Frozen-Density Embedding Theory based simulations with experimental electron densities

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The basic idea of Frozen-Density Embedding Theory (FDET) is the constrained minimisation of the Hohenberg-Kohn density functional $E^{HK}[ρ]$ performed using the auxiliary functional $E^{FDET}_{vAB}[Ψ_A, ρ_B]$, where $Ψ_A$ is the embedded $N_A$-electron wavefunction and $ρ_B(\mathbf{r})$ a non-negative function in real space integrating to a given number of electrons $N_B$. This choice of independent variables in the total energy functional $E^{FDET}_{vAB}[Ψ_A, ρ_B]$ makes it possible to treat the corresponding two components of the total density using different methods in multi-level simulations. We demonstrate, for the first time, the applications of FDET using $ρ_B(\mathbf{r})$ reconstructed from X-ray diffraction data on a molecular crystal. For eight hydrogen-bonded clusters involving a chromophore (represented with $Ψ_A$) and the glycylglycine molecule (represented as $ρ_B(\mathbf{r})$), FDET is used to derive excitation energies. It is shown that experimental densities are suitable to be used as $ρ_B(\mathbf{r})$ in FDET based simulations.

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I. INTRODUCTION

Frozen-Density Embedding Theory (FDET) is the Hohenberg-Kohn theorems based formal framework for multi-level simulations. The total electron density is built up from two components $\rho_A(\vec{r})$ and $\rho_B(\vec{r})$ of which only the first is constructed from quantum-mechanical descriptors. FDET was originally formulated for variational methods used to obtain such descriptors of the embedded species as: a) non-interacting reference system described with a Kohn-Sham determinant, b) interacting system described with a multi-determinant wave-function, and c) one-matrix. Extension of FDET for non-variational methods has been recently formulated. Extensions of FDET for excited states can be made based either on response theory for non-interacting or interacting systems. Another possibility to describe excited states relies on the Perdew-Levy theorem on extrema of the ground-state energy functional. It makes it possible to interpret other-than-the-lowest energy stationary embedded wave-functions obtained in FDET as excited states as pointed out by Khait and Hoffmann. In any of these variants of FDET, the embedded wave-function depends on the chosen $\rho_B(\vec{r})$. Several computational methods sharing with FDET some elements but differing in some key aspects such as: the choice of independent variables, self-consistency between embedding potential and the embedded wave-function, locality of the embedding potential, etc. have been developed in various groups. We address the reader to reviews concerning - besides the methods based on FDET - also related computational approaches.

At the present state of development of approximations for the FDET embedding functional, applications of FDET are limited to such systems where $\rho_A(\vec{r})$ and $\rho_B(\vec{r})$ do not overlap significantly. As a rule of thumb, FDET based methods are only applicable to such cases where the environment is not covalently bound to the embedded species. In such cases, the overlap between $\rho_A(\vec{r})$ and $\rho_B(\vec{r})$ is small and simple local- and semi-local approximations are sufficiently accurate. FDET based simulations can be seen as the variant of QM/MM simulations, in which the modeller decides about the procedure to generate $\rho_B(\vec{r})$ instead of parametrising the force-field parameters describing the energy contributions due to the interactions between the quantum system and its environment. Various system- and property specific protocols for generating $\rho_B(\vec{r})$ for FDET based simulations are possible. Some examples of different treatments of the environment density are given below. If the environment comprises several weakly bound molecules, the
corresponding $\rho_B(\mathbf{r})$ can be obtained either from quantum mechanical calculations for the whole cluster comprising all molecules in the environment or, in a simplified manner, as a superposition of molecular densities derived from some quantum-mechanical method\textsuperscript{19,20}. If $\rho_B(\mathbf{r})$ is localised in a pre-defined part of the space, the effect of electronic polarisation of the environment by the embedded species can be taken into account by optimising also $\rho_B(\mathbf{r})$\textsuperscript{21} or by "pre-polarising" it using simpler techniques\textsuperscript{22,23}. FDET can be also used for setting up a multi-physics simulation in which $\rho_B(\mathbf{r})$ represents a statistical ensemble averaged electron density ($<\rho_B>(\mathbf{r})$) represented as a continuum derived using classical statistical-mechanics based approaches\textsuperscript{24,25}. Such methods are especially useful for studying electronic structure of solvated molecules\textsuperscript{26}.

