

QM/QM and QM/MM Hybrid Methods

Subsystem and Embedding Methods for Quantum Chemistry

Johannes Neugebauer



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Lecture 2

Contents — QM/QM Methods

- introduction
- energy-based embedding schemes
- many-body expansions (MBEs)
- subsystem DFT and density-based embedding
- “exact embedding” through potential reconstruction
- “exact embedding” through projection
- WF/DFT embedding
- density matrix embedding theory (DMET)

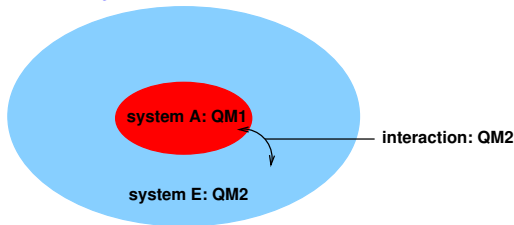
QM/QM Hybrid Methods

Partitioning is possible at different levels:

- energy partitioning
- wavefunction partitioning
- density-matrix partitioning
- Green's function partitioning
- density partitioning
- ...

Energy-Based Partitioning and Many-Body Expansions

Simple QM/QM Hybrid Methods



- ONIOM (Morokuma): a generalization of subtractive QM/MM

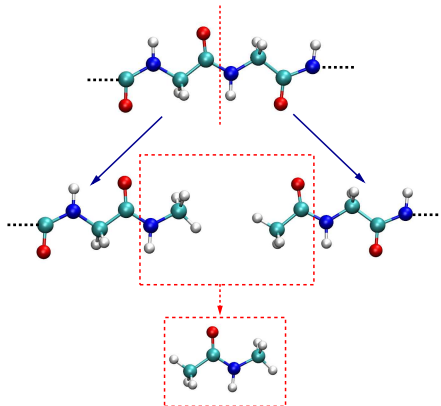
$$E_{\text{tot}}^{\text{QM/QM}} = E_{(A+E)}^{\text{QM2}} + (E_A^{\text{QM1}} - E_A^{\text{QM2}})$$

- interaction defined as

$$E_{A \leftrightarrow E}^{\text{QM2}} = E_{(A+E)}^{\text{QM2}} - E_A^{\text{QM2}} - E_E^{\text{QM2}}$$

- generalizations for many layers (QM1/QM2/MM/continuum) available
- generalization for electrostatic embedding available
- properties require corresponding definitions
(i.e., there is no "ONIOM wavefunction")

Fragmentation Methods



Molecular Fractionation with Conjugated Caps (MFCC)

- developed for proteins; partition into oligopeptides
- use model for neighboring fragments as caps
- sum up energies for capped fragments, subtract “concaps”
- no electrostatic embedding; better with larger caps

Increment Methods

General idea:

- largest part of E_{tot} is due to energies of (isolated) subsystems
- interaction energy: mainly due to pair interactions
- general energy expression:

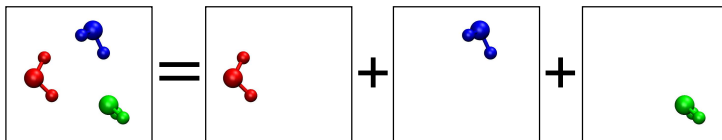
$$E_{\text{tot}} = \sum_I E_I + \sum_{I < J} E_{I \leftrightarrow J} + \sum_{I < J < K} E_{I \leftrightarrow J \leftrightarrow K} + \dots$$

$$E_{I \leftrightarrow J} = E_{IJ} - E_I - E_J$$

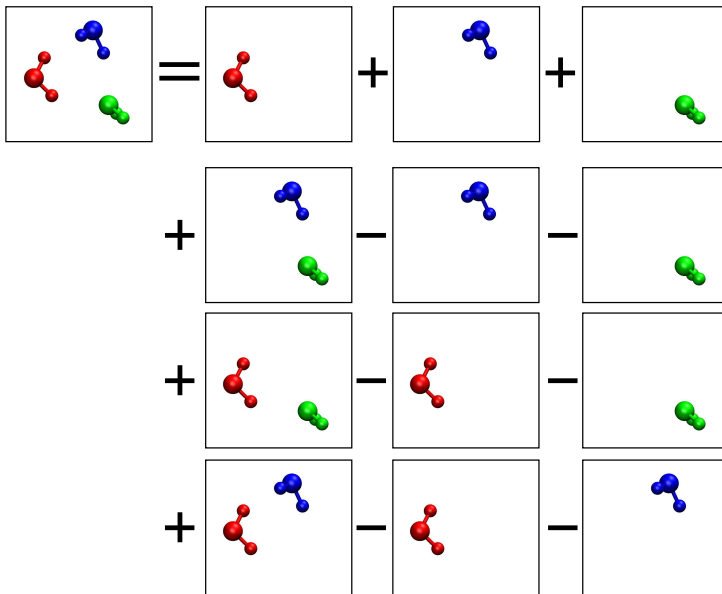
$$E_{I \leftrightarrow J \leftrightarrow K} = E_{IJK} - E_I - E_J - E_K \\ - (E_{IJ} - E_I - E_J) - (E_{IK} - E_I - E_K) - (E_{JK} - E_J - E_K)$$

- n th-order increment method: exact for n subsystems

Increment Methods

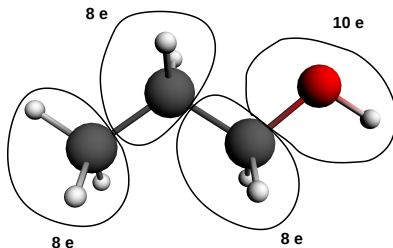


Increment Methods



Fragment Molecular Orbital Method (1)

An embedded increment method

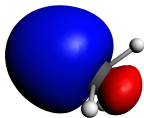


FMO-1

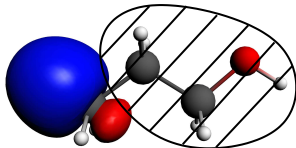
- fragmentation without separation of bond electron pairs
- fragment calculations under full electrostatic embedding
- no capping applied

Fragment Molecular Orbital Method (1)

An embedded increment method



generate localized MOs
for capped fragment



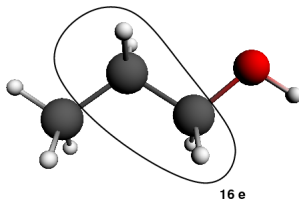
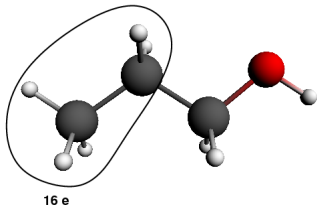
use these LMOs as basis
for "true" fragments

FMO-1

- fragment orbitals are expressed through localized orbitals obtained from reference compound (capped fragment)
- minimal basis is applied $\Rightarrow$ bond electron pairs have no freedom to change compared to reference compound

Fragment Molecular Orbital Method (2)

An embedded increment method



etc.

FMO-2

- 2nd order increment method
 - monomers and dimers are obtained with full electrostatic embedding potential, based on localized orbitals
- ⇒ FMO-2 implicitly contains higher-order terms

A Density-Based Many-Body Expansion

- in a DFT context, use MBE for the electron density,

$$\begin{aligned}\rho_{\text{tot}}^{(n)}(\mathbf{r}) &= \rho_{\text{tot}}^{(1)}(\mathbf{r}) + \Delta\rho_{\text{tot}}^{(2)}(\mathbf{r}) + \Delta\rho_{\text{tot}}^{(3)}(\mathbf{r}) + \dots + \Delta\rho_{\text{tot}}^{(n)}(\mathbf{r}) \\ &= \sum_I \rho_I^{(1)}(\mathbf{r}) + \sum_{I < J} \rho_{I \leftrightarrow J}^{(2)}(\mathbf{r}) + \sum_{I < J < K} \rho_{I \leftrightarrow J \leftrightarrow K}^{(3)}(\mathbf{r}) + \dots\end{aligned}$$

$$\Delta\rho_{I \leftrightarrow J}^{(2)}(\mathbf{r}) = \rho_{IJ}(\mathbf{r}) - \rho_I^{(1)}(\mathbf{r}) - \rho_J^{(1)}(\mathbf{r})$$

$$\begin{aligned}\Delta\rho_{I \leftrightarrow J \leftrightarrow K}^{(3)} &= \rho_{IJK}(\mathbf{r}) - \rho_I^{(1)} - \rho_J^{(1)} - \rho_K^{(1)} - [\rho_{IJ}(\mathbf{r}) - \rho_I^{(1)}(\mathbf{r}) - \rho_J^{(1)}(\mathbf{r})] \\ &\quad - [\rho_{IK}(\mathbf{r}) - \rho_I^{(1)}(\mathbf{r}) - \rho_K^{(1)}(\mathbf{r})] - [\rho_{JK}(\mathbf{r}) - \rho_J^{(1)}(\mathbf{r}) - \rho_K^{(1)}(\mathbf{r})]\end{aligned}$$

and approximate $E_{\text{tot}}[\rho] \approx E_{\text{db-MBE}}^{(n)} = E_{\text{tot}}[\rho_{\text{tot}}^{(n)}]$

- often converges faster than energy-based MBE
- in n -th order db-MBE, we only have access to n -body orbitals
 $\Rightarrow$ How to compute $T_s[\rho_{\text{tot}}^{(n)}]$?

