

The Devil in the Details: What Everybody Should Know When Running DFT Calculations.

A Computational Chemistry Laboratory Notebook

by Pierpaolo Morgante and Roberto Peverati

This set of experiments has been designed with the goal of emphasizing technical details that are often overlooked when performing density functional theory (DFT) calculations. The implementation of graphical user interfaces (GUIs) like IQMol¹ and GaussView² has certainly helped in making computational chemistry programs more accessible. However, GUIs usually do not allow the users to control all the settings that are important when running a calculation. As a consequence, users end up with a lot of default parameters. Precautions have been taken to make the default settings up to date with the results of recent studies,^{3,4} but their blind usage does not represent good practice in computational chemistry.

This laboratory notebook is intended mainly as a guide for beginners or non-experts in the field, however, some of the experiments can be useful for experts in a research environment as well, since they highlight several overlooked aspects of DFT. We also show that computational databases are not only important for chemical research, but they can be effectively used as an educational tool as well. In fact, all of our structures are taken from the GMTKN55,⁵ MGCDDB84,⁶ or Minnesota 2015⁷⁻⁹ databases. The exercises are proposed as an introductory approach to DFT and they complement a Computational Chemistry class. They **DO NOT** represent suggestions for functionals or basis sets. Also, this lab notebook **IS NOT** a substitute for a textbook on the theoretical foundation of computational chemistry and DFT. Some pre-requisite notions that are required are: the nature of the many approximations to the exchange–correlation functional, the definition of a basis set, the construction of a real-space integration grid, usage of stability analysis techniques, and partial charges and orbital-localization techniques. A suggested list of textbooks for establishing or reviewing these notions is given at the bottom of the bibliography section at the end of this document.

Instructors will need to set up students to run calculations using a software that can handle Kohn–Sham density functional theory (KS–DFT). Calculations can be run on either commercial or open-source quantum chemistry programs, as long as the software includes the most common exchange–correlation (κ) functional approximations. In developing this lab notebook, we mainly used Gaussian and Q-Chem, but each experiment is easily portable to other quantum chemistry programs. The choice of whether to use a graphical user interface (GUI) or not, is left to the instructor as well. The notebook is structured so that single experiments can be separated from each other and distributed to the students week by week. Each experiment also includes all the necessary references, while an overall reference section with all the cited articles is also reported at the end of the notebook itself.

General advice for students:

- 1) All the calculations are performed in the gas phase.
- 2) All the reference energies are electronic energies and are given in kcal/mol (unless noted otherwise). Thermochemistry calculations are needed only in Experiment 9.
- 3) All the geometries are given in a separate folder.
- 4) Do NOT delete any files until the end of the lab. Try to keep them organized so that you can access them at any time.
- 5) Each calculation can be performed on a desktop computer and it should not take too long, even with the largest basis set.
- 6) Feel free to try more functionals, but do not forget to collect and present the results accordingly.

Experiment 0: An introductory note on how to classify *xc* functionals.

The design of a computational experiment should start with the identification of the chemical problem you wish to study. Then you should read the published literature⁵⁻¹³ to identify the best performing method for the problem at hand, and only after thorough bibliographical research you can start submitting calculations and experimenting with the analysis of the results. The next decision that you have to make when setting up a good computational experiment is the choice of an exchange-correlation (*xc*) functional and basis set. We usually use the term “method” to indicate a specific combination of *xc* functional and basis set.

In general, choosing a good method is not easy, and this is why you should rely on suggestions coming from experts in the field.^{4,16} The functionals you are going to use in this notebook represent suggestions for educational purpose, and we are not implicitly encouraging their use in a general research context. As stated at the beginning of this paragraph, we refer you to other publications⁵⁻¹⁶ for such suggestions. For good reviews of DFT, you can read refs. 6, 14, 15 or 16.