The above examples show clearly that the choice of the procedure to generate $\rho_B(\mathbf{r})$ is the key element of any FDET based simulation. This can be made in an "automatic" way by making some system-independent procedures/choices/approximations or made in a system dependent manner involving user provided information about $\rho_B(\mathbf{r})$ such as: a) using as $\rho_B(\mathbf{r})$ the ground-state density of some system obtained without putting any information about embedded species, b) localising $\rho_B(\mathbf{r})$ in a pre-defined region of space by choosing a limited set of atom-centred basis functions, c) allowing it to spread over the whole system, d) optimising $\rho_B(\mathbf{r})$ by means of the "freeze-and-thaw" minimisation of the total energy\textsuperscript{21} e) or any combination of the above. In principle, the density $\rho_B(\mathbf{r})$ obtained from the unique partitioning of the total density using the approach developed by Carter and collaborators\textsuperscript{27,28} could be used as a possible "automatic" procedure to generate $\rho_B(\mathbf{r})$ in FDET. The strategy, in which $\rho_B(\mathbf{r})$ is obtained form quantum mechanical calculations for the environment only, i.e., in the absence of the embedded species, is particularly attractive. Although the effect of the polarisation of the environment by the embedded species is not treated explicitly, the dominant effect of the environment on the embedded wave-function is well described. This is partially owing to the fact that $\rho_A(\mathbf{r})$ and $\rho_B(\mathbf{r})$ usually do overlap in real space and the effect of embedded species on the electron density distribution in the vicinity of atoms formally treated as environment is also taken into account to some extent in the implicit manner. The more flexible is the basis set used for $\Psi_A$ the better this implicit treatment works\textsuperscript{23,29}.

The present work concerns yet another possibility to generate $\rho_B(\mathbf{r})$ for FDET simulations of embedded species in a given environment consisting of non-covalently bound molecules, in
which $\rho_B(\vec{r})$ is obtained from experimental data concerning a different system: a molecular crystal of the environment molecule. Recent years brought a number of works showing that both, electron densities\cite{30} and wavefunctions\cite{31} can be reconstructed from X-ray diffraction data. It is tempting, therefore, to explore these new possibilities generate $\rho_B(\vec{r})$ for the use in FDET based simulations. We have to underline that several approximations may undermine the use of X-ray based densities for FDET. The most important issues can be listed as it follows: a) the link to any experimental quantity is of course affected by experimental errors, which are unavoidable and may affect both precision and accuracy; b) the electron density and wavefunction that are extracted from experiment are static, whereas atoms are not steady in the crystal; c) the sampling of the diffraction in the reciprocal space is necessarily incomplete; d) only the intensity of the diffracted ray is measured, but not the phase; e) the crystal sample is imperfect. For these reasons, the possibility to use experimental densities as $\rho_B(\vec{r})$ in FDET, hinges critically on robust and numerically stable protocols to generate such densities and it is hence important to investigate the dependence of FDET results on such procedures. The state of the art in the wavefunction and electron density reconstruction from X-ray diffraction data is encouraging this attempt. In particular the above mentioned pitfalls may be tackled as follows: a) modern instrumentation enables measuring the diffraction intensities with high precision; b) the deconvolution of thermal motion is reliable, if the measurements are carried out at sufficiently low temperature and if the resolution of the diffraction is sufficiently large; c) complementary input from theory can compensate for the missing information; d) appropriate modelling enables the phasing of the diffracted rays; e) data correction from ideal kinematic theory of diffraction allows for sufficiently accurate data. The present work reports an exploratory study on the use of densities from X-ray restricted wavefunctions in FDET.

