

Tackling An Accurate Description of Molecular Reactivity with Double-Hybrid Density Functionals

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Communication:**Tackling An Accurate Description of Molecular Reactivity with Double-Hybrid Density Functionals**

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In this communication, we assess a panel of 18 double-hybrid (DH) density functionals for the modeling of the thermochemistry and kinetics properties of an extended dataset of 449 organic chemistry reactions belonging to the BH9 database. We show that most of DHs provide a statistically robust performance to model barrier height and reaction energies in reaching the ‘chemical accuracy’. In particular, we show that nonempirical DHs like PBE0-DH and PBE-QIDH, or minimally parameterized alternatives like ω B2PLYP and B2K-PLYP succeed to model accurately both properties in a balanced fashion. We demonstrate however that parameterized approaches like ω B97X-2 or DSD-like DHs are more biased to only one of both properties.

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Thermochemistry and kinetics rule the chemical reactivity of molecular systems. The former studies the equilibrium state between reactants and products and delivers the concept of reaction yield. The latter focuses on the path followed by the transformation of reactants into products, and particularly to the rate constant driving the reversibility of the reaction. Both fields rely on two different energy quantities that have been routinely assessed at theoretical chemistry level along the last century as the reaction and barrier height energies (RE and BH, respectively).¹

RE is the energy variation between products (P) and reactants (R). Here dubbed ΔE_{RE} , it is defined as

$$\Delta E_{\text{RE}} = E_{\text{P}} - E_{\text{R}}, \quad (1)$$

where E_{R} and E_{P} are the energies of the reactant and product at their minimum-energy structures, respectively. Dubbed ΔE_{BH}^i , the BH energy involves a third quantity, namely the energy of the transition-state (TS) structure E_{TS} which connects R and P. According to its definition, ΔE_{BH}^i characterizes a forward ($i = f$) or reverse ($i = r$) reaction

$$\Delta E_{\text{BH}}^i = E_{\text{TS}} - E_{\text{min}}, \quad (2)$$

where E_{min} refers to the minimum energy structure of R or P whether a forward or reverse process is targeted.

The computation of these energy quantities requires a robust computational chemistry protocol that guarantees an homogeneous and reproducible accuracy while conserving a daily affordable cost when applied to sizable molecular systems.²⁻⁵ Within the computational energy landscape, highly accurate *ab initio* composite methods (*e.g.*, WnX)^{4,6,7} are often claimed as being the ‘Holy Grail’ of reactivity. However, even alleviated by the domain-based local pair natural orbital (DLPNO) framework,⁸⁻¹¹ their computational cost prevents them from being applied to very large molecules commonly employed in chemistry. For these reasons, electronic structure methods, and notably the Kohn-Sham variant of density-functional theory (KS-DFT), has continuously drawn attention since the middle of the 80’s.^{12,13}

KS-DFT cost/accuracy trade-off has indeed regularly improved with the recurrent efforts done by the community to develop new and sophisticated density-functional approximations (DFAs).^{14,15} The double-hybrid (DH) class of approximations is one of their modern (striking) representation.¹⁶⁻¹⁹ By adding nonlocality to both the exchange and correlation energies, it systematically improves the well-known and widely used global-hybrid class of approximations.²⁰

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The exchange-correlation energy term is now defined as

$$E_{xc}^{\text{DH}}[\rho] = a_x E_x^{\text{EXX}}[\{\phi_i\}] + (1 - a_x) E_x^{\text{DFA}}[\rho] + a_c E_c^{\text{PT2}}[\{\phi_i, \phi_a\}] + (1 - a_c) E_c^{\text{DFA}}[\rho], \quad (3)$$

where a_x and $(1 - a_x)$ govern the fractions of nonlocal exact-like (EXX) and semilocal DFA exchange energies, respectively, which depend on the set of occupied orbitals $\{\phi_i\}$. a_c and $(1 - a_c)$ denote the parts of second-order perturbation theory (PT2) correlation energy and its semilocal complementary, respectively, the former adding also a dependence on the set of virtual orbitals $\{\phi_a\}$.

In literature, the DH class of approximation and its adaptations into range-separated exchange and/or correlation,^{21–24} and/or spin-component-scaled variants,^{25–29} are often found as overperforming other exchange-correlation approximations in extensive benchmark sets probing for energy,^{30–32} structure^{33,34} and density-based properties.^{35,36} On the one hand, their large fraction of EXX energy (mostly $a_x > 50\%$) helps to cancel the self-interaction error (SIE)^{37,38} which spuriously contaminates elongated bonds in TS structures resulting in an underestimation of energy BHs. On the other hand, their PT2 energy term brings the nonlocal dynamic correlation required to accurately describe covalent bond energies, and thus REs. It is thus expected, and confirmed on some previous benchmark sets, that DHs are excellent candidates to model reactivity of molecular systems.^{27,29,39–42}

In kinetics and thermochemistry, 1.4 kcal mol⁻¹ is often recalled as being the ‘chemical accuracy’ threshold for an accurate determination of BHs and REs.¹ At room temperature, it corresponds to an error of about one order of magnitude for equilibrium or rate constants. With the aim to identify which variant of DHs is able to reach this energy threshold for a wide variety of molecular reactions, we will thus assess these expressions on the newly developed BH9 comprehensive benchmark set for BHs and REs.⁴³ The dataset contains a total of 449 real-size molecular reactions and 898 barrier heights (*i.e.*, 449 forward and 449 reverse BHs), all of them characterized by reference energies computed at the DLPNO coupled-cluster singles and doubles plus perturbative triples [CCSD(T)] level of theory at the complete basis set limit (CBS). DLPNO-CCSD(T) is indeed becoming a standard owing to its linearly-scaled computational cost and high accuracy (tenth of kcal mol⁻¹) with respect to pristine CCSD(T). It is thus an excellent compromise to obtain reference energy values for large systems like those implied in BH9.^{43,44}

During the reviewing process of this communication, one of the reviewer warned us about the presence of some unreliable reference barrier height and reaction energies in the original publi-

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cation of the BH9 dataset. According to his advise and after discussion with the original authors of the dataset, we removed 15 entries,⁴⁵ reducing thus the size of the dataset to 434 real-size molecular reactions and 868 barrier heights.

