Group functions, Löwdin partition, and hybrid QC/MM methods for large molecular systems

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The problem of developing an exact form of the junction between the quantum and classical parts in a hybrid QC/MM approach is considered. We start from the full Hamiltonian for the whole system and assume a specific form of the electron wavefunction, which allows us to separate the electron variables relevant to the reactive (quantum) part of the system from those related to the inert (classical) part. Applying the Löwdin partition to the full Hamiltonian for the molecular system results in general formulae for the potential energy surfaces of a molecular system composed of different parts provided some of these parts are treated quantum mechanically whereas others are treated with use of molecular mechanics. These principles of separating electron variables have been applied to construct an efficient method for analysis of electronic structure and d-electron excitation spectra of transition metal complexes. This method has been also combined with the MM approximation in order to get a description for potential energy surfaces of the complexes and to develop a consistent approach to the known problem of extending molecular mechanics to transition metals.

1 Introduction

The problem of quantum theoretical description of molecular potential energy surfaces (PESs) is nowadays considered to be resolved. Numerous *ab initio* packages available both commercially or on a donation basis are able to simulate key elements of the PESs of relatively small molecules. However, the demand of the *ab initio* methods for computing power is very high for the systems which are of interest from the chemical point of view. For this reason the attempts to bypass the N^n scale problem in the quantum chemical studies are being undertaken with use of the hybrid QC/MM (quantum chemistry/molecular mechanics) approaches. These methods are based upon a natural observation: even in the case when reacting molecules contain hundreds of atoms the chemical transformation itself affects only their small fragments. This induced development of the methods where a part of the molecular system where chemical transformations take place is treated with the use of quantum chemical methods whereas the rest which is chemically inert is treated with use of molecular mechanics.[1] This approach (see ref. 2–7) drastically reduces the requirements for the computer power since only a small fraction of the entire molecular system is treated at the quantum level. The fundamental problem which arises in this context is that of constructing a consistent form of junction between the parts of the molecular system treated at different approximation levels.

This problem is closely related to the general problem of separating electron variables in quantum chemistry. From a fairly early time it was clear that the SCF approximation[8,9] is not the only possible way of doing that.[10,11] An alternative to the SCF approximation is that of the group functions (GF) product presented in detail in ref. 12. According to this approximation the whole set of N orthonormal one-electron states is divided into M disjoint subsets (groups). The trial wavefunction for an N_e-electron system in the GF approximation is then represented as an antisymmetrized product of M antisymmetrized n_α-electron functions Φ_α ($\alpha = 1, \ldots, M$). Each of these functions is a linear combination of the n_α-electron Slater determinants constructed from the one-electron states of the α-th group.

The approximation where the wavefunction is of the GF form immediately solves the problems mentioned above. First, when the electron variables are separated in a way that matrix elements of the operators transferring electrons between different groups of electrons are vanishing one may treat the group functions at different levels of approximation. This is clearly a prerequisite for any combined QC/MM treatment. In addition, if the size of each group is significantly smaller than that of the whole system, the demand for the computational resources for methods based on the GF approximation scales as $M(N/M)^n$ *i.e.* it grows linearly with the growth of the number of groups M. The GF approximation in the strict sense applies only to the systems where the groups of electrons are clearly distinguishable so that one-electron transfers between the groups vanish. It rarely takes place exactly. In order to reach the variable separation one has to eliminate the matrix elements of electron transfer between the groups. Two methods of doing that are reported in the literature. First, one can follow the method[13,14] and eliminate the intergroup one-electron transfer matrix elements by corresponding adjustment of the one-electron basis sets for each group. This can be done either in a variational manner as in ref. 14 or perturbatively as it has been originally proposed in ref. 13. Another possibility is to eliminate these matrix elements directly from the Hamiltonian by the Löwdin partition.[15] It leads to the perturbative treatment as well, but in this case it applies to many-electron wavefunctions rather than to the one-electron states. In the present paper we employ the Löwdin partition in order to reach approximate separation of electronic variables. Then the electron wavefunction in the GF form will be used to apply different levels of approximation to different groups of electrons and to derive the form for the PES of a molecular system composed of different parts provided some of these parts are treated quantum mechanically whereas others are treated with use of molecular mechanics. As far as we know no derivation of that sort has been published before. Next, several examples which use this way of

separating electron variables will be reviewed.

2 Theory

2.1 Approximate separation of electron variables by Löwdin partition

The ground state wavefunction of electrons in the GF approximation has the form:[12]

$$\Psi_0 = \bigwedge_{\alpha=1}^{M} \Phi^\alpha \qquad (1)$$

The sign $\bigwedge$, denotes the antisymmetrized product of the multipliers. From the practical point of view it means that in eqn. (1) all the operators creating electrons in the one-electron states of the α-th group stand to the left from those of the β-th group, provided $\beta < \alpha$. This form of the trial wavefunction is, of course, an approximation, since, in general, the matrix elements of electron transfer between the groups are not vanishing. We use the Löwdin partition in order to derive this approximate form for the wavefunction. To do so we start from a general form[16–18] of the wavefunction. It differs from the GF approximation in the respect that the number of electrons in each group is not fixed, and this generalized group function (GGF) expansion is a linear combination of functions which are antisymmetrized products of multipliers with a different number of electrons in the groups:[16–18]

$$\Psi_k = \sum_{\{n_\alpha\}} \sum_{\{i_\alpha\}} C^k_{\{i_\alpha\}}(\{n_\alpha\}) \bigwedge_\alpha \Phi^\alpha_{i_\alpha}(n_\alpha) \qquad (2)$$

In the expansion eqn. (2) each distribution $\{n_\alpha\}$ of electrons among the groups satisfies the condition:

$$\sum_\alpha n_\alpha = N_e \; ; \; \forall \alpha, \, n_\alpha \geqslant 0$$

here $\Phi^\alpha_{i_\alpha}(n_\alpha)$ is the i-th n_α-electron function where only the one-electron states of the α-th group may be occupied. Expansion coefficients $C^k_{\{i_\alpha\}}(\{n_\alpha\})$ are thought to be determined on the basis of the variational principle.

The GGF representation is very general. Any many-electron wavefunction can be rewritten in the GGF form. We assume that we can make a justified division of the one-electron basis into the groups and that we have physical grounds to assign specific number of electrons to each group as well. This is a usual formulation of the GF approach given in the literature.[11,12] Its exact meaning is that in the GGF expansion eqn. (2) only the product functions with a certain fixed distribution $\{\bar{n}_\alpha\}$ of electrons among the groups give the dominating contribution.

Now we consider the total electron Hamiltonian $\hat{H}(q)$ which depends on the nuclear coordinates q parametrically. It can be rewritten with the use of the second quantization formalism according to the division of the one-electron basis set introduced above:

$$\hat{H}(q) = \sum_\alpha \hat{H}_\alpha(q) + \sum_{\alpha < \beta} \hat{V}_{\alpha\beta}(q) \qquad (3)$$

where $\hat{H}_\alpha(q)$ contains only the products of fermion operators creating/annihilating electrons in the one-electron states of the group α. The interaction operators $\hat{V}_{\alpha\beta}(q)$ are those which contain the mixed products of the creation/annihilation operators of the groups α and β. (There are, of course, the terms in the Hamiltonian containing products of the operators belonging to three and four different groups. We, however, omit them for the sake of simplicity. Apart from the latter restriction the above form of the electronic Hamiltonian is quite general.)

The separation of electronic variables is reached by projecting exact electronic wavefunctions eqn. (2) to the subspace spanned by the functions with the fixed number $(\bar{n}_\alpha)$ of electrons in the α-th group. Let $\hat{P}$ be the operator projecting N_e-

electron functions eqn. (2) to this subspace. The projection operator $\hat{P}$ when acting on the GGF type wavefunction cuts off all the states with the electron distribution different from that we have fixed above. The target states in the Im$\hat{P}$ subspace (Im$\hat{P}$—image $\hat{P}$—stands here for the set of vectors of a linear space which are obtained by action of the linear operator $\hat{P}$ upon all vectors of the linear vector space) have the form:

$$\Psi_k = \sum_{\{i_\alpha\}} C^k_{\{i_\alpha\}}(\{\bar{n}_\alpha\}) \bigwedge_{\alpha=1}^{M} \Phi^\alpha_{i_\alpha}(\bar{n}_\alpha) \qquad (4)$$

For the sake of simplicity we restrict ourselves with the interaction operator containing only one-electron transfer terms (resonance interaction) and the two-electron interactions which conserve number of electrons in the groups (Coulomb interaction). Thus the interaction terms in eqn. (3) acquire the form:

$$\hat{V}_{\alpha\beta}(q) = \hat{V}^r_{\alpha\beta}(q) + \hat{V}^c_{\alpha\beta}(q)$$
$$\hat{V}^r_{\alpha\beta}(q) = \sum_{a \in \alpha, \, b \in \beta} v^r_{ab}(q)(a^+ b + b^+ a) \qquad (5)$$
$$\hat{V}^c_{\alpha\beta}(q) = \sum_{aa' \in \alpha, \, bb' \in \beta} (aa' \parallel bb') a^+ b^+ b' a'$$

Here $(aa' \parallel bb')$ is the symmetrized two-electron matrix element of the electron–electron Coulomb repulsion.