Before starting with the experiments in this notebook, you should know the most used acronyms in the DFT literature. As an example, you should be familiar with the common jargon that is used in the “Jacob’s Ladder of Density Functional Approximations” introduced by Perdew and Schmidt in 2001.¹⁷ Local Spin-Density Approximation (LSDA), Generalized Gradient Approximation (GGA), meta-GGA (mGGA), and hybrid and double-hybrid functionals, should not be a new concept to you. If they are, use the reference below to review these concepts before moving on to the next experiment. Verify your knowledge using the following problem.

Problem: Try to classify the following functionals as LSDA, GGA, mGGA, hybrid GGA (H-GGA), or hybrid mGGA (H-mGGA). Refer to the literature^{5-16,18} if you need help identifying some functionals. Hint: We will not deal with double-hybrids, so there are none in this table. For the appropriate references, see the following experiments.

Functional	SPW92	SVWN5	BP86	BLYP	PBE
Form					
Functional	M06-L	M11-L	MN15-L	SCAN	B97M-V
Form					
Functional	B3LYP	B3PW91	M05-2X	M06	M06-2X
Form					
Functional	M06-HF	M11	MN15	PBE0	ωB97M-V
Form					

References:

- 4) N. Mardirossian, and M. Head-Gordon, *J. Chem. Theory Comput.*, **2016**, 12, 4303–4325.
- 5) L. Goerigk, A. Hansen, C. Bauer, S. Ehrlich, A. Najibi and S. Grimme, *Phys. Chem. Chem. Phys.*, **2017**, 19, 32184–32215.
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Experiment 1: Applying DFT to Organic Chemistry – Part A.

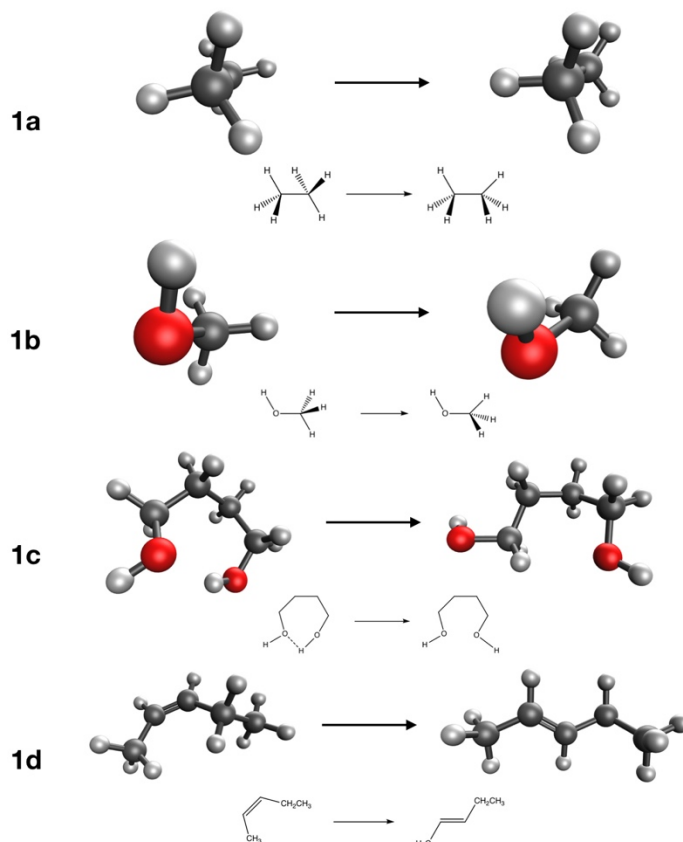


Figure 1 Reactions studied in Experiment 1. Rotational barrier of ethane (**1a**) and methanol (**1b**). Conformational change in two isomers of butane-1,4-diol (**1c**). Cis-trans isomerization reaction of pent-2-ene (**1d**). The carbon atoms are black, the oxygen atoms are red, and the hydrogen atoms are white. The dotted lines show hydrogen bonds.