The originality of BH9 is not only its extensive size which guarantees the calculation of robust error bars, but also the chemical diversity of the molecular systems (reaching 71 atoms) involved and the energy diversity of their reactions. More precisely, it probes for 9 types of reactions involved in highly important organic and biochemistry reactions. They belong to (i) radical rearrangement and addition, (ii) pericyclic, (iii) halogen atom transfer, (iv) hydrogen atom transfer, (v) hydride transfer, (vi) B- and Si- containing reactions, (vii) proton transfer, (viii) nucleophilic substitution, and (ix) nucleophilic addition.

Table I gathers the performance of a set of 10 pristine DHs augmented by their dispersion-corrected variants on the BH9 barrier height energy database (see Table SI of Supplementary Material⁴⁶ for more detailed informations about their composition). They are selected to be representative of the modern DH variety, *i.e.*, to belong to (i) nonempirical, minimally or highly parameterized DHs,⁴⁷ (ii) global or range-separated exchange DHs, (iii) spin-component-scaled DHs, and (iv) dispersion-corrected with Grimme's -D3(BJ) model.^{48,49} For the BH energy property, the total mean absolute deviations (MADs) span between 1.71 (PBE0-DH) and 4.89 kcal mol⁻¹ (RSX-0DH), and the MADs calculated from subsets are relatively homogeneous with the related total MAD. We notice however that in average DHs tend to better perform on subsets (vi), (vii), and (ix), but obtain worse MADs on subset (iii).

The best performance is reached by the PBE0-DH nonempirical global DH (1.71 kcal mol⁻¹), and by the dispersion-corrected and uncorrected variants of ω B2PLYP, a minimally parameterized range-separated exchange (RSX) DH trained to accurately reproduce excitation energies (1.72 and 1.73 kcal mol⁻¹, respectively). They are followed by the PBE-QIDH nonempirical global DH (1.93 kcal mol⁻¹), by B2K-PLYP (2.08 kcal mol⁻¹), a minimally parameterized DH trained for kinetics purpose, and by their dispersion-corrected variants (2.38 and 2.53 kcal mol⁻¹, respectively). We find then the highly parameterized ω B97X-2 RSX-DH (2.80 kcal mol⁻¹), its dispersion corrected variant (2.81 kcal mol⁻¹), and PBE0-DH-D3(BJ) (2.86 kcal mol⁻¹). The remaining 8 DHs considered in this work provide deviations larger than 3 kcal mol⁻¹, *i.e.* deviations larger than ~ 2 times the 'chemical accuracy' threshold.

Even if it seems difficult to rationalize trends between the nature of the DHs and their performances, it is easy to realize that the on-top addition of the -D3(BJ) correction systematically

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deteriorates, or at least marginally improves for few of them, the estimation of BH energies (Table I). It is generally found an overstabilization of the TS with respect to reactants and products, leading to underestimation of BHs induced by a double counting of dispersion forces (see mean signed deviations in Table SII of Supplementary Material⁴⁶). This behavior confirms some previous investigations showing that a dispersion correction does not *a fortiori* improve the accuracy of nonempirical DHs.⁵⁰ However, it contradicts some others which highly recommend to systematically add it on-top of a DH.^{31,51}

In terms of performance/features rationalization, it is worth noting that nonempirical global DHs including between 50 to 70% of EXX, and between 10 to 35% of PT2 correlation energies, provide promising results. It is however not the case of their RSX variants. We remark also that to get an accurate measure of BH energies, minimally parameterized global DHs need to include a large fraction of EXX ($\sim 70\%$) and PT2 correlation energies ($\sim 40\%$) like in B2K-PLYP, while the performance of B2-PLYP ($a_x = 0.53$ and $a_c = 0.27$) remains more modest. Finally, we note the excellent performance of ω B2PLYP which is the only RSX-DH able to well behave with respect to BHs.

At this point, it is also important to compare the DH performances with respect to other (non-DH) density-functional approximations reported in Ref. 43. The comparison is of course not completely strict since we removed here 30 troublemaker BHs energies from the original BH9 dataset.⁴⁵ However, it provides a (slightly overestimated) flavour of their MADs. On this line, only some global- or RSX-hybrid approximations displays MADs lower than 3 kcal mol⁻¹. Among them, we note highly parameterized density functionals from the Head-Gordon (*e.g.*, ω B97M-V⁵² and ω B97XD⁵³) or Truhlar (*e.g.*, M05-2X,⁵⁴ M06-2X⁵⁵ and MN15⁵⁶) groups for which the BH property is an integral part of their training set, and MADs compete with the best DHs (MADs between 2.1 and 2.3 kcal mol⁻¹). Good results are also found with the CAM-B3LYP⁵⁷ minimally parameterized RSX and PBE0^{58,59} nonempirical global hybrids when coupled with the XDM dispersion correction^{60,61} (2.37 and 2.85 kcal mol⁻¹, respectively). Unlike with DHs (exception made with Minnesota density functionals), we notice here that the on-top addition of a dispersion correction is recommended.

Looking now at the BH9 database from the thermochemistry point of view, Table II gathers the performance of all DHs on REs. For most of the DHs, the total MADs are here better than for BHs. They span from 1.37 to 6.24 kcal mol⁻¹ with a better average performance on subsets (v) and (vii) than on subset (i). The best approach is the highly parameterized ω B97X-2 range-separated

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exchange DH (1.37 kcal mol⁻¹). It is directly followed by the minimally parameterized DSD-PBEP86-D3(BJ) and DSD-BLYP-D3(BJ) spin-component scaled, and B2K-PLYP-D3(BJ) global DHs (1.56, 1.63 and 1.72 kcal mol⁻¹, respectively), all of them being corrected for dispersion forces. We find then the ω B2PLYP range-separated exchange DH (2.10 kcal mol⁻¹), and the PBE0-DH and PBE-QIDH nonempirical DHs (2.23 and 2.48 kcal mol⁻¹, respectively). The last one yielding a MAD below 3 kcal mol⁻¹ is B2-PLYP-D3(BJ), a minimally parameterized DH corrected for dispersion interactions. The 6 other approaches considered in this work are above this threshold.