Density Partitioning

Some Flavors of DFT

- orbital-free DFT: formulated directly in terms of $\rho(\mathbf{r})$

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$$\rho(\mathbf{r}) = \sum_i |\phi_i(\mathbf{r})|^2$$

(called v_s -representability in the following)

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- orbital-free DFT: formulated directly in terms of $\rho(\mathbf{r})$
- Kohn–Sham DFT: non-interacting v -representability assumed,

$$\rho(\mathbf{r}) = \sum_i |\phi_i(\mathbf{r})|^2$$

(called v_s -representability in the following)

- subsystem DFT:

$$\rho(\mathbf{r}) = \sum_I \rho_I(\mathbf{r})$$

v_s -representability assumed for every ρ_I :

$$\rho_I(\mathbf{r}) = \sum_i |\phi_{i_I}(\mathbf{r})|^2$$

(but not necessarily for the total density $\Rightarrow$ different search space than in KS-DFT)

Some Flavors of DFT

Frozen-Density Embedding:

$$\rho(\mathbf{r}) = \rho_1(\mathbf{r}) + \rho_2^{\text{fixed}}(\mathbf{r}); \quad \rho_1(\mathbf{r}) = \sum_i |\phi_{i_1}(\mathbf{r})|^2$$

- “sDFT without optimization of $\rho_2(\mathbf{r})$ ” (no “freeze-and-thaw”)

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- “sDFT without optimization of $\rho_2(\mathbf{r})$ ” (no “freeze-and-thaw”)
- no orbital representation needed for ρ_2 , can be taken from:
 - simple superpositions of atomic/fragment densities
J. Neugebauer, M.J. Louwerse, E.J. Baerends, T.A. Wesolowski, *J. Chem. Phys.* **122** (2005) 094115.
 - statistically averaged densities
J.W. Kaminski, S. Gusarov, T.A. Wesolowski, A. Kovalenko, *J. Phys. Chem. A* **114** (2010), 6082.
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N. Ricardi, M. Ernst, P. Macchi, T.A. Wesolowski, *Acta Cryst. A* **76** (2020), 571.

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N. Ricardi, M. Ernst, P. Macchi, T.A. Wesolowski, Acta Cryst. A 76 (2020), 571.
- useful for properties of embedded molecules
- but: not well suited/not intended for total-energy calculations
- can only lead to exact solution if $\rho(\mathbf{r}) \geq \rho_2^{\text{fixed}}(\mathbf{r}) \quad \forall \mathbf{r}$

Subsystem DFT

- KS energy expression with partitioning $\rho(\mathbf{r}) = \sum_I \rho_I(\mathbf{r})$

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

- if ρ is given as sum of subsystem densities:

$$V_{\text{ext}}[\rho] = V_{\text{ext}}[\rho_1 + \rho_2 + \dots]$$

$$J[\rho] = J[\rho_1 + \rho_2 + \dots]$$

$$\tilde{E}_{\text{xc}}[\rho] = \tilde{E}_{\text{xc}}[\rho_1 + \rho_2 + \dots]$$

(where $\tilde{E}_{\text{xc}}[\rho]$ is an approximation to the unknown exact functional $E_{\text{xc}}[\rho]$)

- problematic in sDFT context: $T_s[\rho] = T_s[\{\phi_i^{\text{opt}}\}]$

G. Senatore, K. R. Subbaswamy, *Phys. Rev. B* **34** (1986), 5754;

P. Cortona, *Phys. Rev. B* **44** (1991), 8454;

T.A. Wesolowski, J. Weber, *Chem. Phys. Lett.* **248** (1996), 71;

recent review: C.R. Jacob, J. Neugebauer, *WIREs Comput. Mol. Sci.* **14** (2024), e1700.

Subsystem DFT

- write T_s formally exactly as

$$T_s[\rho] = \sum_I T_s[\rho_I] + \left[T_s[\rho] - \sum_I T_s[\rho_I] \right]$$

or

$$T_s[\rho] = \sum_I T_s[\rho_I] + T_s^{\text{nad}}[\rho, \{\rho_I\}]$$

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- exact T_s^{nad} :

$$\begin{aligned} T_s^{\text{nad}}[\rho, \{\rho_I\}] = & \min_{\{\phi_i\} \rightarrow \rho} \sum_{i=1}^n \langle \phi_i | -\nabla_i^2/2 | \phi_i \rangle \\ & - \sum_I \left(\min_{\{\phi_{i_I}\} \rightarrow \rho_I} \sum_{i=1}^n \langle \phi_{i_I} | -\nabla_i^2/2 | \phi_{i_I} \rangle \right) \end{aligned}$$

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- introduce density-dependent approximation,

$$T_s^{\text{nad}}[\rho, \{\rho_J\}] \approx \tilde{T}_s^{\text{nad}}[\rho, \{\rho_J\}] = \tilde{T}_s[\rho] - \sum_I \tilde{T}_s[\rho_I]$$

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$$T_s^{\text{nad}}[\{\rho_J\}] \approx \tilde{T}_s^{\text{nad}}[\{\rho_J\}] = \tilde{T}_s[\rho_1 + \rho_2 + \dots] - \sum_I \tilde{T}_s[\rho_I]$$

One-Particle Equations in Subsystem DFT

- energy functional:

$$E[\{\rho_J\}] = V_{\text{ext}}[\rho] + J[\rho] + E_{\text{xc}}[\rho] + \sum_I T_s[\rho_I] + T_s^{\text{nad}}[\{\rho_J\}],$$

- choose no. of electrons per subsystem (n_J)
- construct Lagrangian

$$L[\{\rho_J\}] = E[\{\rho_J\}] - \sum_I \mu_I \left(\int d^3r \rho_I(\mathbf{r}) - n_I \right)$$

and minimize w.r.t. ρ_K

⇒ Euler–Lagrange equations:

$$0 = v_{\text{ext}}(\mathbf{r}) + v_{\text{Coul}}[\rho](\mathbf{r}) + v_{\text{xc}}[\rho](\mathbf{r}) + \frac{\delta T_s[\rho_K]}{\delta \rho_K(\mathbf{r})} + \frac{\delta T_s^{\text{nad}}[\{\rho_J\}]}{\delta \rho_K(\mathbf{r})} - \mu_K$$

One-Particle Equations in Subsystem DFT

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⇒ Euler–Lagrange equations:

$$0 = v_{\text{eff}}[\rho](\mathbf{r}) + \frac{\delta T_s[\rho_K]}{\delta \rho_K(\mathbf{r})} + \frac{\delta T_s^{\text{nad}}[\{\rho_J\}]}{\delta \rho_K(\mathbf{r})} - \mu_K$$

Frozen-Density Embedding

- assume all subsystem densities are v_s -representable
- ⇒ subsystem orbitals can be obtained from

$$\left(-\frac{1}{2}\nabla^2 + v_{\text{eff}}^{\text{sub}}[\rho, \rho_K](\mathbf{r}) \right) \phi_{i_K} = \epsilon_{i_K} \phi_{i_K},$$

- ⇒ if we choose

$$v_{\text{eff}}^{\text{sub}}[\rho, \rho_K](\mathbf{r}) = v_{\text{eff}}[\rho](\mathbf{r}) + \frac{\delta T_s^{\text{nad}}[\{\rho_J\}]}{\delta \rho_K(\mathbf{r})}$$

the systems of non-interacting particles fulfill

$$v_{\text{eff}}^{\text{sub}}[\rho, \rho_K](\mathbf{r}) + \frac{\delta T_s[\rho_K]}{\delta \rho_K(\mathbf{r})} - \mu_K = 0$$

- ⇒ these are the sought-for densities

Embedding Potential

- define “environmental” density for system I [complementary to $\rho_I(\mathbf{r})$]:

$$\rho_I^{\text{env}}(\mathbf{r}) = \sum_{J, J \neq I} \rho_J(\mathbf{r})$$

- one-particle equations for FDE calculation become

$$\left(-\frac{1}{2} \nabla^2 + v_{\text{eff}}[\rho_I](\mathbf{r}) + v_{\text{emb}}[\rho_I, \rho_I^{\text{env}}](\mathbf{r}) \right) \phi_{i_I} = \epsilon_{i_I} \phi_{i_I}$$

(Kohn–Sham equations with constrained electron density, KSCED)

- embedding potential

$$\begin{aligned} v_{\text{emb}}[\rho_I, \rho_I^{\text{env}}](\mathbf{r}) &= \sum_{J, J \neq I} v_{\text{ext}}^J(\mathbf{r}) + \sum_{J, J \neq I} v_{\text{Coul}}[\rho_J](\mathbf{r}) \\ &\quad + \{v_{\text{xc}}[\rho](\mathbf{r}) - v_{\text{xc}}[\rho_I](\mathbf{r})\} + \frac{\delta T_s^{\text{nad}}[\{\rho_J\}]}{\delta \rho_K(\mathbf{r})} \end{aligned}$$

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Solution of the KSCED equations

Approximations that have to be selected:

- non-additive kinetic energy functional $\tilde{T}_s^{\text{nad}}$
(and corresponding potential)

- XC functional:

- either regard $E_{\text{xc}}[\rho]$ as *one* energy contribution,

$$E_{\text{xc}}[\rho] \approx \tilde{E}_{\text{xc}}[\rho_1 + \rho_2 + \dots]$$

- or approximate components of $E_{\text{xc}}[\rho]$,

$$E_{\text{xc}}[\rho] = \sum_I E_{\text{xc}}[\rho_I] + E_{\text{xc}}^{\text{nad}}[\{\rho_I\}] \approx \sum_I \tilde{E}_{\text{xc}}^{(I)}[\rho_I] + \tilde{E}_{\text{xc}}^{\text{nad}}[\{\rho_I\}]$$

(facilitates use of different XC approximations for different subsystems and/or the non-additive part)

Important special case:

- use exact exchange within subsystems, but not for inter-subsystem part
⇒ avoid costly evaluation of inter-system exchange integrals

Non-additive kinetic-energy functionals

Common decomposable approximations:

- general structure: $T_s^{\text{nad}}[\{\rho_I\}, \rho] = T_s[\rho] - \sum_I T_s[\rho_I]$
- Thomas–Fermi approximation

$$T_s[\rho] \approx T_{\text{TF}}[\rho] = C_F \int \rho^{5/3}(\mathbf{r}) d\mathbf{r}$$