In this first experiment, you will analyze four reactions that can be usually found in introductory organic chemistry textbooks (**Figure 1**). For the first reaction (**1a**) you will calculate the energy difference between the staggered and the eclipsed conformations of ethane. In the second reaction (**1b**), you will analyze the staggered and eclipsed conformation in methanol. For the third reaction (**1c**), you will look at a change of conformation in the butane-1,4-diol molecule. The last reaction (**1d**) is the isomerization reaction of *cis*-pent-2-ene to *trans*-pent-2-ene. The molecules in **1a-d** come from the BHROT27,⁵ the BUT14DIOL¹⁹ and FH51²⁰ subsets of the GMTKN55 database.⁵

The κ functional approximations we suggest to use are: SPW92^{21,22} (if not available, use SVWN5^{21,23}), BP86,^{24,25} BLYP,^{24,26} B3LYP,^{23,24,26-28} B3LYP-D3(BJ),^{23,24,26-29} B3PW91,^{22,24,27,30} PBE,³¹ PBE-D3(BJ),^{29,31} PBE0,³² M06-2X,³³ M11,³⁴ SCAN³⁵ (if not available, use TPSS)³⁶, MN15,⁹ B97M-V^{37,38} (if not available, use MN15-L⁸), ω B97M-V^{38,39} (if not available, use ω B97X-D)⁴⁰ and the Hartree-Fock (HF)⁴¹ method. The basis set you should use is def2-QZVP.⁴² We also recommend the Ultrafine grid in Gaussian, which correspond to the (99,590) Lebedev grid in Q-Chem.

The reference energies for the reactions are 2.73 kcal/mol (**1a**), 1.01 kcal/mol (**1b**), 3.29 kcal/mol (**1c**) and -1.15 kcal/mol (**1d**). After submitting calculations with each one of the functionals introduced above, you should calculate the reaction energies as the difference between the energies of the products and the reactants and then put them in a table. After that, you should also calculate the absolute error $|\varepsilon|$ with respect to the reference data as the difference:

$$|\varepsilon| = |E_{\text{comp}} - E_{\text{ref}}|$$

Report them in the same table that collects the results.

Problems:

1) Which functional has the most negative error?

2) Which functional has the most positive error?

3) Which functional is the best performer for each reaction?

4) Which functional is the best overall?

5) Are there functionals that perform badly for these reactions?

6) Collect the total computational timing and divide it by the number of SCF steps that it takes to reach convergence for each functional. How do they perform? Report the results in the following table. Compare B3LYP with the other hybrid functionals and the HF method (add more pages if needed to report all results).

	SPW92 (SVWN5)	BP86	BLYP	B3LYP	B3LYP-D3(BJ)
Total time					
	B3PW91	PBE	PBE-D3(BJ)	PBE0	M06-2X
Total time					
	M11	SCAN (TPSS)	MN15	B97M-V (MN15-L)	ωB97M-V (ωB97X-D)
Total time					

We will comment more extensively on the results after Experiment 3 has been completed.

References:

- 5) L. Goerigk, A. Hansen, C. Bauer, S. Ehrlich, A. Najibi and S. Grimme, *Phys. Chem. Chem. Phys.*, **2017**, 19, 32184–32215.
- 8) H. S. Yu, X. He, and D. G. Truhlar, *J. Chem. Theory Comput.*, **2016**, 12, 1280–1293.
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Experiment 2: Applying DFT to Organic Chemistry – Part B.