Except for B2K-PLYP and B2-PLYP, we notice that -D3(BJ) overcorrects REs of all DHs considered in this work. The larger improvements are of about 0.5 kcal mol⁻¹ for the former and 1.4 kcal mol⁻¹ for the latter. They are obtained for pericyclic reactions [subset (ii)]. Just like within the Diels-Alder reaction (DARC) testset,⁶² the repulsive nonbonded interactions at highly compressed distance ruling the reactants are overestimated, leading to their larger destabilization with respect to the product (see mean signed deviations in Table SIII of Supplementary Material⁴⁶). Even if this error is claimed to be closely related to SIE,⁶² -D3(BJ) artificially stabilizes the product and improves the estimation of the RE property. This observation is confirmed by the good performance of the ω B2PLYP RSX-DH variant which better corrects SIE. The other subsets are revealed as less affected by the use of the *a posteriori* correction.

The performance/features trade-off is less restrictive for the estimation of RE than for BH energies. Except nonempirical RSX-DHs and B2-PLYP, most of the DHs tested in this work provide excellent performances with respect to this property. This is however not the case for other density-functional approximations as semilocal or hybrids. Like for BHs, highly parameterized global and RSX hybrids from the Head-Gordon and Truhlar groups compete with the best DHs even if MADs are biased by 15 more troublemaker REs.^{43,45} The best performance is found for ω B97M-V (1.62 kcal mol⁻¹) and the deviations remain below 3 kcal mol⁻¹ for M05-2X, M06-2X and ω B97XD. Other approximations are found less accurate than DHs.

Since the accuracy in kinetics and thermochemistry is ruled by the ‘chemical accuracy’ energy threshold, Figure 1 depicts the success of DHs in reaching it for BH and RE properties. It is calculated as the number of reactions included in the BH9 database with an absolute energy error lower than 1.4 kcal mol⁻¹ divided by the total number of reactions. The higher this percentage is, the better a DH fulfills the ‘chemical accuracy’ criteria. At a first glance, most of the DHs investigated here gather a similar success for BH and RE properties. Only the ω B97X-2 and

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ω B97X-2-D3(BJ) highly, and DSD-PBEP86-D3(BJ), DSD-BLYP-D3(BJ) and B2-PLYP-D3(BJ) minimally parameterized DHs display unbalanced performance *versus* both properties. ω B97X-2 is by far the most successful in predicting REs (67.5%). Its parameterization is likely the source of its large success. However, it is also probably at the origin of its poor success with respect to BHs (27.4%). Similar remarks can be made for DSD-PBEP86-D3(BJ) and DSD-BLYP-D3(BJ), and in a lower extent to B2-PLYP-D3(BJ).

The other DHs provide a well balanced and more stable success *versus* both properties, proving that the parameterization of a DFA can give an unbalanced performance (Figure 1). The best DH is ω B2PLYP while the worse is B2-PLYP-D3(BJ). Their successes are of about 51.7% (41.7%) and 17.5% (42.4%) for BH (RE), respectively. In between, the B2K-PLYP minimally parameterized, and PBE0-DH and PBE-QIDH nonempirical global DHs are found as very promising with a success ranging from 45 to 49% for BH, and from 35 and to 49% for REs. The other DHs present a more moderate success positioned around 30% for both properties.

Despite their excellent performance, DHs are often criticized for their larger computational cost with respect to more standard DFAs. It scales as $O(n^5)$ (n referring to the size of the basis set) compared with $O(n^4)$ for standard hybrids. Even if it is common practice to alleviate their computational effort by using the resolution-of-the-identity (RI) or similar fitting techniques, we recently developed a novel protocol able to reduce again the computational cost, and extend in the same time their domain of applicability (in terms of molecular size). Dubbed *DHthermo*,⁶³ the protocol rests on the development of a small split-valence basis set (DH-SVPD),⁶⁴ which by error compensation between basis set superposition and basis set incompleteness errors (BSSE and BSIE, respectively), assures a good performance for a DH at a relatively cheap computational effort. Since *DHthermo* turns out to be a protocol of choice to model the thermochemistry properties of hydrocarbons,^{63,65,66} we investigate here its impact while assessing the kinetics and thermochemistry properties of reactions gathered into the BH9 database. Figure 2 compares the MADs of 8 DHs uncorrected for dispersion forces and calculated over the 9 subsets with the very large def2-QZVPP and small DH-SVPD basis sets. At a first glance, we observe that most of the correlation points (*i.e.*, 83% for BHs and 83% for REs) are located lower to the diagonal, *i.e.* that DHs better perform at def2-QZVPP level than at DH-SVPD level. However, this loss of accuracy goes well with a large saving in computational effort. For instance, the full assessment of the BH9 database costs 130.4 *versus* 27.5 wall-time hours on Intel Xeon Gold 6134 (3.20GHz) CPUs at def2-QZVPP and DH-SVPD levels, respectively, that corresponds to a saving factor of 4.7.

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Going deeper into details, we remark that just like dispersion corrections, the loss of accuracy provided by DH-SVPD is a consequence of an underestimation of BHs and REs (see mean signed deviations in Tables SIV and SV of Supplementary Material⁴⁶). Over the 8 dispersion-uncorrected DHs assessed in this work, 21% (54%) of subsets are in the conic area of $\pm 20\%$ ($\pm 40\%$) error for the BH property. It is of about 33% (60%) for the RE property. Nevertheless, coupling DH-SVPD to a DH tends to improve the estimation of BHs for subsets (i), (iii) and (viii), and of REs for subsets (iv), (v) and (vii).

