R_I\},\{\alpha_v\}] \qquad [8.91]$$

where $\{\mathbf{R}_I\}$ are the nuclear coordinates, $\{\alpha_v\}$ are all the possible external constraints imposed on the system (e.g., the volume Ω). The functional U contains the inter-nuclear Coulomb repulsion and the effective electronic potential energy, including external nuclear, Hartree, and exchange and correlation contributions.

In the conventional approach, the minimization of the energy functional (eq. [8.91]) with respect to the orbitals ψ_i subject to the orthonormalization constraint leads to a set of self-consistent equations (the Kohn-Sham equations), i.e.:

$$\left\{-\frac{h^2}{2m}\nabla^2 + \frac{\partial U}{\partial \rho(r)}\right\}\psi_i(r) = \varepsilon_i \psi_i(r) \qquad [8.92]$$

whose solution involves repeated matrix diagonalizations (and rapidly growing computational effort as the size of the system increases).

It is possible to use an alternative approach, regarding the minimization of the functional as an optimization problem, which can be solved by means of the simulated annealing procedure.[71] A simulated annealing technique based on MD can be efficiently applied to minimize the KS functional: the resulting technique, called "dynamical simulated annealing" allows the study of finite temperature properties.

In the "dynamical simulated annealing," the $\{R_i\}$, $\{\alpha_v\}$ and $\{\psi_i\}$ parameters can be considered as dependent on time; then the Lagrangian is introduced, i.e.:

$$L = \sum_i \frac{1}{2}\mu \int_\Omega d^3r |\dot{\psi}_i|^2 + \sum_I \frac{1}{2} M_I \dot{R}_I + \sum_v \frac{1}{2}\mu_v \dot{\alpha}_v^2 - V[\{\psi_i\},\{R_I\},\{\alpha_v\}] \qquad [8.93]$$

with:

$$\int_\Omega d^3r \psi_i^*(r,t)\psi_j(r,t) = \delta_{ij} \qquad [8.94]$$

In eq. [8.94] the dot indicates time derivative, M_I are the nuclear masses and μ are arbitrary parameters having the dimension of mass.

Using eq. [8.94] it is possible to generate a dynamics for $\{R_i\}$, $\{\alpha_v\}$ and $\{\psi_i\}$ through the following equations:

$$M_I \ddot{R}_I = -\nabla_{R_I} V \qquad [8.95]$$

$$\mu_v \ddot{\alpha}_v = -\left(\frac{\partial V}{\partial \alpha_v}\right) \qquad [8.96]$$

$$\mu\ddot{\psi}(r,t) = -\frac{\partial V}{\partial \psi_i^*(r,t)} + \sum_k \Lambda_{ik}\psi_k(r,t) \qquad [8.97]$$

In eq. [8.97] the Λ are the Lagrange multipliers introduced to satisfy eq. [8.94]. It is worth noticing that, while the nuclear dynamics [8.95] can have a physical meaning, that is not true for the dynamics associated with the $\{\alpha_v\}$ and $\{\psi_i\}$: this dynamics is fictitious, like the associated "masses" μ.

If μ and the initial conditions $\{\psi_i\}_0$ and $\{d\psi_i/dt\}_0$ are chosen such that the two classical sets of degrees of freedom (nuclear and electronic) are only weakly coupled, the transfer of energy between them is small enough to allow the electrons to adiabatically follow the nuclear motion, then remaining close to their instantaneous BO surface. In such a metastable situation, meaningful temporal averages can be computed. The mentioned dynamics is meant to reproduce what actually occurs in real matter, that is, electrons adiabatically following the nuclear motion.

QM potentials have been widely used in molecular dynamics simulation of liquid water using the CP DFT algorithm. See, for example, refs. [72,73].

8.7.2.2 Semi-classical simulations

Computer simulations are methods addressed to perform "computer experimentation". The importance of computer simulations rests on the fact that they provide quasi-experimental data on well-defined models. As there is no uncertainty about the form of the interaction potential, theoretical results can be tested in a way that is usually impossible with results obtained by experiments on real liquids. In addition, it is possible to get information on quantities of no direct access to experimental measures.

There are basically two ways of simulating a many-body system: through a stochastic process, such as the Monte Carlo (MC) simulation,[74] or through a deterministic process, such as a Molecular Dynamics (MD) simulation.[75,76] Numerical simulations are also performed in a hybridized form, like the Langevin dynamics[42] which is similar to MD except for the presence of a random dissipative force, or the Brownian dynamics,[42] which is based on the condition that the acceleration is balanced out by drifting and random dissipative forces.

Both the MC and the MD methodologies are used to obtain information on the system via a classical statistical analysis but, whereas MC is limited to the treatment of static properties, MD is more general and can be used to take into account the time dependence of the system states, allowing one to calculate time fluctuations and dynamic properties.

In the following, we shall briefly describe the main features of MD and MC methodologies, focusing the attention to their use in the treatment of liquid systems.

Molecular dynamics

Molecular Dynamics is the term used to refer to a technique based on the solution of the classical equation of motion for a classical many-body system described by a many-body Hamiltonian H.

In a MD simulation, the system is placed within a cell of fixed volume, usually of cubic shape. A set of velocities is assigned, usually drawn from a Maxwell-Boltzmann distribution suitable for the temperature of interest and selected to make the linear momentum equal to zero. Then the trajectories of the particles are calculated by integration of the classical equation of motion. It is also assumed that the particles interact through some forces, whose calculation at each step of the simulation constitutes the bulk of the computational demand of the calculation. The first formulation of the method, due to Alder,[75] referred to a system of hard spheres: in this case, the particles move at constant velocity between perfectly elastic collisions, so that it is possible to solve the problem without making any approximations. More difficult is the solution of the equations of motion for a set of Lennard-Jones particles: in fact, in this case an approximated step-by-step procedure is needed, since the forces between the particles change continuously as they move.

Let us consider a point Γ in the phase space and suppose that it is possible to write the instantaneous value of some property A as a function A(Γ). As the system evolves in time, Γ and hence A(Γ) will change. It is reasonable to assume that the experimentally observable "macroscopic" property A_{obs} is really the time average of A(Γ) over a long time interval:

$$A_{obs} = \langle A \rangle_{time} = \langle A(\Gamma(t)) \rangle_{time} = \lim_{t\to\infty} \frac{1}{t} \int_0^t A(\Gamma(t))dt \qquad [8.98]$$

The time evolution is governed by the well-known Newton equations, a system of differential equations whose solution is practical. Obviously it is not possible to extend the integration to infinite time, but the average can be reached by integrating over a long finite time, at least as long as possible as determined by the available computer resources. This is exactly what is done in a MD simulation, in which the equations of motion are solved step-by-step, taking a large finite number τ of steps, so that:

$$A_{obs} = \frac{1}{\tau} \sum_{\bar{\tau}} A(\Gamma(\bar{\tau})) \qquad [8.99]$$

It is worth stressing that a different choice in the time step is generally required to describe different properties, as molecular vibrations (when flexible potentials are used), translations and rotations.

A problem arising from the methodology outlined above is whether or not a suitable region of the phase space is explored by the trajectory to yield good time averages (in a relatively short computing time) and whether consistency can be obtained with simulations with identical macroscopic parameters but different initial conditions. Generally, thermodynamically consistent results for liquids can be obtained provided that careful attention is paid to the selection of initial conditions.

Monte Carlo

As we have seen, apart from the choice of the initial conditions, a MD simulation is entirely deterministic. By contrast, a probabilistic (stochastic) element is an essential part of any Monte Carlo (MC) simulation.

The time-average approach outlined above is not the only possible: it is in fact practical to replace the time average by the ensemble average, being the ensemble a collection of points Γ distributed according to a probability density ρ(Γ) in the phase space. The density is determined by the macroscopic parameters, NPT, NVT, etc., and generally will evolve in time. Making the assumption that the system is "ergodic", the time average in eq. [8.98] can be replaced by an average taken over all the members of the ensemble at a particular time:

$$A_{obs} = \langle A \rangle_{ensemble} = \sum_{\Gamma} A(\Gamma) \rho_{ensemble}(\Gamma) \qquad [8.100]$$

Sometimes, instead of using the $\rho(\Gamma)$, a "weight" function $w(\Gamma)$ is used:

$$\rho(\Gamma) = \frac{w(\Gamma)}{Q} \qquad [8.101]$$

$$Q = \sum_{\Gamma} w(\Gamma) \qquad [8.102]$$

$$\langle A \rangle_{ensemble} = \frac{\sum_{\Gamma} w(\Gamma) A(\Gamma)}{\sum_{\Gamma} w(\Gamma)} \qquad [8.103]$$

Q is the partition function of the system.

From Eq. [8.102], it is possible to derive an approach to the calculation of thermodynamics properties by direct evaluation of Q for a particular ensemble. Q is not directly estimated, but the idea of generating a set of states in phase space sampled in accordance with the probability density $\rho(\Gamma)$ is the central idea of MC technique. Proceeding exactly as done for MD, replacing an ensemble average as in Eq. [8.103] with a trajectory average as in Eq. [8.99], a succession of states is generated in accordance with the distribution function ρ_{NVE} for the microcanonical NVE ensemble. The basic aim of the MC method (so-called because of the role that random numbers play in the method), which is basically a technique for performing numerical integration, is to generate a trajectory in phase space that samples from a chosen statistical ensemble. It is possible to use ensembles different from the microcanonical: the only request is to have a way (physical, entirely deterministic or stochastic) of generating from a state $\Gamma(\tau)$ a next state $\Gamma(\tau + 1)$. The important point to be stressed is that some conditions have to be fulfilled: these are that the probability density $\rho(\Gamma)$ for the ensemble should not change as the system evolves, any starting distribution $\rho(\Gamma)$ should tend to a stationary solution as the simulation proceeds, and the ergodicity of the systems should hold. With these recommendations, we should be able to generate from an initial state a succession of points that in the long term are sampled with the desired probability density $\rho(\Gamma)$. In this case, the ensemble average will be the same as a "time average" (see Eq. [8.99]). In a practical simulation, τ runs over the succession of states generated following the previously mentioned rules, and is a large finite number. This approach is exactly what is done in an MC simulation, in which a trajectory is generated through phase space with different recipes for the different ensembles. In other words, in a MC simulation a system of particles interacting through some known potential is assigned a set of initial coordinates (arbitrarily chosen) and a sequence of configurations of the particles is then generated by successive random displacements (also called 'moves').