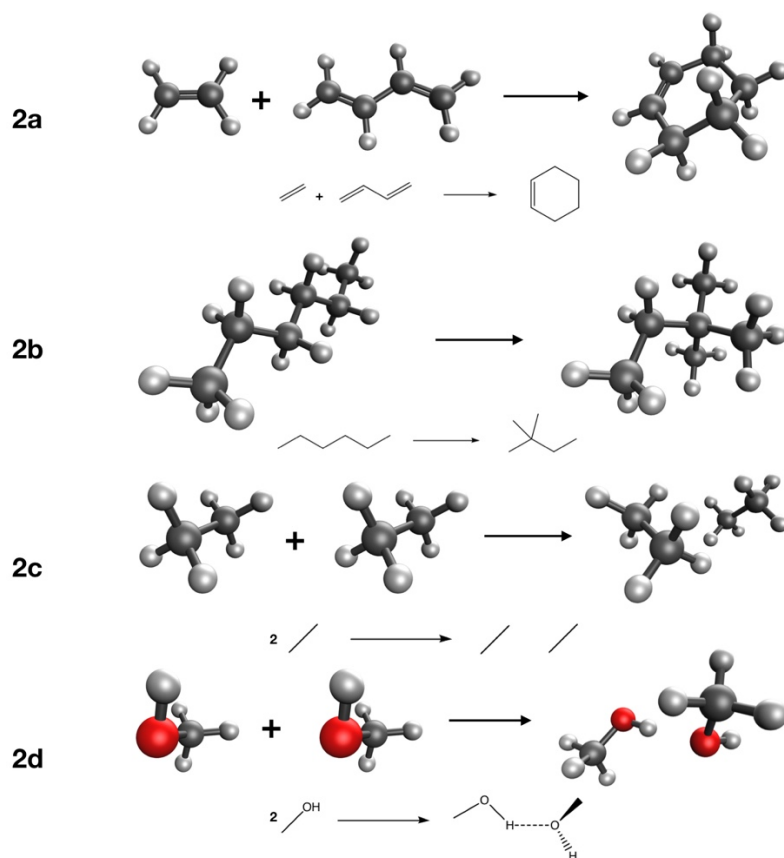


Figure 2 Reactions studied in the Experiment 2. Diels-Alder reaction of ethene and butadiene (**2a**). Isomerization of n-hexane to neo-hexane (**2b**). Formation of the ethene (**2c**) and the methanol (**2d**) dimers. The carbon atoms are black, the oxygen atoms are red, and the hydrogen atoms are white. The dotted line shows hydrogen bond.

In this second experiment, you will deal with four additional organic reactions commonly found in textbooks (**Figure 2**). The first one (**2a**) is a Diels-Alder reaction between ethene and butadiene and it has a reference energy of -45.40 kcal/mol. The second one (**2b**) is the isomerization reaction of neo-hexane (2,2-dimethylbutane) to hexane with a reference energy of -2.49 kcal/mol. The third one describes the formation of the ethane dimer (**2c**), kept together only by van der Waals (dispersion) interactions, and it has a reference energy of -1.34 kcal/mol. In the last one, you will analyze the methanol dimer (**2d**), which is kept together by hydrogen bonding, having a reference energy of -5.81 kcal/mol. These structures come from the DARC^{5,43,44} and ADIM6^{5,45} subsets of the GMTKN55 database,⁵ and the AlkIsomer11^{46,47} and S66^{48,49} subsets of the MGCDDB84 database.⁶

Similarly to Experiment 1, you will use the following functionals: SPW92^{21,22} (or SVWN5^{21,23}), BP86,^{24,25} BLYP,^{24,26} B3LYP,^{23,24,26-28} B3LYP-D3(BJ),^{23,24,26-29} B3PW91,^{22,24,27,30} PBE,³¹ PBE-D3(BJ),^{29,31} PBE0,³² M06-2X,³³ M11,³⁴ SCAN³⁵ (or TPSS)³⁶, MN15,⁹ B97M-V^{37,38} (or MN15-L⁸), ω B97M-V^{38,39} (or ω B97X-D)⁴⁰ and the Hartree-Fock (HF)⁴¹ method. The basis set you should use is def2-QZVP.⁴² We also recommend the Ultrafine grid in Gaussian, which correspond to the (99,590) Lebedev grid in Q-Chem. After submitting calculations with each one of these functionals, you should calculate the computed reaction energies, and then put them in a table together with the absolute error $|\epsilon|$.

Problems:

1) Which functional has the most negative error?

2) Which functional has the most positive error?

3) Which functional is the best performer for each reaction?

4) Which functional is the best overall?

5) Are there functionals that perform badly for these reactions?

6) Collect the total computational timing and divide it by the number of SCF steps that it takes to reach convergence for each functional. How do they perform? Report the results in the following table. Compare B3LYP with the other hybrid functionals and the HF method (add more pages if needed to report all results).