L.A. Thomas, *Proc. Camb. Phil. Soc.* **23** (1927) 542; E. Fermi, *Z. Physik* **48** (1928) 73.

exact for homogeneous electron gas (“LDA” for kinetic energy)

- von Weizsäcker approximation

$$T_s[\rho] \approx T_{\text{vw}}[\rho] = \frac{1}{8} \int \frac{|\nabla \rho(\mathbf{r})|^2}{\rho(\mathbf{r})} d\mathbf{r}$$

C.F. von Weizsäcker, *Z. Physik* **96** (1935) 431.

exact for one-orbital systems

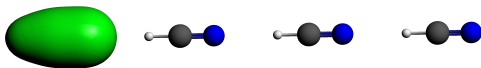
- conjoint construction:
choose enhancement factor in GGA-type T_s as in GGA-X functionals

H. Lee, C. Lee, R.G. Parr, *Phys. Rev. A* **44** (1991), 768.

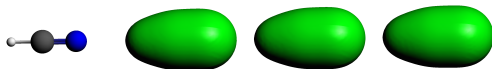
Subsystem DFT at Work

Step 1

active system



environment

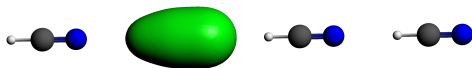


- calculate ρ_{active} with frozen environment
- iterate over all subsystems ("freeze-and-thaw")

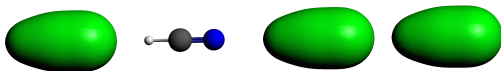
Subsystem DFT at Work

Step 2

active system



environment

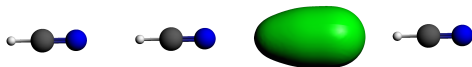


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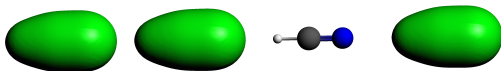
Subsystem DFT at Work

Step 3

active system



environment

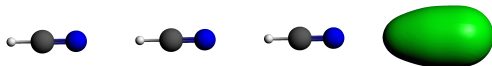


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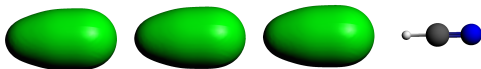
Subsystem DFT at Work

Step 4

active system



environment

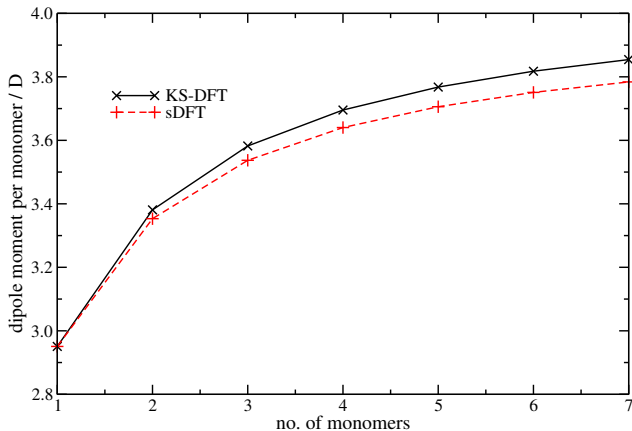


- calculate ρ_{active} with frozen environment
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Dipole Moment of (HCN)_N

Average dipole moment as a function of chain length

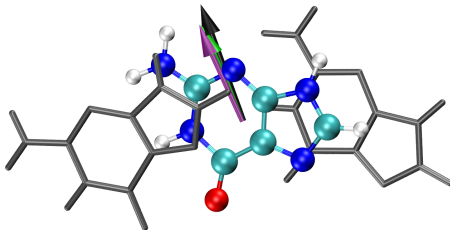
BP86/TZP



Are Subsystem Properties Meaningful?

Dipole moment of the central guanine in a trimer

Structure: R. Sedlak *et al.*, *J. Chem. Theory Comput.* **9** (2013), 3364.



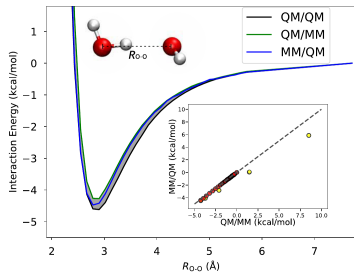
(PW91/PW91k/TZP; black: isolated; purple: sDFT; green: Bader analysis of KS-DFT)

	$ \mu_{\text{central}} $ / Debye	angle to $\vec{\mu}_{\text{iso}}$ / °
iso	7.48	
sDFT	5.99	4.2
Bader	5.95	5.1

T. Dresselhaus, JN, *Theor. Chem. Acc.* **134** (2015), 97.

Density-Functionalizing QM/MM with sDFT

Pavanello and co-workers: Compare QM/MM to MM/QM



X. Chen, J.A. Martinez B, X. Shao, M. Riera Rimbau, O. Andreussi, F. Paesani, M. Pavanello, *J. Chem. Theory Comput.* 2025, **21**, 10340, DOI: 10.1021/acs.jctc.5c01440; published under CC-BY 4.0, see <https://creativecommons.org/licenses/by/4.0/>

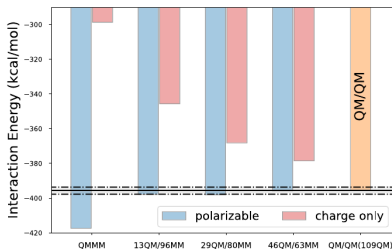
- MM energies often inconsistent with QM counterparts (even electrostatics)
- idea: *density-functionalize* MM energy contributions,

$$E^{\text{QM/MM}} = E[\rho_{\text{QM}}, \rho_{\text{MM}}] = E[\rho_{\text{QM}}] + E[\rho_{\text{MM}}] + E^{\text{int}}[\rho_{\text{QM}}, \rho_{\text{MM}}]$$

- ρ_{MM} : Gaussian function for valence electrons, pseudopotential for core
- energy is evaluated as in sDFT

Density-Functionalizing QM/MM with sDFT

Convergence for $[\text{Pd}(\text{H}_2\text{O})_4]\text{Cl}_2$ in water

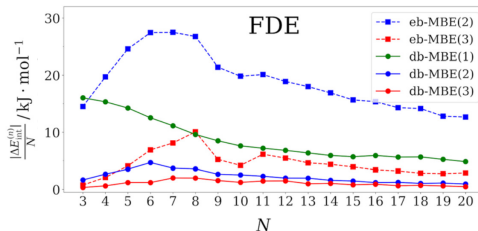


X. Chen, J.A. Martinez B, X. Shao, M. Riera Rimbau, O. Andreussi, F. Paesani, M. Pavanello, *J. Chem. Theory Comput.* 2025, **21**, 10340, DOI: 10.1021/acs.jctc.5c01440; published under CC-BY 4.0, see <https://creativecommons.org/licenses/by/4.0/>

- much faster convergence for polarizable, *density-functionalized* QM/MM (compared to conventional charge-only QM/MM)
- *density-functionalized* QM/MM contains repulsive short-range term (T_s^{nad})
⇒ avoids electron spill-out (electron leaking)
- related earlier work: “Polarizable Density Embedding”
(combines elements from FDE, polarizable force fields, and Huzinaga-type embedding)
J.M.H. Olsen, C. Steinmann, K. Ruud, J. Kongsted, *J. Phys. Chem. A* 2015, **119**, 5344.

sDFT for Density-Based Many-Body Expansions

Interaction-energy errors for $\text{Ca}^{2+}(\text{H}_2\text{O})_N$ clusters:



S. Schürmann, J.R. Vornweg, M. Wolter, C.R. Jacob, *Phys. Chem. Chem. Phys.* 2023, **25**, 736, DOI: 10.1039/d2cp04539g; published under CC-BY 4.0, see <https://creativecommons.org/licenses/by/4.0/>

- energy in db-MBE:

$$E_{\text{db-MBE}}^{(n)} = E_{\text{tot}}[\rho_{\text{tot}}^{(n)}] = E_{\text{eb-MBE}}^{(n)} + (E_{\text{tot}}[\rho_{\text{tot}}^{(n)}] - E_{\text{eb-MBE}}^{(n)}) = E_{\text{eb-MBE}}^{(n)} + E_{\text{db-cor}}^{(n)}$$

- $E_{\text{db-cor}}^{(n)}$ contains electrostatic terms as well as

$$T_s^{\text{nad}}[\{\rho_I\}, \{\rho_{IJ}\}, \dots] \quad \text{and} \quad E_{\text{xc}}^{\text{nad}}[\{\rho_I\}, \{\rho_{IJ}\}, \dots]$$

⇒ evaluated as in sDFT

From DFT/DFT to
WF/DFT embedding

DFT-in-DFT Hybrid Methods

Subsystem DFT

- fragmentation scheme,
KS-DFT for subsystems, OF-DFT for interaction

$$E^{\text{sDFT}}[\rho_{\text{tot}}] = E^{\text{KS}}[\rho_1] + E^{\text{KS}}[\rho_2] + E^{\text{OF}}_{(1 \leftrightarrow 2)}[\rho_1, \rho_2]$$

FDE (without orbital representation of ρ_{env})

- QM/QM embedding scheme, KS-DFT/OF-DFT

$$E^{\text{FDE}}[\rho_{\text{tot}}] = E^{\text{KS}}[\rho_1] + E^{\text{OF}}[\rho_2] + E^{\text{OF}}_{(1 \leftrightarrow 2)}[\rho_1, \rho_2]$$

Wavefunction-in-DFT Hybrid Methods

Can this idea be transferred to WF-in-DFT embedding?

