Supporting Information

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SI Text

Computational Details and Accuracy Test Database. Perdew has formulated the hierarchy of density functional theory (DFT) approximations as a "Jacob's ladder" rising from the "earth of Hartree" to the "heaven of chemical accuracy" (1). We tested here the performance of some representative functionals of each rung (2–23). These functionals are the first rung: SVWN (2, 3); the second rung: BLYP (4, 5), PW91 (6, 7), PBE (8); the third rung: M06-L (9), TPSS (10); the forth rung: B3LYP (4, 5,11–13), X3LYP (14), PBE0 (15), M06-2X (16), M06 (16); and the fifth rung: XYG3 (17), XYGJ-OS, MC3BB (18), B2PLYP (19), B2GP-LYP (20), and ωB97X-2(LP) (21). The corresponding dispersion corrected methods: B3LYP-D (22), B3LYP-D3 (23), and B2PLYP-D (22) are also tested.

Single point DFT calculations were performed with the G3Large basis set (24) for heats of formation (HOFs), ionization potentials (IPs), electron affinities (EAs), proton affinities (PAs), bond dissociation enthalpies (BDEs), reaction barrier heights (RBHs), and nonbonded interactions (NBIs). Only HOFs of the G3/99 set (24–26) were used as the training set to optimize the parameters in XYG3 and XYGJ-OS. All other data were used as the testing sets. The results are summarized in Table S1.

For HOFs (at 298 K and 1 atm), the G3/99 set (24–26) was used as reference. The geometries were optimized using B3LYP with the 6-31G(2df,p) basis set. Analytical vibrational frequencies were calculated at the same level and scaled by 0.9854 to estimate zero-point energies and thermo corrections. The same strategy is used in the G3X method (24). Spin-orbit corrections were included as in the Gn method (24–26). HOFs were calculated via atomization procedure.

For IPs, EAs, and PAs (at 0 K), the G2-1 set (24–26) was used as reference. These properties were calculated as energy differences between the neutral species and the corresponding ionic species. As in the Gn method (24–26), the geometries were optimized using MP2(full) with the 6-31G(d) basis set. Analytical vibrational frequencies were calculated at the level of HF/6-31G (d) and scaled by 0.8929 to estimate zero-point energies.

For BDEs, the BDE92/07 set (27) was used as reference. BDEs were calculated according to the enthalpy change of the following reaction in the gas phase at 298 K and 1 atm:

$$X - Y(g) = X \cdot (g) + Y \cdot (g),$$
$$BDE(X - Y) = \Delta_f H^{\varnothing}_{298}(X \cdot) + \Delta_f H^{\varnothing}_{298}(Y \cdot) - \Delta_f H^{\varnothing}_{298}(X - Y).$$

For RBHs, Truhlar's nonhydrogen transfer barrier height (NHTBH) set and hydrogen transfer barrier height (HTBH) set were used as reference. The geometries are taken from Truhlar database website (28, 29).

For NBIs, Truhlar's noncovalent interaction energy (NCIE) set was used as reference. The geometries are taken from Truhlar database website (29).

We also included some wave function based methods: HF, MP2, SCS-MP2 (30), SOS-MP2 (31) for comparison. Composite methods such as G2 and G3 (24–26) were used as references. Geometries and thermo corrections were all done using the standard procedure built in the Gn method. For RBHs and NBIs, the Gn results are replaced with QCISD(T)/6-311+G(3df,2p) ones, where the geometries are taken from Truhlar database website (28, 29).

The performances of various methods are summarized as follows (see Table S1).

We tested various methods in describing the whole $H + CH_4 \rightarrow H_2 + CH_3$ reaction path using CCSD(T)/6-311++G(3df,2pd) data (32) as the reference. The results are depicted in Fig. S1. XYGJ-OS results are nearly identical to the XYG3 and CCSD(T) results before the barrier. But XYGJ-OS overestimates the reaction endothermicity by 1.21 kcal/mol. Note that RBH are not included in the training set of XYG3 and XYGJ-OS.

We tested various methods in describing the intermolecular potentials of the CH_4-C_6H_6 complex calculated by various methods as shown in Fig. S2. The CCSD(T) results at the complete basis set (CBS) limit are used as reference (33). An unpruned (250,590) grid is used in calculations to avoid spurious oscillations on potential energy curves for dispersion-bound complexes with MC3BB and the M06 family of functionals (34). As shown in Fig. S2, XYGJ-OS data are nearly on top of those of XYG3. Note that nonbonded interaction is not included in the training set of XYG3 and XYGJ-OS. However we do not include BSSE corrections with XYG3 and XYGJ-OS in comparing to the G3 and M06 data bases.