In summary, by assessing 868 BHs and 434 REs contained into the novel and extended BH9 database, we show that DHs can provide a statistically-verified and accurate answer to the kinetics and thermochemistry modeling issue. Over the whole set of BHs and REs, minimally parameterized DHs like ω B2PLYP or B2K-PLYP, and nonempirical DHs like PBE0-DH and PBE-QIDH succeed to reach the ‘chemical accuracy’ energy threshold by more than 40% for both properties in a balanced fashion. This success corresponds to MADs lower than $2.5 \text{ kcal mol}^{-1}$. Other DHs like the highly parameterized ω B97X-2, or minimally parameterized DSD-PBEP86-D3(BJ) and DSD-BLYP-D3(BJ) spin-component-scaled DHs provide also an excellent estimate of RE properties. Their performance remains however lower than expected probably due to their empirical parameterization. Furthermore, we notice that coupling an empirical dispersion correction like -D3(BJ) to a DH tends to deteriorate its accuracy. Unlike with more standard semilocal or hybrid DFAs,⁴³ we thus discourage their use for this type of investigation.

Computational details: All the computations are performed with the release 5.0 of Orca.⁶⁷ For each energy single point, a tight SCF convergence criteria together with the DefGrid3 integration grid are taken as default. The BH9 database is both assessed with the very large def2-QZVPP Ahlrichs’ quadruple- ζ ⁶⁸ and small DH-SVPD split-valence⁶⁴ basis sets, the former assuring a nearly complete basis set convergence and minimizing BSSE while the latter assuming compensation between BSSE and BSIE. The DH-SVPD basis set being only available for H, C, N and O, we replace it by def2-SVPD for the missing elements.^{68,69} The resolution-of-the-identity in combination with the ‘chain-of-spheres’ algorithm⁷⁰ (COSX) and an automatic construction of a general purpose auxiliary basis set is systematically turned on.

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SUPPLEMENTARY MATERIAL

Mean signed and absolute deviations regarding all the subsets and density-functional approximations investigated herein are reported within the Supplementary Material.

DATA AVAILABILITY

The data that supports the findings of this study are available within the article [and its supplementary material].

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REFERENCES

- ¹K. N. Houk and F. Liu, *Acc. Chem. Res.* **50**, 539 (2017).
- ²J. M. Martin, *Annu. Rep. Comput. Chem.* **1**, 31 (2005).
- ³D. A. Dixon, D. Feller, and K. A. Peterson, *Annu. Rep. Comput. Chem.* **8**, 1 (2012).
- ⁴A. Karton, *WIREs Comput. Mol. Sci.* **6**, 292 (2016).
- ⁵E. Semidalas and J. M. Martin, *J. Chem. Theory Comput.* **18**, 883 (2022).
- ⁶A. Karton, N. Sylvetsky, and J. M. L. Martin, *J. Comput. Chem.* **38**, 2063 (2017).
- ⁷B. Chan, *Pure Appl. Chem.* **89**, 699 (2017).
- ⁸C. Riplinger and F. Neese, *J. Chem. Phys.* **138**, 034106 (2013).

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- ⁹P. Pinski, C. Riplinger, E. F. Valeev, and F. Neese, *J. Chem. Phys.* **143**, 034108 (2015).
- ¹⁰C. Riplinger, P. Pinski, U. Becker, E. F. Valeev, and F. Neese, *J. Chem. Phys.* **144**, 024109 (2016).
- ¹¹Y. Guo, C. Riplinger, U. Becker, D. G. Liakos, Y. Minenkov, L. Cavallo, and F. Neese, *J. Chem. Phys.* **148**, 011101 (2018).
- ¹²W. Kohn and L. J. Sham, *Phys. Rev.* **140**, A1133 (1965).
- ¹³P. Hohenberg and W. Kohn, *Phys. Rev.* **136**, B864 (1964).
- ¹⁴H. S. Yu, S. L. Li, and D. G. Truhlar, *J. Chem. Phys.* **145**, 130901 (2016).
- ¹⁵A. D. Becke, *J. Chem. Phys.* **140**, 18A301 (2014).
- ¹⁶J. C. Sancho-Garcia and C. Adamo, *Phys. Chem. Chem. Phys.* **15**, 14581 (2013).
- ¹⁷L. Goerigk and S. Grimme, *WIREs Comput. Mol. Sci.* **4**, 576 (2014).
- ¹⁸N. Q. Su and X. Xu, *WIREs Comput. Mol. Sci.* **6**, 721 (2016).
- ¹⁹J. M. L. Martin and G. Santra, *Isr. J. Chem.* **60**, 787 (2020).
- ²⁰E. Brémond, M. Savarese, A. J. Pérez-Jiménez, J. C. Sancho-García, and C. Adamo, *J. Phys. Chem. Lett.* **6**, 3540 (2015).
- ²¹É. Brémond, Á. J. Pérez-Jiménez, J. C. Sancho-García, and C. Adamo, *J. Chem. Phys.* **150**, 201102 (2019).
- ²²M. Casanova-Páez, M. B. Dardis, and L. Goerigk, *J. Chem. Theory Comput.* **15**, 4735 (2019).
- ²³É. Brémond, M. Savarese, Á. J. Pérez-Jiménez, J. C. Sancho-García, and C. Adamo, *J. Chem. Theory Comput.* **14**, 4052 (2018).
- ²⁴I. Y. Zhang and X. Xu, *J. Phys. Chem. Lett.* **4**, 1669 (2013).
- ²⁵É. Brémond, M. Savarese, J. C. Sancho-García, Á. J. Pérez-Jiménez, and C. Adamo, *J. Chem. Phys.* **144**, 124104 (2016).
- ²⁶I. Y. Zhang, N. Q. Su, E. Brémond, C. Adamo, and X. Xu, *J. Chem. Phys.* **136**, 174103 (2012).
- ²⁷S. Kozuch and J. M. L. Martin, *Phys. Chem. Chem. Phys.* **13**, 20104 (2011).
- ²⁸I. Y. Zhang, X. Xu, Y. Jung, and W. A. Goddard, *Proc. Natl. Acad. Sci. USA* **108**, 19896 (2011).
- ²⁹S. Kozuch, D. Gruzman, and J. M. L. Martin, *J. Phys. Chem. C* **114**, 20801 (2010).
- ³⁰A. Najibi, M. Casanova-Páez, and L. Goerigk, *J. Phys. Chem. A* **125**, 4026 (2021).
- ³¹L. Goerigk, A. Hansen, C. Bauer, S. Ehrlich, A. Najibi, and S. Grimme, *Phys. Chem. Chem. Phys.* **19**, 32184 (2017).
- ³²E. Brémond, I. Ciofini, J. C. Sancho-García, and C. Adamo, *Acc. Chem. Res.* **49**, 1503 (2016).
- ³³C. Puzzarini and V. Barone, *Acc. Chem. Res.* **51**, 548 (2018).