If f(R) is an arbitrary function of all the coordinates of the molecule, its average value in the canonical ensemble is:

$$\langle f \rangle = \frac{\int f(r) e^{-\beta V(R)} dR}{\int e^{-\beta V(R)} dR} \qquad [8.104]$$

where $\beta = 1/kT$ and V(R) is the potential energy.

In the MC methods the integration is done by re-writing <f> in terms of the probabilities P_k of finding the configuration R_k:

$$\langle f \rangle = \sum_k f(R_k) P_k \qquad [8.105]$$

$$P_k = \frac{e^{-\beta V(R_k)}}{\sum_k e^{-\beta V(R_k)}} \qquad [8.106]$$

The search for the most probable configuration R_k is done using Markov's chain theory, so that after setting the system at a given configuration R_i, another configuration R_j is selected, making a random move in the coordinates. Not all configurations are accepted; the decision on whether or not to accept a particular configuration is made in such a way as to ensure that asymptotically the configuration space is sampled according to the probability density appropriate to a chosen ensemble. In particular:

if $$V(R_j) < V(R_i)$$

the move is accepted in the chain. Otherwise,

if $$V(R_j) > V(R_i)$$

the move is subjected to a second screening and accepted

if $$e^{-\beta(V_j - V_i)} < \gamma$$

where γ is a random number between 0 and 1.

The original models used in MC were highly idealized representations of molecules, such as hard spheres and disks, but nowadays MC simulations are carried out on the basis of more reliable interaction potential. The use of realistic molecule-molecule interaction potential makes it possible to compare data obtained from experiments with the computer generated thermodynamic data derived from a model. The particle momenta do not enter the calculation, there is no scale time involved, and the order in which the configurations occur has no special significance.

It is worth noticing that, because only a finite number of states can be generated in a simulation, the results obtained from a MC simulation are affected by the choice of initial conditions, exactly as previously said for the MD results.

As we have already said, it is possible to extend the MC method, originally formulated in the microcanonical ensemble, to other ensembles. Particularly important in the study of liquid systems is the extension of the Monte Carlo method to the grand canonical μVT ensemble:[76] that is due to the fact that such an extension permits to calculate the free energy of the system, a quantity of particular significance in the chemistry and physics of liquids. The grand canonical MC involves a two-stage process: the first stage is exactly identical to what is done in the conventional MC, with the particles moving and the move accepted or rejected as previously said. The second stage involves an attempt either to insert a particle at a randomly chosen point in the cell or to remove a particle that is already present. The decision whether to make an insertion or a removal is made randomly with equal probabilities. The trial configuration is accepted if the pseudo-Boltzmann factor:

$$W_N = e^{\left[N\beta\mu - \log N! - \beta V_N(r^N)\right]} \qquad [8.107]$$

increases. If it decreases, the change is accepted when equal to:

$$\frac{W_{N+1}}{W_N} = \frac{1}{N+1} e^{[\beta\mu - \beta(V_{N+1} - V_N]} \qquad [8.108]$$

for the insertion, or to:

$$\frac{W_{N-1}}{W_N} = N e^{[-\beta\mu - \beta(V_{N+1} - V_N]} \qquad [8.109]$$

for the removal.

This method works very well at low and intermediate densities. As the density increases, it becomes difficult to apply, because the probability of inserting or removing a particle is very small.

As we have already said, the grand canonical Monte Carlo provides a mean to determining the chemical potential, and hence, the free energy of the system. In other MC and MD calculations a numerical value for the free energy can always be obtained by means of an integration of thermodynamic relations along a path which links the state of interest to one for which the free energy is already known, for example, the dilute gas or the low-temperature solid. Such a procedure requires considerable computational effort, and it has a low numerical stability. Several methods have been proposed and tested.

The difficulties in using MC and MD arise from the heavy computational cost, due to the need of examining a large number of configurations of the system usually consisting of a large number of particles. The size of the system one can study is limited by the available storage on the computer and by the speed of execution of the program. The time taken to evaluate the forces or the potential energy is proportional to N^2.

Other difficulties in molecular simulations arise from the so-called quasi-ergodic problem,[77] i.e., the possibility that the system becomes trapped in a small region of the phase space. To avoid it, whatever the initial conditions, the system should be allowed to equilibrate before starting the simulation, and during the calculation, the bulk properties should be carefully monitored to detect any long-time drift.

As already said, apart from the initial conditions, the only input information in a computer simulation are the details of the inter-particle potential, almost always assumed to be pair-wise additive. Usually in practical simulations, in order to economize the computing time, the interaction potential is truncated at a separations r_c (the cut-off radius), typically of the order of three molecular diameters. Obviously, the use of a cut-off sphere of small radius is not acceptable when the inter-particle forces are very long ranged.

The truncation of the potential differently affects the calculation of bulk properties, but the effect can be recovered by using appropriate "tail corrections". For energy and pressure for monoatomic fluids, for example, these "tail corrections" are obtained by evaluating the following integrals [8.110] and [8.111] between the limits $r=r_c$ and $r=\infty$, and assuming that $g(r)=1$ for $r>r_c$:

$$\frac{E}{N}=2\pi\rho\int v(r)\,g(r)\,r^2dr \qquad [8.110]$$

$$\frac{\beta P}{\rho}=1-\frac{2\pi\beta\rho}{3}\int v(r)\,g(r)\,r^3dr \qquad [8.111]$$

As already mentioned above, the extent of "tail corrections" strongly depends on the property under study. In the case of pressure, this correction can be very large; for example, in the case of a Lennard-Jones potential truncated at $r_c=2.5\sigma$, at conditions close to the triple point, $E/N\varepsilon=-6.12$, to which the tail correction contributes -0.48, but $\beta P/\rho=0.22$, of which -1.24 comes to the tail. The neglecting of the tail correction would lead to a strongly positive value for pressure.[42]

Usually, when a cut-off radius is exploited, for the calculation of the interaction between a particle and the others, the "nearest-neighbor" convention is used. It means that, assuming the particles of interest lie in a cell and that this basic unit is surrounded by periodically repeated images of itself, a particle i lying on the central cell will interact only with the nearest image of any other particle j. The interaction is then set to zero if the distance between i and the nearest image is greater than r_c. The usual assumption $r_c<L/2$, with L the cell length, means it is assumed that at most one image of j lies in any sphere of radius $r<L/2$ centered on the particle i.

For the calculations of properties of a small liquid system, like a very small liquid drop, the cohesive forces between molecules may be sufficient to hold the system together during the course of a simulations: otherwise the system of molecules may be confined by a potential acting as a container. Such an arrangement is, however, not satisfactory for the simulation of bulk liquids, being the main obstacle the large fraction of molecules which lie on the surface. Molecules on the surface will experience quite different forces from molecules in the bulk.

To overcome the problem, in the simulation of bulk liquids a possible solution is to impose periodic boundary conditions. The system is in a cubic box, which is replicated throughout space to form an infinite lattice. During the simulation, as a molecule moves in the original box, its image in each of the neighboring boxes moves exactly in the same way. In particular as a molecule leaves the central box, one of its images will enter the central box through the opposite face. A common question to ask about the use of periodic boundary conditions is if the properties of a small, infinitely periodic system and the macroscopic system that it represents are the same. This will usually depend both on the range of the intermolecular potential and the phenomenon under investigation. In some cases, periodic boundary conditions have little effect on the equilibrium thermodynamic properties and structure of fluids away from phase transitions and where the interactions are short-ranged, but in other cases this is not true.

It is worth mentioning an alternative method to the standard periodic boundary conditions for simulating bulk liquids. A three dimensional system can be embedded in the surface of an hypersphere: the hypersphere is a finite system and cannot be considered as part of an infinitely repeating periodic system. Effects coming from the curved geometry (non-Euclidean geometry has to be considered) are expected to decrease as the system increases, so that in the case of solutes of large size, "spherical boundary conditions" are expected to be a noticeable method for simulating bulk liquids. In this case, boundary conditions can be obtained by inserting the spherical cell into a large sphere and then by performing a simulation of a lower computational level in the extended region. However, recent versions of the method tend to replace the second portion of the liquid, described at a molecular level, with a description by means of continuum models (see Section 8.7.3), which can be easily extended up to $r=\infty$.

Turning attention to the accuracy gained in the calculation of liquids properties by molecular simulations, it turns out that certain properties can be calculated more accurately than others. For example, the mean potential energy can be obtained with an uncertainty less than 1%; larger errors are associated with the calculation of thermodynamic properties, such as, the specific heat, that are linked to fluctuations in a microscopic variable. Typically, an uncertainty of the order of 10% is expected.[42]

The dynamical properties of liquids can be generally computed by calculating the time-correlation functions. They provide a quantitative description of the microscopic dynamics in liquids. Here, computer simulations play a key role, since they give access to a large variety of correlation functions, many of which are not measurable by laboratory experiments. In a MD simulation, the value of the correlation function $C_{AB}(t)$ at time t is calculated by averaging the product $A(t+s)B(s)$ of two dynamical variables, A(t) and B(t) over many choices of the time origin s. It has been shown that the uncertainty in time correlations between events separated by an interval τ increases as $\tau^{1/2}$. In addition, the correlated motion of large numbers of particles determines many dynamical properties. These collective properties are usually subjected to larger errors than in the case of single particle properties, and their calculation is very demanding from a computational point of view.[42]

QM/MM

As final remark of this section, we would like to briefly mention the so-called QM/MM method.[78,79]

In this approach, a part of the system (the solute M) is treated explicitly by a quantum mechanical (QM) method, while another part (the bulk solvent S) is approximated by a standard Molecular Mechanics (MM) force field. It is clear that such a method takes advantage of the accuracy and generality of the QM treatment, and of the computational efficiency of the MM calculation.