The total CPU timings are compared for XYG3-RI, XYGJ-OS, and local XYGJ-OS (see Fig. S3). We used n-alkanes as examples. The calculations were performed with cc-pVDZ basis sets with the same basis set as the auxiliary basis. The numbers of basis functions are 250 for C_{10}, 1,210 for C_{50}, and up to 2,410 for C_{100}. For local XYGJ-OS, a cutoff criterion of 5×10^{-6} for local screening and the ω value of 0.2 a.u. for the attenuated Coulomb fitting metric (Eq. **S17** below) were used (35). As compared to XYGJ-OS, the local algorithm errors for total energies of n-alkanes are less than 0.01 eV (0.25 kcal/mol) up to C_{100}. For the atomization energies of G2 set, we obtained the same statistical results (less than 0.001 eV of difference) for both XYGJ-OS and its local version.

The ωB97X-2(LP) results are taken from ref. 21. The ωB97X-2 (LP) yields a very high accuracy comparable to XYGJ-OS for HOF, IP, EA, PA, NHTBH, and HTBH, where the key difference in terms of accuracy is that, in ωB97X-2(LP) all the latter properties were part of the training set used in the fitting process while in XYGJ-OS only the HOF was used as a training set. XYGJ-OS contains four fitting parameters while parameters in Becke88 exchange and LYP correlation functionals are fixed at their original values. The ωB97X-2 (LP) contains 16 fitting parameters. Another difference is that, the parameters in the ωB97X-2 (LP) were fitted assuming the large Pople basis 6-311++G(3df, 3pd). There is also a computational difference between ωB97X-2 (N^5) and XYGJ-OS (N^3 for the default local implementation and N^4 for canonical).

From Table S1, it is clear that HOF calculations are very basis set dependent, where the calculations with the basis sets used for DHDF functional parameterization lead to the best results. Changing basis sets from 6-311+G(3df,2p) to G3Large increases XYG3 MAD for HOF by 1.63 kcal/mol. Changing basis sets from CQZV3P (quadruple basis sets plus three set of polarization and core polarization functions) to G3Large increases B2PLYP MAD by 4.85 kcal/mol and B2PLYP-D MAD by 4.22 kcal/mol. Changing basis sets from 6-311++G(3df,3pd) to G3Large increases ωB97X-2 (LP) MAD for HOF by 3.82 kcal/mol. For other properties, basis set dependence associated with DHDFs is relatively mild.

Dispersion-correction methods could increase the errors for RBH and hydrogen bond interactions, but they should significantly improve the performance for systems (clusters) dominated by weak (vdw) interactions. Thus for RBH (Truhlar datasets

NHTBH38 and HTBH38 in Table S2), we find MAD = 4.47 kcal/mol (B3LYP), 5.12 (B3LYP-D) and 4.98 (B3LYP-D3). Grimme, et al. (57) found MAD = 4.7 (B3LYP), 5.4 (B3LYP-D) and 5.2 kcal/mol (B3LYP-D3), which are slightly different due to differences in the basis sets. For nonbonded interactions (Truhlar dataset NCIE31 in Table S3), we find MAD = 0.95 kcal/mol (B3LYP), 0.71 (B3LYP-D), and 0.70 (B3LYP-D3). In fact, B3LYP is much worse for the π-π stacking complexes than these numbers suggest, because we assess the error at the correct geometry. B3LYP-D and -D3 give correct geometry and lead to decreased error. On the other hand, for the hydrogen bond and charge-transfer complexes, the agreement is worse for the dispersion corrected methods.

All calculations reported in this article were performed using a development version of Q-Chem (36).

XYG3 vs. XYGJ-OS. In this section of SI, we summarize some basic physics associated with XYG3 and XYGJ-OS. The way of deviation of XYG3 and XYGJ-OS presented here complements that in the main text.

The Holy Grail in Kohn-Sham (KS) DFT is to find the exact, yet unknown, exchange-correlation functional $E_{xc}[\rho]$ using density ρ as the basic variable (37–39). The density functional approximation (DFA) often partitions E_{xc} into exchange and correlation parts

$$E_{xc}[\rho] \approx E_x^{\mathrm{DFA}}[\rho] + E_c^{\mathrm{DFA}}[\rho]. \qquad \textbf{[S1]}$$

Various approximations to this divine functional have been developed and tested in recent decades, but the accuracy of the best methods practical for important applications is often not adequate.