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- ³⁴E. Brémond, M. Savarese, N. Q. Su, A. J. Pérez-Jiménez, X. Xu, J. C. Sancho-García, and C. Adamo, *J. Chem. Theory Comput.* **12**, 459 (2016).
- ³⁵É. Brémond, V. Tognetti, H. Chermette, J. C. Sancho-García, L. Joubert, and C. Adamo, *J. Chem. Theory Comput.* **18**, 293 (2022).
- ³⁶G. L. Stoychev, A. A. Auer, and F. Neese, *J. Chem. Theory Comput.* **14**, 4756 (2018).
- ³⁷J. L. Bao, L. Gagliardi, and D. G. Truhlar, *J. Phys. Chem. Lett.* **9**, 2353 (2018).
- ³⁸A. J. Cohen, P. Mori-Sánchez, and W. Yang, *Science* **321**, 792 (2008).
- ³⁹G. Santra, M. Cho, and J. M. L. Martin, *J. Phys. Chem. A* **125**, 4614 (2021).
- ⁴⁰I. Y. Zhang, N. Q. Su, É. A. G. Brémond, C. Adamo, and X. Xu, *J. Chem. Phys.* **143**, 187102 (2015).
- ⁴¹A. Karton, A. Tarnopolsky, J.-F. Lamère, G. C. Schatz, and J. M. L. Martin, *J. Phys. Chem. A* **112**, 12868 (2008).
- ⁴²A. Tarnopolsky, A. Karton, R. Sertchook, D. Vuzman, and J. M. L. Martin, *J. Phys. Chem. A* **112**, 3 (2008).
- ⁴³V. K. Prasad, Z. Pei, S. Edelmann, A. Otero-de-la Roza, and G. A. DiLabio, *J. Chem. Theory Comput.* **18**, 151 (2022).
- ⁴⁴D. G. Liakos, Y. Guo, and F. Neese, *J. Phys. Chem. A* **124**, 90 (2020).
- ⁴⁵Due to the presence of unreliable reference energies, we removed the following 15 entries from the pristine BH9 dataset. They are: 41: 01_41, 45: 01_45, 47: 01_47, 197: 03_9, 204: 03_16, 205: 03_17, 207: 03_19, 263: 04_32, 264: 04_33, 265: 04_34, 271: 04_40, 306: 04_75, 311: 04_80, 317: 04_86, 319: 04_88.
- ⁴⁶See supplementary material at [URL will be inserted by AIP] for details about the definition of the density functionals used herein and a detailed description of their performance.
- ⁴⁷The parameterization of DHs is considered as (i) nonempirical in case its constants are identified to limit physical constraints, (ii) minimally parameterized in case it contains few empirical parameters, typically 1 to 5, and (iii) highly parameterized in case it contains more than 5 empirical parameters.
- ⁴⁸S. Grimme, J. Antony, S. Ehrlich, and H. Krieg, *J. Chem. Phys.* **132**, 154104 (2010).
- ⁴⁹S. Grimme, S. Ehrlich, and L. Goerigk, *J. Comput. Chem.* **32**, 1456 (2011).
- ⁵⁰D. Bousquet, E. Brémond, J. C. Sancho-García, I. Ciofini, and C. Adamo, *Theor. Chem. Acc.* **134**, 1602 (2014).
- ⁵¹N. Mehta, M. Casanova-Páez, and L. Goerigk, *Phys. Chem. Chem. Phys.* **20**, 23175 (2018).