Using the BO approximation and assuming that no charge transfer occurs between S and M, the Hamiltonian of the system can be separated into three terms:

$$\hat{H}=\hat{H}_M+\hat{H}_{MS}+\hat{H}_{SS} \qquad [8.112]$$

where the first term is the Hamiltonian of the solute in vacuo, the second one represents the QM/MM solute-solvent interaction and couples solvent effects into QM calculations. It can be separated in an electrostatic term, a van der Waals terms and a polarization term, i.e.:

$$\hat{H}_{MS}=\hat{H}_{MS}^{el}+\hat{H}_{MS}^{vdW}+\hat{H}_{MS}^{pol} \qquad [8.113]$$

The third term in eq. [8.112] is the interaction energy between solvent molecules. It is usually approximated by the molecular mechanics force field, which in general contains bond stretching, angle bending, dihedral torsion and non-bonded terms (see Section 8.4.5).

Once the Hamiltonian of the system is defined, the total energy of an instantaneous configuration sampled during an MC or MD simulation is determined as:

$$E = \left\langle \Phi \middle| \hat{H} \middle| \Phi \right\rangle = E_M + E_{MS} + E_{SS} \qquad [8.114]$$

More details on the procedure can be found in literature.[78]

The forces used to integrate Newton's equation of motion in MD simulations are determined by differentiating eq. [8.114] with respect to nuclear coordinates.

In the practical QM/MM calculation, the solvent S is equilibrated first using simulations (or a RISM version of the integral equation approach, see Section 8.7.1.1), and then the electronic structure of the solute M is modified via an iterative QM procedure in the presence of a fixed potential of the S component. The procedure is repeated iteratively; at the next step the S distributions is determined again, now taking into account the modified description of M. This sequence of steps is repeated until convergence. A problem of such a methodology is that changes in the internal geometry of M must be treated apart, scanning point-by point the relevant PES, not being available analytical expressions for first and second derivatives of the energy with respect to nuclear coordinates, which would be necessary to take into account any modification in the solute geometry.

To overcome problems arising from the finite system size used in MC or MD simulation, boundary conditions are imposed using periodic-stochastic approximations or continuum models.[75] In particular, in stochastic boundary conditions the finite system is not duplicated but a boundary force is applied to interact with atoms of the system. This force is set as to reproduce the solvent regions that have been neglected. Anyway, in general any of the methods used to impose boundary conditions in MC or MD can be used in the QM/MM approach.

8.7.3 CONTINUUM MODELS

Originally, continuum models of solvent were formulated as dielectric models for electrostatic effects. In a dielectric model the solvent is modeled as a continuous medium, usually assumed homogeneous and isotropic, characterized by a scalar, static dielectric constant ε. This model of the solvent, that can be referred to the original work by Born, Onsager and Kirkwood 60-80 years ago, assumes linear response of the solvent to a perturbing electric field due to the presence of the molecular solute.

This simple definition then has been largely extended to treat more complex phenomena, including not only electrostatic effects; and nowadays continuum solvation models represent very articulate methodologies able to describe different systems of increasing complexity.

The history of, and the theory behind, continuum solvation models have been described exhaustively in many reviews[31a,80,81] and articles[82-84] in the past, so we prefer not to repeat them here. In addition, so large and continuously increasing is the amount of examples of theoretical developments on one hand, and of numerical applications on the other, that we shall limit our attention to a brief review of the basic characteristics of these models which have gained wide acceptance and are in use by various research groups.

Trying to give a more theoretically-stated definition of continuum models, but still keeping the same conciseness of the original one reported above, we have to introduce some basic notions of classical electrostatics.

The electrostatic problem of a charge distribution ρ_M (representing the molecular solute) contained in a finite volume (the molecular cavity) within a continuum dielectric can be expressed in terms of the Poisson equation:

$$\vec{\nabla}\left[\varepsilon(\vec{r})\vec{\nabla}\phi(\vec{r})\right] = -4\pi\rho_M(\vec{r}) \qquad [8.115]$$

where ϕ is the total electrostatic potential.

Eq. [8.115] is subject to the constraint that the dielectric constant inside the cavity is $\varepsilon_{in}=1$, while at the asymptotic boundary we have:

$$\lim_{r\to\infty} r\phi(\vec{r}) = \alpha \qquad \lim_{r\to\infty} r^2\phi(\vec{r}) = \beta \qquad [8.116]$$

with α and β finite quantities.

At the cavity boundary the following conditions hold:

$$\phi_{in}(\vec{r}) = \phi_{out}(\vec{r}) \qquad \frac{\partial\phi_{in}}{\partial\hat{n}} = \varepsilon_{out}(\vec{r})\frac{\partial\phi_{out}}{\partial\hat{n}} \qquad [8.117]$$

where subscripts in and out indicate functions defined inside and outside the cavity, and $\hat{n}$ is the unit vector perpendicular to the cavity surface and pointing outwards.

Further conditions can be added to the problem, and/or those shown above (e.g., the last one) can be modified; we shall consider some of these special cases later.

As said above, in several models an important simplification is usually introduced, i.e., the function $\varepsilon_{out}(\vec{r})$ is replaced by a constant ε (from now on we skip the redundant subscript out). With this simplification we may rewrite the electrostatic problem by the following equations:

$$\text{inside the cavity: } \nabla^2\phi(\vec{r}) = -4\pi\rho_M(\vec{r}), \text{ outside the cavity: } \nabla^2\phi(\vec{r}) = 0 \qquad [8.118]$$

Many alternative approaches have been formulated to solve this problem.

In biochemistry, methods that discretize the Poisson differential operator over finite elements (FE) have long been in use. In general, FEM approaches do not directly use the molecular cavity surface. Nevertheless, as the whole space filled by the continuous medium is partitioned into locally homogeneous regions, a careful consideration of the portion of space occupied by the molecular solute has still to be performed.

There is another family of methods, known as FD (finite difference) methods,[85] which exploit point grids covering the whole space, but conversely to the FEM point, in FD methods the points are used to replace differential equations by algebraic ones.

These methods can be applied both to the "simplified" model with constant ε, and to models with space dependent $\varepsilon(\vec{r})$ or real charges dispersed in the whole dielectric medium. They aim at solving the Poisson equation (1) expressed as a set of finite difference equations for each point of the grid. The linear system to be solved has elements depending both on ε

and ρ_M, and its solution is represented by a set of ϕ values in the grid points. These values have to be reached iteratively.

Many technical details of the methods have been changed in the years. We signal, among others, the strategy used to define the portion of the grid, especially near the molecular surface where there is a sharp change in ε, and the mathematical algorithms adopted to improve convergence in the iterative processes. Almost all FD methods have been conceived for, and applied to, classical descriptions of solutes, generally represented by atomic charges. The latter are usually drawn from previous QM calculations in vacuo or from Molecular Mechanics effective potentials, as in the study of large molecules, usually proteins. The deficiencies due to the use of rigid charges are partially alleviated by introducing a dielectric constant greater than one for the inner space (ε between 2 and 4), and/or by including atomic polarization functions (akin to atomic dipole polarizabilities).

The DelPhi program[85a] is one of these proposals. This method, which has been extensively improved during the years, exists now in a QM version[86] exploiting a recent high level QM method, called PS-GVB,[87] based on a synthesis of grid point integration techniques and standard Gaussian orbital methods. From a PS-GVB calculation in vacuo, a set of atomic charges, the potential derived (PD) charges, is obtained by a fitting of the molecular electrostatic potential (MEP). These charges are used in DelPhi to solve the Poisson equation in the medium, and then to get, with the aid of a second application of DelPhi in vacuo, the reaction field (RF). The latter is represented by a set of point charges on the cavity surface, which define the solute-solvent interaction potential to be inserted in the PS-GVB Hamiltonian. Then a new computational cycle starts, and the whole process is repeated until convergence is reached.

In parallel, the classical FD procedure of Bashford and Karplus[88] has been coupled with the Amsterdam density fuctional theory (DFT)[89] code to give another version of QM-FD methods. Starting from a DFT calculation in vacuo, the RF potential is obtained as the difference between the solutions of the Poisson equation obtained with a FD method in the medium and in vacuo (in both cases, the electrostatic potential ϕ_M is expressed in terms of PD atomic charges). The RF potential is then re-computed to solve a modified Kohn-Sham equation. The calculations are repeated until convergence is achieved.

An alternative to the use of finite differences or finite elements to discretize the differential operator is to use boundary element methods (BEM).[90] One of the most popular of these is the polarizable continuum model (PCM) developed originally by the Pisa group of Tomasi and co-workers.[32] The main aspect of PCM is to reduce the electrostatic Poisson equation (1) into a boundary element problem with apparent charges (ASCs) on the solute cavity surface.

A method that is very similar to PCM is the conductor-like screening model (COSMO) developed by Klamt and coworker[91] and used later by Truong and coworkers,[92] and by Barone and Cossi.[93] This model assumes that the surrounding medium is well modeled as a conductor (thus simplifying the electrostatics computations) and corrections are made *a posteriori* for dielectric behavior.

Electrostatic BE methods can be supported by nonelectrostatic terms, such as dispersion and exchange, in different ways, and their basic theory can be extended to treat both classical and quantum mechanical solutes; in addition, many features, including analytical gradients with respect to various parameters, have been added to the original models so as to make BE methods one of the most powerful tools to describe solvated systems of increasing complexity. More details on their main aspects will be given in the following.