- within DFT, $v_{\text{emb}}(\mathbf{r})$ is formally exact
(contains all non-electrostatic contributions)
 - simple idea:
include $\langle \chi_{\mu} | v_{\text{emb}}(\mathbf{r}) | \chi_{\nu} \rangle$ into one-electron part of WF calculation
- ⇒ gives access to “embedded WF” and properties

Wavefunction-in-DFT Hybrid Methods

- WF/DFT energy functional:

$$E^{\text{WF/DFT}}[\Psi_A, \rho_B] = \langle \Psi_A | \hat{H}_A | \Psi_A \rangle + E_B^{\text{KS}}[\rho_B] + E_{(A \leftrightarrow B)}^{\text{OFDFT}}[\rho_A, \rho_B]$$

(ρ_A : density obtained from Ψ_A)

- minimization w.r.t. Ψ_A yields (ρ_B fixed):

$$\hat{H}'_A \Psi_A = \left(\hat{H}_A + \sum_{i=1}^{n_A} v_{\text{emb}}^A[\rho_A, \rho_B](\mathbf{r}_i) \right) \Psi_A = \tilde{E}_A \Psi_A$$

where

$$v_{\text{emb}}^A[\rho_A, \rho_B](\mathbf{r}) = v_{\text{ext}}^B(\mathbf{r}) + v_{\text{Coul}}[\rho_B](\mathbf{r}) + v_{\text{xc}}[\rho](\mathbf{r}) - v_{\text{xc}}[\rho_A](\mathbf{r}) + v_t^{\text{nad}}[\rho_A, \rho_B](\mathbf{r})$$

⇒ same form as in sDFT! (but often evaluated with approximate ρ_A, ρ_B)

Wavefunction-in-DFT Embedding

$$\begin{aligned} v_1^{\text{emb}}[\rho_1, \rho_2](\mathbf{r}) = & \sum_{A_2} -\frac{Z_{A_2}}{|\mathbf{r} - \mathbf{R}_{A_2}|} + \int \frac{\rho_2(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}' \\ & + \left. \frac{\delta E_{\text{xc}}[\rho]}{\delta \rho(\mathbf{r})} \right|_{\rho=\rho_1+\rho_2} - \left. \frac{\delta E_{\text{xc}}[\rho]}{\delta \rho(\mathbf{r})} \right|_{\rho=\rho_1} + \left. \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \right|_{\rho=\rho_1+\rho_2} - \left. \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \right|_{\rho=\rho_1} \end{aligned}$$

Wavefunction-in-DFT Embedding

$$\begin{aligned}
 v_1^{\text{emb}}[\rho_1, \rho_2](\mathbf{r}) = & \underbrace{\sum_{A_2} -\frac{Z_{A_2}}{|\mathbf{r} - \mathbf{R}_{A_2}|}}_{\text{constant}} + \underbrace{\int \frac{\rho_2(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}'}_{\text{changes in every macroiteration}} \\
 & + \underbrace{\frac{\delta E_{\text{xc}}[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1+\rho_2} - \frac{\delta E_{\text{xc}}[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1}}_{\text{changes in every microiteration}} + \underbrace{\frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1+\rho_2} - \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1}}_{\text{changes in every microiteration}}
 \end{aligned}$$

Wavefunction-in-DFT Embedding

$$v_1^{\text{emb}}[\rho_1, \rho_2](\mathbf{r}) = \underbrace{\sum_{A_2} -\frac{Z_{A_2}}{|\mathbf{r} - \mathbf{R}_{A_2}|}}_{\text{constant}} + \underbrace{\int \frac{\rho_2(\mathbf{r}')}{|\mathbf{r}' - \mathbf{r}|} d\mathbf{r}'}_{\text{changes in every macroiteration}} + \underbrace{\frac{\delta E_{\text{xc}}[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1+\rho_2} - \frac{\delta E_{\text{xc}}[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1}}_{\text{changes in every microiteration}} + \underbrace{\frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1+\rho_2} - \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \bigg|_{\rho=\rho_1}}_{\text{changes in every microiteration}}$$

Note: Self-consistent embedding for excited states leads to non-orthogonal active-system states!

Wavefunction-in-DFT Embedding

Rigorous DFT derivation of “WF-in-DFT” embedding:

- DFT description where ρ_2 is described through a KS system ...
 - ... and ρ_1 is described through a many-body wavefunction
 - if $\Psi_1 = \Psi_1^{\text{exact}}$, then $E_1^{\text{WF}}[\Psi_1] = E_1^{\text{KS}}[\rho_1]$ (for exact functionals)
- ⇒ formally, a correction is needed for $E_1^{\text{WF}}[\Psi_1]$ if $\Psi_1 \neq \Psi_1^{\text{exact}}$

T.A. Wesolowski, *Phys. Rev. A* **77** (2008), 012504.

CASSCF-in-DFT Embedding

How to choose ρ_1^{CAS} for energy-difference calculations?

$$E_{(1+2)}^{\text{CAS/DFT}} = E_1^{\text{CAS}}[\Psi_1] + E_2^{\text{DFT}}[\rho_2] + E_{(1\leftrightarrow 2)}^{\text{int}}[\rho_1^{\text{CAS}}, \rho_2]$$

- require consideration especially in state-average CASSCF
- affects the corresponding embedding potential
- has consequences on mutual orthogonality of states

Frequent simplifications in early work:

- ρ_1 -dependent terms obtained from DFT, fixed in WF part
- ground-state embedding potential also used for excited states

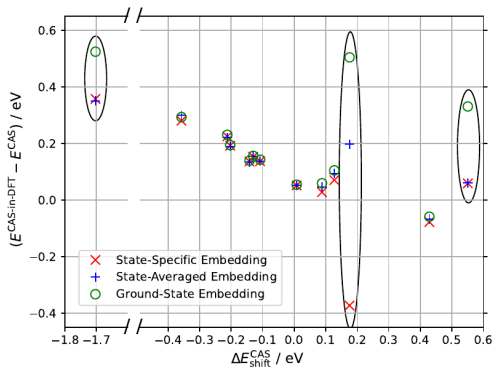
More work on CASSCF/DFT:

T. Klüner, N. Govind, Y.A. Wang, E.A. Carter, *Phys. Rev. Lett.* **86** (2001), 5954;
T. Klüner, N. Govind, Y.A. Wang, E. Carter, *J. Chem. Phys.* **116** (2002), 42;
S. Sharifzadeh, P. Huang, E.A. Carter, *J. Phys.: Condens. Matter* **21** (2009), 355501;
D.K. Kanan, S. Sharifzadeh, E.A. Carter, *Chem. Phys. Lett.* **519–520** (2012), 18;
C. Daday, C. König, O. Valsson, J.N. C. Filippi, *J. Chem. Theory Comput.* **9** (2013), 2355;
C. Daday, C. König, J.N. C. Filippi, *ChemPhysChem* **15** (2014), 3205;
N. Schieschke, T. Bodenstern, S. Höfener, *J. Chem. Phys.* **154** (2021), 084120;
L. Schreder, S. Lubner, *J. Chem. Phys.* **161** (2024), 144110.

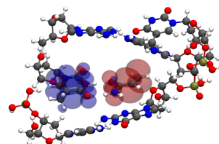
CASSCF-in-DFT Embedding

Influence of the choice of embedding:

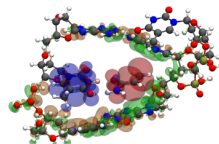
- SA-CASSCF/PW91/PW91k, cc-pVDZ



Difference Densities



State-Averaged Embedding

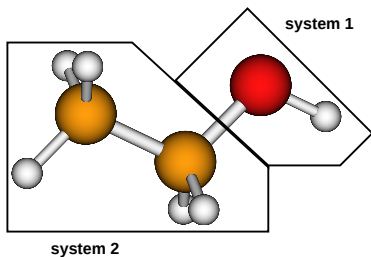


State-Specific Embedding

“Exact” Density-Based Embedding

Covalent Bonds through Exact Embedding Potentials

Approximations for v_t^{nad} break down for covalent bonds



- What do we know about the exact $v_t^{\text{nad}}(\mathbf{r})$?
- Can we reconstruct the *exact* embedding potential for subsystems 1, 2 that reproduces $\rho_{\text{super}}(\mathbf{r}) = \rho_1(\mathbf{r}) + \rho_2(\mathbf{r})$?

("exact" here excludes errors introduced by finite basis sets, errors introduced in the calculation of ρ_{super} (usually through E_{xc}), and numerical errors in the construction of the potential, e.g., due to finite grid size)

Functional Derivative of T_s^{nad}

- problems arise due to

(here: system K = active system)

$$\frac{\delta T_s^{\text{nad}}[\{\rho_I\}]}{\delta \rho_K(\mathbf{r})} = \frac{\delta T_s[\rho]}{\delta \rho_K(\mathbf{r})} - \sum_I \frac{\delta T_s[\rho_I]}{\delta \rho_K(\mathbf{r})}$$

with $\rho(\mathbf{r}) = \sum_I \rho_I(\mathbf{r})$

- first term:

$$\begin{aligned} \frac{\delta T_s[\rho]}{\delta \rho_K(\mathbf{r})} &= \int \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r}')} \cdot \frac{\delta \rho(\mathbf{r}')}{\delta \rho_K(\mathbf{r})} d\mathbf{r}' \\ &= \int \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r}')} \cdot \delta(\mathbf{r}' - \mathbf{r}) d\mathbf{r}' = \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \end{aligned}$$

- second term:

$$\sum_I \frac{\delta T_s[\rho_I]}{\delta \rho_K(\mathbf{r})} = \sum_I \frac{\delta T_s[\rho_K]}{\delta \rho_K(\mathbf{r})} \cdot \delta_{KI} = \frac{\delta T_s[\rho_K]}{\delta \rho_K(\mathbf{r})}$$