The matrix elements of the $\hat{V}^r_{\alpha\beta}(q)$ operator are vanishing for the pair of the states when they both belong to the Im$\hat{P}$ subspace spanned by the functions eqn. (4). The operators $\hat{V}^r_{\alpha\beta}(q)$ are responsible for electron transfers between the groups α and β. When acting upon a state from the Im$\hat{P}$ subspace the $\hat{V}^r_{\alpha\beta}(q)$ operator results in the states which all have distributions of electrons among the groups different from that characteristic for the states from Im$\hat{P}$. On the other hand the states with different distributions of electrons among the groups are orthogonal. For that reason the matrix elements of $\hat{V}^r_{\alpha\beta}(q)$ between two states from the Im$\hat{P}$ subspace are vanishing. This is obviously the defect of the GF approximation since in fact the intergroup electron transfers do take place. The contributions from the states with the electron transfers between the groups are taken into account by the Löwdin partition procedure:[11,12,15]

$$\hat{H}_{\text{eff}}(q, E) = \hat{P}\hat{H}^0(q)\hat{P} + \hat{P}\hat{V}^{rr}(q, E)\hat{P}$$
$$\hat{V}^{rr}(q, E) = \hat{V}^r(q)\hat{Q}\hat{R}(E)\hat{Q}\hat{V}^r(q) \qquad (6)$$
$$\hat{R}(E) = (E\hat{Q} - \hat{Q}\hat{H}^0\hat{Q})^{-1}$$

where

$$\hat{H}^0(q) = \sum_\alpha \hat{H}_\alpha(q) + \sum_{\alpha < \beta} \hat{V}^c_{\alpha\beta}(q) \qquad (7)$$

and $\hat{Q} = 1 - \hat{P}$ is the complementary projection operator. By this the total Hamiltonian acting in the total functional space is projected to the subspace Im$\hat{P}$ and the intergroup one-electron transfers are replaced by the virtual ones which are included in the correction term $\hat{V}^{rr}(q, E)$ containing the resolvent of the operator $\hat{H}^0(q)$ in the Im$\hat{Q}$ subspace. The eigenvalues of the effective Hamiltonian by construction coincide with those of the original Hamiltonian.

After projecting to the Im$\hat{P}$ subspace with the fixed distribution of electrons among the groups we can seek the ground state of electrons in the class of the wavefunctions of the GF form eqn. (1). At this stage the GF form of the trial wavefunction remains an approximation. The reason is that the functions of the Im$\hat{P}$ subspace are not the GF type functions. They are the linear combinations of the GFs with the fixed electron distribution $\{\bar{n}_\alpha\}$. Thus a single GF function must be selected on the basis of the variational principle. This is completely analogous to the standard SCF approximation: the exact wavefunction is a linear combination of the Slater

determinants, but a single Slater determinant is used in order to approximate the whole expansion.

Applying the variational principle to the GF trial wavefunction yields a system of interconnected eigenvalue problems with the effective Hamiltonians $\hat{H}^\alpha_{\text{eff}}$ for the functions Φ^α for the corresponding groups. Each of the group effective Hamiltonians depends on the ground state wavefunctions of all remaining groups:[12]

$$\hat{H}^\alpha_{\text{eff}}(q, E)\Phi^\alpha_0 = E^\alpha(q, E)\Phi^\alpha_0$$

$$\hat{H}^\alpha_{\text{eff}}(q, E) = \hat{P}\hat{H}_\alpha(q)\hat{P} + \Sigma_{\beta \neq \alpha}\langle\Phi^\beta_0 | \hat{P}\hat{W}_{\beta\alpha}\hat{P} | \Phi^\beta_0\rangle \quad (8)$$

$$\hat{P}\hat{W}_{\beta\alpha}\hat{P} = \hat{P}\hat{V}^c_{\beta\alpha}(q)\hat{P} + \hat{P}\hat{V}^{rr}_{\beta\alpha}(q, E)\hat{P}$$

Averaging the intergroup interaction terms over the ground states of the groups $\beta \neq \alpha$ leaves intact the fermion operators related to the α-th group itself. By virtue of this both two-electron operators $\hat{V}^c$ and $\hat{V}^{rr}$ result in renormalization of one-electron terms in the Hamiltonians for each group $\alpha = 1$, ..., M. The averaging of the Coulomb interaction operator can be easily performed following the recipe given in ref. 12:

$$\langle\Phi^\beta_0 | \hat{P}\hat{V}^c_{\beta\alpha}\hat{P} | \Phi^\beta_0\rangle = \sum_{\alpha\alpha' \in \alpha} a^+ a' \sum_{bb' \in \beta} (aa'\|bb')\langle\langle b^+ b'\rangle\rangle_\beta \quad (9)$$

where

$$\langle\langle b^+ b'\rangle\rangle_\beta = \langle\Phi^\beta_0 | b^+ b' | \Phi^\beta_0\rangle \quad (10)$$

The averages $\langle\langle b^+ b'\rangle\rangle_\beta$ are the one-electron densities and thus eqn. (9) has the standard SCF form.

The situation with the averages $\langle\Phi^\beta_0 | \hat{P}\hat{V}^{rr}_{\beta\alpha}\hat{P} | \Phi^\beta_0\rangle$ is more complicated: the operator $\hat{P}\hat{V}^{rr}_{\beta\alpha}\hat{P}$ has the form:

$$\hat{P}\hat{V}^{rr}_{\beta\alpha}\hat{P} = \sum_{aa' \in \alpha,\, bb' \in \beta} v^r_{ab}(q)v^r_{a'b'}(q)(a^+ b\hat{R}(E)b'^+ a'$$

$$+ b^+ a\hat{R}(E)a'^+ b') \quad (11)$$

Averaging the latter expansion over the ground state of the β-th group Φ^β_0 yields the following one-electron operator acting on the electron quantum numbers of the α-th group:

$$\langle\langle\hat{P}\hat{V}^{rr}_{\beta\alpha}\hat{P}\rangle\rangle_\beta = \sum_{aa' \in \alpha} \sum_{bb' \in \beta} (v^r_{ab}(q)v^r_{a'b'}(q)a^+$$

$$\times \langle\langle b\hat{R}(E)b'^+\rangle\rangle_\beta a'$$

$$+ v^r_{ab}(q)v^r_{a'b'}(q)a\langle\langle b^+ \hat{R}(E)b'\rangle\rangle_\beta a'^+) \quad (12)$$

One can check that despite their asymmetric appearance the operators $\langle\langle\hat{P}\hat{V}^{rr}_{\beta\alpha}\hat{P}\rangle\rangle_\beta$ eqn. (12) are hermitian. The averages $\langle\langle b\hat{R}(E)b'^+\rangle\rangle_\beta$ and $\langle\langle b^+ \hat{R}(E)b'\rangle\rangle_\beta$ will be considered in more detail below.

2.2 Derivation of hybrid QC/MM methods

2.2.1 Effective Hamiltonian for the combined molecular system.
As we already mentioned in the Introduction the idea to treat the chemically transforming part at the quantum mechanical level and to treat the rest with the use of molecular mechanics is very naturally based on the whole set of experimental data of synthetic chemistry. More formally this idea is expressed in an assumption that the PES of molecular systems of interest (say, of chemically transforming large molecules) can be presented as a sum of quantum chemical and molecular mechanical contributions. (The origins of this approach date back to the theory of conjugated hydrocarbons presenting the energy as a sum of the π-electron energy and of the σ-frame energy respectively either calculated by the quantum chemical (Hückel) methods or taken in the harmonic approximation.[19] Obviously, this approach is prototypic for the modern QC/MM techniques.) Though the above assumption concerning the form of the PES function is verisimilar, neither itself nor the form for the junction between the QC and MM parts parametrized by different authors have ever been derived by a sequential analysis of the molecular Hamiltonian with explicitly formulated assumptions concerning the form of the electronic wavefunction. In the current literature only numerical recipes parametrizing one or another arbitrary

form of the junction have been proposed.[2,4-6] The formulae for the junction employed in these papers are introduced *ad hoc* which in the final run may lead to various inconsistencies. In this section we, using the general formalism of the previous section, shall perform an approximate separation of electronic variables in the molecular Hamiltonian and pass to the effective Hamiltonian. Next, averaging the effective Hamiltonian over the ground state of the chemically inert part results in formulae representing the PES of a molecular system, containing contributions from chemically active and inert parts in the form allowing the standard QC/MM treatment. The junction between the QC and MM parts of the system falls as we shall see into parts. The first appears as contributions from the chemically inert system which renormalize parameters of the electronic Hamiltonian for the chemically active system. The second renormalizes the parameters of the MM treated inert part of the molecular system. We shall consider both contributions.