	SPW92 (SVWN5)	BP86	BLYP	B3LYP	B3LYP-D3(BJ)
Total time					
	B3PW91	PBE	PBE-D3(BJ)	PBE0	M06-2X
Total time					
	M11	SCAN (TPSS)	MN15	B97M-V (MN15-L)	ωB97M-V (ωB97X-D)
Total time					

7) Do the functionals that include -D3 corrections perform better than the corresponding uncorrected ones?

References:

- 5) L. Goerigk, A. Hansen, C. Bauer, S. Ehrlich, A. Najibi and S. Grimme, *Phys. Chem. Chem. Phys.*, **2017**, 19, 32184–32215.
- 6) N. Mardirossian, and M. Head-Gordon, *Mol. Phys.*, **2017**, 115, 2315–2372.
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- 21) J. C. Slater, *Phys. Rev.*, **1951**, 81, 385–390.
- 22) J. P. Perdew, and Y. Wang, *Phys. Rev. B*, **1992**, 45, 13244–13249. Erratum: J. P. Perdew, and Y. Wang, *Phys. Rev. B*, **2018**, 45, 079904.
- 23) S. H. Vosko, L. Wilk, and M. Nusair, *Can. J. Phys.*, **1980**, 58, 1200–1211.
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Experiment 3: Difficult Cases for DFT.

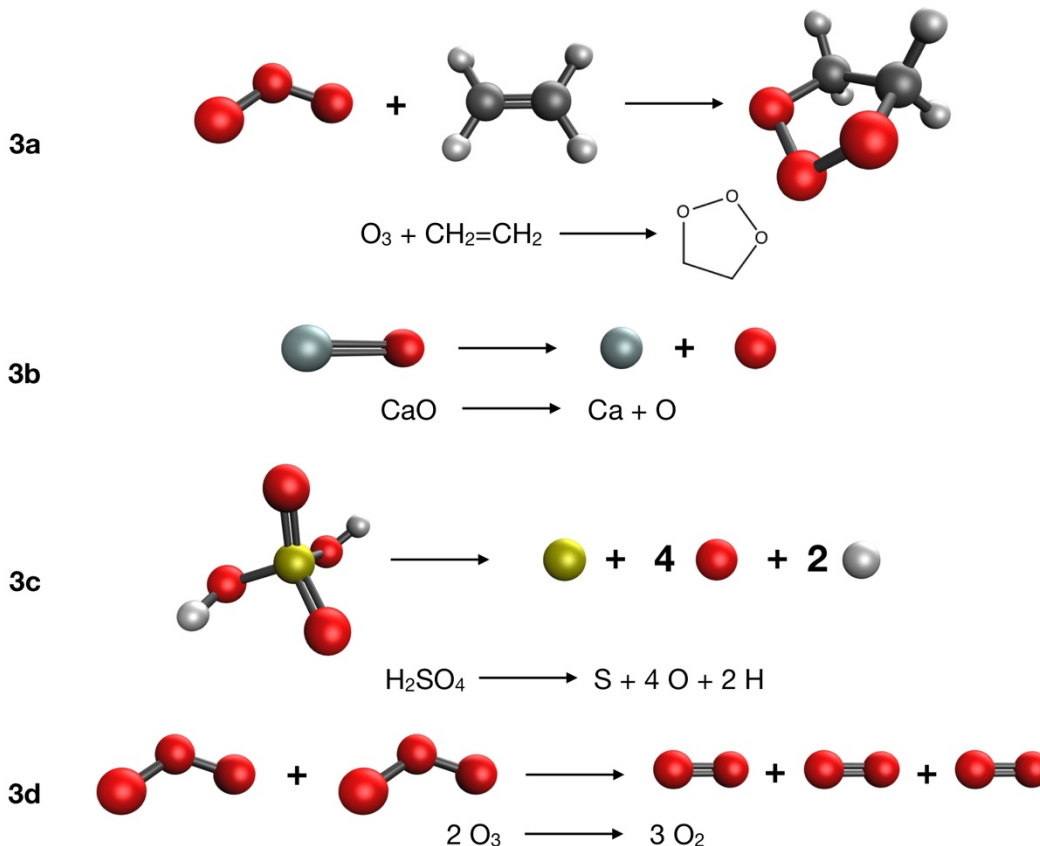


Figure 3 Reactions studied in Experiment 3. The ozonolysis reaction (**3a**), the dissociation of the CaO bond (**3b**), the atomization reaction of sulfuric acid (**3c**), and the conversion of ozone to oxygen (**3d**). The carbon atoms are black, the oxygen atoms are red, the hydrogen atoms are white, the sulfur atom is dark yellow, and the calcium atom is grey.