Functional Derivative of T_s^{nad}

⇒ we need to calculate

$$v_t^{\text{nad}}[\rho_K, \rho_{\text{super}}](\mathbf{r}) = \frac{\delta T_s^{\text{nad}}[\{\rho_I\}]}{\delta \rho_K(\mathbf{r})} = \frac{\delta T_s[\rho_{\text{super}}]}{\delta \rho_{\text{super}}(\mathbf{r})} - \frac{\delta T_s[\rho_K]}{\delta \rho_K(\mathbf{r})}$$

• or, in other words, we need to find

$$v_t[\rho](\mathbf{r}) = \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})}$$

for two different densities ($\rho = \rho_{\text{super}}$ and $\rho = \rho_K$)

Euler–Lagrange Equation: Kohn–Sham Formalism

- Euler–Lagrange Equation:

$$\mu = \left. \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \right|_{\rho=\rho_{\text{target}}} + v_s[\rho_{\text{target}}](\mathbf{r})$$

⇒ “Kinetic-energy potential:”

$$v_t[\rho_{\text{target}}](\mathbf{r}) = \left. \frac{\delta T_s[\rho]}{\delta \rho(\mathbf{r})} \right|_{\rho=\rho_{\text{target}}} = \mu - v_s[\rho_{\text{target}}](\mathbf{r})$$

- μ is just a constant shift in the potential (will be ignored here)

⇒ If we know the potential $v_s[\rho_{\text{target}}](\mathbf{r})$ that results in a set of orbitals $\{\phi_i^{\text{target}}\}$ such that

$$\sum_i |\phi_i^{\text{target}}(\mathbf{r})|^2 = \rho_{\text{target}}(\mathbf{r}),$$

then we also have access to $v_t[\rho_{\text{target}}](\mathbf{r})$

Why Use “Exact” Embedding at All?

⇒ we can obtain the exact v_t^{nad} as

$$v_t^{\text{nad}}[\rho_A, \rho_{\text{super}}](\mathbf{r}) = v_s[\rho_A](\mathbf{r}) - v_s[\rho_{\text{super}}](\mathbf{r}) + \Delta\mu$$

(two subsystems assumed for simplicity; v_t^{nad} is given for subsystem A)

Exact embedding is expensive:

- either, we first have to solve a KS-DFT calculation for the total system
- or, we have to do (several) reconstructions of total-system potentials

Why Use “Exact” Embedding at All?

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- either, we first have to solve a KS-DFT calculation for the total system
- or, we have to do (several) reconstructions of total-system potentials

Possible benefits:

- “exact” potential may serve as basis for approximations
- “exact” potential may be transferred to more expensive WF/DFT
- ground-state calculation is not the bottleneck (e.g., response)

S. Fux, C.R. Jacob, J. Neugebauer, L. Visscher, M. Reiher, *J. Chem. Phys.* **132** (2010), 164101;

J.D. Goodpaster, N. Ananth, F.R. Manby, T.F. Miller III, *J. Chem. Phys.* **133** (2010), 084103;

D. Schnieders, J. Neugebauer, *J. Chem. Phys.* **149** (2018), 054103.

Potential Reconstruction

Densities in search of Hamiltonians:

- we need to find $v_s[\rho](\mathbf{r})$ that yields a specific $\rho = \rho^{\text{target}}$
- ⇒ “inverse Kohn–Sham problem”
- ⇒ has been solved several times in the context of v_{xc} development:
 - Wang and Parr *Phys. Rev. A* **47** (1993), R1591.
 - van Leeuwen and Baerends *Phys. Rev. A* **49** (1994), 2421.
 - Zhao, Morrison and Parr *Phys. Rev. A* **50** (1994), 2138.
 - Wu and Yang *J. Chem. Phys.* **118** (2003), 2498.
 - ...

van Leeuwen–Baerends Reconstruction

- KS-equation

$$\epsilon_i \phi_i(\mathbf{r}) = \left[-\frac{\nabla^2}{2} + v_s(\mathbf{r}) \right] \phi_i(\mathbf{r})$$

$$\sum_i \epsilon_i \phi_i^*(\mathbf{r}) \phi_i(\mathbf{r}) = \sum_i \phi_i^*(\mathbf{r}) \left[-\frac{\nabla^2}{2} \right] \phi_i(\mathbf{r}) + v_s(\mathbf{r}) \sum_i \phi_i^*(\mathbf{r}) \phi_i(\mathbf{r})$$

$$v_s(\mathbf{r}) \rho(\mathbf{r}) = \sum_i \phi_i^*(\mathbf{r}) \left[\frac{\nabla^2}{2} \right] \phi_i(\mathbf{r}) + \sum_i \epsilon_i \phi_i^*(\mathbf{r}) \phi_i(\mathbf{r})$$

$$v_s(\mathbf{r}) = \frac{1}{\rho(\mathbf{r})} \sum_i \left\{ \phi_i^*(\mathbf{r}) \left[\frac{\nabla^2}{2} \right] \phi_i(\mathbf{r}) + \epsilon_i \phi_i^*(\mathbf{r}) \phi_i(\mathbf{r}) \right\}$$

van Leeuwen–Baerends Reconstruction

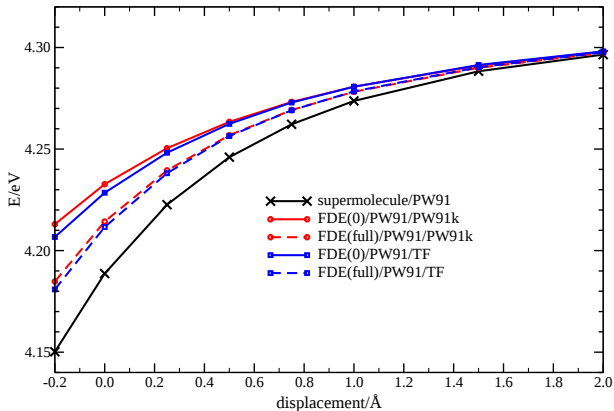
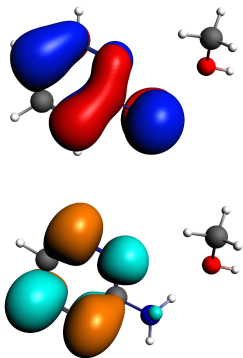
- iterative scheme, iteration $(k + 1)$,

$$\begin{aligned} v_s^{(k+1)}(\mathbf{r}) &= \frac{1}{\rho^{\text{target}}(\mathbf{r})} \sum_i \left\{ \phi_i^{(k)*}(\mathbf{r}) \left[\frac{\nabla^2}{2} \right] \phi_i^{(k)}(\mathbf{r}) + \epsilon_i^{(k)} \phi_i^{(k)*}(\mathbf{r}) \phi_i^{(k)}(\mathbf{r}) \right\} \\ &= \frac{\rho^k(\mathbf{r})}{\rho^{\text{target}}(\mathbf{r})} \cdot v_s^{(k)} \end{aligned}$$

R. van Leeuwen, E.J. Baerends, *Phys. Rev. A* **49** (1994), 2421.

Excitation Energies with Reconstructed Potentials

Aminopyridine ··· methanol

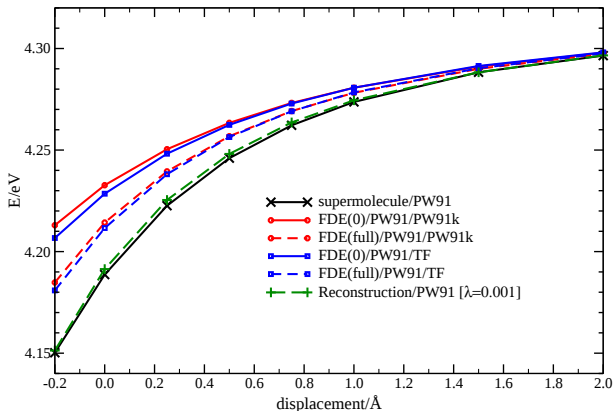
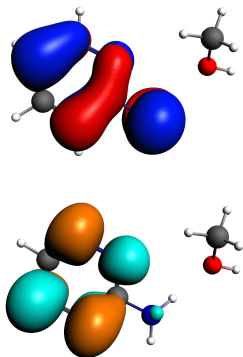


D. Artiukhin, C.R. Jacob, JN, *J. Chem. Phys.* **142** (2015), 234101.

● $\pi \rightarrow \pi^*$ excitation of aminopyridine ··· MeOH (PW91/TZP)

Excitation Energies with Reconstructed Potentials

Aminopyridine ··· methanol



D. Artiukhin, C.R. Jacob, JN, *J. Chem. Phys.* **142** (2015), 234101.

- $\pi \rightarrow \pi^*$ excitation of aminopyridine ··· MeOH (PW91/TZP)
- reconstruction using Wu–Yang algorithm, ALDA kernel

“Exact” Projection-Based Embedding

T_s^{nad} for Orthogonal Subsystem Orbitals

- assume two-partitioning ($A + B$); determine supersystem KS orbitals
- define

$$\rho_A(\mathbf{r}) = \sum_{j=1}^{n_A} |\phi_j^{\text{super}}(\mathbf{r})|^2 \quad \text{and} \quad \rho_B(\mathbf{r}) = \sum_{k=n_A+1}^{n_A+n_B} |\phi_k^{\text{super}}(\mathbf{r})|^2 = \rho_{\text{env}}(\mathbf{r})$$

- kinetic energy:

$$\begin{aligned} T_s[\{\phi_i^{\text{super}}\}] &= \sum_{i=1}^n \langle \phi_i^{\text{super}} | -\nabla^2/2 | \phi_i^{\text{super}} \rangle \\ &= \sum_{j=1}^{n_A} \langle \phi_j^{\text{super}} | -\nabla^2/2 | \phi_j^{\text{super}} \rangle + \sum_{k=n_A+1}^{n_A+n_B} \langle \phi_k^{\text{super}} | -\nabla^2/2 | \phi_k^{\text{super}} \rangle \\ &= T_s^A + T_s^B \end{aligned}$$

⇒ apparently, no non-additive kinetic-energy approximation needed!