The adiabatic connection approach provides a powerful tool for developing and understanding E_{xc} (40, 41). This approach defines a family of partially interacting N-electron systems for a fixed ρ,

$$\hat{H}_\lambda = \hat{T} + \hat{V}_{\mathrm{ee},\lambda} + \hat{V}_{\mathrm{ext},\lambda} = \hat{T} + \lambda \hat{V}_{\mathrm{ee}} + \sum_i^N v_\lambda(r_i), \qquad \textbf{[S2]}$$

where both the two-electron operator $\hat{V}_{\mathrm{ee}} = \sum_{i<j}^N 1/r_{ij}$ and the external potential depends upon the coupling strength λ. Here $\lambda = 0$ corresponds to the noninteracting KS system with $\hat{H}_s$, while $\lambda = 1$ leads to the physical system. E_{XC} is then given by (40, 41):

$$E_{xc}[\rho] = \int_0^1 U_{xc,\lambda}[\rho] d\lambda, \qquad \textbf{[S3]}$$

where $U_{xc,\lambda}$ is the potential energy of exchange-correlation at intermediate coupling strength λ. Regretfully, the exact integrand $U_{xc,\lambda}$ is unknown. Eq. **S2** may be reformulated as

$$\hat{H}_\lambda = \hat{H}_s + \lambda \hat{H}'_\lambda, \qquad \textbf{[S4]}$$

where the perturbation term is given by

$$\hat{H}'_\lambda = \hat{V}_{\mathrm{ee}} + \frac{1}{\lambda} \sum_{i=1}^N \left[v_\lambda(r_i) - v_s(r_i) \right]. \qquad \textbf{[S5]}$$

From perturbation theory and relations based on uniform coordinate scaling (42), we obtain

$$U_{xc,\lambda} = E_x^{\mathrm{HF}} + 2\lambda E_c^{\mathrm{GL2}} + O(\lambda^2). \qquad \textbf{[S6]}$$

Here E_c^{GL2} is the Görling-Levy theory of coupling-constant perturbation expansion to second order (43):

$$E_c^{\mathrm{GL2}} = \sum_i \sum_a \frac{|\langle \varphi_i | v_x - \hat{k}_x | \varphi_a \rangle|^2}{\varepsilon_i - \varepsilon_a}$$
$$+ \frac{1}{4} \sum_{ij} \sum_{ab} \frac{|\langle \varphi_i \varphi_j | \varphi_a \varphi_b \rangle - \langle \varphi_i \varphi_j | \varphi_b \varphi_a \rangle|^2}{\varepsilon_i + \varepsilon_j - \varepsilon_a - \varepsilon_b}, \qquad \textbf{[S7]}$$

where subscripts (i, j) denote occupied KS orbitals, and (a, b) denote virtual orbitals. Here v_x is the local exchange operator defined by the exchange part of Eq. **S8**,

$$v_{xc}(r) = \frac{\delta E_{xc}[\rho]}{\delta \rho}, \qquad \textbf{[S8]}$$

while $\hat{k}_x$ in Eq. **S7** is the Fock-like nonlocal exchange operator, leading to E_x^{HF}:

$$E_x^{\mathrm{HF}} = -\frac{1}{2} \sum_{ij} \iint d^3r' d^3r \frac{\varphi_i^*(r)\varphi_j(r)\varphi_j^*(r')\varphi_i(r')}{|r'-r|}. \qquad \textbf{[S9]}$$

The superscript "HF" emphasizes that it has the same form as in Hartree-Fock (HF) theory. Eq. **S9** is exact if the KS orbitals give the true density. Inserting Eq. **S6** into Eq. **S3** leads to:

$$E_{xc}[\rho] \approx E_x^{\mathrm{HF}}[\{\varphi_i[\rho]\}] + E_c^{\mathrm{GL2}}[\{\varphi_i[\rho]\}]. \qquad \textbf{[S10]}$$

If $U_{xc,\lambda}$ depends linearly on λ, the higher order term $O(\lambda^2)$ in Eq. **S6** is zero, such that the higher order term $O(\lambda^3)$ in **[S10]** vanishes; i.e., **[S10]** provides an exact expression in this condition. The $\{\varphi[\rho]\}$ indicates an orbital dependent functional. For practical uses, one needs an $E_{xc}^{\mathrm{DFA}}[\rho]$ that generates good KS orbitals (17, 44, 45, 46).

To improve the linear approximation of $U_{xc,\lambda}$, we define a doubly hybrid density functional (DHDF) that combines **[S10]** and **[S1]**:

$$E_{xc}^{\mathrm{DHDF}}[\rho] = c_1 E_x^{\mathrm{LDA}} + c_2 \Delta E_x^{\mathrm{GGA}} + c_3 E_x^{\mathrm{HF}}$$
$$+ c_4 E_c^{\mathrm{LDA}} + c_5 \Delta E_c^{\mathrm{GGA}} + c_6 E_c^{\mathrm{GL2}}. \qquad \textbf{[S11]}$$

Here $\{E_x^{\mathrm{LDA}}, E_c^{\mathrm{LDA}}\}$ are the exchange and correlation components within the local density approximation (LDA), and $\{\Delta E_x^{\mathrm{GGA}}, \Delta E_c^{\mathrm{GGA}}\}$ are the corresponding correction terms to LDA within the generalized gradient approximation (GGA). The meta-GGA functionals that include kinetic energy density or the Laplacian of density can also be used in replace of GGAs. **[S10]** is more appropriate near $\lambda = 0$, while **[S1]** is more appropriate near $\lambda = 1$. Therefore Eq. **S11** combines both to embrace local and nonlocal parts of both exchange and correlation contributions, which we expect to provide a good form for general applications. MC3BB (18), B2PLYP (19) and ωB97X-2 (21), which are derived and constructed differently, are examples of other doubly hybrid functionals (18–21, 47–49). Neglecting the nonlocal correlation effects, Eq. **S11** leads to such conventional hybrid functionals as Becke's half-and-half (50) and B3LYP (12).