Now we pass to the formal derivations. We assume that the one-electron states forming the one-electron basis for the entire molecular system may be ascribed either to the chemically inactive rest of the system (medium or M-states). The numbers of electrons in the R-system (chemically active subsystem) N_R and in the M-system (chemically inactive subsystem) $N_M = N_e - N_R$, respectively, are good quantum numbers at least at low energies. We also assume that the one-electron basis in both the systems is formed by strictly localized orbitals proposed in ref. 20. The strictly localized orbitals are orthonormalized linear combinations of the AOs centered on a single atom. In that sense they are the classical hybrid orbitals (HO):

$$|t(A)\rangle = \sum_{\tau \in A} h^t_\tau(A)|\tau\rangle \quad (13)$$

where the expansion coefficients $h^t_\tau(A)$ are defined by some procedure to be discussed elsewhere. In a degenerate case when the expansion coefficients are equal to 0s and 1s the HOs of eqn. (13) are the original AOs.

Applying the general technique described in the previous section leads to the effective Hamiltonian with the interaction containing two contributions: the Coulomb interaction between the electrons of the R- and M-systems and the projected resonance interaction between the M- and R-systems.

$$\hat{H}_{\text{eff}}(q, E) = \hat{P}\hat{H}_R(q)\hat{P} + \hat{P}\hat{H}_M(q)\hat{P}$$

$$+ \hat{P}\hat{V}^c(q)\hat{P} + \hat{P}\hat{V}^{rr}(q, E)\hat{P}$$

$$\hat{V}^{rr}(q, E) = \hat{V}^r(q)\hat{Q}(E - \hat{Q}\hat{H}^0\hat{Q})^{-1}\hat{Q}\hat{V}^r(q) \quad (14)$$

with

$$\hat{V}(q) = \hat{V}^r(q) + \hat{V}^c(q)$$

$$\hat{V}^r(q) = \sum_{r \in R,\, m \in M} v_{rm}(q)(r^+ m + m^+ r) \quad (15)$$

$$\hat{V}^c(q) = \sum_{rr' \in R,\, mm' \in M} (rr'\|mm')r^+ m^+ m'r'$$

where

$$(rr'\|mm') = (rr'|mm') - (rm'|mr')$$

and

$$\hat{H}^0(q) = \hat{H}_R(q) + \hat{H}_M(q) + \hat{V}^c(q)$$

If the approximate ground state in the Im$\hat{P}$ subspace is sought in the form:

$$\Psi_0 = \Phi^R_0 \bigwedge \Phi^M_0 \quad (16)$$

the functions Φ^R_0 and Φ^M_0 satisfy the system of interconnected eigenvalue problems with the effective Hamiltonians for the

respective subsystems:

$$\hat{H}^{R}_{eff}(q, E)\Phi^{R}_0 = E^{R}(q, E)\Phi^{R}_0$$

$$\hat{H}^{M}_{eff}(q, E)\Phi^{M}_0 = E^{M}(q, E)\Phi^{M}_0$$

$$\hat{H}^{R}_{eff}(q, E) = \hat{P}\hat{H}_R(q)\hat{P} + \langle\Phi^{M}_0|\hat{P}\hat{W}\hat{P}|\Phi^{M}_0\rangle \qquad (17)$$

$$\hat{H}^{M}_{eff}(q, E) = \hat{P}\hat{H}_M(q)\hat{P} + \langle\Phi^{R}_0|\hat{P}\hat{W}\hat{P}|\Phi^{R}_0\rangle$$

$$\hat{P}\hat{W}\hat{P} = \hat{P}\hat{V}^c(q)\hat{P} + \hat{P}\hat{V}^{rr}(q, E)\hat{P}$$

At this point we must deviate from the route prescribed by eqn. (8). The general scheme of the previous section has to be modified in order to conform the requirements imposed upon the target QC/MM description. Indeed, our goal is to develop a combined method in which the chemically inert part of the system (M-system) is treated with use of the MM. The MM approach presumes that the potential energy of the M-system is evaluated (parametrized) without explicit calculation of the electronic wavefunction of M-electrons. The quantities related to the M-system itself must be independently parametrized in a transferable fashion: the parameters describing the M-system must be universally usable for any R-system and also without any R-system at all as happens in the standard MM techniques. This makes any theory which takes the wavefunction Φ^{M}_0 calculated in the presence of the R-system as a basic quantity inappropriate for our purposes. We notice that the ground state of the effective Hamiltonian of the M-system Φ^{M}_0 eqn. (17) is in a certain sense close to that of the free M-system calculated without any R-system at all. Indeed, the electronic Hamiltonian for the M-system $\hat{H}^M(q)$ contains the one-electron terms describing attraction of electrons in the M-system to the bare cores of the atoms of the R-system and thus has the form:

$$\hat{H}^M(q) = \hat{H}^M_0(q) + \mathscr{V}^R(q) \qquad (18)$$

where

$$\mathscr{V}^R(q) = -e^2 \sum_A \frac{Z^R_A}{|r - R_A|}$$

(The core charge of an atom A is distributed between the R- and M-systems according to ref. 21):

$$Z_A = Z^M_A + Z^R_A \qquad (19)$$

The condition which specifies the distribution of the core charge Z_A between the R- and M-systems is that the cores of the R-system must be as much as possible screened by the electrons of the R-system i.e. the effective Hamiltonian $\hat{H}^M_{eff}$ must be as much as possible close to the Hamiltonian of the free M-system $\hat{H}^M_0(q)$. They, of course, can be reduced to the electron counting rules ultimately based on the concept of the formal oxidation state (see ref. 21 for details). The screening in the Hamiltonian $\hat{H}^M_{eff}$ is due to the $\langle\langle\hat{P}\hat{V}^c(q)\hat{P}\rangle\rangle_R$ term, so we can write:

$$\hat{H}^M_{eff} = \hat{H}^M_0 + \delta\hat{V}^R + \langle\langle\hat{P}\hat{V}^{rr}\hat{P}\rangle\rangle_R$$

$$\delta\hat{V}^R = \mathscr{V}^R + \langle\langle\hat{P}V^c\hat{P}\rangle\rangle_R \approx 0$$

The integer positive values Z^R_A are to be chosen in order to make the $\delta\hat{V}^R$ as small as possible.

In order to be in a position to justify the usage of an MM-like scheme for the M-system we have to use the ground state wavefunction Φ^M_{00} for the free M-system as a multiplier in eqn. (16) instead of Φ^M_0. Thus the ground state for the combined system is to be sought in the form:

$$\Psi_0 = \Phi^R_0 \wedge \Phi^M_{00} \qquad (20)$$

In order to get a better description for the energy with this trial wavefunction we have to replace the effective Hamiltonian eqn. (14) acting in the subspace $\text{Im}\hat{P}$ eqn. (4) by another

effective operator acting in the subspace of the functions of the form eqn. (20). This will be done with use of the Löwdin partition[12,15] as well. Averaging the resulting effective Hamiltonian acting in the subspace eqn. (20) over the ground state of the M-subsystem reduces the problem to finding the eigenstates of the effective Hamiltonian for R-electrons only.