Further alternative methods for solving the Poisson equation are to represent the solute and the solvent reaction field by single-center multipole expansions (MPE), as first pioneered by the Nancy group of Rivail and coworkers.[94] Originally, this formalism was adopted because it simplified computation of solvation free energies and analytic derivatives for solute cavities having certain ideal shapes, e.g., spheres and ellipsoids. The formalism has been extended to arbitrary cavity shapes and multipole expansions at multiple centers. An alternative method still adopting the same MPE approach is that of Mikkelsen and coworkers;[95] this method has been implemented in the Dalton computational package.[96]

The idea of a distributed multipole expansion to represent the charge distribution is also employed by the so-called generalized Born (GB) approach to continuum solvation. In this case, however, only monopoles (i.e., atomic partial charges) are employed and instead of solving the Poisson equation with this charge distribution, one uses the generalized Born approximation. The most widely used solvation models adopting this procedure are the original generalized Born/surface area (GBSA) approach of Still and co-workers,[97] including the subsequent extensions and adaptations of several groups in which the GB electrostatics are combined with a classical MM treatment of the solute, and the SMx models of Cramer, Truhlar and coworkers[98] in which GB electrostatics are employed in a quantum mechanical treatment of the solute. In both of these approaches, semiempirical atomic surface tensions are used to account for nonelectrostatic solvation effects. For the SMx models, the value of x ranges from 1 to 5.42, corresponding to successively improved versions of the prescriptions for atomic charges and radii, the dielectric descreening algorithm, and the functional forms for the atomic surface tensions.

8.7.3.1 QM-BE methods: the effective Hamiltonian

As anticipated above, in BE methods for solvation the basic feature is to solve the Poisson equation [8.115] with the related boundary conditions [8.117] (or in a simpler isotropic case the system [8.118]) by defining an apparent charge distribution σ on the solute cavity surface (such charge is usually indicated as ASC).[31a] This continuous charge which depends on both the solvent dielectric constant and the solute charge and geometry, is then discretized in terms of point charges each placed on a different portion of surface identified by a collocation point s_k and an area a_k. This partition of the cavity surface into patches, or tesserae, represents one of the main features of the method as well as the shape of the cavity itself, which here has not been limited to analytical simple shapes (as in the original MPE methods), but it can be well modeled according to the actual solute geometry.

The particular aspect we shall treat here is the generalization of the basic theory of these methods to QM descriptions of the solute. To do that, one has to introduce the concept of the Effective Hamiltonian (EH); for the isolated system, the fundamental equation to solve is the standard Schrödinger equation

$$H^0\Psi^0 = E^0\Psi^0 \qquad [8.119]$$

where the superscript 0 indicates the absence of any interactions with other molecules.

In the presence of a solvent treated in the ASC-BE framework, an external perturbation has to be taken into account: the reaction field due to the apparent charges placed on the cavity surface. Such perturbation can be represented in terms of an electrostatic potential V^R

to be added to the Hamiltonian H^0 so to obtain an effective Hamiltonian H which will satisfy a different Schrödinger equation with respect to [8.119], namely, we have

$$H\Psi = E\Psi \qquad [8.120]$$

Both the wave function and the eigenvalue E will be modified with respect to [8.119], due to the presence of the solvent perturbation.

An important aspect, until now not introduced, is that the solvent apparent charges, and consequently the reaction operator V^R, depend on the solute charge, i.e., in the present QM framework, on the wave function they contribute to define. This mutual interactions between Ψ and V^R induces a complexity in the problem which can be solved through the standard iterative procedures characterizing the self-consistent (SC) methods. Only for an aspect the calculation in solution has to be distinguished from that in vacuo way; the energy functional to be minimized in a variational solution of [8.120] is not the standard functional E but the new free energy functional G

$$G = \left\langle \Psi \middle| H^0 + 1/2V^R \middle| \Psi \right\rangle \qquad [8.121]$$

The 1/2 factor in front of V^R accounts for the linear dependence of the operator on the solute charge (i.e., the quadratic dependence on Ψ). In a more physical description, the same factor is introduced when one considers that half of the interaction energy has been spent in polarizing the solvent and it has not been included in G.

In the standard original model the perturbation V^R is limited to the electrostatic effects (i.e., the electrostatic interaction between the apparent point charges and the solute charge distribution); however, extensions to include dispersion and repulsion effects have been formulated. In this more general context the operator V^R can be thus partitioned in three terms (electrostatic, repulsive and dispersive), which all together contribute to modify the solute wave function.

For clarity's sake in the following we shall limit the analysis to the electrostatic part only, referring the reader to refs. [31,83], and to the original papers quoted therein, for details on the other terms. For a more complete report we recall that nonelectrostatic effects can be also included *a posteriori*, i.e., independently of the QM calculation, through approximated or semiempirical models still exploiting the definition of the molecular cavity. In PCM and related methods, the term corresponding to the energy spent in forming the solute cavity in the bulk liquid, is usually computed using the SPT integral equation method (see Section 8.7.1.1).

Until now no reference to the specific form of the operator V^R has been given, but here it becomes compulsory. Trying to remain at the most general level possible, we start to define the apparent charges $q(s_k)$ through a matrix equation, i.e.,

$$\boldsymbol{q} = -\boldsymbol{M}^{-1}\boldsymbol{f}(\rho) \qquad [8.122]$$

where **M** is a square matrix depending only on the geometry of the system (e.g., the cavity and its partition in tesserae) and the solvent dielectric constant and $\mathbf{f}(\rho)$ is a column vector containing the values of a function f, which depends on the solute distribution charge ρ, computed on the cavity tesserae. The form of this function is given by the specific solvation model one uses; thus, for example, in the original version of PCM it coincides with the normal component of the electrostatic field to the cavity surface, while for both the COSMO model[91-93] and the revised PCM version, known as IEF (integral equation formalism),[99] it is represented by the electrostatic potential. In any case, however, this term induces a dependence of the solvent reaction to the solute charge, and finally to its wave function; in a standard SC procedure it has to be recomputed (and thus also the apparent charges **q**) at each iteration.

Also, the form of **M** depends on the solvation model; contrary to **f**, it can be computed once, and then stored, if the geometry of the system is not modified during the calculation.

Once the apparent charges have been defined in an analytical form through eq. [8.122], it is possible to define the perturbation V^R as

$$V^R = \int \frac{q(sk)}{|r - sk|} \rho(\rho) dr \qquad [8.123]$$

In particular, by distinguishing the source of ρ, i.e., the solute nuclei and electrons, we can always define two equations [8.122], one for each source of f, and thus compute two sets of apparent charges, $\mathbf{q}^N$ and $\mathbf{q}^e$, depending on the solute nuclei and electrons, respectively. This allows one to partition the reaction operators in two terms, one depending on the geometry of the system and the solute nuclear charge, and the other still depending on the geometry and on the solute wave function.

Such partition is usually introduced to get an effective Hamiltonian whose form resembles that of the standard Hamiltonian for the isolated system. In fact, if we limit our exposition to the Hartree-Fock approximation in which the molecular orbitals are expressed as an expansion over a finite atomic orbital basis set, the Fock operators one defines for the two systems, the isolated and the solvated one, become (over the atomic basis set)

$$\boldsymbol{F}^0 = \boldsymbol{h} + \boldsymbol{G}(\boldsymbol{P}) \qquad \boldsymbol{F} = \boldsymbol{h} + \boldsymbol{j} + \boldsymbol{G}(\boldsymbol{P}) + \boldsymbol{X}(\boldsymbol{P}) \qquad [8.124]$$

where **h** and **G**(**P**) are the standard one and two-electron interaction matrices in vacuo (**P** represents the one-electron density matrix). In [8.124] the solvent terms are expressed by two matrices, **j** and **X**(**P**), whose form follows directly from the nuclei and electron-induced equivalents of expression [8.122], respectively; for the electronic part, ρ has to be substituted by **P**.

The parallel form of $\mathbf{F}^0$ and **F** in [8.124] shows that the two calculations can be performed exactly in the same way, i.e., that solvent does not introduce any complication or basic modification to the procedure originally formulated for the isolated system. This is a very important characteristic of continuum BE solvation methods which can be generalized to almost any quantum mechanical level of theory. In other words, the definition of ‘pseudo’ one and two-electron solvent operators assures that all the theoretical bases and the formal issues of the quantum mechanical problem remain unchanged, thus allowing a stated solution of the new system exactly as in vacuo.

Above, we have limited the exposition to the basic features of single point HF calculations, and to the thermodynamic functions (the solvation free energy is immediately given by eqs. [8.121-8.124]). However, extensions to other QM procedures as well as to other types of analysis (the evaluation of molecular response functions, the study of chemical reactivity, the reproduction of spectra of various nature, just to quote the most common applications) have been already successfully performed.[83] Many of these extensions have been made possible by the formulation and the following implementation of efficient procedures to get analytical derivatives of the free energy in solution with respect to various parameters.[100] To understand the role of this methodological extension in the actual development of the solvation models we just recall the importance of an efficient computation of analytical gradients with respect to nuclear coordinates to get reliable geometry optimizations and dynamics.[101]

It is here important to recall that such improvements are not limited to BE solvation methods; for example, Rivail and the Nancy group[102] have recently extended their multipole-expansion formalism to permit the analytic computation of first and second derivatives of the solvation free energy for arbitrary cavity shapes, thereby facilitating the assignment of stationary points on a solvated potential energy surface. Analytic gradients for SMx models at ab initio theory have been recently described[103] (even if they have been available longer at the semiempirical level[104]), and they have been presented also for finite difference solutions of the Poisson equation and for finite element solutions.

Many other extensions of different importance have been added to the original BE models in the last few years. Here it may be worth recalling a specific generalization which also has made BE models preferable in particular applications until now almost completely restricted to FE and FD methods.

At the beginning of the present section we indicated the simplified system (4), valid only in the limit of an homogeneous and isotropic dielectric, the commonly studied problem; actually, this has been the only affordable system until recently, with some exceptions represented by systems constituted by two isotropic systems with a definite interface. The situation changed only a few years ago (1997-1998) when BE-ASC methods were extended to treat macroscopically anisotropic dielectrics (e.g., liquid crystals),[99] ionic solutions (e.g., isotropic solutions with nonzero ionic strength),[99] and supercritical liquids.[105]

Another important feature included in BE methods, as well in other continuum methods, are the dynamical effects.

In the previous section devoted to Physical Models, we have recalled that an important issue of all the solvation methods is their ability to treat nonequilibrium, or dynamical, aspects. There, for clarity's sake, we preferred to skip the analysis of this feature, limiting the exposition to static, or equilibrium problems; here, on the contrary, some comments will be added.