Based on Eq. **S11**, we have developed a DHDF, namely XYG3 (17), which is remarkably accurate for a wide range of systems and important chemical properties (17, 44, 45, 46). Nevertheless, including the PT2 term in DHDFs (17–21) leads to a formal scaling as N^5, as opposed to a formal scaling of N^4 as in B3LYP. This unfavorable scaling raises an issue for the practicality to apply XYG3 to large systems.

Here we propose a new opposite-spin (OS) ansatz for DHDF, namely XYGJ-OS, that yields a balanced description of nonlocal correlation effects while considerably reducing computational time. Our OS ansatz is motivated by the observation that the most important electron correlation effects involves correlation of the

OS electrons in the same orbital. The OS ansatz leads to N^4 scaling [using auxiliary basis expansions and Laplace quadrature approximations (31, 35)]. In XYGJ-OS, the same-spin (SS) correlation effects are included within the standard DFA. A local version of XYGJ-OS is further developed that introduces the local approximation for the OS electron correlation. Local XYGJ-OS scales as N^3 by recognizing the "nearsightedness of electron correlation" as emphasized by Kohn (51), while retaining the accuracy of the original XYGJ-OS (described below).

Thus our proposed functional form (XYGJ-OS) is

$$E_{xc}^{\text{XYGJ-OS}}[\rho] = e_x E_x^{HF} + (1-e_x)E_x^S + (e_{VWN}E_c^{VWN} + e_{LYP}E_c^{LYP}) + e_{PT2}E_{c,\text{os}}^{PT2}. \qquad \text{[S12]}$$

In Eq. S12 we normalize the HF exchange and Slater exchange, while eliminating the ΔE_x^{GGA} contribution. The superscript "PT2" indicates that only the MP2-like perturbation part in Eq. S7 is evaluated as also done in the B2PLYP (19) and other DHDFs (17, 20, 21). The correlation part consists of E_c^{VWN}, E_c^{LYP}, and $E_{c,\text{os}}^{PT2}$, where the first term includes both the SS and OS effects while the second and third terms include only OS components. Our concept is that the combination of VWN, LYP, and PT2-OS yields a balanced description of both local and nonlocal spin dependent correlation terms. To determine the optimal four parameters in Eq. S12, we use the experimental HOF data for the G3/99 set of 223 molecules (24–26) as the training set, leading to $\{e_x, e_{VWN}, e_{LYP}, e_{PT2}\} = \{0.7731, 0.2309, 0.2754, 0.4364\}$.

We would like to emphasize that we use fully optimized B3LYP orbitals to generate the density and to calculate each term in Eq. S12 (17, 44, 45, 46). Other DHDFs have either used HF orbitals for PT2 evaluation (18), or the density and orbitals from a truncated functional with incomplete correlation (19–21, 47–49).

Summary of local OS PT2 approximations. In this section of SI, we summarize the approximations associated with the local OS PT2 ansatz, and a brief introduction of how the locality is exploited in the present algorithm. That is, we here summarize ref. 31 for completeness.

In order to be able to use locality of electron correlation, one has to transform the canonical-orbital based PT2 expression to the local-orbital based expression. To this end, we eliminate the energy denominator via the Laplace transform $1/x = \int_0^\infty dt e^{-xt}$ (56):

$$E_{\text{OS-PT2}} = -\sum_{ia}^{\alpha}\sum_{jb}^{\beta} \frac{(ia|jb)^2}{\varepsilon_a + \varepsilon_b - \varepsilon_i - \varepsilon_j}$$
$$= -\int_0^\infty dt \sum_{ia}^{\alpha}\sum_{jb}^{\beta} e^{-(\varepsilon_a+\varepsilon_b-\varepsilon_i-\varepsilon_j)t}(ia|jb)^2, \qquad \text{[S13]}$$

where ε_i, ε_j, ε_a, ε_b are the orbital energies of the occupied levels i, j and the virtual levels a, b. The two-electron MO repulsion integrals are given by:

$$\langle ij|ab \rangle = (ia|jb) = \int d\mathbf{r_1} \int d\mathbf{r_2} \phi_i(\mathbf{r_1})\phi_a(\mathbf{r_1})\frac{1}{|\mathbf{r_1}-\mathbf{r_2}|}\phi_j(\mathbf{r_2})\phi_b(\mathbf{r_2}). \qquad \text{[S14]}$$