Concerning a particular variant of FDET and system to be investigated, we have chosen to evaluate the excitation energies obtained from LinearizedFDET\cite{32,33} for several organic chromophores, each, hydrogen bonded to its environment. Our extensive benchmarking of the performance of FDET for such cases indicate that the errors of FDET excitation energies due to the used approximations for the explicit density functional for non-electrostatic components of the FDET embedding potential (see the next section) are small. In a benchmark set of embedded organic chromophores, the average deviation from the reference amounts to about 0.04 eV\cite{34}. This magnitude of the deviation define the threshold for complexation
induced shifts in the excitation energy above which analysis of the dependence on the shift on $\rho_B(\vec{r})$ is meaningful. In the embedded chromophores chosen for the present study these shifts vary between 0.15 to 0.6 eV.

II. EMBEDDED CHROMOPHORES

Concerning the molecules for which $\rho_B(\vec{r})$ is generated, we have chosen glycylglycine (GlyGly). For this exploratory study, it is crucial that the molecule(s) corresponding to $\rho_B(\vec{r})$ are capable to form hydrogen bonds with the chromophore. GlyGly satisfies this condition. Moreover, the molecular density of GlyGly reconstructed from X-ray diffraction data reflects the features arising from intermolecular hydrogen bonds present in the crystal. Figure 1 shows the GlyGly molecule together with its nearest neighbours in the crystal.

![Figure 1](image.png)

FIG. 1. The hydrogen-bonding pattern for the glycylglycine molecule in the crystal taken from Ref.36. Only nearest atoms involved in hydrogen bonding are shown: oxygen (red) and nitrogen (blue).

The densities reconstructed from experimental data on glycylglycine, are used in the
present work as $\rho_B(\vec{r})$ in FDET calculations of excitation energies for eight different hydrogen-bonded complexes formed by one organic chromophore (acrolein, acrylic acid, or acetone) and glycyglycine. Figure 2 shows the considered clusters.
FIG. 2. The complexes of three different chromophores with glycylglycine.

The hydrogen-bonding networks shown in Figures 1 and 2 are not the same. In the
crystal, all donors and acceptors are involved in hydrogen bonding which is not the case in
the investigated clusters. Nevertheless, each individual hydrogen bond in the clusters has
its corresponding partner in the crystal. It can be expected, therefore, that the effect of the
hydrogen bonding on \( \rho_B(\vec{r}) \) in the cluster is also reflected in the density obtained from the
crystal.

III. FDET APPROACH TO MULTI-LEVEL SIMULATIONS

For a system comprising \( N_{AB} \) electrons in an external potential \( v_{AB}(\vec{r}) \), the functional
\( E_{v_{AB}}^{FDET}[\Psi_A, \rho_B] \) is defined to satisfy by construction the following relation:

\[
\min_{\Psi_A} E_{v_{AB}}^{FDET}[\Psi_A, \rho_B] = E_{v_{AB}}^{FDET}[\Psi^o_A, \rho_B] = E_{v_{AB}}^{HK}[\rho^o_A + \rho_B],
\]

where \( E_{v_{AB}}^{HK}[\rho] \) is the Hohenberg-Kohn ground-state energy functional\(^{37}\) and \( \rho^o_A(\vec{r}) = \langle \Psi^o_A | \sum_i \delta(\vec{r} - \vec{r}_i) | \Psi^o_A \rangle \).

By virtue of the second Hohenberg-Kohn theorem, Eq. (1) leads to:

\[
E_{v_{AB}}^{FDET}[\Psi^o_A, \rho_B] \geq E_0
\]

where \( E_0 = E_{v_{AB}}^{HK}[\rho_0] \) and \( \rho_0(\vec{r}) \) is the ground-state energy and density of the total system.
Equality is reached for a large class of densities \( \rho_B(\vec{r}) \):

\[
E_{v_{AB}}^{FDET}[\Psi^o_A, \rho_B] = E_0 \quad \text{if } \forall \vec{r} (\rho_0(\vec{r}) > \rho_B(\vec{r})).
\]