Communication

- ⁵²N. Mardirossian and M. Head-Gordon, *Phys. Chem. Chem. Phys.* **16**, 9904 (2014).
- ⁵³J.-D. Chai and M. Head-Gordon, *Phys. Chem. Chem. Phys.* **10**, 6615 (2008).
- ⁵⁴Y. Zhao, N. E. Schultz, and D. G. Truhlar, *J. Chem. Theory Comput.* **2**, 364 (2006).
- ⁵⁵Y. Zhao, N. E. Schultz, and D. G. Truhlar, *Theor. Chem. Acc.* **120**, 215 (2008).
- ⁵⁶H. S. Yu, X. He, S. L. Li, and D. G. Truhlar, *Chem. Sci.* **7**, 5032 (2016).
- ⁵⁷T. Yanai, D. P. Tew, and N. C. Handy, *Chem. Phys. Lett.* **393**, 51 (2004).
- ⁵⁸C. Adamo and V. Barone, *J. Chem. Phys.* **110**, 6158 (1999).
- ⁵⁹M. Ernzerhof and G. E. Scuseria, *J. Chem. Phys.* **110**, 5029 (1999).
- ⁶⁰A. D. Becke and E. R. Johnson, *J. Chem. Phys.* **127**, 154108 (2007).
- ⁶¹A. D. Becke and E. R. Johnson, *J. Chem. Phys.* **127**, 124108 (2007).
- ⁶²E. R. Johnson, P. Mori-Sánchez, A. J. Cohen, and W. Yang, *J. Chem. Phys.* **129**, 204112 (2008).
- ⁶³H. Li, B. Tirri, E. Brémond, J. C. Sancho-García, and C. Adamo, *J. Org. Chem.* **86**, 5538 (2021).
- ⁶⁴J. S. García, É. Brémond, M. Campetella, I. Ciofini, and C. Adamo, *J. Chem. Theory Comput.* **15**, 2944 (2019).
- ⁶⁵H. Li, E. Brémond, J. C. Sancho-García, and C. Adamo, *RSC Adv.* **11**, 26073 (2021).
- ⁶⁶A. Gosset, S. N. Lachmanová, S. Cherraben, G. Bertho, J. Forté, C. Perruchot, H.-P. J. de Rouville, L. Pospíšil, M. Hromadová, É. Brémond, and P. P. Lainé, *Chem. Eur. J* **27**, 17889 (2021).
- ⁶⁷F. Neese, F. Wennmohs, U. Becker, and C. Riplinger, *J. Chem. Phys.* **152**, 224108 (2020).
- ⁶⁸F. Weigend and R. Ahlrichs, *Phys. Chem. Chem. Phys.* **7**, 3297 (2005).
- ⁶⁹D. Rappoport and F. Furche, *J. Chem. Phys.* **133**, 134105 (2010).
- ⁷⁰F. Neese, F. Wennmohs, A. Hansen, and U. Becker, *Chem. Phys.* **356**, 98 (2009).
- ⁷¹E. Brémond and C. Adamo, *J. Chem. Phys.* **135**, 024106 (2011).
- ⁷²E. Brémond, J. C. Sancho-García, A. J. Pérez-Jiménez, and C. Adamo, *J. Chem. Phys.* **141**, 031101 (2014).
- ⁷³J. C. Sancho-García, E. Brémond, M. Savarese, A. J. Pérez-Jiménez, and C. Adamo, *Phys. Chem. Chem. Phys.* **19**, 13481 (2017).
- ⁷⁴A. Karton and L. Goerigk, *J. Comput. Chem.* **36**, 622 (2015).
- ⁷⁵J.-D. Chai and M. Head-Gordon, *J. Chem. Phys.* **131**, 174105 (2009).
- ⁷⁶S. Kozuch and J. M. L. Martin, *J. Comput. Chem.* **34**, 2327 (2013).
- ⁷⁷S. Grimme, *J. Chem. Phys.* **124**, 034108 (2006).
- ⁷⁸L. Goerigk and S. Grimme, *Phys. Chem. Chem. Phys.* **13**, 6670 (2011).

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TABLE I. Mean absolute deviations (kcal mol^{-1}) over the 9 subsets of the BH9 barrier height energy database (868 entries) computed with the 18 double hybrids considered in this work at the def2-QZVPP level of theory.

	Ref.	(i)	(ii)	(iii)	(iv)	(v)	(vi)	(vii)	(viii)	(ix)	total
PBE0-DH	71	1.53	1.95	1.51	1.58	1.84	1.34	1.55	2.72	1.25	1.71
ω B2PLYP-D3(BJ)	22	1.69	2.23	0.94	1.69	1.23	1.47	1.73	1.68	1.47	1.72
ω B2PLYP	22,30	1.69	2.23	1.00	1.60	1.41	1.52	1.69	1.74	1.47	1.73
PBE-QIDH	72	2.04	2.39	1.62	1.31	2.52	1.52	1.28	2.06	1.46	1.93
B2K-PLYP	42	2.08	2.96	1.32	1.32	2.78	1.74	0.62	1.21	1.16	2.08
PBE-QIDH-D3(BJ)	72,73	2.06	2.88	1.13	1.94	4.64	1.79	1.50	1.06	1.82	2.38
B2K-PLYP-D3(BJ)	42,74	2.02	3.58	1.21	1.69	5.32	0.87	0.74	1.44	1.47	2.53
ω B97X-2	75	1.98	3.95	1.77	2.22	4.49	1.35	1.38	2.02	1.67	2.80
ω B97X-2-D3(BJ)	51,75	1.98	3.96	1.77	2.22	4.50	1.36	1.38	2.02	1.67	2.81
PBE0-DH-D3(BJ)	50,71	1.98	2.99	1.80	3.39	4.87	2.53	1.91	0.93	2.33	2.86
DSD-PBEP86-D3(BJ)	76	2.30	3.70	1.65	2.55	7.29	1.47	1.29	2.15	1.98	3.11
B2-PLYP	77	1.46	5.00	2.57	1.91	3.69	2.52	1.19	1.85	2.34	3.15
RSX-QIDH-D3(BJ)	21,23,30	3.35	5.41	3.27	1.11	1.50	2.48	1.79	3.29	3.12	3.28
RSX-QIDH	21,23	3.34	5.35	3.52	1.06	1.82	2.52	1.71	3.58	3.07	3.32
DSD-BLYP-D3(BJ)	76	1.92	5.12	2.19	2.76	7.73	1.36	1.07	2.73	2.27	3.68
B2-PLYP-D3(BJ)	77,78	1.53	5.72	4.80	3.99	8.10	2.06	1.31	3.94	3.00	4.49
RSX-0DH-D3(BJ)	21,30	3.79	7.46	4.34	0.98	5.36	3.04	1.96	5.41	3.92	4.61
RSX-0DH	21	3.74	7.42	5.13	1.30	6.82	3.18	1.76	6.22	3.91	4.89

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TABLE II. Mean absolute deviations (kcal mol^{-1}) over the 9 subsets of the BH9 reaction energy database (434 entries) computed with the 18 double hybrids considered in this work at the def2-QZVPP level of theory.