To proceed further it is practical to rewrite the effective Hamiltonian eqn. (14) in terms of the Hamiltonian for the free M-system. It reads:

$$\hat{H}_{eff}(q, E) = \hat{P}\hat{H}^R(q)\hat{P} + \hat{P}\hat{H}^M_0(q)\hat{P} + \hat{P}\hat{\mathscr{W}}\hat{P} \qquad (21)$$

where

$$\hat{P}\hat{\hat{V}}^c(q)\hat{P} = \hat{P}\hat{V}^c(q)\hat{P} - \langle\langle\hat{P}\hat{V}^c(q)\hat{P}\rangle\rangle_R$$

$$\hat{P}\hat{\mathscr{W}}\hat{P} = \hat{P}\hat{\hat{V}}^c\hat{P} + \hat{P}\delta\hat{V}^R\hat{P} + \hat{P}\hat{V}^{rr}\hat{P} \qquad (22)$$

Now let $\hat{\mathscr{P}}$ be the operator projecting to Φ^M_{00}—to the ground state of the free M-system, and $\hat{\mathscr{Q}} = 1 - \hat{\mathscr{P}}$ is the coprojector. In the basis of the eigenstates of the bare M-Hamiltonian:

$$\hat{\mathscr{P}} = |\Phi^M_{00}\rangle\langle\Phi^M_{00}|; \quad \hat{\mathscr{Q}} = \sum_{p \neq 0}|\Phi^M_{0p}\rangle\langle\Phi^M_{0p}| \qquad (23)$$

The effective Hamiltonian acting in the subspace of the states eqn. (20) and having the eigenvalues coinciding with those of the Hamiltonian eqn. (14) and (21) has the form:[12,15]

$$\hat{\mathscr{H}}_{eff}(q, E, \omega) = \hat{\mathscr{P}}\hat{\mathscr{H}}_{eff}(q, E)\hat{\mathscr{P}} + \hat{\mathscr{P}}\hat{\mathscr{H}}_{eff}(q, E)$$
$$\times \hat{\mathscr{Q}}\hat{\mathscr{R}}(\omega)\hat{\mathscr{Q}}\hat{\mathscr{H}}_{eff}(q, E)\hat{\mathscr{P}} \qquad (24)$$

$$\hat{\mathscr{R}}(\omega) = [\omega\hat{\mathscr{Q}} - \hat{\mathscr{Q}}\hat{\mathscr{H}}_{eff}(q, E)\hat{\mathscr{Q}}]^{-1} \qquad (25)$$

Projection operators $\hat{\mathscr{P}}$ and $\hat{\mathscr{Q}}$ affect the quantum numbers of the M-electrons only and for that reason they do not change (commute with) the Hamiltonian $\hat{P}\hat{H}_R(q)\hat{P}$ which depends on the quantum numbers of R-electrons only. For that reason we get:

$$\hat{\mathscr{H}}_{eff}(q, E, \omega) = \hat{P}\hat{H}^R(q)\hat{P}\hat{\mathscr{P}} + \hat{\mathscr{P}}\hat{P}\hat{H}^M_0(q)\hat{P}\hat{\mathscr{P}}$$
$$+ \hat{\mathscr{P}}\hat{P}\hat{\mathscr{W}}(q, E)\hat{P}\hat{\mathscr{P}} + \hat{\mathscr{P}}\hat{P}\hat{\mathscr{W}}(q, E)\hat{P}\hat{\mathscr{Q}}\hat{\mathscr{R}}(\omega)$$
$$\times \hat{\mathscr{Q}}\hat{P}\hat{\mathscr{W}}(q, E)\hat{P}\hat{\mathscr{P}} \qquad (26)$$

where

$$\hat{\mathscr{P}}\hat{H}_{eff}\hat{\mathscr{Q}} = \hat{\mathscr{P}}\hat{P}\hat{H}^M_0(q)\hat{P}\hat{\mathscr{Q}} + \hat{\mathscr{P}}\hat{P}\delta\hat{V}^R\hat{P}\hat{\mathscr{Q}} + \hat{\mathscr{P}}\hat{P}\hat{W}\hat{P}\hat{\mathscr{Q}}$$
$$= \hat{\mathscr{P}}\hat{P}\hat{\mathscr{W}}\hat{P}\hat{\mathscr{Q}} \qquad (27)$$

(since $\hat{\mathscr{P}}$ projects to an eigenstate of the operator $\hat{H}^M_0$, the corresponding term in the formula just above vanishes).

In the operator eqn. (26) the description of the electronic structure of the M-system is reduced as much as possible—its exact wavefunction is replaced by the fixed wavefunction for electrons for the free M-system.

2.2.2 Effective Hamiltonian for the quantum system. In the target QC/MM theory the wavefunction for electrons in the quantum R-system Φ^R_0 must be found by a QC procedure. According to the general theory this function satisfies the Schrödinger equation with the effective Hamiltonian $\hat{\mathscr{H}}^R_{eff}(q, E, \omega)$ for the electrons in the R-system. This operator is obtained by averaging the operator $\hat{\mathscr{H}}_{eff}(q, E, \omega)$ eqn. (26) over the ground state of the M-system (i.e. over the function Φ^M_{00}). The latter effective Hamiltonian acts only on the quantum numbers of electrons in the R-system. With use of the definitions of the Hamiltonian $\hat{H}^R_{eff}(q, E)$ eqn. (17) and of the projecting operator $\hat{\mathscr{P}}$ eqn. (23) we get the effective Hamiltonian for R-electrons in the form:

$$\mathscr{H}_{\mathrm{eff}}^{\mathrm{R}}(q, E, \omega) = \hat{H}_{\mathrm{eff}}^{\mathrm{R}}(q, E) + \langle \Phi_{00}^{\mathrm{M}} | \hat{P}\hat{\mathscr{W}}(q, E)$$
$$\times \hat{P}\hat{\mathscr{Q}}\hat{\mathscr{R}}(\omega)\hat{\mathscr{Q}}\hat{P}\hat{\mathscr{W}}(q, E)\hat{P} | \Phi_{00}^{\mathrm{M}} \rangle$$
$$+ \langle \Phi_{00}^{\mathrm{M}} | \hat{P}\,\delta\hat{V}^{\mathrm{R}}\hat{P} | \Phi_{00}^{\mathrm{M}} \rangle$$
$$- \langle \Phi_{00}^{\mathrm{M}} | \langle\langle \hat{P}\hat{V}^c\hat{P}\rangle\rangle_{\mathrm{R}} | \Phi_{00}^{\mathrm{M}} \rangle$$
$$+ \langle \Phi_{00}^{\mathrm{M}} | \hat{P}\hat{H}_0^{\mathrm{M}}(q)\hat{P} | \Phi_{00}^{\mathrm{M}} \rangle \tag{28}$$

It is convenient to represent the effective Hamiltonian $\hat{H}_{\mathrm{eff}}^{\mathrm{R}}(q, E)$ also in terms of the $\hat{H}_0^{\mathrm{R}}(q)$ operator, which is the Hamiltonian for the free R-system:

$$\hat{H}_{\mathrm{eff}}^{\mathrm{R}}(q, E) = \hat{H}_0^{\mathrm{R}}(q) + \delta\hat{V}^{\mathrm{M}} + \langle\langle \hat{P}\hat{V}^{rr}\hat{P}\rangle\rangle_{\mathrm{M}}$$
$$\delta\hat{V}^{\mathrm{M}} = \hat{\mathscr{V}}^{\mathrm{M}} + \langle\langle \hat{P}\hat{V}^c\hat{P}\rangle\rangle_{\mathrm{M}} \approx 0$$

Here $\hat{\mathscr{V}}^{\mathrm{M}}$ stands for the operator of attraction of electrons in the R-system to the M-system cores. So that

$$\mathscr{H}_{\mathrm{eff}}^{\mathrm{R}}(q, E, \omega) = \hat{H}_0^{\mathrm{R}}(q) + \delta\hat{V}^{\mathrm{M}} + \langle\langle \hat{P}\hat{V}^{rr}\hat{P}\rangle\rangle_{\mathrm{M}}$$
$$+ \langle \Phi_{00}^{\mathrm{M}} | \hat{P}\hat{\mathscr{W}}(q, E)\hat{P}\hat{\mathscr{Q}}\hat{\mathscr{R}}(\omega)$$
$$\times \hat{\mathscr{Q}}\hat{P}\hat{\mathscr{W}}(q, E)\hat{P} | \Phi_{00}^{\mathrm{M}} \rangle$$
$$+ \langle \Phi_{00}^{\mathrm{M}} | \hat{P}\,\delta\hat{V}^{\mathrm{R}}\hat{P} | \Phi_{00}^{\mathrm{M}} \rangle - \langle \Phi_{00}^{\mathrm{M}} |$$
$$\times \langle\langle \hat{P}\hat{V}^c\hat{P}\rangle\rangle_{\mathrm{R}} | \Phi_{00}^{\mathrm{M}} \rangle$$
$$+ \langle \Phi_{00}^{\mathrm{M}} | \hat{P}\hat{H}_0^{\mathrm{M}}(q)\hat{P} | \Phi_{00}^{\mathrm{M}} \rangle \tag{29}$$

The operator eqn. (28) and (29) contains renormalization terms (1) originating from the Coulomb interaction with the net charges in the M-system $\delta\hat{V}^{\mathrm{M}}$, (2) originating from the resonance interaction with the M-system $\langle\langle \hat{P}\hat{V}^{rr}\hat{P}\rangle\rangle_{\mathrm{M}}$, and (3) those containing the resolvent $\hat{\mathscr{R}}(\omega)$, which is in fact a collection of one- and two-electron operators (see below). It also contains three c-number mean values of the operators for M-electrons over the ground state of the M-system. They do not affect the motion of R-electrons and can be omitted while the electronic structure of the R-system is considered.