Using conventional density functionals representing components of the total energy, and
arbitrary partitioning of the external potential \( v_{AB}(\vec{r}) = v_A(\vec{r}) + v_B(\vec{r}) \), leads to the form
of \( E_{v_{AB}}^{FDET}[\Psi_A, \rho_B] \) more suitable for further discussions:

\[
E_{v_{AB}}^{FDET}[\Psi_A, \rho_B] = \langle \Psi_A | \hat{H}_A | \Psi_A \rangle + V_B[\rho_A] + J_{AB}[\rho_A, \rho_B]
+ E_{xc}^{nad}[\rho_A, \rho_B] + \Delta F[\rho_A]
+ E_{eb}^{HK}[\rho_B] + V_A[\rho_B] + V_{NANB}
\]

where

\[
V_A[\rho_B] = \int v_A(\vec{r})\rho_B(\vec{r})d\vec{r}
\]

\[
V_B[\rho_A] = \int v_B(\vec{r})\rho_A(\vec{r})d\vec{r}
\]

\[
J_{AB}[\rho_A, \rho_B] = \int \int \frac{\rho_A(\vec{r})\rho_B(\vec{r}')}{|\vec{r} - \vec{r}'|} d\vec{r}' d\vec{r}
\]

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and $V_{N_A N_B}$ is the interaction energy between the nuclei defining $v_A(r)$ and $v_B(r)$. The non-additive bi-functional $E^{nad}_{xcT}[\rho_A, \rho_B]$ is related to the functionals $E_{xc}[\rho]$ and $T_s[\rho]$ defined in the constrained search formulation of the Kohn-Sham formalism\cite{38}. It is defined as:

$$E^{nad}_{xcT}[\rho_A, \rho_B] = E_{xc}[\rho_A + \rho_B] - E_{xc}[\rho_A] - E_{xc}[\rho_B] + T_s[\rho_A + \rho_B] - T_s[\rho_A] - T_s[\rho_B]$$  

(5)

The functional $\Delta F[\rho]$ on the other hand depends on the form of the wavefunction $\Psi$ used in Eq. 1 and also is defined via the constrained search\cite{3}. For instance, if $\Psi_A$ is a single determinant ($\Phi$), it reads:

$$\Delta F^{SD}[\rho] = \min_{\Phi \rightarrow \rho} \left< \Phi | \hat{T}_{N_A} + \hat{V}_{ee N_A} \Phi \right> - T[\rho] - V_{ee}[\rho]$$

(6)

$$= \left< \Phi^{o}[\rho] | \hat{T}_{N_A} + \hat{V}_{ee N_A} \Phi^{o}[\rho] \right> - T[\rho] - V_{ee}[\rho] = E_{c}[\rho]$$

and is just the correlation functional defined in constrained-search formulation of density functional theory\cite{38,39}. For $\Psi$ of the full CI form, $\Delta F^{FCI}[\rho] = 0$ by definition.

Euler-Lagrange optimisation of $\Psi_A$ leads to the Schrödinger-like equation:

$$\left( \hat{H}_A + \hat{v}_{emb} \right) \Psi_A = \lambda \Psi_A$$

(7)

where

$$v_{emb}[\rho_A, \rho_B, v_B](\vec{r}) = v_B(\vec{r}) + \int \frac{\rho_B(\vec{r}')}{|\vec{r} - \vec{r}'|} d\vec{r}'$$

$$+ v^{nad}_{xcT}[\rho_A, \rho_B](\vec{r}) + v_F[\rho_A](\vec{r})$$

(8)

with $v^{nad}_{xcT}[\rho_A, \rho_B](\vec{r})$, and $v_F[\rho_A](\vec{r})$ being the first functional derivatives of $E^{nad}_{xcT}[\rho, \rho_B]$ and $\Delta F[\rho]$, respectively.

The lowest energy solution of Eq. 7 will be denoted as $\Psi^{EL}_A$. Note that the energy is given not by the Lagrange multiplier $\lambda$ but in Eq. 4. For exact density functionals, any variational method can be used to obtain $\Psi^{EL}_A$ and the corresponding density $\rho^{EL}_A(\vec{r})$, which satisfy be construction the basic FDET equality given in Eq. 1.