In Experiment 2, we found that it is possible to improve the error in reaction energies by using the -D3 correction for dispersion interactions. Unfortunately, the -D3 correction and all other schemes designed to account for dispersion are not a universal solution when dealing with more complicated problems.

In this last experiment on functionals, you will deal with four reactions. The first one (**3a** in **figure 3**) is the reaction between ethene and ozone to form the first intermediate in an ozonolysis reaction as found in many textbooks. The second one (**3b**) is the homolytic bond dissociation energy of CaO into atomic calcium and oxygen. The third one (**3c**) is the total atomization energy of sulfuric acid. The last one (**3d**) is the reaction energy of the conversion between ozone and molecular oxygen. The first reaction comes from the DC13^{5,33,43,50,51} subset of the GMTKN55 database,⁵ while the second and the third one come from the MR-MGM-BE4⁵² and DC9^{15,53} subsets of the Minnesota 2015B database.⁹ The last reaction has been obtained combining two datapoints of the W4-17 database.⁵⁴ The reference energies are -58.7 kcal/mol, 96.15 kcal/mol, 602.18 kcal/mol, and -67.60 kcal/mol respectively.

You should once again use the following functionals: SPW92^{21,22} (or SVWN5^{21,23}), BP86,^{24,25} BLYP,^{24,26} B3LYP,^{23,24,26-28} B3LYP-D3(BJ),^{23,24,26-29} B3PW91,^{22,24,27,30} PBE,³¹ PBE-D3(BJ),^{29,31} PBE0,³²

M06-2X,³³ M11,³⁴ SCAN³⁵ (or TPSS)³⁶, MN15,⁹ B97M-V^{37,38} (or MN15-L⁸), ω B97M-V^{38,39} (or ω B97X-D)⁴⁰ and Hartree-Fock (HF)⁴¹. The basis set you should use is def2-QZVP,⁴² as usual. Again, we also recommend the Ultrafine grid in Gaussian, which correspond to the (99,590) Lebedev grid in Q-Chem. After submitting calculations with each one of these functionals, you should calculate the computed reaction energies, and then put them in a table together with the absolute error $|\epsilon|$.

Problems:

1) Which functional has the most negative error?

2) Which functional has the most positive error?

3) Which functional is the best performer for each reaction?

4) Which functional is the best overall?

5) Are there functionals that perform badly for these reactions?

8) Collect the total computational timing and divide it by the number of SCF steps that it takes to reach convergence for each functional. How do they perform? Report the results in the following table. Compare B3LYP with the other hybrid functionals and the HF method (add more pages if needed to report all results).

	SPW92 (SVWN5)	BP86	BLYP	B3LYP	B3LYP-D3(BJ)
Total time					
	B3PW91	PBE	PBE-D3(BJ)	PBE0	M06-2X
Total time					
	M11	SCAN (TPSS)	MN15	B97M-V (MN15-L)	ω B97M-V (ω B97X-D)
Total time					

- 6) Do the D3-corrected functionals perform better or worse than the respective uncorrected ones?

Overall Problems for Experiments 1-3:

- 1) Which functional or method is the best overall performer?

- 2) Which functional or method is the worst overall performer?

- 3) Is B3LYP faster than other functionals/methods?

- 4) Do you think that adding the -D3 correction helps? For which reactions?

Tip: The reactions studied in the previous experiments can be found in organic chemistry textbooks, and they involve very simple organic molecules. However, even in these conceptually simple cases, we saw that the results are unpredictable, and different functionals behave in different ways. It is worth remarking that if a functional fails, it is not a failure of DFT as a whole. It is a failure of the approximation in use. DFT is in principle exact, but we have to rely on approximations to the exact theory. The results we get are dependent on how good the approximations (or functionals) are.