Numerical integration over t is performed by introducing a discrete quadrature (over n points, which is typically 6–8):

$$E_{\text{OS-PT2}} = -\sum_q^n w_q \sum_{ia}^{\alpha}\sum_{jb}^{\beta} e^{-(\varepsilon_a+\varepsilon_b-\varepsilon_i-\varepsilon_j)t_q}(ia|jb)^2$$
$$= -\sum_q^n w_q \sum_{ia}^{\alpha}\sum_{jb}^{\beta} (\tilde{i}\,\tilde{a}|\tilde{j}\,\tilde{b})_q^2. \qquad \text{[S15]}$$

t-dependent Laplace transformed orbitals $\tilde{\phi}_i$ and $\tilde{\phi}_a$ are given in terms of canonical orbitals that are exponentially damped:

$$\tilde{\phi}_i = \phi_i e^{\varepsilon_i t_q/2} \qquad \text{[S16]}$$

$$\tilde{\phi}_a = \phi_a e^{-\varepsilon_a t_q/2}. \qquad \text{[S17]}$$

In Eqs. S16, S17 and below, we use a notation for simplicity that $\tilde{\phi}_i$ implies the transformed orbital at the quadrature point q. We next introduce an auxiliary basis $\{\Phi_Q\}$ expansion for the product density (Eq. S18) to reduce the number of expensive four-center two-electron integrals into much more affordable two- and three-center integrals.

$$\rho = |\varphi_i\varphi_{\tilde{a}}\rangle \approx \rho_{\text{fitted}} = \sum_Q^M C_Q^{\tilde{i}\tilde{a}}|\Phi_Q\rangle. \qquad \text{[S18]}$$

This approximation is also known as Resolution of Identity (RI) or density fitting technique (53, 54). The auxiliary basis expansion coefficients, C, are determined by minimizing the self interaction of the difference between the fitted distribution and the actual distribution, $\rho_{\text{diff}} = \rho_{\text{fitted}} - \rho_{\text{actual}}$, defined as,

$$(\rho_{\text{diff}}|\rho_{\text{diff}}) = \int d\mathbf{r_1} \int d\mathbf{r_2}\rho_{\text{diff}}(\mathbf{r_1})g(\mathbf{r_1},\mathbf{r_2})\rho_{\text{diff}}(\mathbf{r_2}), \qquad \text{[S19]}$$

where $g(\mathbf{r_1},\mathbf{r_2}) = 1/|\mathbf{r_1}-\mathbf{r_2}|$. Differentiation of Eq. S19 with respect to C and setting it to zero leads to the following solution for C, which involves only the two-index two-electron and three-index two-electron integrals:

$$C_Q^{\tilde{i}\tilde{a}} = \sum_P (\tilde{i}\,\tilde{a}|P)(P|Q)^{-1}. \qquad \text{[S20]}$$

Inserting Eqs. S18 and S20 into Eq. S14 results in the following integral approximation:

$$(\tilde{i}\,\tilde{a}|\tilde{j}\,\tilde{b}) \approx \sum_Q B_Q^{\tilde{i}\tilde{a}}B_Q^{\tilde{j}\tilde{b}}, \qquad \text{[S21]}$$

where B is the matrix defined as:

$$B_Q^{\tilde{i}\tilde{a}} = \sum_P (\tilde{i}\,\tilde{a}|P)(P|Q)^{-1/2}. \qquad \text{[S22]}$$

Substituting Eq. S21 into Eq. S15 finally leads to the following working expression for the OS PT2 correlation energy:

$$E_{\text{OS-PT2}} = -\sum_q^n w_q \sum_{PQ} X_{PQ}\bar{X}_{PQ}. \qquad \text{[S23]}$$

X_{PQ} and $\bar{X}_{PQ}$ are defined as:

$$X_{PQ} = \sum_{ia}^{\alpha} B_P^{\tilde{i}\tilde{a}}B_Q^{\tilde{i}\tilde{a}} \qquad \text{[S24]}$$

$$\bar{X}_{PQ} = \sum_{jb}^{\beta} B_P^{\tilde{j}\tilde{b}}B_Q^{\tilde{j}\tilde{b}}. \qquad \text{[S25]}$$

Formation of X from the B matrices, Eqs. **S24** and **S25**, is the most expensive fourth-order step in OS-PT2.