### A. Reconstruction of $\rho_B(\vec{r})$ from X-ray diffraction data

X-ray restrained wavefunctions (XRW), in literature commonly (but incorrectly) termed X-ray constrained wavefunctions, were initially developed by Jayatilaka\cite{31,40,41}. Instead of
applying the variational principle, like in conventional SCF, a special functional $L$ is defined, based on a classical Hamiltonian and a function of the square difference between calculated and experimentally measured structure factors, which ideally distributes with a $\chi^2$ statistics. Thus, the minimization of $L$ implies finding the minimal energy AND the best agreement with experiment. Of course, this cannot be simultaneously achieved and a parameter $\lambda_j$ must be defined in order to weight the two parts of the functional. Therefore, the functional takes the form $L = E + \lambda_j\chi^2$. This procedure allows to construct molecular wavefunctions from experimental observations in crystals. By increasing $\lambda_j$, both long and short range interactions in the crystal are progressively taken into account. In this work, we used structure factors measured for GlyGly to calculate X-ray restrained wave-functions with $\lambda_J$ values from 0.0 to 1.0, as for higher values the SCF procedure does not converge. We stress that such value of $\lambda_J=1.0$ has no specific meaning because the electronic energy of the Hamiltonian and the electron density difference in the $\chi^2$ function have two different units, thus $\lambda_J$ is not dimensionless but it depends on the number of electrons, the molecular volume, and the diffraction resolution. Moreover, the structure factors in the $\chi^2$ function are weighted by the variance of their measurement statistics. The aforementioned wavefunctions were then used to calculate $\rho_B$.

B. Computational Details

The following approximations were used in the reported FDET calculations: $i$) ADC(2) treatment of correlation for embedded $N_A$ electrons as implemented in Ref.43, $ii$) decomposable approximations for $v^{\text{nad}}_t[\rho_A, \rho_B](\vec{r})$ (LDA) and $v^{\text{nad}}_{xc}[\rho_A, \rho_B](\vec{r})$ (note that in the LinearizedFDET used here approximations for the energy components $E^{\text{nad}}_{xcT}[\rho_A, \rho_B]$ and $\Delta F[\rho_A]$ are not used at all), $iii$) neglect the $v_F[\rho_A]$ contribution to the embedding potential, $iv$) monomer expansion of $\rho_A(\vec{r})$ (only atomic basis sets centred on the chromophore), $v$) monomer expansion of $\rho_B(\vec{r})$ (only atomic basis sets centred on GlyGly), $vi$) chromophore-independent generation of $\rho_B(\vec{r})$ using one of the following methods for the isolated GlyGly: Hartree-Fock, first-order Møller-Plesset perturbation theory, Kohn-Sham with PBE approximation for $E_{xc}[\rho]$, CCSD44, or the reconstruction from experimental structure factors (see the next section).

The FDET results for each cluster are compared to the reference obtained from ADC(2)
calculations. The reported reference shifts in the excitation energy are evaluated as $\Delta \epsilon_{\text{ref}} = \epsilon_{AB}^{\text{ADC(2)}} - \epsilon_{A(B)}^{\text{ADC(2)}}$, where $AB$ denotes the complex and $A(B)$ denotes the chromophore alone but with the basis set expanded by the functions localised on GlyGly (similarly as it is made in the counterpoise technique of Boys and Bernardi\textsuperscript{45} for intermolecular interaction energy). In all calculations including also the reconstruction of the electron density of GlyGly from the X-ray structure factors, the 6-311G basis set was used.

At $\lambda_J = 0$, the wave-function obtained from X-ray structure data is just the Hartree-Fock molecular wave-function. The numerical results should be identical regardless the used software to generate $\rho_B(\vec{r})$. We used this fact to check the numerical soundness of the procedures to export-import densities $\rho_B(\vec{r})$ obtained with different software. Tonto\textsuperscript{46} was used for X-ray restrained wavefunction calculations, Psi-4\textsuperscript{47} for to generate the CCSD GlyGly density, and Q-Chem\textsuperscript{48} for all other calculations, including FDE-ADC(2) ones.

Throughout the text, $\epsilon_{\text{emb}}[\rho_B^{\text{method}}]$ (and $\Delta \epsilon_{\text{emb}}[\rho_B^{\text{method}}]$) denote the FDET derived excitation energy (and environment induced shift), where the subscript in $\rho_B^{\text{method}}(\vec{r})$ specifies the method used to generate $\rho_B(\vec{r})$.