In continuum models no explicit reference to the discrete microscopical structure of the solvent is introduced; on one hand, this largely simplifies the problem, but on the other hand it represents a limit which can effect the quality of the calculations and their extensibility to more complex problems such as those involving dynamical phenomena. However, since the first formulations of continuum models, different attempts to overcome this limit have been proposed.

One of the theories which has gained more attention identifies the solvent response function with a polarization vector depending on time, P(t), which varies according to the variations of the field from which it is originated (i.e., a solute and/or an external field). This vector accounts for many phenomena related to different physical processes taking place inside and among the solvent molecules. In practice, strong approximations are necessary in order to formulate a feasible model to deal with such complex quantity. A very simple but also effective way of seeing this problem is to partition the polarization vector in terms accounting for the main degrees of freedom of the solvent molecules, each one determined by a proper relaxation time (or by the related frequency).

In most applications, this spectral decomposition is limited to two terms representing "fast" and "slow" phenomena, respectively[106,107]

$$P(t) = P_{fast} + P_{slow} \qquad [8.125]$$

In particular, the fast term is easily associated with the polarization due to the bound electrons of the solvent molecules which can instantaneously adjust themselves to any change of the inducing field. The slow term, even if it is often referred to as a general orientational polarization, has a less definite nature. Roughly speaking, it collects many different nuclear and molecular motions (vibrational relaxations, rotational and translational diffusion, etc.) related to generally much longer times. Only when the fast and the slow terms are adjusted to the actual description of the solute and/or the external field, on one hand, and to each other on the other hand, do we have solvation systems corresponding to full equilibrium. Nonequilibrium solvation systems, on the contrary, are characterized by only partial response of the solvent. A very explicative example of this condition, but not the only one possible, is represented by a vertical electronic excitation in the solute molecule. In this case, in fact, the immediate solvent response will be limited to its electronic polarization only, as the slower terms will not able to follow such fast change but will remain frozen in the equilibrium status existing immediately before the transition.

This kind of analysis is easily shifted to BE-ASC models in which the polarization vector is substituted by the apparent surface charge in the representation of the solvent reaction field.[107] In this framework, the previous partition of the polarization vector into fast and slow components leads to two corresponding surface apparent charges, σ_f and σ_s, the sum of which gives the total apparent charge σ. The definition of these charges is in turn related to the static dielectric constant $\varepsilon(0)$ (for the full equilibrium total charge σ), to the frequency dependent dielectric constant $\varepsilon(\omega)$ (for the fast component σ_f), and to a combination of them (for the remaining slow component σ_s).

The analytical form of the frequency dependence of $\varepsilon(\omega)$ in general is not known, but different reliable approximations can be exploited. For example, if we assume that the solvent is polar and follows a Debye-like behavior, we have the general relation:

$$\varepsilon(\omega) = \varepsilon(\infty) + \frac{\varepsilon(0) - \varepsilon(\infty)}{1 - i\omega\tau_D} \qquad [8.126]$$

with $\varepsilon(0)=78.5$, $\varepsilon(\infty)=1,7756$, and $\tau_D=0.85\times10^{-11}$s in the specific case of water.

It is clear that at the optical frequencies usually involved in the main physical processes, the value of $\varepsilon(\omega)$ is practically equal to $\varepsilon(\infty)$; variations with respect to this, in fact, become important only at $\omega\tau_D <<1$, where $\varepsilon(\omega)$ is close to the static value. In practice, this means that for a polar solvent like water, where $\varepsilon(\infty)$ is much smaller than the static value, the dynamical solvent effects are small with respect to the static ones. Numerically, this means that all processes described in terms of a static or a dynamic solvent approach, as well as solute response properties computed in the full solute-solvent equilibrium or, instead in a condition of nonequilibrium, will present quite different values.

As a last note we underline that, while it is easy to see that nonequilibrium effects have to be taken into account in the presence of fast changes in the electronic distribution of the solute, or of an oscillating external field (as that exploited to measure molecular optical properties), nonequilibrium approaches for nuclear vibrational analyses are still open.

8.8 PRACTICAL APPLICATIONS OF MODELING

In this section we will present some examples of how to determine properties of pure liquids by means of the previously-shown computational procedures. In spite of the fact that most literature in this field is concerned with the study of the properties of water, we will rather focus the attention on the determination of the properties of a few organic solvents of common use (for a review of studies on water, we address interested readers to the already quoted paper of Floris and Tani).[40] Obviously, the following discussion cannot be considered as a complete review of all the literature in the field, but it is rather intended to give the reader a few suggestions on how the previously-shown computational methodologies can be used to obtain data about the most usual properties of pure liquids.

From what we said in the previous section, it should be clear to the reader that continuum models cannot properly be used in order to determine liquid properties: they are in fact concerned in the treatment of a solute in a solvent, and so not of direct use for the study of the solvent properties. For this reason, we will present in the following some examples concerning the application of integral equations and computer simulations.

The analysis will be limited to the examination of the most usual static and dynamic properties of liquids.

Dielectric constant

Let us begin the discussion by considering a couple of examples regarding the calculation of the dielectric constant of pure liquids.

The critical role of the dielectric constant in determining the properties of a liquid and in particular in moderating the intermolecular interactions cannot be overemphasized. It is then extremely important that potential energy functions used, for example, in computer simulations are able to reproduce the experimental value of the dielectric constant and that such a calculation can be used to estimate the validity of any empirical potential to be used in simulations. The problem of the calculation of the dielectric response is complex:[108] many theories and methods are available, giving sometimes different and contrasting results.

It is accepted that for the calculation of the dielectric constant (as well as other properties dependent on intermolecular angular correlations) via computer simulations, it is compulsory to include long-range electrostatic interactions in the treatment. Such interactions can be taken into account by using either the Ewald summation approach or using the reaction field approach. Without going into details, we simply recall here that in the Ewald approach, electrostatic interactions are evaluated using an infinite lattice sum over all periodic images, i.e., by imposing a pseudo-crystalline order on the liquid. In the reaction field approach, however, electrostatic interaction beyond the spherical cutoff (see Section 8.7.2 for details) are approximated by treating the part of the system outside the cutoff radius as a polarizable continuum of a given dielectric constant ε_{rf}.

Several methods exist for the calculation of the dielectric constant by means of computer simulations. The most widely used is the calculation of the average of the square of the total dipole moment of the system, $<M^2>$ (fluctuation method). Using reaction field boundary conditions, the dielectric constant ε of the liquid within the cutoff radius is calculated by applying the following expression, where V is the volume of the system, k the Boltzmann constant and T the temperature:

$$\frac{4\pi}{9}\frac{\langle M^2\rangle}{kVT}=\left(\frac{\varepsilon-1}{3}\right)\frac{2\varepsilon_{rf}+1}{2\varepsilon_{rf}+\varepsilon} \qquad [8.127]$$

In the application of eq. [8.127] careful attention has to be paid to the choice of ε_{rf}, the dielectric constant to use for the continuum part of the system. Usually, rapid convergence in calculations is obtained by choosing $\varepsilon_{rf} \approx \varepsilon$.

A different approach to the calculation of the dielectric constant via computer simulations is given by the polarization response method, i.e., to determine the polarization response of a liquid to an applied electric field E_0. If <P> is the average system dipole moment per unit volume along the direction of E_0, ε can be calculated using the following expression:

$$\frac{4\pi}{9}\frac{\langle P\rangle}{E^0}=\left(\frac{\varepsilon-1}{3}\right)\frac{2\varepsilon_{rf}+1}{2\varepsilon_{rf}+\varepsilon} \qquad [8.128]$$

Even if this second approach is more efficient than the fluctuation method, it requires the perturbation of the liquid structure following the application of the electric field.

As an example, such a methodology has been applied by Essex and Jorgensen[109] to the calculation of the dielectric constant of formamide and dimethylformamide using Monte Carlo statistical mechanics simulations (see Section 8.7.2 for details). The simulation result for dimethylformamide, 32±2, is reasonably in agreement with respect to the experimental value, 37. However, in the case of formamide, the obtained value, 56±2, underestimates the experimental value of 109.3. The poor performance here addresses the fact that force field models with fixed charges underestimate the dielectric constant for hydrogen-bonded liquids.

Other methodologies exist for the calculation of the static dielectric constant of pure liquids by means of computer simulations. We would like to recall here the use of ion-ion potentials of mean force,[110] and an umbrella sampling approach whereby the complete probability distribution of the net dipole moment is calculated.[111]

Computer simulations are not the only methods which can be used to calculate the dielectric constant of pure liquids. Other approaches are given by the use of integral equations, in particular, the hypernetted chain (HNC) molecular integral equation and the molecular Ornstein-Zernike (OZ) theory (see Section 8.7.1 for details on such methodologies).

The molecular HNC theory gives the molecular pair distribution function g(12) from which all the equilibrium properties of a liquid can be evaluated. It is worth recalling here that the HNC theory consists for a pure liquid in solving a set of two equations, namely, the OZ equation [8.76] and the HNC closure relation [8.78] and [8.80].

In order to solve the HNC equations, the correlation functions are written in terms of a series of rotational invariants $\Phi^{mnl}_{\mu\nu}(12)$, which are defined in terms of cosines and sines of the angles defining the relative orientation of two interacting particles 1 and 2:

$$c(12) = \sum_{\substack{mnl \\ \mu v}} c_{\mu v}^{mnl}(R)\Phi_{\mu v}^{mnl}(12) \qquad [8.129]$$

where the coefficients $c_{\mu\nu}^{mnl}(12)$ depend only on the distance between the mass centers of the particles, and the indexes m, n, l, μ, and v are integers satisfying the following inequalities:

$$|m - n| \le l \le m + n, \quad -m \le \mu \le m, \quad -n \le v \le n \qquad [8.130]$$

The dielectric constant can be obtained from the rotational invariant coefficients of the pair correlation function. For example, following Fries et al.,[112] it can be evaluated using the Kirkwood g factor:

$$g = 1 - \frac{4\pi}{\sqrt{3}}\rho\int_0^\infty R^2 h_{00}^{110}(R)dR \qquad [8.131]$$

$$\frac{4\pi}{9}\beta\rho m_e^2 g = \frac{(\varepsilon - 1)(2\varepsilon + 1)}{9\varepsilon} \qquad [8.132]$$

In the previous relations, ρ is the number density of molecules, β=1/kT, and m_e is the effective dipole of molecules along their symmetry axes.