	Ref.	(i)	(ii)	(iii)	(iv)	(v)	(vi)	(vii)	(viii)	(ix)	total
ω B97X-2	75	2.51	0.91	1.90	1.89	0.62	1.33	0.52	1.47	0.96	1.37
ω B97X-2-D3(BJ)	51,75	2.51	0.91	1.90	1.89	0.62	1.33	0.52	1.47	0.96	1.37
DSD-PBEP86-D3(BJ)	76	2.90	1.09	1.95	2.07	0.62	1.51	0.67	1.47	1.59	1.56
DSD-BLYP-D3(BJ)	76	2.43	1.48	1.77	2.02	1.08	1.38	0.55	1.52	1.28	1.63
B2K-PLYP-D3(BJ)	42,74	2.27	2.06	1.72	1.83	1.30	0.92	0.48	1.17	1.12	1.72
ω B2PLYP	22	2.14	3.27	1.01	1.10	1.71	1.88	0.49	1.05	2.60	2.10
ω B2PLYP-D3(BJ)	22,30	2.15	3.33	1.01	1.10	1.70	1.99	0.49	1.06	2.66	2.13
PBE0-DH	71	2.98	3.06	2.33	1.53	1.28	1.24	0.96	1.50	2.22	2.23
B2K-PLYP	42	2.26	3.33	1.77	1.85	1.37	1.71	0.48	1.26	1.44	2.23
PBE-QIDH	72	3.70	3.79	1.36	1.72	0.90	1.46	0.67	1.19	2.82	2.48
B2-PLYP-D3(BJ)	77,78	1.87	5.06	1.48	1.44	1.40	0.99	1.03	1.77	1.77	2.64
PBE-QIDH-D3(BJ)	72,73	3.86	4.67	1.33	1.74	0.83	2.32	0.67	1.14	3.54	2.89
PBE0-DH-D3(BJ)	50,71	3.91	4.98	1.89	1.49	1.15	3.30	0.95	1.49	4.43	3.18
B2-PLYP	77	2.57	7.99	1.90	1.52	1.54	3.82	1.03	1.83	3.75	4.07
RSX-QIDH	21,23	6.11	9.92	1.37	1.56	1.29	3.33	0.61	1.12	6.09	5.06
RSX-QIDH-D3(BJ)	21,23,30	6.14	10.07	1.37	1.56	1.28	3.56	0.61	1.14	6.22	5.14
RSX-0DH	21	7.44	12.05	1.59	1.19	1.85	3.79	0.81	1.45	6.97	6.00
RSX-0DH-D3(BJ)	21,30	7.54	12.51	1.55	1.21	1.83	4.55	0.81	1.54	7.36	6.24

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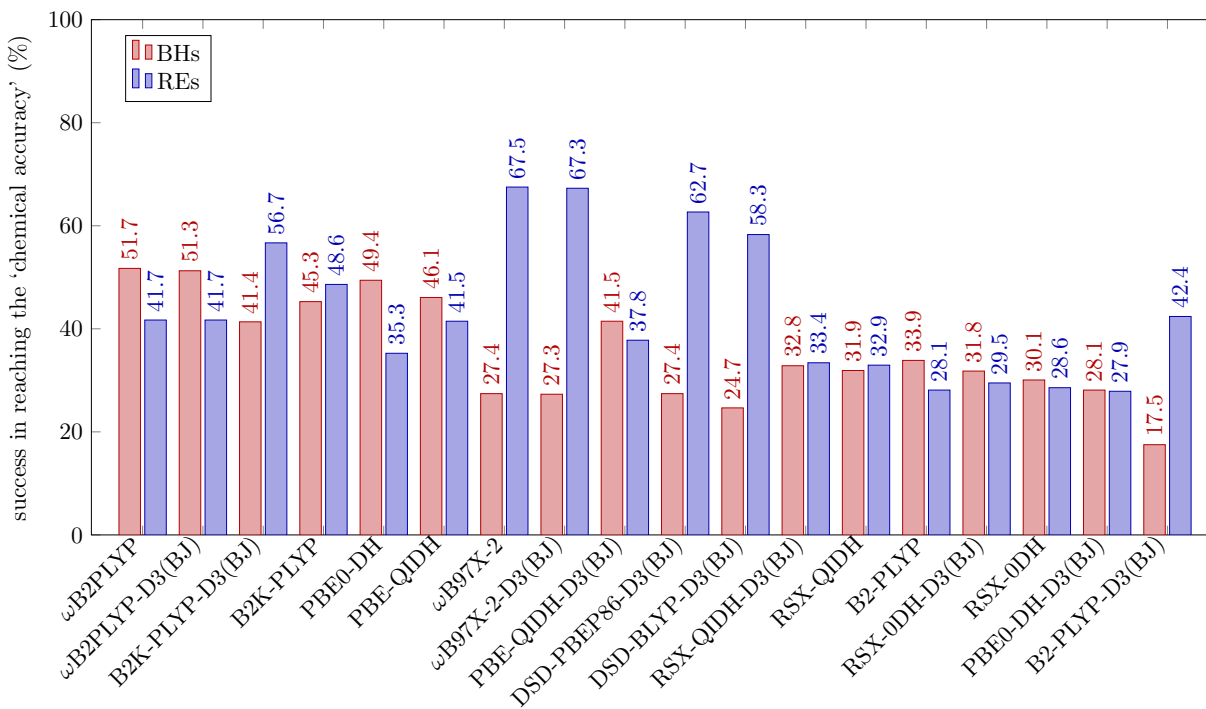


FIG. 1. Percentage of success of each DH in reaching the ‘chemical accuracy’ threshold ($1.4 \text{ kcal mol}^{-1}$) for the (red) 868 barrier height (BH) energies, and (blue) 434 reaction energies (RE). From left to right, DHs are ranked from the more to the less successful in reaching the ‘chemical accuracy’ threshold for both BH and RE properties.