Practice comment: In the first group of “easy” reactions, you may have realized that almost all functionals provide good results. After all, for each reaction we are comparing electronic energies of very similar molecules, since their conformation, or the configuration in the case of pent-2-ene, is the only thing that is changing. Their electron density exhibits very little changes, so even if a functional gets the total density fundamentally wrong in certain regions, it can still provide good results, as long as it is consistent in describing the changes. That is, errors in regions of the density that are not subject to change cancel out when calculating the difference between the product and reactants. This is known as “cancellation of errors”. However, error cancellations are not easy to generalize. Therefore, we cannot say that rotations around a single bond, or conformational changes, or *cis-trans* isomerizations are all easy to study computationally. In fact, there is no way to know in advance whether the reaction at hand falls in the easy, medium or hard category. Before starting a computational investigation, we should analyze in great detail the subsets of the databases that include molecules (or chemical properties) close to the ones we want to study.

For the reactions in the second group, we need a good functional capable of obtaining a correct electron density. Since reactants and products are very different from each other in general, we cannot rely on the beneficial error cancellation that happened for simpler cases. For example, in the case of the Diels-Alder reaction, we combine two fragments to get a larger molecule. The same is valid for isomerization reactions, which are very difficult for DFT. The other two reactions deal with dimers of simple molecules held together by van der Waals interactions. In the 1990s, it was acknowledged that many κ functionals fail to describe bonding in the van der Waals region.⁵⁵ In 2012, correctly modeling van der Waals interactions was still listed as a challenge for DFT.⁵⁶ This problem has been approached several times,^{29,38,57-59} but the two most used corrections available today are the -D correction of Grimme, Goerigk and co-workers,^{29,57,58} and the VV10 functional of Vydrov and Van Voorhis.³⁸ As you may have noticed, the inclusion of the -D3 correction for B3LYP and PBE improved the results of the uncorrected functional. It is certainly a good idea to use the -D3 correction when possible, mainly when performing geometry optimizations,⁶⁰ but we also have to keep in mind that it can sometimes result in an overcorrection. The B97M-V and ω B97M-V approximations include the VV10 correction, and they are among the best performing functionals overall. -D3 corrections for the Minnesota functionals have been proposed,^{5,61,62} but since the functionals have been parametrized using van der Waals complexes too, they are not necessary in principle.

The third group of reactions is the one that yielded the worst results. For this group there is no functional that performs satisfactorily, besides random exceptions (MN15 performs well for CaO because it was included in its training set, i.e. MN15 was parametrized using the database that includes this molecule). If we think about it, those reactions do not look complicated from a chemical point of view. In fact, the two largest molecules have only five atoms that are bigger than hydrogen. This is why we cannot deal with calculations blindly. Our suggestion is to always seek for expert advice when different functionals provide wildly discordant results. In a recent editorial on Organometallics,⁶³ Kathrin Hopmann talks about what makes a computational paper interesting, and she says, “Do not

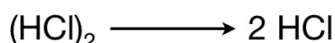
use DFT for mechanisms it cannot handle”. This nicely summarizes the take-home message of these first three experiments. All the functionals that appeared in the literature over the past 40 years have strengths and weaknesses.⁶⁴ Much of the effort in functional development has been devoted to broadening the former and narrowing the latter. As a result, *xc* functional approximations are statistically improving, meaning that in general the results obtained using modern functionals are better than the ones obtained with older functionals. But it is always up to the researchers to use judgment when choosing among them.

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Experiment 4: Basis Set Incompleteness Error.



Scheme 1 The reaction studied in Experiments 1 and 2.

Part A: Split valence.