Such an approach has been used to evaluate the dielectric constant of liquid acetonitrile, acetone and chloroform by means of the generalized SCMF-HNC (self-consistent mean field hypernetted chain), and the values obtained are 30.8 for acetonitrile, 19.9 for acetone, and 5.66 for chloroform. The agreement with the experimental data, 35.9 for acetonitrile, 20.7 for acetone, and 4.8 for chloroform (under the same conditions), is good.

Another way of evaluating the dielectric constant is that used by Richardi et al.[113] who applied molecular Ornstein-Zernike theory and eq. [8.131] and [8.132]. The obtained values for both acetone and chloroform are low with respect to experimental data, but in excellent agreement with Monte Carlo simulation calculations. In this case, the dielectric constant is evaluated by using the following expressions:

$$\frac{(\varepsilon - 1)(2\varepsilon_{rf} + 1)}{3(2\varepsilon_{rf} + \varepsilon)} = \frac{\rho\mu^2}{9kT\varepsilon_0}\frac{\left\langle \sum_{i=1}^{N}\sum_{j=1}^{N}\mu_i\mu_j \right\rangle}{N\mu^2} \qquad [8.133]$$

where ε_{rf} is the dielectric constant of the continuum part of the system, i.e., the part outside the cutoff sphere, N the number of molecules of the system and μ the dipole moment.

A further improvement in the mentioned approach has been achieved by Richardi et al.[114] by coupling the molecular Ornstein-Zernike theory with a self-consistent mean-field approximation in order to take the polarizability into account. For the previously-mentioned solvents (acetone, acetonitrile and chloroform), the calculated values are in excellent agreement with experimental data, showing the crucial role of taking into account polarizability contributions for polar polarizable aprotic solvents.

Thermodynamical properties

Paying attention again to calculations for acetone and chloroform, we would like to mention two papers by the Regensburg group[113,114] exploiting molecular Ornstein-Zernike (MOZ) theory and site-site Ornstein-Zernike (SSOZ) theory for the calculation of excess internal energies. In the MOZ framework, the internal excess energy per molecule is computed by a configurational average of the pair potential V acting between molecules:

$$E^{ex} = \frac{\rho}{2\Omega^2} \int\int\int V(R_{12}, \Omega_1, \Omega_2)\, g(R_{12}, \Omega_1, \Omega_2)\, dR_{12}\, d\Omega_1\, d\Omega_2 \qquad [8.134]$$

with ρ the density of molecules.

Using instead SSOZ, E^{ex} can be directly calculated from the site-site distribution function, $g_{\alpha\beta}$, as:

$$E^{ex} = 2\pi\rho \int_0^\infty \sum_{\alpha=1}^{k} \sum_{\beta=1}^{k} g_{\alpha\beta}(r) V_{\alpha\beta}(r) r^2 dr \qquad [8.135]$$

where k is the number of sites per molecule.

In both cases the calculated values are in good agreement with experimental data and with calculations done exploiting the Monte Carlo computer simulation. In this case, E^{ex} can be obtained as:

$$E^{ex} = \frac{1}{N} \sum_{i=1}^{N} \sum_{j>1}^{N} \sum_{\alpha=1}^{k} \sum_{\beta=1}^{k} V_{\alpha\beta}\left(r_{\alpha\beta,ij}\right) + \frac{\varepsilon_{rf} - 1}{2\varepsilon_{rf} + 1} \frac{z_\alpha z_\beta e_0^2 r_{\alpha\beta,ij}^2}{4\pi\varepsilon_0 r_{cutoff}^3} \qquad [8.136]$$

where k is the number of sites per molecule, $r_{\alpha\beta,ij}$ is the distance between site α of molecule i and site β of molecule j. Only pairs i,j of molecules for which $r_{ij}<r_{cutoff}$ are considered.

Further refinements of the mentioned approach have been proposed in the already quoted paper by Richardi et al.[114] by coupling the molecular Ornstein-Zernike theory with a self-consistent mean-field approximation. Here again, computed data are in excellent agreement with experiments.

As already said, the use of integral equation methodologies is not the only possible way of obtaining thermodynamical properties for liquids. Computer simulations are also widely used, and it is then possible to obtain equilibrium properties by mean of both Monte Carlo and Molecular Dynamics simulations.

As an example, we would like to mention some calculations on equilibrium properties for liquid ethanol at various temperatures.[115] The calculated values for the heat of vaporization are in overall agreement with experiments, showing an error of the order of 1-1.5%.

Compressibilities

As an example of how to determine compressibilities by mean of integral equations, we would like to quote here the already cited paper of Richardi et al.[113] in which molecular Ornstein-Zernike (MOZ) theory and site-site Ornstein-Zernike (SSOZ) theory have been exploited. In particular, using the MOZ, the compressibility κ_T can be evaluated using the equation:

$$\rho kT\kappa_T = 1 + 4\pi\rho\int_0^\infty \left(g_{00}^{000}(R_{12}) - 1\right)R_{12}^2 dR_{12} \qquad [8.137]$$

and exploiting SSOZ can be calculated from any site-site distribution function $g_{\alpha\beta}$ as:

$$\rho kT\kappa_T = 1 + 4\pi\rho\int_0^\infty \left(g_{\alpha\beta}(r) - 1\right)r^2 dr \qquad [8.138]$$

For acetone and chloroform, the obtained results are too large.

Relaxation times and diffusion coefficients

Let us now consider an example of how to calculate dynamic properties of pure liquids by computational methodologies. As already said in Section 8.7.2, molecular dynamics simulations are able to take into account the time-dependence in the calculation of liquid properties.

Paying attention to pure acetone, Brodka and Zerda[116] have calculated rotational relaxation times and translational diffusion coefficients by molecular dynamics simulations. In particular, the calculated rotational times of the dipole moment can be compared with a molecular relaxation time τ_M obtained from the experimentally determined τ_D by using the following expression, which considers a local field factor:

$$\tau_M = \frac{2\varepsilon_s + \varepsilon_\infty}{3\varepsilon_s}\tau_D \qquad [8.139]$$

where ε_s and ε_∞ are the static and optical dielectric constants, respectively. The calculated data are in good agreement with experimental values.

Diffusion coefficients can be calculated directly from the velocity correlation functions or from mean square displacements, as:

$$D^{vcf} = \frac{1}{3}\int_0^\infty \langle v(t)v(0)\rangle dt \qquad [8.140]$$

$$D^{msd} = \lim_{i\to\infty}\frac{1}{6t}\left\langle \left|r(t)r(0)\right|^2\right\rangle \qquad [8.141]$$

The values obtained by using the [8.140] or the [8.141] are almost the same, and properly describe the experimental temperature and density dependencies of the diffusion coefficients, even if about 30% smaller than obtained using NMR spin-echo techniques.

Among the pure solvents we have treated so far, other available data regard the calculation of the self diffusion coefficient (D) for liquid ethanol at different temperatures.[115d] The D parameter was obtained from the long-time slope of the mean-square displacements of the center of mass: experimental changes of D over the 285-320K range of temperatures were acceptably reproduced by molecular dynamics simulations.

Shear viscosity

To end this section, we would like to report an example of calculation of the shear viscosity again taking as an example pure acetone.

The viscosity can be computed by using molecular dynamics simulations from the virial form of the molecular pressure tensor P, which can be represented as a sum of four contributions:

$$PV = \sum_{i=1}^{N} \frac{p_i p_i}{m_i} + P_S V + P_R V + P_C V \qquad [8.142]$$

where V is the volume of the cell, N the number of molecules, p_i and m_i the momentum and mass of molecule i.

The first term in eq. [8.142] is the kinetic contribution, while P_S is the short-range potential interaction contribution, P_R the reciprocal-space portion of the pressure tensor, and P_C a correction tensor term.

From the xy elements of the time-averaged molecular pressure tensor [8.142] and the applied shear (or strain) rate $\gamma = \partial v_x / \partial y$, the viscosity η can be computed using the constitutive relation:

$$\eta = -\frac{\langle P_{xy} - P_{yx} \rangle}{2\gamma} \qquad [8.143]$$

the calculated values for acetone (extrapolated data) are in reasonable agreement with experimental data, as well as results for acetone/methanol and acetone/water mixtures.[117]

8.9 LIQUID SURFACES

Until now our task has been relatively easy, as we have only considered the general methodological aspects of the computational description of liquids.

To proceed further, we have to be more specific, entering into details of specific problems, all requiring the introduction and the characterization of different properties, and of the opportune methodological (computational) tools to treat them. We also note that, as additional complication, it can happen that things change considerably when the full range of macroscopic variables (temperature, pressure, volume) is considered, and when other components are added to the liquid system.

Not much effort is needed to convince readers of the overwhelming complexity of the task we are here considering. Let us take a simple pure liquid: to span the range of the thermodynamical variables means to consider systems in which the liquid is in presence of the solid, of the vapor, including supercritical as well as super-cooled states, and all the related phenomena, as ebullition, vaporization, condensation and freezing.

All states and all dynamical processes connecting states are of interest for chemistry, chemical engineering, and physical chemistry. Some properties can be defined for all the states (such as the thermodynamic basic quantities); others are specific for some situations, such as the surface tension. But also for properties of general definition, the techniques to use have often to be very different. It is not possible, for example, to use the same technique to study the temperature dependence of the Helmholtz free energy in a bulk liquid or in the same liquid under the form of a fog near condensation.

Things become more complex when a solute is added to the liquid, and more and more complex when the system contains three or more components.

We are not sure whether any case occurring in this field has been subjected to theoretical analysis and modeling; however, the number of problems considered by theoretical research is very large, and there are models, generally based on the use of molecular potentials, that can give hints, and often useful computational recipes.