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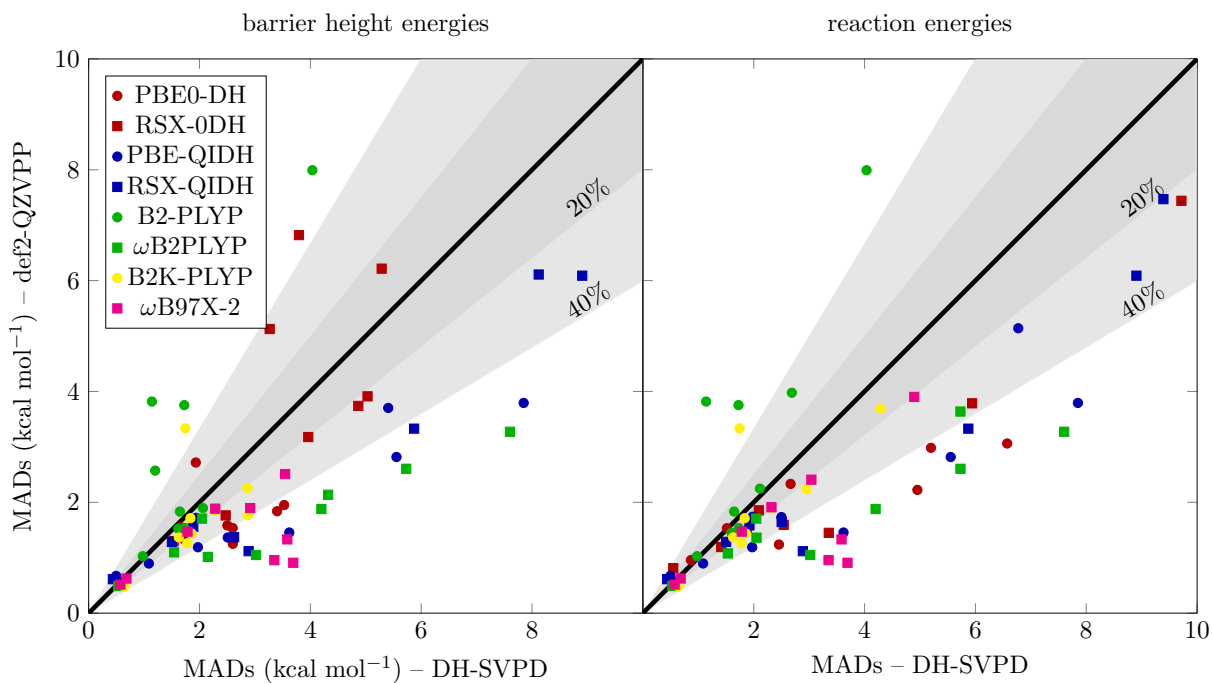
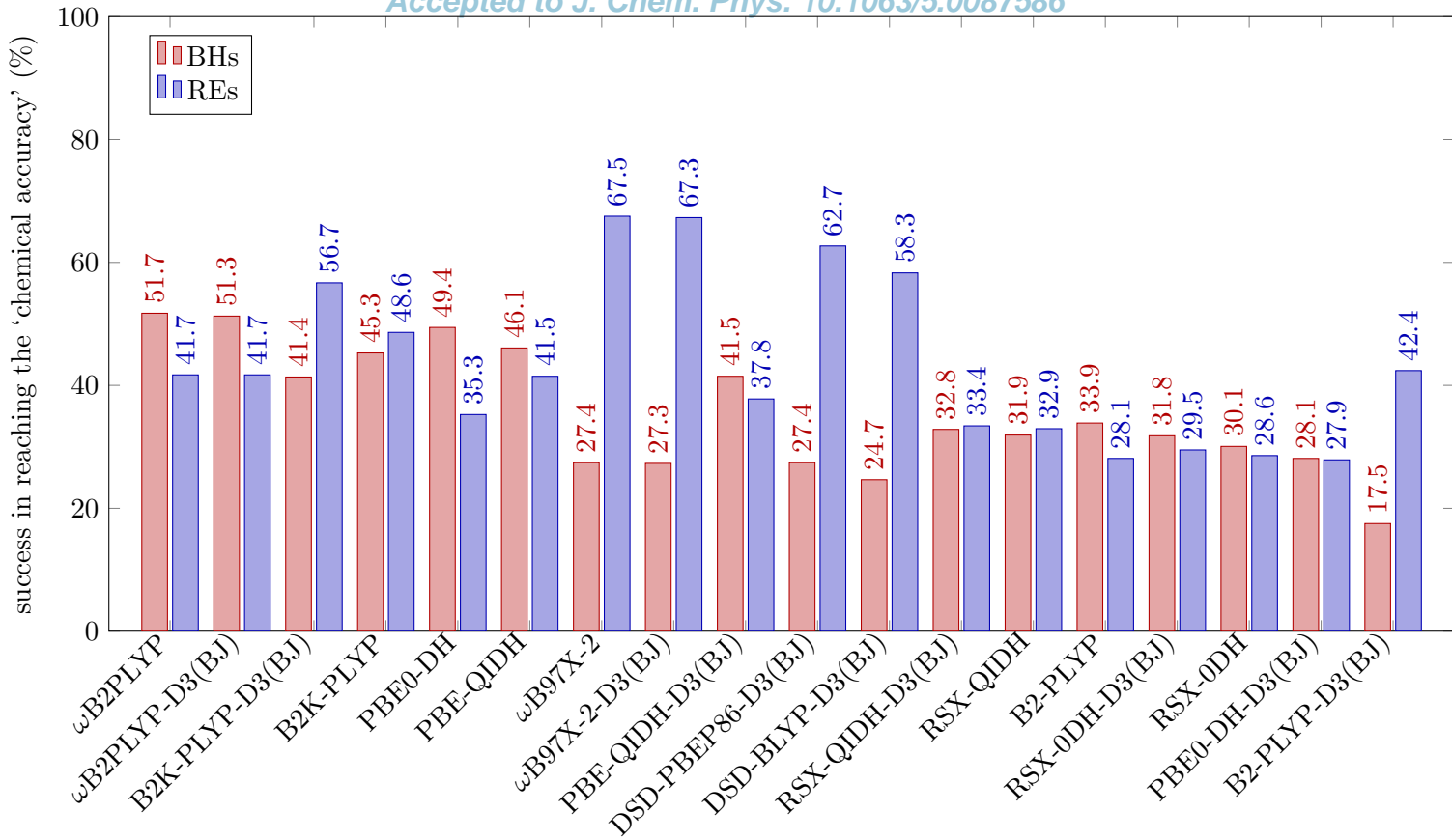


FIG. 2. Correlation diagrams comparing the mean absolute deviations (MAD in kcal mol^{-1}) calculated over the 9 subsets of the BH9 dataset at DH-SVPD and def2-QZVPP level of theories for (left) barrier height (BH) and (right) reaction energy (RE) properties. The thin and large gray areas depict a ± 20 and $\pm 40\%$ error with respect to the diagonal, respectively. A lower deviation to the diagonal indicates a better performance with the def2-QZVPP basis set.



barrier height energies

reaction energies