T_s^{nad} for Orthogonal Subsystem Orbitals

- but: even in case of orthogonal ϕ_i^{super} and exact ρ_A, ρ_B , in general

$$\begin{aligned} & \sum_{j=1}^{n_A} \langle \phi_j^{\text{super}} | -\nabla^2/2 | \phi_j^{\text{super}} \rangle + \sum_{k=n_A+1}^{n_A+n_B} \langle \phi_k^{\text{super}} | -\nabla^2/2 | \phi_k^{\text{super}} \rangle \\ & \geq \min_{\{\phi_{i_A}\} \rightarrow \rho_A} \sum_i^{n_A} \langle \phi_{i_A} | -\nabla^2/2 | \phi_{i_A} \rangle + \min_{\{\phi_{i_B}\} \rightarrow \rho_B} \sum_i^{n_B} \langle \phi_{i_B} | -\nabla^2/2 | \phi_{i_B} \rangle \end{aligned}$$

T_s^{nad} for Orthogonal Subsystem Orbitals

- but: even in case of orthogonal ϕ_i^{super} and exact ρ_A, ρ_B , in general

$$\begin{aligned} & \sum_{j=1}^{n_A} \langle \phi_j^{\text{super}} | -\nabla^2/2 | \phi_j^{\text{super}} \rangle + \sum_{k=n_A+1}^{n_A+n_B} \langle \phi_k^{\text{super}} | -\nabla^2/2 | \phi_k^{\text{super}} \rangle \\ & \geq \min_{\{\phi_{i_A}\} \rightarrow \rho_A} \sum_i^{n_A} \langle \phi_{i_A} | -\nabla^2/2 | \phi_{i_A} \rangle + \min_{\{\phi_{i_B}\} \rightarrow \rho_B} \sum_i^{n_B} \langle \phi_{i_B} | -\nabla^2/2 | \phi_{i_B} \rangle \end{aligned}$$

- reason: not both subsets of $\{\phi_i^{\text{super}}\}$ are, in general, ground-state of some effective potential
- still: subsets of $\{\phi_i^{\text{super}}\}$ can be obtained from projected KS problem without v_t^{nad}

Externally Orthogonal Subsystem Orbitals

In sDFT, orbitals of different subsystems are not necessarily orthogonal:

$$\langle \phi_i | \phi_j \rangle = \delta_{ij}, \quad \text{but} \quad \langle \phi_i | \phi_{j'} \rangle \quad \text{can be} \quad \neq 0$$

How can we determine orthogonal embedded subsystem orbitals?

Three (related) strategies:

- projection-based embedding

F.R. Manby, M. Stella, J.D. Goodpaster, T.F. Miller III, *J. Chem. Theory Comput.* 2012, **8**, 2564.

- external orthogonality through extra Lagrangian multipliers

Y.G. Khait, M.R. Hoffmann, *Ann. Rep. Comput. Chem.* 2012, **8**, 53-70;

P.K. Tamukong, Y.G. Khait, M.R. Hoffmann, *J. Phys. Chem. A* 2014, **118**, 9182.

- Huzinaga equation (transferred to KS-DFT)

S. Huzinaga and A.A. Cantu, *J. Chem. Phys.* 1971, **55**, 5543;

B. Hégely, P.R. Nagy, G.G. Ferency, M. Kállay, *J. Chem. Phys.* 2016, **145**, 064107.

Exact Embedding through Projection

Basic Idea:

- 1st step: KS-DFT calculation on $(A + B)$
- 2nd step: localization of KS orbitals $\Rightarrow \{\phi_i^A\}, \{\phi_i^B\}$
- then: construct Fock operator for electrons in subsystem A ,

$$\hat{f}^A = -\frac{\nabla^2}{2} + v_{\text{nuc}}^A(\vec{r}) + v_{\text{nuc}}^B(\vec{r}) + v_{\text{Coul}}[\rho_A + \rho_B](\vec{r}) + v_{\text{xc}}[\rho_A + \rho_B](\vec{r}) + \mu \hat{P}^B$$

with projection operator $\hat{P}^B$,

$$\hat{P}^B = \sum_{i \in B} |\phi_i^B\rangle \langle \phi_i^B|$$

- for $\lim_{\mu \rightarrow \infty}$: eigenfunctions of $\hat{f}^A$ are orthogonal to $\{\phi_i^B\}$

Externally Orthogonal Subsystem Orbitals

Enforce external orthogonality through extra constraints

- consider sDFT energy as functional of two orbital sets,

$$E^{\text{sDFT}} = E^{\text{sDFT}}[\{\phi_i^A\}, \{\phi_i^B\}]$$

- introduce orthonormality constraints through Lagrangian multipliers,

$$E^{\text{sDFT}} \rightarrow L^{\text{sDFT}} = E^{\text{sDFT}} - \sum_{I=A,B} \sum_{\substack{i \in I \\ j \in I}} \lambda_{ij}^I (\langle \phi_i^I | \phi_j^I \rangle - \delta_{ij}) - \sum_{\substack{i \in A \\ j \in B}} \lambda_{ij}^{AB} \langle \phi_i^A | \phi_j^B \rangle - \sum_{\substack{i \in B \\ j \in A}} \lambda_{ij}^{BA} \langle \phi_i^B | \phi_j^A \rangle$$

- optimization w.r.t. ϕ_i^A yields (for ϕ_i^B fixed),

$$\left(-\frac{\nabla^2}{2} + v_{\text{eff}}^{\text{KS}}[\rho](\mathbf{r}) \right) \phi_i^A(\mathbf{r}) = \epsilon_i^A \phi_i^A(\mathbf{r}) + \sum_{j \in B} \lambda_{ij}^{AB} \phi_j^B(\mathbf{r})$$

- multiply with $\langle \phi_k^B |$; make use of external orthogonality already,

$$\langle \phi_k^B | \hat{f}^{\text{KS}} | \phi_i^A \rangle = \lambda_{ik}^{AB}$$

Externally Orthogonal Subsystem Orbitals

- from this it follows that,

$$\hat{f}^{\text{KS}}|\phi_i^A\rangle = \epsilon_i^A|\phi_i^A\rangle + \sum_{j \in B} |\phi_j^B\rangle \langle \phi_j^B | \hat{f}^{\text{KS}} | \phi_i^A \rangle$$

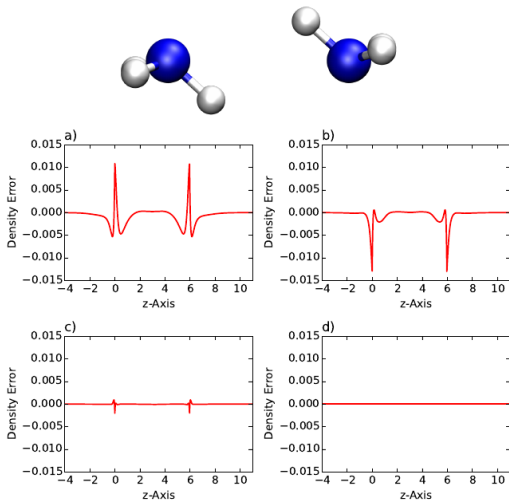
$$\Rightarrow \underbrace{\left(1 - \sum_{j \in B} |\phi_j^B\rangle \langle \phi_j^B|\right)}_{\hat{f}'} \hat{f}^{\text{KS}} |\phi_i^A\rangle = (1 - \hat{P}^B) \hat{f}^{\text{KS}} |\phi_i^A\rangle = \epsilon_i^A |\phi_i^A\rangle$$

- note: $\hat{f}'$ is not Hermitian
- under external orthogonality: $(1 - \hat{P}^B)|\phi_i^A\rangle = |\phi_i^A\rangle$

$$\Rightarrow \underbrace{(1 - \hat{P}^B) \hat{f}^{\text{KS}} (1 - \hat{P}^B)}_{\hat{f}''} |\phi_i^A\rangle = \epsilon_i^A |\phi_i^A\rangle$$

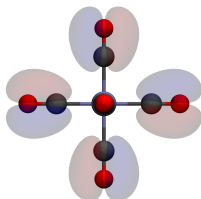
note: $\hat{f}''$ is Hermitian!

Comparing Density-Based Embedding Schemes



PBE/def2-QZVP; a) sum-of-isolated densities; b) PBE-type τ_s^{nad} ; c) potential reconstruction d) projection

How To Select the Active System?

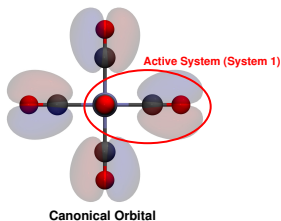


Canonical Orbital

Standard Approach: Manual Selection

- 1 run standard KS-DFT calculation on supersystem

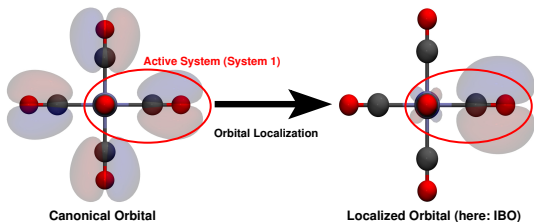
How To Select the Active System?



Standard Approach: Manual Selection

- 1 run standard KS-DFT calculation on supersystem
- 2 select set of active atoms

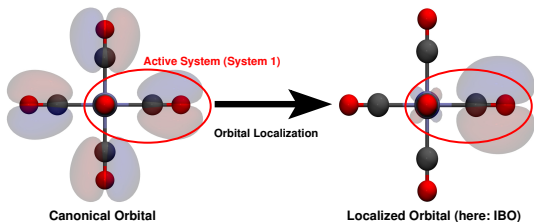
How To Select the Active System?