While Eq. **S15** is specific to the canonical-orbital basis, expressions in a generalized orthogonal basis can be given as follows:

$$E_{\text{OS-PT2}} = -\sum_q^n w_q \sum_{IA}^{\alpha} \sum_{JB}^{\beta} (\tilde{I}\tilde{A}\,|\tilde{J}\tilde{B})^2_q \qquad [\textbf{S26}]$$

$$\tilde{\phi}_I = \sum_K \phi_K (\phi_K | e^{\hat{f}t_q/2} | \phi_I) = \sum_K \phi_K W_{KI} \qquad [\textbf{S27}]$$

$$\tilde{\phi}_A = \sum_C \phi_C (\phi_C | e^{-\hat{f}t_q/2} | \phi_A) = \sum_C \phi_C W_{CA}, \qquad [\textbf{S28}]$$

where indices $I, J, K \ldots$ and $A, B, C \ldots$ refer to localized functions that span occupied and virtual spaces. In Eqs. **S27** and **S28**, we again assume that $\tilde{\phi}_I$ implies the transformed orbital at the quadrature point q. We chose to use orthogonal Boys functions for the localized occupied orbitals, and the generalized orthogonal projected atomic orbitals (AO)'s for the localized virtual orbitals, defined as $|A\rangle = \hat{Q}(s^{-1/2})|\mu\rangle$, where $\hat{Q}$ is the virtual projection operator, and $\mu, \nu, \cdots$ are the AO indices. We could have used Boys virtual orbitals instead of the projected AOs since the projected AOs partly destroy the locality of AOs by applying $s^{-1/2}$. But Boys localization using the Jacobi sweeps becomes computationally very demanding due to poor convergence for large systems. Therefore we used the projected AOs for the localization of virtual orbitals.

We next introduce the auxiliary basis expansion, as before, for the product distribution $\tilde{\phi}_I \tilde{\phi}_A$, and obtain the same solution for C, except that here we choose to employ the short-range two-electron operator $g(\mathbf{r_1}, \mathbf{r_2}) = erfc(\omega|\mathbf{r_1}-\mathbf{r_2}|)/|\mathbf{r_1}-\mathbf{r_2}|$, which is denoted with a subscript ω, to remove the long-range artifact of Coulomb metric (55).

$$C_Q^{\tilde{I}\tilde{A}} = \sum_P (\tilde{I}\tilde{A}\,|P)_\omega (P|Q)_\omega^{-1}. \qquad [\textbf{S29}]$$

Finally, we rewrite Eq. **S14** as the following working expression for the local OS-PT2 algorithm:

$$E_{\text{OS-PT2}} = -\sum_q^n w_q \sum_{PQRS} Y_{PR}(P|Q) \bar{Y}_{QS}(R|S) \qquad [\textbf{S30}]$$

$$Y_{PR} = \sum_{IA}^{\alpha} C_P^{\tilde{I}\tilde{A}} C_R^{\tilde{I}\tilde{A}} \qquad [\textbf{S31}]$$

$$\bar{Y}_{QS} = \sum_{JB}^{\beta} C_Q^{\tilde{J}\tilde{B}} C_S^{\tilde{J}\tilde{B}}. \qquad [\textbf{S32}]$$

To exploit the locality and sparsity of the various matrices, we use a scheme called "natural blocking," where the entire rows or columns of large matrices can be removed for processing due to the physical nature (structure) of given matrices.

Eq. **S31** is the most time-consuming step in a straightforward 4th order scaling implementation of OS PT2 method (like

Eqs. **S24** and **S25**). But because the occupied and virtual functions (I, A) are localized and the auxiliary expansion functions Q are also local, the fitting coefficients $C_Q^{\tilde{I}\tilde{A}}$ (where the quadrature point q is implied as in Eq. **S27** and **S28**) must also be local. In other words, for a given occupied orbital I, only those virtual and auxiliary functions (matrix elements) that are local to I will be nonzero, and so $Y_{PQ} = \sum_B C_P^{\tilde{I}\tilde{B}} C_Q^{\tilde{I}\tilde{B}}+ = (P_{\text{sig}}, B_{\text{sig}})_I (B_{\text{sig}}, Q_{\text{sig}})_I$, where $P_{\text{sig}}, B_{\text{sig}}, Q_{\text{sig}}$ mean that P, B, and Q are local to I, can be evaluated with a linear scaling effort. In a natural blocking scheme, the (P, B) batches of the three-index C "matrix" are examined and the entire rows and columns are removed if they are not local to I. Furthermore, $C_Q^{\tilde{I}\tilde{A}}$ is arranged optimally for this operation, which is performed as an efficient dense matrix multiply over the significant virtual (B_{sig}) and auxiliary (P_{sig}) indices, using the natural blocking scheme. In deleting the rows and columns, we have used a numerical cutoff of 5×10^{-6} and the error associated with it is insignificant as shown below.