Let us consider the contributions renormalizing the Hamiltonian for the free R-system.

(1) This type of the renormalizing contribution to the effective Hamiltonian of the R-system contains the average of the Coulomb intersystem interaction over the ground state of the M-system:

$$\langle\langle \hat{P}\hat{V}^c\hat{P}\rangle\rangle_{\mathrm{M}} = \langle \Phi_{00}^{\mathrm{M}} | \hat{P}\hat{V}^c\hat{P} | \Phi_{00}^{\mathrm{M}} \rangle \tag{30}$$

Inserting the explicit expression for the Coulomb operator we get:

$$\langle\langle \hat{P}\hat{V}^c\hat{P}\rangle\rangle_{\mathrm{M}} = \sum_{rr'} r^+ r' \left[\sum_{mm'} (rr' \| mm')\langle\langle m^+ m'\rangle\rangle_{\mathrm{M}} \right] \tag{31}$$

The expression eqn. (31) is valid for arbitrary pairs of the states in the respective systems. In the ZDO approximation for the two-center two-electron integrals we have for arbitrary AO pairs $\mu v \in \mathrm{A}$ and $\kappa\lambda \in \mathrm{B}$:

$$(\mu v | \kappa\lambda) = \delta_{\mu v}\,\delta_{\kappa\lambda}(\mu\mu | \lambda\lambda) = \gamma_{\mathrm{AB}} \tag{32}$$

For the HO pairs $rr' \in \mathrm{A}$, $mm' \in \mathrm{B}$ we get:

$$(rr' \| mm') = (rr' | mm') = \gamma_{\mathrm{AB}}\,\delta_{rr'}\,\delta_{mm'} \tag{33}$$

due to the HOs orthonormality. Making summation over all HOs $m \in \mathrm{M}$ of the atom B we get the renormalization of the one-electron parameters for the HO $r \in \mathrm{A}$ in the R-system:

$$r^+ r\gamma_{\mathrm{AB}}\left[\sum_{m \in \mathrm{B}} \langle\langle m^+ m\rangle\rangle_{\mathrm{M}} \right] = r^+ r\gamma_{\mathrm{AB}} P_{\mathrm{B}}^{\mathrm{M}} \tag{34}$$

where P_{B} is the electron density of the M-system residing on the valence orbitals of the atom B. Following our general semi-empirical approach we neglect the penetration effects[22]

and assume the matrix element of electron attraction at any AO centered on the atom A to the core of the atom B to be equal to γ_{AB}. Then the operator of electron attraction to the M-system cores acquires the form:

$$\hat{\mathscr{V}}^{\mathrm{M}}(q) = -e^2 \sum_{\mathrm{B}} \frac{Z_{\mathrm{B}}^{\mathrm{M}}}{|r - R_{\mathrm{B}}|} \approx$$
$$- \sum_{\mathrm{A} \neq \mathrm{B}} \sum_{r \in \mathrm{A}} r^+ r \sum_{\mathrm{B}} \gamma_{\mathrm{AB}} Z_{\mathrm{B}}^{\mathrm{M}}$$

and the total contribution of the atom B to the one-electron parameter of an HO centered on the atom $\mathrm{A} \neq \mathrm{B}$ equals to:

$$\gamma_{\mathrm{AB}}(P_{\mathrm{B}}^{\mathrm{M}} - Z_{\mathrm{B}}) = \gamma_{\mathrm{AB}}(P_{\mathrm{B}}^{\mathrm{M}} - Z_{\mathrm{B}}^{\mathrm{M}} - Z_{\mathrm{B}}^{\mathrm{R}})$$
$$= \gamma_{\mathrm{AB}}(Q_{\mathrm{B}}^{\mathrm{M}} - Z_{\mathrm{B}}^{\mathrm{R}})$$

where $Q_{\mathrm{B}}^{\mathrm{M}}$ is the charge on the atom B of the M-system. One can easily check, that the formula above is in agreement with the intuitively transparent choice of the core charges in the already classical example of effective electronic Hamiltonians i.e. in the π-electron PPP Hamiltonian (see ref. 23).

(2) This type of the renormalizing contribution of the effective Hamiltonian for the R-system is due to the virtual one-electron transfers between the systems. The term in the effective Hamiltonian which takes into account these transfers is:

$$\hat{P}\hat{V}^{rr}(q, E)\hat{P} = \sum_{rmr'm'} v_{rm}(q)v_{r'm'}(q)$$
$$\times [(r^+ m\hat{R}(E)m'^+ r')$$
$$+ (m^+ r\hat{R}(E)r'^+ m')] \tag{35}$$

The resolvent $\hat{R}(E)$ can be presented as:

$$\hat{R}(E) = \sum_{i \in \mathrm{Im}\hat{Q}} \frac{|i\rangle\langle i|}{E - E_i} \tag{36}$$

It has the poles at the energies of the states which differ by transfer of one-electron from (or to) the M-system to (or from) the R-system. We denote the states $|i\rangle \in \mathrm{Im}\hat{Q}$ as $|\mu \to \rho\rangle$ or $|\rho \to \mu\rangle$ corresponding respectively to one-electron transfers from the M-system to the R-system and vice versa. The estimates for the energies E_i of these states are $I_\mu - A_\rho - g_{\mu\rho}$ and $I_\rho - A_\mu - g_{\mu\rho}$, where Is and As are the ionization potentials and electron affinities corresponding to the ρ and μ eigenstates of the respective systems. The renormalizing correction is obtained by averaging eqn. (35) over the ground state of the M-system:

$$\langle\langle \hat{P}\hat{V}^{rr}(q, E)\hat{P}\rangle\rangle_{\mathrm{M}} = \sum_{rr'} \sum_{mm'} v_{rm}(q)v_{r'm'}(q)$$
$$\times \{r^+ \langle\langle m\hat{R}(E)m'^+\rangle\rangle_{\mathrm{M}} r'$$
$$+ r\langle\langle m'\hat{R}(E)m^+\rangle\rangle_{\mathrm{M}} r'^+\} \tag{37}$$

We notice that the resolvent operator $\hat{R}(E)$ acts in a subspace spanned by two types of the product functions, namely by the $(N_{\mathrm{M}} + 1)$-electron functions of the M-system multiplied by the $(N_{\mathrm{R}} - 1)$-electron functions of the R-system and by the $(N_{\mathrm{M}} - 1)$-electron functions of the M-system multiplied by the $(N_{\mathrm{R}} + 1)$-electron functions of the R-system. It can be shown[24] that the above expression acquires the form:

$$\langle\langle \hat{P}\hat{V}^{rr}(q, E)\hat{P}\rangle\rangle_{\mathrm{M}} = \sum_{rr'} \sum_{mm'} v_{rm}(q)v_{r'm'}(q)$$
$$\times \left\{ \sum_{\rho \in \mathrm{Im}\mathscr{O}_{\mathrm{R}}(N_{\mathrm{R}} + 1)} r^+ |\rho\rangle \right.$$
$$\times \langle\rho | r' G_{mm'}^{(\mathrm{adv})}(A_\rho - E)$$
$$+ \sum_{\rho \in \mathrm{Im}\mathscr{O}_{\mathrm{R}}(N_{\mathrm{R}} - 1)} r|\rho\rangle$$
$$\left. \times \langle\rho | r'^+ G_{mm'}^{(\mathrm{ret})}(I_\rho - E) \right\} \tag{38}$$

where $G^{(\mathrm{ret})}(\epsilon)$ and $G^{(\mathrm{adv})}(\epsilon)$ are the one-electron Green's func-

tions of the M-system. (For the reference concerning the Green's function technique in the finite fermion systems see ref. 23, 25 and 26). It can be easily checked, that the renormalizing contributions of the type discussed in this paragraph do not appear in the π-electron Hamiltonians: due to the planar symmetry the resonance matrix elements $v_{\sigma\pi}$ vanish. The situation when they are crucially important will be discussed below.