IV. RESULTS

For eight considered clusters, the lowest excitation energies obtained from FDET/ADC(2) calculations ($\epsilon_{\text{emb}}[\rho_B]$) using several choices for $\rho_B(\vec{r})$ are shown in Figure 3 together with the corresponding reference supermolecular ADC(2) results. These excitations have the n-$\pi^*$ character and are blue-shifted due to the interactions with the environment. The magnitude of the reference shift falls in the 0.15-0.6 eV range, which makes the shift in these complexes a suitable observable for discussing the effect of the $\rho_B$-dependency of the FDET results. For this type of excitations, the combined effect of the approximation used for the FDET embedding potential and the use of the isolated environment density as $\rho_B(\vec{r})$ results in the average error in the excitation energy of the magnitude of 0.04 eV\textsuperscript{23,34}. 
FIG. 3. Complexation induced shifts of the excitation energy ($\Delta \epsilon_{\text{emb}}[\rho_B]$) for eight chromophores hydrogen bonded to GlyGly. For each complex, FDET calculations (embedded ADC(2)) used the electron density of GlyGly obtained from three different methods: Hartree-Fock or CCSD for the isolated GlyGly or density reconstructed from X-ray structure factors for GlyGly molecular crystal at $\lambda_J = 1$. Reference values ($\Delta \epsilon_{\text{ref}}^{\text{ref}}$) are obtained from ADC(2) calculations for the whole complex.

We start with the analysis of the results obtained without taking any experimental information from the molecular crystal, i.e., $\Delta \epsilon_{\text{emb}}[\rho_B^{\lambda_J=0}]$. $\Delta \epsilon_{\text{emb}}[\rho_B^{\lambda_J=0}]$ correspond to a "standard" FDET protocol in which the Hartree-Fock density of the isolated environment is used as $\rho_B(\vec{r})$. The deviation from the reference are small and their magnitude is consistent with the benchmark results published elsewhere. The effect of correlation on $\rho_B(\vec{r})$ (see the
shifts obtained with $\rho_{CCSD}^{\vec{r}}$ results in a slight reduction of the shifts in all cases.

At $\lambda_J > 0$, both the correlation- and the crystal-field effects are taken into account in $\rho_B^{\vec{r}}$ leading to a further reduction of the shifts. The deviations of FDET shifts from the reference increase (see the values of $\Delta\epsilon_{emb}[\rho_{B}^{\lambda_J=1}]$ in Figure 3).

As previously mentioned, we could not extend the restraint to values of $\lambda_J$ larger than 1, because the procedure became numerically unstable. Unfortunately, although the effect of correlation and polarisation by the crystal field are reflected in $\rho_{B}^{\lambda_J}(\vec{r})$ they cannot be separated. Moreover, the environment of GlyGly in the molecular crystal and in the clusters analysed in the present work are different. As a result, even if the reconstruction of the density of GlyGly from X-ray structure factors were exact, this would not guarantee that such density would yield the best FDET results for the clusters under investigation. The values $\Delta\epsilon_{emb}[\rho_{B}^{\lambda_J}]$ at $\lambda_J = 0$ and $\lambda_J = 1$ represent, therefore, a good estimate of the maximum scatter (minimal and maximal bounds) of the FDET results due to the $\rho_{B}$-dependency of the FDET embedding potential. Within these bounds, the deviations from the reference do not exceed 0.1 eV (or 30% in terms of the relative error). This also points out the need for a thorough analysis of the disentangled effects of correlation and polarisation in $\Delta\epsilon[\rho_{B}^{\lambda_J}]$.

The subsequent part concerns the numerical stability of the FDET derived complexation induced shifts of the lowest excitation energy with respect to variations of $\rho_{B}(\vec{r})$ correspondent to the change of the parameter $\lambda_J$ from 0 to 1.