In another step, the AO to occupied-MO transformation $(I\nu|P)_\omega = \sum_\mu C_{\mu I}(\mu\nu|P)_\omega$ is $O(M^4)$ work. For a large enough system, it asymptotically approaches $O(M^3)$ because the magnitude of the $\mu\nu$ function product decays as a Gaussian with the inter-function distance. Because the integral operator is short-ranged, as denoted by a subscript ω, only those integrals that involve basis functions (μ, ν, and P) that are close each other in real space will have nonzero values. A significant number of arithmetic operations can be saved by using this integral sparsity, namely by inserting an IF statement in which the first MO transformation is skipped if the integral value is zero against some numerical threshold. We have used 10^{-6} as an integral threshold criterion, which is sufficiently tight that it adds no additional error numerically as shown below. This utilization of sparsity makes the cost of occupied-index AO-to-MO transformation formally $O(M^2)$, instead of $O(M^3)$.

Other steps involved in the transformations and evaluations of various quantities that lead to Eqs. **S31** and **S32** have also been accelerated by using the similar blocking scheme and integral screening (see ref. 35 for more details). The resulting algorithm is formally cubic scaling (localization, local transformation, and inspection of the matrices), but due to a relatively small prefactor of the latter cubic steps it shows a quadratic scaling for favorable cases before these cubic steps become dominant.

As seen in Fig. S3, linear alkane chains show a quadratic scaling and a significant speedup as compared to the calculation without using local algorithm. On the other hand, the fully three-dimensional (3D) dense systems like the diamonoid do not show a significant speedup up to C100 due to the small length scale of this system even with 100 carbon atoms, $\approx$10 Å. In contrast, the length scale of linear alkane with 100 carbon atoms is about $\approx$125 Å, thus showing a substantial speedup. This relatively modest speedup means that, for fully 3D structures like the diamond structure, we have simply not yet reached the quadratic or cubic regime where sparsity can make a significant difference. There will be a significant speedup using the local algorithm even for dense 3D systems, however, if one considers large enough systems. The memory and disk requirement for the local PT2 calculation are also quadratically scaling, moderate to be applicable for large systems.

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Fig. S1. Accuracy of various theoretical methods for calculating the potential energy curve of the $H + CH_4 \rightarrow H_2 + CH_3$ reaction. Reaction coordinate is defined as [R(CH)-R(HH)] (in Å). CCSD(T)/6-311++G(3df,2pd) results (32) are used as reference. Note that RBH are not included in the training set of XYG3 and XYGJ-OS.

Fig. S2. The intermolecular potentials for the CH$_4$-C$_6$H$_6$ complexes from various methods. *R* is defined as carbon of CH$_4$ to the ring center of C$_6$H$_6$ (in Å). Data in red are the coupled-cluster method with single and double as well as perturbative triple excitations (CCSD)(T) at the complete basis set limit from ref. 33. XYGJ-OS data are nearly on top of those of XYG3. Note that nonbonded interaction is not included in the training set of XYG3 and XYGJ-OS. But BSSE corrections are NOT included in the calculations. XYG3 and XYGJ-OS are making use of BSSE to have this good agreement.

XYG3-RI

A

$y = 4.651x - 7.0226$
$R^2 = 0.9999$

(y-axis: Log(Total CPU); x-axis: Log(alkane))

XYGJ-OS

B

$y = 3.6566x - 5.6575$
$R^2 = 0.9998$

(y-axis: Log(Total CPU); x-axis: Log(alkane))

Local XYGJ-OS

C

$y = 2.0822x - 3.2755$
$R^2 = 0.9931$

(y-axis: Log(Total CPU); x-axis: Log(alkane))

Fig. S3. Scaling of the XYG3, XYGJ-OS, and its local version method as measured by the log of total CPU time vs the alkane chain length.

Table S1. Mean absolute deviations (MADs, in kcal/mol) for various benchmark sets with the G3Large basis set. BSSE correction is not included unless otherwise stated