(3) The last term renormalizing the Hamiltonian for the R-system appears due to a collection of terms eqn. (22). It contains both one- and two-electron terms. In general the theory of the polarization conditioned modification of the effective Hamiltonian for the R-system parallels the theory of weak interactions between molecules as it is given in ref. 27. The important difference is that the two systems considered in the present paper are not equivalent, whereas in the theory of molecular interactions the interacting molecules are considered on equal footing. Nevertheless all the terms present in the theory of weak interactions have their analogs in the present theory with an important addition of the terms derived from the projected resonance interaction. They are somewhat cumbersome and thus they will be described in detail elsewhere. The preliminary results can be found in ref. 28.

2.2.3 Potential energy surface for the combined systems.

Now we derive the combined QC/MM description for the PES. The total PES of a molecular system $\mathscr{U}(q)$ is a sum of its electronic energy $\mathscr{E}_0(q)$ and of the internuclear Coulomb repulsion $U(q)$:

$$\mathscr{U}(q) = \mathscr{E}_0(q) + U(q)$$
$$U(q) = e^2/2 \sum_{A \neq B} Z_A Z_B / R_{AB}(q)$$
$$\approx 1/2 \sum_{A \neq B} Z_A Z_B \gamma_{AB}(q) \qquad (39)$$

where Z_A and Z_B are the nuclear (core) charges of the atoms A and B, $R_{AB}(q)$ are the internuclear separations which depend on the independent nuclear coordinates q, and $\gamma_{AB}(q)$ are the two-center electron Coulomb repulsion integrals used in the ZDO approximation to parametrize the internuclear repulsion as well. The electronic energy is the average of the effective electronic Hamiltonian $\mathscr{H}_{\text{eff}}(q, E, \omega)$ eqn. (24) which is acting in the $\text{Im}(\mathscr{P}\hat{P})$ subspace over the wavefunction Ψ_0 eqn. (20) of the combined R $\oplus$ M-system. Taking this all into account one obtains:[12]

$$\mathscr{E}_0(q) = \langle \Psi_0 | \mathscr{H}_{\text{eff}}(q, E, \omega) | \Psi_0 \rangle = \mathscr{E}_0^R(q) + E_{00}^M(q)$$
$$E_{00}^M(q) = \langle \Phi_{00}^M(q) | \hat{H}_0^M(q) | \Phi_{00}^M(q) \rangle$$
$$\mathscr{E}_0^R(q) = \langle \Phi_0^R(q) | \mathscr{H}_{\text{eff}}^R | \Phi_0^R(q) \rangle \qquad (40)$$

The electronic energy of the R-system $\mathscr{E}_0^R(q)$ is the minimal eigenvalue of the effective electron Hamiltonian for the R-system eqn. (28) which has to be found with use of a QC procedure with involves an explicit construction of the many-electron wavefunction Φ_0^R in each point q of the nuclear configuration space. The effective Hamiltonian to be used for this end is outlined in the previous section.

The electronic energy of the M-system $E_{00}^M(q)$ has to be evaluated without explicit construction of the wavefunction $\Phi_{00}^M(q)$ of its electrons by an MM-like procedure. However, we notice that the MM-like approaches parametrize not the electronic energy, but the total energy *i.e.* the sum of the electronic energy and that of the nuclear repulsion. When $E_{00}^M(q)$ is supplied with the corresponding sum of the core–core Coulomb repulsion terms it becomes the PES of the M-system. One can hope that this can be already parametrized in an MM-like fashion (see below).

We notice also that the MM-like parametrization for the M-system cannot coincide with any standard MM parametrization since for some atoms in the combined system their AOs are distributed between the R- and M-systems and, thus, some part of the potential energy related to these atoms must be treated on the basis of a QC calculation and only some other part with use of an MM approach. Clearly, the parameters of any MM-like scheme related to these atoms must be renormalized. Let us consider the renormalization of the electrostatic contribution to the PES first. We restrict ourselves with the MM parametrization schemes which explicitly include the Coulomb interaction of the effective atomic charges in the expression for the potential energy and presume that the charges are extracted from some QC calculation. The corresponding (electrostatic) term in the MM type PES is:

$$E_{\text{el–st}}(q) = e^2 \sum_{A < B} R_{AB}^{-1} Q_A Q_B \approx \tfrac{1}{2} \sum_{A \neq B} Q_A Q_B \gamma_{AB}(q)$$
$$Q_A = (P_A - Z_A) \qquad (41)$$

where Q_A is the total effective charge of the atom A, P_A is the electron density on the atom A which corresponds to the wavefunction Φ_{00}^M. In the MM schemes the quantities Q_A are considered as parameters of the method.

Previously [eqn. (19)] we evoked a possibility of distributing the total effective charges between the R- and M-systems:

$$Q_A = Q_A^R + Q_A^M$$
$$Q_A^R = P_A^R - Z_A^R$$
$$Q_A^M = P_A^M - Z_A^M \qquad (42)$$

The general conditions allowing us to determine Z_A^R and Z_A^M are mentioned above. It can be checked that the off-diagonal matrix elements of the one-electron density matrix between the HOs of the different systems are vanishing due to the structure of the wavefunction Ψ_0:

$$\langle \Psi_0 | r^+ m | \Psi_0 \rangle = \langle \Psi_0 | m^+ r | \Psi_0 \rangle = 0$$

Then for any atom A we can write:

$$P_A = P_A^M + P_A^R$$
$$P_A^R = \sum_{r \in A} \langle\langle r^+ r \rangle\rangle_R$$
$$P_A^M = \sum_{m \in A} \langle\langle m^+ m \rangle\rangle_M$$

The electron density P_A^R is found by a QC calculation on the R-system, whereas P_A^M is parametrized as a sum of the averages $\langle\langle m^+ m \rangle\rangle_M$ over all HOs m of the M-system centered on the atom A. This scheme is nontrivial only for those atoms in the molecular system which bear the HOs which belong to the different systems (frontier atoms or FA). However, formally it can be extended to those atoms where all HOs belong to the same system (non-frontier atoms or non-FA). Inserting the expansion eqn. (42) in the above formula for the electrostatic part of the MM-type PES eqn. (41) we get:

$$E_{\text{el–st}}(q) = \tfrac{1}{2} \sum_{A \neq B} (Q_A^R + Q_A^M)(Q_B^R + Q_B^M)\gamma_{AB}(q)$$
$$= \tfrac{1}{2} \sum_{A \neq B} (Q_A^R Q_B^R + Q_A^M Q_B^R + Q_A^R Q_B^M$$
$$+ Q_A^M Q_B^M)\gamma_{AB}(q) \qquad (43)$$

Clearly, the electrostatic contribution to the MM PES for two non-FA atoms from the M-system is not renormalized due to separation of the R-system. The same applies to a pair of two non-FA atoms from the R-system. For them the electrostatic contribution is estimated with use of the charges calculated by the adopted QC procedure and thus must be excluded from the MM contribution to the PES. The nontrivial renormalization of the MM-part of the PES happens to the FA only. Only the parts Q_A^M of the total effective charge residing on an FA A must be used in the electrostatic part of the PES of the

M-system instead of the total effective charges. This is how the renormalization of the electrostatic term of the MM part of the PES takes place.

The standard MM schemes usually involve van der Waals (dispersion) interactions between nonbonded atoms. As it was in the case of the electrostatic contribution the van der Waals terms must be renormalized. It can be shown that the dispersion interactions between the R- and M-systems arise from the

$$\langle \Phi_{00}^{M}| \hat{P}\hat{\bar{V}}^{c}\hat{P}\hat{\mathscr{R}}(\omega)\hat{P}\hat{\bar{V}}^{c}\hat{P} |\Phi_{00}^{M}\rangle \tag{44}$$

term in the effective Hamiltonian for the R-system eqn. (29). The average of this term over the ground state of the R-system Φ_{0}^{R} appears in the PES of the combined system. Following the general scheme formulated in ref. 12 and 27 one can reduce the mentioned average of eqn. (44) to the sum of integrals having the form:

$$E_{\text{disp}}^{\text{RM}} = - \sum_{pr \in R,\, tv \in M} (pp\,|\,tt)(rr\,|\,vv)$$
$$\times \int_{0}^{\infty} d\omega\, \pi_{rp}^{R}(i\omega)\pi_{vt}^{M}(i\omega) \tag{45}$$

where $\pi_{rp}^{R}(i\omega)$ and $\pi_{vt}^{M}(i\omega)$ are the reduced polarization propagators for the R- and M-systems. In the MM context the dispersion interaction is normally represented by a sum of the pair atom–atom contributions. The simplest method to include intersystem dispersion interactions is to add the corresponding diatomic terms to the PES.[4] However, in the case of the chemically transforming R-system the different electronic terms change their relative energies and thus the positions of the poles of the $\pi_{rp}^{R}(i\omega)$ function change along the reaction path. This affects the value of the above integral but is not reflected by the atom–atomic scheme. Thus the explicit consideration of the intersystem dispersion interaction may result in noticeable renormalization of the latter. It will be considered in detail elsewhere.