These remarks, which are trivial for every reader, with even a minimal experience in working with solvents, have been added here to justify our choice of not trying to give a schematic overview, and also to justify the extremely schematic presentation of the unique specific more advanced subject we shall here consider, the interfacial properties of liquids.

8.9.1 THE BASIC TYPES OF LIQUID SURFACES

The surface of a liquid is often represented as a very small fraction of the liquid specimen, and it may be neglected. This statement is not of general validity, however, and often the surface plays a role; in some cases, the dominant role. To be more specific, it is convenient to consider a classification of liquid surfaces, starting from a crude classification, and introducing more details later.

The basic classification can be expressed as follows:

- Liquid/gas surfaces;
- Liquid/liquid surfaces;
- Liquid/solid surfaces.

Liquid/gas surfaces may regard a single substance present in both phases, liquid and vapor at equilibrium or out of equilibrium, but they may also regard a liquid in the presence of a different gas, for example, air (in principle, there is always a given amount of solvent in the gas phase). In the presence of a different gas, one has to consider it in the description of the liquid, both in the bulk and in the interface. In many cases, however, the role of the gas is marginal, and this is the reason why in many theoretical studies on this interface the gas is replaced by the vacuum. This is a very unrealistic description for liquids at equilibrium, but it simply reflects the fact that in simplifying the model, solvent-solute interactions may be sacrificed without losing too much in the description of the interfacial region.

The potentials used to describe these interfaces are those used to describe bulk liquids. The differences stay in the choice of the thermodynamical ensemble (grand canonical ensembles are often necessary), in the boundary conditions to be used in calculations, and in the explicit introduction in the model of some properties and concepts not used for bulk liquids, like the surface tension. Much could be said in this preliminary presentation of liquid/gas interfaces, but we postpone the few aspects we have decided to mention, because they may be treated in comparison with the other kind of surfaces.

Liquid/liquid surfaces regard, in general, a couple of liquids with a low miscibility coefficient, but there are also cases of one-component systems presenting two distinct liquid phases, for which there could be interest in examining the interfacial region at the coexistence point, or for situations out of the thermodynamical equilibrium.

If the second component of the liquid system has a low miscibility with the first, and its molar ratio is low, it is easy to find situations in which this second component is arranged as a thin layer on the surface of the main component with a depth reducing, in the opportune conditions, to the level of a single molecule. This is a situation of great practical importance to what we experience in our everyday life (petrol on the surface of water); however, it has to be related to a finer classification of liquid interfaces we shall consider later.

Once again the potentials used for liquid/liquid surfaces are in general those used for bulk liquids eventually with the introduction of a change in the numerical values of the parameters.[118] The difference from the bulk again regards the thermodynamical ensemble, the boundary conditions for the calculations and the use of some additional concepts.

The liquid/solid surfaces may be of very different types. They can be classified according to the electrical nature of the solid as:

- Liquid/conductor
- Liquid/dielectric

The presence of mobile electrons in metals and other solid substances (to which some liquids may be added, like mercury[119]), introduces in the modelling of the liquid interface new features not present in the previously-quoted interfaces nor in the bulk liquids. For many phenomena occurring at such interfaces there is the need for taking into explicit account electrons flowing from one phase to the other, and of related electron transfers occurring via redox mechanisms. The interaction potentials have to be modified and extended accordingly.[120]

The good electrical conductivity of the solid makes more sizeable and evident the occurrence of phenomena related to the presence of electric potentials at the interface (similar phenomena also occur at interfaces of different type, however[121]). A well-known example is the double layer at the liquid side of an electrolyte/electrode surface. For the double layer, actually there is no need of interaction potentials of special type: the changes in the modelling mainly regard the boundary conditions in the simulation or in the application of other models, of continuum or integral equation type.

It is clear that attention must be paid to the electrostatic part of the interaction. Models for the solid part similar to those used for bulk liquids play a marginal role. There are models of LJ type, but they are mainly used to introduce in the solid component the counterpart of the molecular motions of molecules, already present in the description of the liquid (vibrations of the nuclei: phonons, etc.).

The electrostatic problem may be treated with techniques similar to those we have shown for the continuum electrostatic model for solutions but with a new boundary condition on the surface, e.g., V=constant. In this case, a larger use is made (especially for planar surfaces) of the image method,[122] but more general and powerful methods (like the BEM) are gaining importance.

An alternative description of the metal that can be profitably coupled to the continuum electrostatic approach is given by the jellium model. In this model, the valence electrons of the conductor are treated as an interacting electron gas in the neutralizing background of the averaged distribution of the positive cores (some discreteness in this core distribution may be introduced to describe atomic motions). The jellium is described at the quantum level by the Density Functional Theory (DFT) and it represents a solid bridge between classical and full QM descriptions of such interfaces:[123] further improvements of the jellium which introduce a discrete nature of the lattice[124] are now often used.[125]

The liquid/dielectric surfaces exhibit an even larger variety of types. The dielectric may be a regular crystal, a microcrystalline solid, a glass, a polymer, an assembly of molecules held together by forces of different type.

The potentials in use for crystals and those used for covalently bound systems are cognate with those used for liquids, so it is not compulsory to open here a digression on this theme. We have already quoted the MM methods generally used for solids of molecular type; for more general classes of compounds, a variety of 'atom-atom' potentials have been given.[126] The difference with respect to the bulk is mainly due, again, to different ways of handling the opportune boundary conditions. It is evident that the techniques used to describe a water-protein interface greatly differ, in microscopic detail, time scale, etc., to those used to describe the surfaces between a liquid and a regular crystal surface.

For many problems, the solid surface in contact with the liquid may be held fixed: this characteristic has been amply exploited in simulation studies. We quote here two problems for which this simplification is not possible: problems in which the structure of the solid (or solid-like) component is subjected to conformational changes, and problems in which a progressive expansion (or reduction) of the solid phase plays the main role.

To the first case belong problems addressing the structure of the interfacial zone in the case of biopolymers (e.g., proteins) or similar covalently bound massive molecules, and ordered assemblies of molecules held together by strong non-covalent interactions (as membranes or similar structures). In both cases, the liquid and the solid component of the systems are generally treated on the same footing: interaction force fields are used for both components, introducing, where appropriate, different time scales in the molecular dynamics calculations.

The second case mainly regards the problem of crystal growth or dissolution in a liquid system (pure liquid or solution). A mobile surface of this type is not easy to treat with standard methods: it is better to pass to more specialistic approaches, for which there is the need of introducing a different mathematical treatment of the (mobile) boundary surface conditions. This is a subject that we cannot properly treat here.

8.9.2 SYSTEMS WITH A LARGE SURFACE/BULK RATIO

To complete this quick presentation of the three main types of liquid surfaces, it is convenient to consider systems in which the interfacial portion of the liquid is noticeably larger than in normal liquids.

Some among them are denoted in literature as constrained liquids, others as dispersed systems. This classification is not universal, and it does not take in account other cases.

A typical example of constrained liquid is that present in pores or capillaries. The surface is of liquid/solid type, and the same remarks about interaction potentials and computational methods we have already offered may be applied here. More attention must be paid in computations of interactions among separate portions of the liquid interface. In the slit pore case (i.e., in a system composed of two parallel plane solid surfaces, with a thin amount of liquid between them), there may be an interference between the two distinct surfaces, more evident when the thickness of the liquid is small, or when there is an electrical potential between the two faces. The slit pore model is extensively used to describe capillarity problems: in the most usual cylindrical capillary types there is a radial interaction similar in some sense to the interaction with a single solid surface.

Pores of different shape are present in many solid materials: zeolites and other aluminosilicates are outstanding examples. When the pore is very small there is no more distinction between superficial and bulk molecules of the liquid. Nature (and human ingenuity) offers examples over the complete range of situations. For all the systems we have here introduced (quite important in principle and for practical reasons), there is no need of introducing important changes in the standard theoretical approach with respect to that used for other liquid systems. Computer simulations are the methods more largely used to describe pores and micro-pores in molecular sieves of various nature.

A different type of confined liquid is given by a thin layer spread on a surface. The difference with respect to the micro-pore is that this is a three-component system: the surface may be a solid or a liquid, while the second boundary of the layer may regard another liquid or a gas. An example is a thin layer liquid on a metal, in the presence of air (the prodrome of many phenomena of corrosion); a second example is a layer on a second liquid (for example, oil on water). The standard approach may be used again, but other phenomena occurring in these systems require the introduction of other concepts and tools: we quote, for example, the wetting phenomena, which require a more accurate study of surface tension.

The thin layer in some case exhibits a considerable self-organization, giving rise to organized films, like the Blodgett-Langmuir films, which may be composed by several layers, and a variety of more complex structures ending with cellular membranes. We are here at the borderline between liquid films and covalently held laminar structures. According to the degree of rigidity, and to the inter-unit permeation interaction, the computational model may tune different potentials and different ways of performing the simulation.

Another type of confined liquid regards drops or micro-drops dispersed in a medium. We are here passing from confined liquids to the large realm of dispersed systems, some among which do not regard liquids.

For people interested in liquids, the next important cases are those of a liquid dispersed into a second liquid (emulsions), or a liquid dispersed in a gas (fogs), and the opposite cases of a solid dispersed in a liquid (colloids) or of a gas dispersed in a liquid (bubbles).

Surface effects on those dispersed systems can be described, using again the standard approach developed in the preceding sections: intermolecular potentials, computer simulations (accompanied where convenient by integral equation or continuum approaches). There is not much difference with respect to the other cases.

A remark of general validity but particular for these more complex liquid systems must be expressed, and strongly underlined.

We have examined here a given line of research on liquids and of calculations of pertinent physico-chemical properties. This line starts from QM formal description of the systems, then specializes the approach by defining intermolecular potentials (two- or many-body), and then it uses such potentials to describe the system (we have paid more attention to systems at equilibrium, with a moderate extension to non-equilibrium problems).

This is not the only research line conceivable and used, and, in addition, it is not sufficient to describe some processes, among them, those regarding the dispersed systems we have just considered.