	Methods	HOF (223)	IP (38)	EA (25)	PA (8)	BDE (92)	NHTBH (38)	HTBH (38)	NCIE (31)	All (493)
1st rung	SVWN (SPL)	130.88	15.14	17.30	5.68	18.14	12.53	17.95	3.29	67.28
2nd	BLYP	10.16	6.02	2.47	1.75	7.00	8.29	7.68	1.49	7.84
Rung	PW91	22.04	5.19	3.19	1.53	3.75	8.95	9.76	1.31	12.78
	PBE	20.71	5.13	2.40	1.56	3.91	8.57	9.48	1.17	12.10
3rd	M06-L	5.20	5.31	3.56	1.60	4.17	3.81	4.33	0.59	4.41
Rung	TPSS	5.01	5.36	2.41	1.66	5.88	9.04	8.26	1.14	5.33
4th	B3LYP	6.08	3.74	2.45	1.40	5.51	4.84	4.26	0.98	4.98
Rung	B3LYP-D	3.58	3.77	2.46	1.09	4.16	5.22	5.21	0.65	3.67
	B3LYP-D3	4.15	3.77	2.47	1.18	4.29	5.17	4.97	0.64	3.93
	X3LYP	5.04	3.69	2.11	1.62	5.09	4.70	4.52	0.84	4.41
	PBE0	5.64	3.84	2.97	1.25	3.67	3.56	4.38	0.71	4.36
	M06-2X	2.26	2.72	2.37	1.94	1.40	1.26	1.25	0.28	1.86
	M06	3.37	3.63	2.04	1.78	1.95	2.31	2.16	0.43	2.67
5th	XYG3	3.44	1.30	1.98	1.65	1.86	1.31	0.81	0.32	2.31
	XYG3*	1.81	1.31	1.84	1.61	1.56	1.29	0.75	0.32	1.51
Rung	XYGJ-OS	**1.65**	**1.23**	**1.97**	**1.68**	**0.71**	**1.18**	**0.87**	**0.35**	**1.28**
	MC3BB	3.28	2.78	4.01	1.03	2.43	1.44	0.80	0.58	2.58
	B2PLYP	7.59	2.48	2.15	1.52	3.30	2.23	1.73	0.55	4.71
	B2PLYP[†]	2.74[†]	2.48	2.15	1.52	2.95[†]	2.23	1.73	0.55	2.45
	B2PLYP-D	5.89	2.48	2.15	1.34	2.60	2.47	2.11	0.45	3.85
	B2PLYP-D[†]	1.67[†]	2.48	2.15	1.34	2.27[†]	2.47	2.11	0.45	1.88
	B2GP-LYP	7.95	2.24	2.72	1.44	2.72	1.36	0.70	0.40	4.62
	ωB97X-2(LP)	5.34	1.62	1.53	1.52	1.82	1.95	0.71	0.73	3.23
	ωB97X-2(LP)[‡]	1.52	1.73	1.56	1.09	1.62	1.67	0.74	0.47[§]	1.44
Ab	HF	213.42	23.19	26.46	3.09	32.70	9.08	13.51	2.37	107.71
initio	MP2	10.63	3.49	3.59	2.13	7.73	5.42	3.91	0.60	7.49
	SCS-MP2	11.64	4.02	4.94	1.02	6.23	6.53	5.22	0.32	7.93
	SOS-MP2	15.07	4.52	5.82	0.89	6.01	7.09	6.09	0.46	9.64
	G2	1.89	0.97	1.31	1.34	1.80	0.97	1.24	0.57	1.56
	G3	1.06	1.27	1.13	1.06	1.08	0.97	1.24	0.57	1.06

*Taken from ref. 17 with 6-311+G(3df,2p).
†HOF are taken from ref. 22 with very large basis set of CQZV3P. BDEs are calculated using the corresponding HOF.
‡Taken from ref. 21 or calculated with 6-311++G(3df,3pd).
§BSSE corrections are included for the NCIE set.

Table S2. Mean absolute deviation for RBH of Truhlar's NHTBH38 and HTBH38 sets (basis sets: 6-311+G(3df,2p)

RBH	UM10	NS16	HAT12	HT38	NHT38	Total
B3LYP	2.02	3.38	8.50	4.31	4.64	4.47
B3LYP-D	2.50	4.03	8.96	5.06	5.18	5.12
B3LYP-D3	2.37	4.01	8.93	4.83	5.13	4.98

Here HT38 refers to the forward and reverse barrier heights for 19 hydrogen transfer reactions; HAT12 refers to the forward and reverse barrier heights for six heavy-atom transfer reactions, NS16 refers to the forward and reverse barrier heights for eight nucleophilic substitution reactions and UM10 refers to the forward and reverse barrier heights for five association and unimolecular reactions).

Table S3. Mean absolute deviation for Truhlar's NCIE31 set of nonbonded interactions (basis sets: 6-311+G(3df,2p)

RBH		HB6	CT7	DI6	WI7	PPS5	Total(31)
B3LYP		0.63	0.76	0.61	0.27	2.93	0.95
	BSSE corrected	0.55	0.76	0.93	0.38	3.25	1.07
B3LYP-D		0.86	1.49	0.60	0.14	0.34	0.71
	BSSE corrected	1.07	1.40	0.33	0.04	0.46	0.67
B3LYP-D3		0.70	1.60	0.78	0.11	0.21	0.70
	BSSE corrected	0.93	1.48	0.46	0.01	0.29	0.65

NCIE31 consists of six hydrogen bond (HB) complexes, seven charge-transfer (CT) complexes, six dipole interaction (DI) complexes, seven weak interaction (WI) complexes, and five π-π stacking (PPS) complexes. The WI and PPS are dominated by London dispersion)