In the present section we derived general formulae for the PES of a combined molecular system comprising a chemically transforming part of a system to be treated with the use of quantum chemistry and a chemically inert system to be treated with use of molecular mechanics. Applying the general formalism of separating electron variables related to the two systems resulted in a consistent description of the PES of the combined system in a desired form of the sum of the QC and MM contributions. Also the quantities usually referred to as "junctions" between the QC and MM parts of the combined system have been consistently derived. It turned out that the junctions manifest themselves in renormalizations of the electronic Hamiltonian for the QC system and in respective modifications of the MM potential.

3   Implementations of electron variables separation

The previous section presents a survey of a general direction where in our opinion the theory should evolve in order to reach a reliable and cheap methods making electronic structure and chemical transformation of large molecular systems available to quantum chemical treatment. In what follows we present some examples where the aforementioned methodology has been applied in various situations which are difficult for the standard quantum chemistry and where the electronic variable separation performed in the above manner turned out to be effective.

3.1   Effective crystal field method

The main idea of the fundamental paper on the crystal field theory (CFT)[29] was to restrict the explicit consideration by the states of the d-shell of the transition metal ion. The reason

for success of such an economical approach is that the low-energy excitations of transition metal complexes (TMC) or those of transition metal impurity ions in solids are the d–d excitations (excitations of the d-shell) and for that reason the experimental data can be interpreted with use of the theories operating within this restricted subspace of the electronic states. The rest of the electrons and nuclei do not appear in the CFT. The qualitative physical picture provided by the CFT is correct due to the correct form of the electronic wavefunction which it tacitly uses. The implicit wavefunction of a complex in the CFT is a GF function: it is a product of the multiplet (full CI) state for a fixed number of d-electrons (considered explicitly) and of an unspecified closed shell state for the remaining electrons in the ligands. The ligand electrons are not considered explicitly, and that is why the crystal fields cannot be satisfactorily calculated within the CFT's own framework. In order to achieve this the ECF method,[30] which brings the ligand's electron wavefunction into consideration has been proposed. It gives an example of the variable separation performed with use of the Löwdin partition.

The formal derivation of the ECF method is described in ref. 30. The whole set of the valence AOs of a TMC (including the 4s-, 4p-, and 3d-AOs of the metal center and the valence AOs of all ligand atoms) is divided into two parts. The first contains only 3d-orbitals of the transition metal atom or TMA (d-system). The second part contains 4s- and 4p-AOs of the TMA and the valence orbitals of the ligand atoms (ligand system or l-system). The d-shell takes part of the R-system of the previous section and the rest takes part of the M-system. Notice that the present example of the variable separation using the technique described above illustrates the nontrivial distribution of the core charges between the systems. In the TMCs the border between the R- and M-systems crosses the transition metal atom itself. The requirement of the minimality of $\delta\hat{V}^{d}$ immediately leads to $Z_{d} = n_{d}$ which means that the total charge of the d-shell equals zero and thus $\delta\hat{V}^{d} = 0$.

The wavefunction Φ_{n} for the n-th electronic state of a TMC is then taken in the form:

$$\Phi_{n} = \Phi_{d}^{n}(n_{d}) \bigwedge \Phi_{l}(N - n_{d}) \tag{46}$$

where $\Phi_{d}^{n}(n_{d})$ is the spin and symmetry adapted n_{d}-electron wavefunction of the metal d-orbitals, and $\Phi_{l}(=\Phi_{00}^{M})$ is the single determinant $(N - n_{d})$-electron wavefunction for the l-orbitals. Within the ECF theory[30] the l-system is described by a single Slater determinant Φ_{l}. The function Φ_{l} is calculated for a charge of the central ion $Z_{TMI} \to Z_{TMI} - Z_{d}$ which corresponds to the complete screening of the part of the total core charge of the transition metal ion by the d-shell. The solution of the SCF problem for the l-system yields the one electron density matrix P_{kl}, the energies of the molecular orbitals (MO) ϵ_{i}, and MO-LCAO coefficients c_{ik}. These quantities completely describe the electronic structure of the l-system and may be concentrated in the Green's functions for the l-system. They are used to construct the effective Hamiltonian $\hat{H}_{d}^{\text{eff}}$:

$$\hat{H}_{d}^{\text{eff}} = \sum_{\mu\nu\sigma} U_{\mu\nu}^{\text{eff}} d_{\mu\sigma}^{+} d_{\nu\sigma}$$
$$+ \frac{1}{2} \sum_{\mu\nu\rho\eta} \sum_{\sigma\tau} (\mu\nu\,|\,\rho\eta) d_{\mu\sigma}^{+} d_{\nu\sigma} d_{\rho\tau}^{+} d_{\eta\tau} \tag{47}$$

where the d-electron Coulomb interaction term is inherited from the free ion and the effective one-electron parameters $U_{\mu\nu}^{\text{eff}}$ contain contributions from the Coulomb and the resonance interaction of the d- and l-systems:

$$U_{\mu\nu}^{\text{eff}} = \delta_{\mu\nu}\hat{U}_{\text{dd}} + W_{\mu\nu}^{\text{atom}} + W_{\mu\nu}^{\text{field}} + W_{\mu\nu}^{\text{cov}} \tag{48}$$

where

$$W_{\mu\nu}^{\text{atom}} = \delta_{\mu\nu}\left(\sum_{i\in s,\, p} g_{\mu i} P_{ii}\right) \tag{49}$$

is the repulsion of electrons in the d-shell from those in the 4s- and 4p-AOs of the metal:

$$W_{\mu\nu}^{\text{field}} = \sum_L Q_L \hat{V}_{\mu\nu}^L$$

$$Q_L = P_L - Z_L \tag{50}$$

$$P_{LL} = \sum_{l \in L} P_{ll}$$

is the Coulomb interaction of d-electrons with the net charges on the ligand atoms, in the standard CFT form. These two contributions appear from averaging the intersystem Coulomb interaction over the ground state of the free l-system. The contribution $W_{\mu\nu}^{\text{atom}}$ is a result of averaging the Coulomb interaction between electrons occupying the states on the FA. The term

$$W_{\mu\nu}^{\text{cov}} = -\sum_{ll'} \beta_{\mu l} \beta_{\nu l'} [G_{ll'}^{(\text{adv})}(I_d) + G_{ll'}^{(\text{ret})}(A_d)] \tag{51}$$

takes into account the intersystem resonance interaction.[31] Here $\beta_{\mu l}$ are the resonance integrals between the μ-th d-orbital and the l-th orbital in the ligands. The simplification of eqn. (38) is reached here by noticing that the ionization potential I_d and electron affinity A_d of the d-shell do not depend on the one-electron state from (or to) which an electron is extracted (or added). This allows us to factorize the sum over ρ in eqn. (38). Also E is set equal to zero (for details see ref. 30).

It is well known[32] that correct description of the ground state spin and symmetry of TMCs and of their d-d excitation spectra presents a problem for semi-empirical quantum chemistry based on the SCF approximation. The problems are both the poor convergency and incorrect answers. The reason is the strongly correlated behavior of d-electrons (see below) which precludes applying the SCF approximation to them. On the other hand the ligands can be satisfactorily described by a SCF based semi-empirical method. At this point the electron variable separation becomes crucial since the different levels of description are necessary for different parts of a TMC. The d-shell must be described with correlations whereas the ligands may be treated without it. In a series of papers[33] the ECF method has been tested for a variety of TMCs. In the ECF approach the desired variable separation is performed. After that it turns out that for a series of complexes ranging from metal hexahydrate ions to metal porphyrins the ground state spin and symmetry are reproduced in full agreement with experimental data whereas the d–d excitation energies are reproduced with an accuracy of 1000–2000 cm^{-1}.[33] This accuracy is comparable to that of *ab initio* approaches when applied to TMCs. At the same time the ECF method currently can be applied to a TMC containing up to 250 ligand atoms[34] which is clearly beyond the scope of available *ab initio* packages.