Figure 4 shows the dependence of the calculated shifts $\Delta\epsilon_{emb}[\rho_{B}^{\lambda_J}]$ on the parameter $\lambda_J$ for each complex. The dependence of $\Delta\epsilon_{emb}[\rho_{B}^{\lambda_J}]$ on $\lambda_J$ is smooth and monotonic. Above $\lambda_J = 0.5$ till its maximal value used in this study $\lambda_J = 1$, $\Delta\epsilon_{emb}[\rho_{B}^{\lambda_J}]$ remains almost constant (it changes by as little as about 0.01 eV).
FIG. 4. Complexation induced shifts of the excitation energy ($\Delta \epsilon_{\text{emb}}[\rho_B^{\lambda_J}]$) at various values of $\lambda_J$ for 8 clusters.

Turning back to practical applications, we notice that large scale simulations usually apply the monomer expansion for both $\rho_A(\vec{r})$ and $\rho_B(\vec{r})$ and using isolated environment density as $\rho_B(\vec{r})$ already assures good accuracy of the FDET derived environment induced shifts. In such simulations, the modeller has a wide range of available methods to generate $\rho_B(\vec{r})$ (see the Introduction). The data collected in Figure 5 shows how the FDET results depend on the method used to generate $\rho_B(\vec{r})$ including: Hartree-Fock, MP1, CCSD, and KS-DFT(PBE). For reference purposes, the values of $\Delta \epsilon_{\text{emb}}$ obtained from X-ray diffraction data at $\lambda_J = 0.25$ are also given.
FIG. 5. FDET (embedded ADC(2)) derived complexation induced shifts of the excitation energy ($\Delta \epsilon_{emb}$) obtained for eight intermolecular complexes with different choices for $\rho_B(\vec{r})$. Reference values ($\Delta \epsilon_{ref}$) are obtained from ADC(2) calculations for the whole complex.

The results collected in Figure 5 indicate clearly that X-ray derived molecular density is suitable for generating $\rho_B(\vec{r})$ for FDET calculations following the conventional protocol (LinearizedFDET, monomer expansion of $\rho_A(\vec{r})$, monomer expansion for $\rho_B(\vec{r})$, lack of explicit treatment of $\rho_B(\vec{r})$ polarisation by the chromophore). The deviations from the reference are, however, larger than if Hartree-Fock or correlated isolated GlyGly densities are used for this purpose. This does not bear direct relevance to the quality of these densities. The overall error of the FDET derived excitation energy results from the balance of the errors in two
FDET embedding potentials evaluated at two different pairs of densities $v_{\text{emb}}[\rho_A^{ES}, \rho_B, v_B](\vec{r})$ and $v_{\text{emb}}[\rho_A^{GS}, \rho_B, v_B](\vec{r})$, where $\rho_A^{GS}$ and $\rho_A^{ES}$ denote ground and excited state, respectively, in which the non-electrostatic contributions are approximate.

It is worthwhile to note that the use of X-ray derived densities as $\rho_B(\vec{r})$ leads to smaller errors than if the Kohn-Sham PBE calculations are used for this purpose.

V. CONCLUSIONS

The recent developments in techniques to reconstruct the electron density from X-ray diffraction data made it possible not only to determine the maxima of the electron density (coinciding with the position of nuclei) but also reveals its more detailed features. For a molecular crystal, the reconstruction yields a localised density of a single molecule but taking into account its chemical environment. In FDET based simulations, the molecular densities are used as an input quantity providing the complete quantum-mechanical descriptor of the environment of the embedded species. In the present work, we explored the possibility to use molecular density of the glycyglycine derived from X-ray diffraction data collected for the molecular crystal in FDET calculations of complexation induced shift of the excitation energy in eight intermolecular complexes, each consisting of an organic chromophore hydrogen-bonded to one glycyglycine molecule. The usability of such densities for this purpose was not evident before the present study was made. Several factors could, in principle, invalidate such practical applications of X-ray reconstructed densities. First of all, glycyglycine in the crystal and in the complexes analysed in the present work have different environments. This might result in different polarisation of such localised molecular, and as a consequence, contribute to errors in the FDET results. Other group of factors relate rather to the reconstruction procedure. It cannot be made perfect due to a) errors in the experimental measurements, b) the very basic assumption according to which the average of a dynamic quantity (electron density) is represented using as an intermediate object, namely a static single-determinant wave-function, c) incompleteness of the experimental data, d) errors in the phasing procedures, e) crystal defects.