Standard Approach: Manual Selection

- 1 run standard KS-DFT calculation on supersystem
- 2 select set of active atoms
- 3 localize orbitals (our choice: intrinsic bond orbitals, IBO)

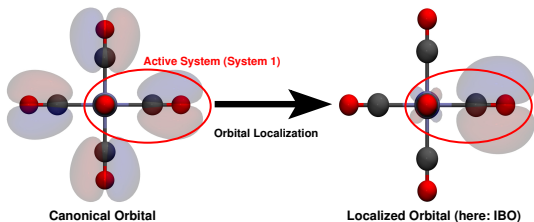
How To Select the Active System?



Standard Approach: Manual Selection

- 1 run standard KS-DFT calculation on supersystem
- 2 select set of active atoms
- 3 localize orbitals (our choice: intrinsic bond orbitals, IBO)
- 4 determine active orbitals (based on Mulliken net population on active atoms)

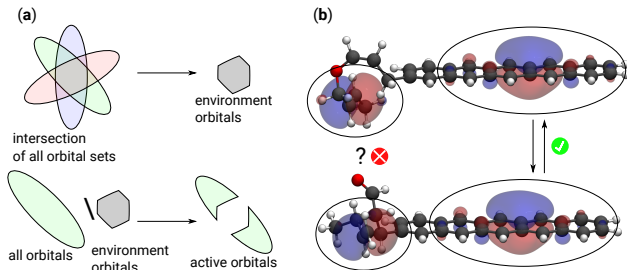
How To Select the Active System?



Standard Approach: Manual Selection

- 1 run standard KS-DFT calculation on supersystem
- 2 select set of active atoms
- 3 localize orbitals (our choice: intrinsic bond orbitals, IBO)
- 4 determine active orbitals (based on Mulliken net population on active atoms)
- 5 construct projection operator and run embedded calculation

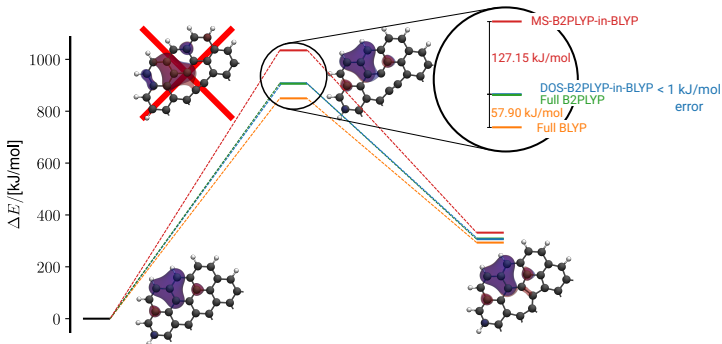
How To Select the Active System?



Direct Orbital Selection for reaction paths:

- compare orbital sets for reactants, transition state, products
(obtained from low-level method)
- select “unchanged” orbitals as non-active = environment
(based on IAO charges and orbital-wise kinetic energies)
- in turn, all non-environment orbitals are active

Stone–Wales Defect Formation



DOS for a ligand dissociation reaction:

- approximate full B2PLYP results by B2PLYP-in-BLYP embedding
- 58 out of 134 orbitals active with DOS, 53 active based on manual selection

Another Exact DFT Embedding Scheme

Density-Matrix partitioning

- consider KS energy expression in terms of density matrix $\mathbf{D}$

$$E[\mathbf{D}] = \text{Tr} \mathbf{h} \mathbf{D} + \frac{1}{2} \text{Tr} \mathbf{D} \mathbf{J}(\mathbf{D}) + E_x[\mathbf{D}] + E_c[\mathbf{D}]$$

with one-particle density matrix

$$\mathbf{D} = \sum_i^{\text{occ}} c_{\mu i} c_{\nu i}$$

- now partition density matrix

$$\mathbf{D} = \mathbf{D}^A + \mathbf{D}^B$$

such that $\mathbf{D}^A$ and $\mathbf{D}^B$ are obtained from orthogonal MO spaces

⇒ exact partitioning, as in projection-based embedding

Multi-Level DFT

Generate a suitable guess density matrix:

- e.g., start from superposition of fragment density matrices, $\mathbf{D}^{\text{SOF}}$
- build initial Fock matrix based on $\mathbf{D}^{\text{SOF}}$ and diagonalize
⇒ yields approximation for total density matrix, $\mathbf{D}^{\text{approx}}$
- partition $\mathbf{D}^{\text{approx}}$ into

$$\mathbf{D}^{\text{approx}} = \mathbf{D}^A + \mathbf{D}_{\text{fixed}}^B$$

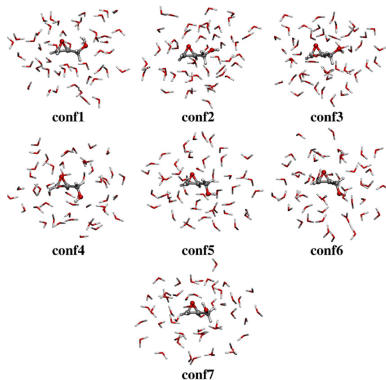
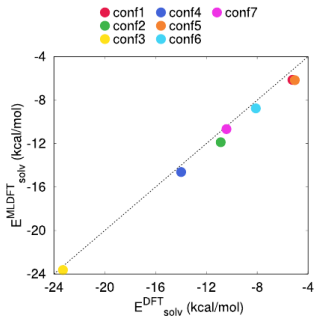
(implies partitioning of orbital spaces)

G. Giovannini, H. Koch, *J. Chem. Theory Comput.* **16** (2020), 139.

- minimize total energy w.r.t. $\mathbf{D}^A$ while keeping $\mathbf{D}_{\text{fixed}}^B$ fixed

G. Marrazzini, G. Giovannini, M. Scavino, F. Egidi, C. Cappelli, H. Koch, *J. Chem. Theory Comput.* **17** (2021), 791.

Multi-Level DFT



G. Marrazzini, G. Giovannini, M. Scavino, F. Egidi, C. Cappelli, H. Koch, *J. Chem. Theory Comput.* **17** (2021), 791;
published under CC-BY; DOI: 10.1021/acs.jctc.0c00940

Application: Solvation energies of glycidol in water

- B3LYP/6-31G* for glycidol
- B3LYP/6-31G for water

Density-Matrix Embedding Theory

Decomposing Total-System States

Consider active system A and environment B :

- states of combined system can be expanded as,

$$|\Psi_{A+B}\rangle = \sum_i^{n_{\text{states}}^A} \sum_j^{n_{\text{states}}^B} c_{ij} |A_i\rangle |B_j\rangle$$

Schmidt Decomposition Theorem:

- any pure state $|\Psi_{A+B}\rangle$ can be written in terms of (orthonormal) *Schmidt states* $|a_i\rangle, |b_i\rangle$

$$|\Psi_{A+B}\rangle = \sum_k^{n_{\min}} \sqrt{p_k} |a_k\rangle |b_k\rangle$$

(where $\sqrt{p_i}$ is a real, non-negative number with $\sum_i p_i = 1$, and $n_{\min} = \min(n_{\text{states}}^A, n_{\text{states}}^B)$)

J. Audretsch, *Entangled Systems — New Directions in Quantum Physics*, Wiley-VCH, Weinheim, 2007, pp. 149-151;

M. Schlosshauer, *Decoherence and the Quantum-to-Classical Transition*, Springer, Berlin, 2007, p. 104.

Decomposing Total-System States

Schmidt Decomposition by SVD

- singular value decomposition of matrix $c = U\lambda V^\dagger$

$$\begin{aligned} |\Psi_{A+B}\rangle &= \sum_i^{n_{\text{states}}^A} \sum_j^{n_{\text{states}}^B} c_{ij} |A_i\rangle |B_j\rangle = \sum_i^{n_{\text{states}}^A} \sum_j^{n_{\text{states}}^B} \sum_k^{n_{\text{min}}} U_{ik} \lambda_k V_{kj}^\dagger |A_i\rangle |B_j\rangle \\ &= \sum_k^{n_{\text{min}}} \lambda_k |a_k\rangle |b_k\rangle \end{aligned}$$

⇒ even if $n_{\text{states}}^B \gg n_{\text{states}}^A$, exact embedding of A is possible with n_{states}^A bath states

- ground state of $\hat{H}$ is also ground state of *embedding* Hamiltonian $\hat{P}\hat{H}\hat{P}$
i.e., active-fragment block of 1-RDM is the same for $|\Psi_{A+B}\rangle$ and $|\Psi_{A,\text{emb}}\rangle$ (with $\hat{P} = \sum_{ij} |a_i b_j\rangle \langle a_i b_j|$)
- but: constructing bath states requires knowledge of full $|\Psi_{A+B}\rangle$

Idea of DMET

- construct bath states from simple approximation $|\Phi\rangle$ to $|\Psi_{A+B}\rangle$
- use bath states to obtain high-level approximation from embedded problem

H.-P. Breuer, F. Petruccione, *The Theory of Open Quantum Systems*, Oxford University Press, Oxford, 2006, pp. 75-76;
G. Knizia, G.K.-L. Chan, *J. Chem. Theory Comput.* 2013, **9**, 1428;
S. Wouters, C.A. Jiménez-Hoyos, Q. Sun, G.K.-L. Chan, *J. Chem. Theory Comput.* 2016, **12**, 2706.