We dedicate here a limited space to these aspects of theoretical and computational description of liquids because this chapter specifically addresses interaction potentials and because other approaches will be used and described in other chapters of the Handbook. Several other approaches have the QM formulation more in the background, often never mentioned. Such models are of a more classical nature, with a larger phenomenological character. We quote as examples the models to describe light diffraction in disordered systems, the classical models for evaporation, condensation and dissolution, the transport of the matter in the liquid. The number is fairly large, especially in passing to dynamical and out of equilibrium properties. Some models are old (dating before the introduction of QM), but still in use.

A more detailed description of molecular interactions may lead to refinements of such models (this is currently being done), but there is no reasonable prospect of replacing them with what we have here called the standard approach based on potentials. The standard approach, even when used, may be not sufficient to satisfactorily describe some phenomena. We quote two examples drawn from the presentation of liquid surfaces in dispersed systems: bubbles and solid small particles.

The description of the energetics of a single bubble, and of the density inside and around it, is not sufficient to describe collective phenomena, such as ebullition or separation of a bubble layer. The description of a single bubble is at a low level in a ladder of models, each introducing new concepts and enlarging the space (and time) scale of the model.

The same holds for small solid particles in a liquid. There is a whole section of chemistry, colloidal chemistry, in which our standard approach gives more basic elements, but there is here, again, a ladder of models, as in the preceding example.

Our standard model extends its range of applicability towards these more complex levels of theory. This is a general trend in physics and chemistry: microscopic approaches, starting from the study of the interaction of few elementary particles, are progressively gaining more and more importance over the whole range of sciences, from biology to cosmology, passing through engineering and, in particular, chemistry. In the case of liquids, this extension of microscopical models is far from covering all the phenomena of interest.

8.9.3 STUDIES ON INTERFACES USING INTERACTION POTENTIALS

To close this section on liquid surfaces, limited to a rapid examination of the several types of surface of more frequent occurrence, we report some general comments about the use of the standard approach on liquid surfaces.

The first information coming from the application of the method regards the density profile across the interface. Density may be assumed to be constant in bulk liquids at the equilibrium, with local deviations around some solutes (these deviations belong to the family of cybotactic effects, on which something will be said later). At each type of liquid surface there will be some deviations in the density, of extent and nature depending on the system.

A particular case is that of mobile surfaces, i.e., liquid/gas and liquid/liquid surfaces. Having liquids a molecularly grained structure, there will always be at a high level of spatial deviation a local deviation of the surface from planarity. If there are no other effects, this deviation (sometimes called corrugation, but the term is more convenient for other cases, like liquid/solid surfaces, where corrugation has a more permanent status) averages to zero.

Entropic forces are responsible for other effects on the density profile, giving origin at a large scale to a smooth behavior of the density profile, connecting the constant values of the two bulk densities. The most natural length unit in liquids is the bulk correlation length, ξ, i.e., the distance at which the pair correlation $g_{AB}(r)$ has decayed to 1. For bulk water ξ is around 5-6 Å. This large scale behavior hides different local behaviors, that range among two extremes, from capillary waves to van der Waals regime.[127] Capillary waves correspond to a sharp boundary (corrugation apart) with “fingers” of a liquid protruding out of the bulk. Capillary waves may happen both at liquid and gas surfaces, in the former, in a more stable status (i.e., with a large mean life) than in the latter.

The van der Waals regime locally corresponds to the large scale energy profile, with a smooth shape.

The behavior of the density profile largely depends on the chemical nature of the composite system. Some phenomenological parameters, like mutual solubility, may give a good guess about the probable energy profile, but "surprises" are not rare events. It may be added that the density profile is sensitive to the quality of the potential and the method using the potentials. It is not clear, in our opinion, if some claims of the occurrence of a thin void (i.e., at very low density) layer separating two liquid surfaces is a real finding or an artifact due to the potentials. Old results must be considered with caution, because computations done with old and less powerful computers tend to reduce the size of the specimen, thus reducing the possibility of finding capillary waves. The dimension of the simulation box, or other similar limiting constraints, is a critical parameter for all phenomena with a large length scale (this is true in all condensed systems, not only for surfaces).

The density profile for liquid/solid surfaces has been firstly studied for hard spheres on hard walls, and then using similar but a bit more detailed models. It is easy to modify the potential parameters to have an increment of the liquid density near the wall (adhesion) or a decrement. Both cases are physically possible, and this effect plays an important role in capillarity studies.

A corrugation at the solid surface can be achieved by using potentials for the solid phase based on the atomic and molecular constitution. This is almost compulsory for studies on systems having a large internal mobility (biomolecules are the outstanding example), but it is also used for more compact solid surfaces, such as metals. In the last quoted example the discreteness of the potential is not exploited to address corrugation effects but rather to introduce mobility (i.e., vibrations. or phonons) in the solid part of the system, in parallel to the mobility explicitly considered by the models for the liquid phase.

Another type of mobility is that of electrons in the solid phase: this is partly described by the continuum electrostatic approach for dielectrics and conductors, but for metals (the most important conductors) it is better to resort to the jellium model. A QM treatment of jellium models permits us to describe electric polarization waves (polarons, solitons) and their mutual interplay with the liquid across the surface.

Jellium, and the other continuum descriptions of the solid, have the problem of exactly defining the boundary surface. This is the analog of the problem of the definition of the cavity boundary for solutes in bulk solvents, occurring in continuum solvation methods (see Section 8.7.3). The only difference is that there are more experimental data for solutes than for liquid/solid surfaces to have hints about the most convenient modeling. The few accurate ab-initio calculations on liquid/metal systems are of little help, because in order to reach an acceptable accuracy, one is compelled to reduce the solid to a small cluster, too small to describe effects with a large length scale.

The disturbances to the bulk density profile are often limited to a few solvent diameters (typically 2-3), but the effect may be larger, especially when external electric fields are applied.

The second information derived from the application of our methods to surfaces regards the preferred orientation of liquid molecules near the surface. To treat this point there is the need of a short digression.

In bulk homogeneous liquids at the equilibrium orientation, the location of a specific molecule is immaterial. We need to know the orientational modes (often reduced to librations) of the components of the liquid system to write the appropriate statistical partition function. In the case of solvation energies, the rotational component of the factorized solute partition function gives a not negligible contribution to ΔG_{solv}. The translational component of the solute partition function can be factorized apart, as first suggested by Ben-Naim,[128] and included in the cratic component of ΔG_{solv} with a small correction (the cratic component is the numerical factor taking into account the relationships between standard states in a change of phase).

In the homogeneous bulk liquid we have to explicitly consider orientations for dynamical relaxation effects. The same holds for translation in other dynamical problems (diffusion, transport, etc.).

Coming back to the static problems, it turns out that near the limiting surface, the free energy of the components of the liquid also depends on positions and orientations. A quantity like ΔG_{solv} for the transfer of M in the solvent S in the bulk must be replaced by $\Delta G_{solv}(r, \Omega)$ specifying position and orientation of M with respect to the surface of S.

This effect must not be confused with the cybotactic effects we have mentioned, nor with the hole in the solute-solvent correlation function $g_{MS}(r)$ (see Figure 8.5). The hole in the radial correlation function is a consequence of its definition, corresponding to a conditional property, namely that it gives the radial probability distribution of the solvent S, when the solute M is kept at the origin of the coordinate system. Cybotactic effects are related to changes in the correlation function $g_{MS}(r)$ (or better $g_{MS}(r, \Omega)$) with respect to a reference situation. Surface proximity effects can be derived by the analysis of the $g_{MS}(r, \Omega)$ functions, or directly computed with continuum solvation methods. It must be remarked that the obtention of $g_{MS}(r)$ functions near the surface is more difficult than for bulk homogeneous liquids. Reliable descriptions of $g_{MS}(r, \Omega)$ are even harder to reach.

Orientational preferences are the origin of many phenomena, especially when at the surface there are electric charges, mobile or fixed. Outstanding examples occur in biological systems, but there is a large literature covering other fields. A relatively simple case that has been abundantly studied is the electric potential difference across the surface.[129]

We have not considered yet the behavior of solutes near the interface. The special, but quite important, case of the charged components of a salt solution near a charged boundary is widely known, and it is simply mentioned here.

More generally, the behavior of solutes largely depends on the chemical composition of the system. Small ions are repelled at the air/gas interface, hydrophobic molecules are attracted to the interface. Even the presence of a simple CH_3 group has some effect: the air interface of dilute solutions of methanol is saturated in CH_3OH over a sizeable molar fraction range.[130] At the liquid/liquid interface between water and hydrocarbon solvents, solutes with a polar head and an alkylic chain tend to find an equilibrium position, with the polar head in water, at a distance from the surface depending on the chain length.[131]

All the quoted results have been obtained at the static level, employing a mean force potential, obtained in some cases with inexpensive continuum models; in other cases, with computer demanding simulations of the free energy profile.

Simulations can give more details than continuum methods, which exploit a simplified and averaged model of the medium. Among the simulation results we quote the recognition that small cations, exhibiting strong interactions with water molecules, tend to keep bound the first solvation layer when forced to pass from water to another solvent. Analogous effects are under examination for neutral polar solutes at water/liquid interfaces in case the bulk solubility of the two partners is not symmetric (a typical example is the water/octanol system).[132]

We have here mentioned the process of transport of a solute from a liquid phase to another. This is a typical dynamic process for which static descriptions based on mean forces simply represent the starting-point, to be completed with an explicit dynamical treatment. Molecular dynamics is the chosen tool for these studies, which are quite active and promise illuminating results. MD simulations also are the main approach to study another important topic: chemical reactions at the surface.[133]

The study of the various aspects of chemical reactions in bulk liquids, from the thermodynamical balance of the reaction, to the mechanistic aspects, to the reaction rates, represents nowadays a well explored field, in which several approaches may be used. The complexity of chemical systems does not permit us to consider this problem completely settled under the methodological and computational point of view, but important advances have been achieved.

Reactions at the surface are a frontier field, and the same remarks hold for reactions in dispersed liquid systems. Interaction potentials, simulations and other methods will find here renewed stimuli for more precise and powerful formulations.

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