On the other hand, our past numerical experience indicates that the dependency of vertical excitation energies derived from FDET on $\rho_B(\vec{r})$ is rather weak. Factors such as choice of the quantum mechanical methods to generate $\rho_B(\vec{r})$, used basis sets, taking into account
the effect on embedded species on $\rho_B(\mathbf{r})$, etc. affect of course the FDET derived excitation energies but this effect is usually of the secondary importance. This weak dependency can be expected and is justified by the fact that it is the total density and not the way as it is partitioned that determines the properties of a given molecular system. In FDET, $\rho_A(\mathbf{r})$ is obtained variationally for any given $\rho_B(\mathbf{r})$, which results in its capacity to approach better the exact total density (see the relevant discussions in Refs.\textsuperscript{12,20}). It could be expected, therefore, that reconstructed densities deviate indeed not significantly from the constraint-free one and, in turn, yield similar excitation energies if used as $\rho_B(\mathbf{r})$. The primary objective of this work was the verification of this expectation. The obtained results demonstrate, indeed, that X-ray reconstructed densities are suitable to be used as $\rho_B(\mathbf{r})$ in FDET in pair with possible alternative techniques. Despite the fact that the X-ray restrained wavefunction procedure does not yield a unique solution but rather a range of density parametrised by $\lambda_J$, the scatter of the excitation energies obtained using the whole range of this parameter is rather narrow. The excitation energies vary within less than 0.1 eV depending on the details of the reconstruction procedure. Taking into account that a typical range of the effect of hydrogen bonding environment on the excitation energy in organic chromophores is in the range of 1 eV, this relatively small scatter makes the FDET simulations using X-ray derived molecular densities an attractive tool for making quantitative predictions and to interpret experimental results. Further reduction of this scatter is probably possible through disentangling the effects of crystal-field polarisation and correlation effect on the density of a molecule in a molecular crystal. We intend to deal with this issue in our subsequent work.

Turning back to possible applications, for such clusters as the ones investigated in the present work, it is easier to generate $\rho_B(\mathbf{r})$ using one of the available standard techniques (applied also in the present work). The use of experimentally derived densities of glycylglycine as $\rho_B(\mathbf{r})$ in FDET simulations does not improve the results obtained using either Hartree-Fock or CCSD densities of isolated glycylglycine. We rather aim at modelling larger molecular environments for which conventional calculations are impossible, too costly, or simply yield densities which are not physical.

We underline also the proposed strategy to generate $\rho_B(\mathbf{r})$ does not take into account the effect of the embedded species on $\rho_B(\mathbf{r})$ unless the embedded species in FDET calculations is the molecule present in the crystal. Numerical experience gathered in the studies of electronic excitations in chromophores in molecular clusters by means of FDET applying
localised basis sets show uniformly that the effect of “polarisation” of $\rho_B(\vec{r})$ by the embedded species on the electronic excitation is of secondary importance. The magnitude of the effect due to explicit treatment of electronic polarisation of $\rho_B(\vec{r})$ is smaller compared to the overall effect of the environment on the electronic polarisation and does not necessarily improve the numerical results. If needed, it can be easily estimated by performing “pre-polarisation” of $\rho_B(\vec{r})$. Here also the experimental derived $\rho_B(\vec{r})$ might prove more useful then alternative techniques. This is the case when the molecules associated with $\rho_B(\vec{r})$ have similar neighbours in the cluster to be investigated and in the molecular crystal used to generate $\rho_B(\vec{r})$.

A. Synopsis

We demonstrate -for the first-time- the use of experiment-derived molecular electron densities as $\rho_B(\vec{r})$ in Frozen Density Embedding Theory based calculations of environment-induced shifts of electronic excitations for chromophores in clusters. $\rho_B(\vec{r})$ was derived from X-ray restrained molecular wavefunctions of glycyglycine in molecular crystals to obtain environment densities for modelling the clusters.

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