DMET in Practice

- (1) perform HF calculation on full system ($A + B$)
 $\Rightarrow$ yields N_{occ} occupied orbitals $\{\phi_i\}$
- (2) perform orbital rotation among $\{\phi_i\}$; specifically:
 - calculate

$$S_{ij} = \sum_{p \in A} \langle \phi_i | p \rangle \langle p | \phi_j \rangle$$

(overlap matrix of orbitals projected onto the L_A "sites" $|p\rangle$ of fragment A)

- eigenvectors of S define a rotation matrix; there are $N_{\text{occ}} - L_A$ eigenvectors with zero eigenvalue
 $\Rightarrow$ environment orbitals $\{\phi_i^{\text{env}}\}$ without overlap with A
 $\Rightarrow$ the remaining L_A "entangled" orbitals $\{\phi_i^{\text{ent}}\}$ do have overlap with A
- (3) project $\{\phi_q^{\text{ent}}\}$ onto environment "sites" $\Rightarrow$ yields L_A "bath orbitals" $|b\rangle$

$$\{|b\rangle\} = \left\{ \sum_{r \in B} |r\rangle \langle r | \phi_i^{\text{ent}} \rangle \right\}$$

DMET in Practice

- ⇒ many-body wavefunction: CAS-CI wavefunction with (half-filled) active space of $\{|p\rangle\}$ (L_A sites of fragment A) and $\{|b\rangle\}$ (L_A bath orbitals)
- (4) project total Hamiltonian $\hat{H}$ into active space, $\hat{H}_{\text{emb}}^A = \hat{P}\hat{H}\hat{P}$, and find high-accuracy approx. to $\hat{H}_{\text{emb}}^A \Psi_{A,\text{emb}} = E_A \Psi_{A,\text{emb}}$ (e.g., FCI)
- (5) adjust one-particle density matrix $\mathbf{D}$ to match that of Ψ_A as close as possible on fragment A . Do that for all fragments and iterate.

DMET in Practice

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- (5) adjust one-particle density matrix $\mathbf{D}$ to match that of Ψ_A as close as possible on fragment A . Do that for all fragments and iterate.

Note: This adjustment minimizes

$$\Delta = \sum_A \sum_{rs \in A} ||\langle \Phi | \hat{a}_r^\dagger \hat{a}_s | \Phi \rangle - \langle \Psi_{A,\text{emb}} | \hat{a}_r^\dagger \hat{a}_s | \Psi_{A,\text{emb}} \rangle||^2$$

by changing the Fock operator

$$\hat{f} \rightarrow \hat{f} + \sum_A \hat{\mu}_A \quad \text{with} \quad \hat{\mu}_A = \sum_{rs \in A} \mu_{rs}^A \hat{a}_r^\dagger \hat{a}_s$$

in the calculation of the mean-field wavefunction $|\Phi\rangle$ (i.e., Δ is minimized w.r.t. all μ_{rs}^A)

DMET in Practice

- ⇒ many-body wavefunction: CAS-CI wavefunction with (half-filled) active space of $\{|p\rangle\}$ (L_A sites of fragment A) and $\{|b\rangle\}$ (L_A bath orbitals)
- (4) project total Hamiltonian $\hat{H}$ into active space, $\hat{H}_{\text{emb}}^A = \hat{P}\hat{H}\hat{P}$, and find high-accuracy approx. to $\hat{H}_{\text{emb}}^A \Psi_{A,\text{emb}} = E_A \Psi_{A,\text{emb}}$ (e.g., FCI)
- (5) adjust one-particle density matrix $\mathbf{D}$ to match that of Ψ_A as close as possible on fragment A . Do that for all fragments and iterate.

Note: This adjustment minimizes

$$\Delta = \sum_A \sum_{rs \in A} ||\langle \Phi | \hat{a}_r^\dagger \hat{a}_s | \Phi \rangle - \langle \Psi_{A,\text{emb}} | \hat{a}_r^\dagger \hat{a}_s | \Psi_{A,\text{emb}} \rangle||^2$$

by changing the Fock operator

$$\hat{f} \rightarrow \hat{f} + \sum_A \hat{\mu}_A \quad \text{with} \quad \hat{\mu}_A = \sum_{rs \in A} \mu_{rs}^A \hat{a}_r^\dagger \hat{a}_s$$

in the calculation of the mean-field wavefunction $|\Phi\rangle$ (i.e., Δ is minimized w.r.t. all μ_{rs}^A)

Full system may be decomposed into multiple active sites, each of which comes with its own embedding; consistency is enforced via common low-level wavefunction $|\Phi\rangle$

G. Knizia, G.K.-L. Chan, *J. Chem. Theory Comput.* **9** (2013), 1428.

Conclusion

QM/QM methods

- offer the full range from “improved QM/MM” to “essentially exact”
- challenge:
QM/QM setup with automatic partitioning and error control

Conclusion

QM/QM methods

- offer the full range from “improved QM/MM” to “essentially exact”
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The Subsystem Quantum Chemistry Code SERENITY

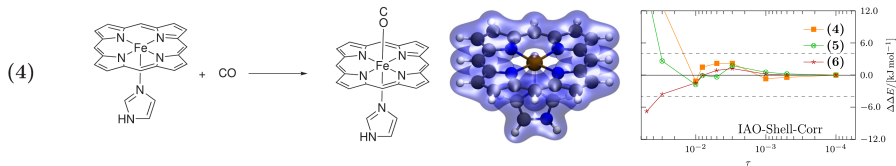


C++; open source; github.com/qcserenity

written with a focus on embedding/fragmentation methods

Appendix: Further Examples

Ligand Dissociation from an Fe-Porphyrin



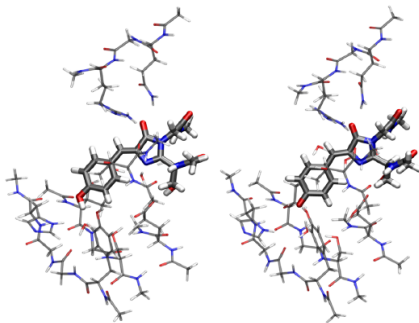
DOS for a ligand dissociation reaction:

- approximate hybrid DFT result by hybrid-in-non-hybrid DFT
- threshold τ controls “similarity” of orbitals
- 25 out of 118 orbitals chosen as active for $\tau = 10^{-2}$
- error: $\Delta\Delta E = \Delta E^{\text{PBE0-in-PBE}} - \Delta E^{\text{PBE0}}$

M. Bensberg, JN, *J. Chem. Phys.* **150** (2019), 184104.

Protein Response Effects on Excitation Energies

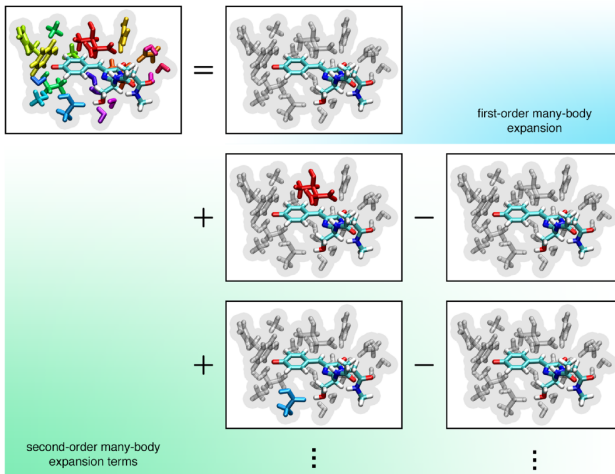
GFP models: A- and B-Form



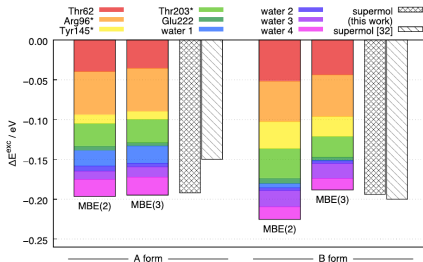
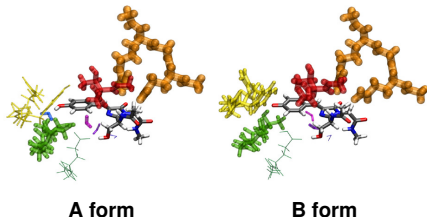
C. Daday, C. Curutchet, A. Sinicropi, B. Mennucci, C. Filippi, *J. Chem. Theory Comput.* **11** (2015), 4825.

- ca. -0.15 eV protein response effect
- not reproduced by embedding potential contributions
(i.e., if off-resonance exciton couplings are neglected)

Embedded Many-Body Expansion



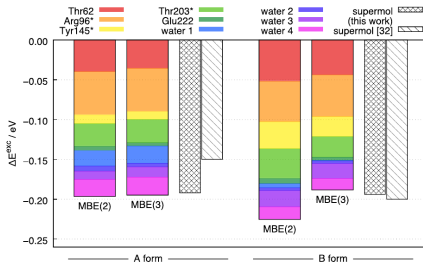
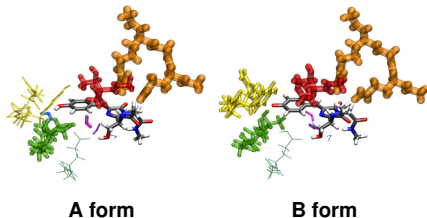
Environmental Response Effects in GFP models



(CAM-B3LYP[BLYP/LLP91]; basis: def2-SVP)

system	GFP279-A		GFP279-B	
	E^{exc}/eV	Δ/eV	E^{exc}/eV	Δ/eV
isolated	3.541	+0.230	3.086	+0.021
MBE(1)	3.504	+0.192	3.258	+0.194
MBE(2)	3.307	-0.005	3.033	-0.032
MBE(3)	3.309	-0.003	3.070	+0.006
reference	3.312	—	3.064	—
env. response	-0.195		-0.188	

Environmental Response Effects in GFP models



(CAM-B3LYP[BLYP/LLP91]; basis: def2-SVP)

system	GFP279-A (emb)		GFP279-A (non-emb)	
	E^{exc}/eV	Δ/eV	E^{exc}/eV	Δ/eV
isolated	3.541	+0.230	3.541	+0.230
MBE(1)	3.504	+0.192	3.541	+0.230
MBE(2)	3.307	-0.005	3.283	-0.029
MBE(3)	3.309	-0.003	3.317	+0.005
reference	3.312	-	3.312	-