3.2 Extending MM to transition metals

In the previous section we presented an account of the ECF theory in the general context of the electron variables separation performed with the use of the Löwdin partition technique. It leads to a family of the methods which use a variety of semi-empirical techniques to calculate the electronic structure of the l-system. If the method employed for calculating the ligands' electronic structure is also parametrized to reproduce the heats of formation and geometries of organic molecules, one may hope that a combination of such a method for the ligands with the ECF approach for the d-shell will lead after proper parametrization to an accurate description of the d–d spectra, geometries and heats of formation of TMCs. Some work is done along this direction,[35,36] however, there is not enough experience yet on applying these methods in structural studies on TMCs. An alternative to the step by step

improvement of semi-empirical descriptions of the ligands for the computation of the PES of TMCs is to use the MM approximation to calculate the ligand's energy E_l. In this approach the ECF/CNDO or ECF/INDO method are only retained for calculating the crystal field felt by the d-shell.[37,38] The ligand's potential energy E_l is simply replaced by E_{mm}, estimated with use of the MM2 procedure.[39] The total energy of the n-th electronic state of a complex then has the form:

$$E_n = E_d^{\text{eff}}(n) + E_{mm} \tag{52}$$

The energies $E_d^{\text{eff}}(n)$ of the d-shells are calculated with the ECF/CNDO method. This brings us into the area of extending the MM technique to transition metals. This is a rapidly growing area (see ref. 40–45) of research. Two aspects are important here: First, the sufficiently quantum character of behavior manifested by the d-shell when many (or at least several) electronic states of different spin and/or symmetry are accessible in a narrow energy range near its ground state. Such a behavior must be attributed to the d-shell since for the ligands the excited states are well separated from the ground state on the energy scale and thus the standard MM description is possible. This puts the very problem of extending MM to transition metals in the general context of the developing QC/MM methods though it is rarely recognized by the workers in the field. The second aspect is not only the quantum but also sufficiently many-particle (correlated) behavior of electrons in the d-shell. Both aspects are adequately covered by the ECF/MM approach based on eqn. (52). This distinguishes the ECF/MM approach from many others in this area.

The ECF/MM approach has been used to study energy profiles of the *cis*-[Fe(bipy)$_2$(NCS)$_2$] molecule which is known to exist in two different spin states.[46,47] This is an important example which demonstrates both the quantum and correlated behavior of the d-shell simultaneously. The ECF/CNDO method[30] has been used for analysis of the spin states and d–d excitations in this molecule[48] and has demonstrated the general validity of the ECF method. It has been completed by the MM potential representing the ligand's energy. The standard MM2 parametrization[39] has been used for all atoms except iron, for which no bending or torsional terms have been used and the bond stretching potential has been modeled by a Morse function:

$$E_b^{\text{Fe–N}} = D_{\text{Fe–N}}(1 - e^{-\alpha_{\text{Fe–N}}(r - r^0_{\text{Fe–N}})})^2 \tag{53}$$

The parameter values were fitted[37] to reproduce the experimentally determined positions of the PESs minima along the Fe—N bond-length coordinates for the low-spin and high-spin states. It is possible to reproduce the whole qualitative picture of the lowest electronic terms derived from experiment[46,47] with a single MM potential for the ligands and with the ECF/CNDO method applied to estimate the d-shell energy. Different Fe—N distances for the high-spin and low-spin forms of the complex appear as a result of a compromise between the single ligand MM-potential and the geometry sensitive d-shell energy obtained by the ECF/CNDO procedure for different values of the total spin of the d-shell. The d-electron energy is specific for each spin state since it is obtained by diagonalization of the n_d-electron effective Hamiltonian of eqn. (48) in each point of the nuclear coordinate space.

In this section we describe a simplest approach for constructing a hybrid QC/MM method for a specific class of molecular systems *i.e.* for TMCs. In a line with the general recipe eqn. (40) the energy of a molecular system is presented as a sum of an average of the effective Hamiltonian for the quantum system (the d-shell) over its ground state (with specific value of the total spin) and of the energy of the classical system. Despite the fact that the quantum system in this example is somewhat degenerate (no geometry of its own) as

compared to the thinkable quantum systems displaying more pronounced "chemical" behavior, all the components of the hybrid QC/MM approach are present here. The geometry dependence of the energy of the quantum system appears *via* the geometry dependence of the contributions eqn. (48)–(51) renormalizing the Hamiltonian for the quantum d-shell.

4 Discussion

In the present paper we described an approach to a noncontradictive derivation of the hybrid quantum chemistry/molecular mechanics (QC/MM) methods, which is based on combining the group function formalism and the Löwdin partition. The area of the hybrid QC/MM methods is rapidly growing now. However, the QC/MM procedures presented in the literature including those implemented in existing quantum chemistry packages do not stem from any sequential derivation.[3,4] This clearly reduces the strength of this potentially powerful approach. This situation must be corrected by constructing a logical derivation based on an adequate form of the trial electron wavefunction of a molecular system. The choice of this form is not simple, particularly in the case when the chemically transforming system (or more precisely, the quantum system with a dense spectrum of electronic states) is a part of a larger molecule, *i.e.* when the R-system to be treated at a QC level is connected to the M-system treated at the MM level by chemical bonds. At this point an alternative appears: to set a borderline between the systems across some bonds or to set it at some atoms. Both methods are present in the literature. In the works which use the SCF based semi-empirical methods[5,49] the first method is adopted. This choice predetermines further problems to be solved within the approaches of this kind. It is necessary to decide how to share one-electron density between two systems. Unfortunately, there is no sequential procedure to perform such a density sharing if the bonds are cut in half. Indeed, if a bond to be cut is even slightly polar then the average numbers of electrons in the R- and M-systems are not integer, which makes applying any standard semi-empirical QC procedure to the R-system questionable, since the existing QC methods are designed on the basis of the SCF approximation operating with the many-electron states which are eigenstates of the number of particles (electrons) operator. Even if the bond to be cut is not polar and the diagonal one-electron densities (the averages of the number of electrons operator) can be set equal to integers and thus the average numbers of electrons in the R- and M-systems are integer as well, it does not change the general situation. The problem is quite general, since according to ref. 17 the one-electron density is separable only for the wavefunctions of the type eqn. (4) *i.e.* for those where the intergroup electron transfers are projected out. It is definitely not a good approximation for two ends of a chemical bond which by definition can exist only in the case of a nontrivial quantum mechanical superposition of the states with different number of electrons on its ends. This is also known as fluctuation of number of electrons[50] which means that even if the average numbers of electrons in the R- and M-systems are integer which may serve as an *ad hoc* solution when a numeric procedure is developed, the numbers of particles in the R- and M-systems are not good quantum numbers. These notions stipulated our choice of the second method of setting the border between the R- and M-systems. If this method is adopted, then the derivations given in the present paper which generalize and refine approaches of ref. 16, 28 and 30 propose a noncontradictive way to approximate the electronic structure of the R- and M-systems by the eigenfunctions of the number of electrons operators and to handle the remaining fluctuations of the corresponding averages arose due to intersystem electron transfer terms in the exact Hamiltonian with use of the perturbative (Löwdin partition) approach.

Following this general direction already allowed us to develop an effective approach to the problems which are traditionally difficult for standard semi-empirical quantum chemistry and for the computational chemistry in general. These are first of all the quantum chemical approach to TMCs and to extending the MM approach to transition metals. The methods of evaluating the PESs of TMCs in the framework of MM-like approaches which exist in the literature either do not presume the possibility of the existence of different spin states of the complexes with open shell, or prescribe usage of different parameter sets for different spin states of the same ion. Our approach, by contrast, allows us to take into account different states of the d-shell and by this allows a single parameter set for the MM part of the system. This is certainly a step forward which became possible only on the basis of electron variables separation.

In the future we are going to extend the area for the present technique. Two directions are particularly important. First is the systematic study of the role played by the projected resonance term eqn. (35). Ironically, it does not appear in the most known theory[23,51] using the GF formalism in order to reach the electron variable separation for π- and σ-systems. Due to the obvious symmetry reasons the intersystem resonance term vanishes and the second component of the proposed approach *i.e.* the Löwdin partitioning is not needed. The resonance term is proven to be crucially important for the ECF theory[30] of TMCs. In the general low symmetry case of a hybrid QC/MM method the resonance contribution must be important. The second point is the renormalization of the electron–electron interaction in the R-system or equivalently the M–R dispersion interaction. Again in the framework of the σ–π electron variable separation it has been shown (see ref. 23 and references therein) that the modifications of the bare Coulomb interaction in the π-system due to polarization of the σ-system are significant. Experimentally the modification of the Coulomb interaction in the d-shell of TMC is well known under the name of nepheloxetic effect.[52] However, our attempt to ascribe this effect to the interaction with the ligand electronic polarization has not been successful so far.[53] Nevertheless it seems rather verisimilar that such an effect must take place in the QC/MM context.

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