After choosing a functional, the following step for picking a good method is choosing a good basis set. There are many different “families” of basis sets,^{65,66} which have been developed in the past sixty years by different computational chemists. Head-Gordon and co-workers⁶⁷ found that the most cost-effective basis sets for DFT belong to the Ahlrichs’ family.⁴² We will analyze their performance for the dissociation reaction of the HCl dimer, coming from the NCCE23^{15,68-71} subset of the Minnesota 2015B⁹ database. The reference energy for this dissociation reaction is 2.01 kcal/mol.

We suggest calculating the dissociation energy of this reaction using the following functionals: SPW92^{21,22} (or SVWN5^{21,23}), BP86,^{24,25} B3LYP,^{23,24,26-28} PBE,³¹ PBE0,³² M06-2X,³³ SCAN³⁵ (or TPSS)³⁶, B97M-V^{37,38} (or MN15-L⁸), ω B97M-V^{38,39} (or ω B97X-D)⁴⁰ and the Hartree-Fock (HF)⁴¹ method. For now, we only use the def2-SVP, def2-TZVP and def2-QZVP basis sets.⁴² These basis sets have been recently redefined, hence the “def2-” prefix. SVP stands for Split-Valence Polarized, TZVP means Triple-Zeta (split-)Valence Polarized, and QZVP stands for Quadruple-Zeta (split-)Valence Polarized. Being split-valence implies that they include one set of functions for the core orbitals, while the number of functions for the valence orbitals depends on the size of the basis set, i.e. on the “zeta”. For example, double- ζ basis sets include two functions for each valence orbital, triple- ζ include three, and so on. Being polarized means that the basis set includes an additional function having higher angular momentum than the valence orbitals. For example, a double- ζ polarized basis set for carbon would include a d function, while for iron it would include an f function. If some of the def2- basis sets are not defined for the program you are using (for instance, the augmented basis sets are not defined as a keyword in the Gaussian program), you can use either use them as external basis set or use the Dunning’s basis sets⁷² instead. However, keep in mind that they are optimized for correlated wave-function calculations,⁷² and they are not the best choice for DFT. For these basis sets, the shorthand notation is cc-pV n Z, where cc means “correlation consistent” and n is either D for double- ζ , T for triple- ζ , or Q for quadruple- ζ . Therefore, the def2-SVP, def2-TZVP and def2-QZVP basis sets can be substituted with the cc-pVDZ, cc-pVTZ, and cc-pVQZ respectively. Once again, we suggest the UltraFine grid in Gaussian, or the (99,590) in Q-Chem. After submitting calculations with each one of these functional/basis-set combinations, you should calculate the reaction energy and then the absolute error $|\varepsilon|$. Report the absolute errors in the table below, and then answer the following questions.

	SPW92 (SVWN5)	BP86	B3LYP	PBE	PBE0
def2-SVP					
def2-TZVP					
def2-QZVP					
	M06-2X	SCAN (TPSS)	B97M-V (MN15-L)	ω B97M-V	HF
def2-SVP					
def2-TZVP					
def2-QZVP					

Problems:

- 1) Is there a trend when going from a double- to a quadruple- ζ basis set? More specifically, what happens to the magnitude of the error? Do all the functionals follow the same pattern?
-
-

- 2) How would you classify the behavior of the functionals you tried? Use one of these definitions to fill the table below.
- a) Functionals whose errors decrease with increasing basis set size.
 - b) Functionals whose errors increase with increasing basis set size.
 - c) Functionals whose behavior does not follow a specific pattern.

	SPW92 (SVWN5)	BP86	B3LYP	PBE	PBE0
Behavior					
	M06-2X	SCAN (TPSS)	B97M-V (MN15-L)	ωB97M-V	HF
Behavior					

In your opinion, which functionals are the best for this reaction?

Part B: Diffuse Functions.

Adding diffuse basis functions is important to describe the behavior of the electron density in regions that are far away from the nuclei. For this reason, the exponents of a diffuse function are smaller than those used in the rest of the functions.

Repeat the calculations for the hydrochloric acid dimer with the def2-SVPD, def2-TZVPD, and def2-QZVPD basis sets⁴² (or the aug-cc-pVDZ, aug-cc-pVTZ, and aug-cc-pVQZ basis sets).⁷² Report the absolute errors in the table below, and then answer the following questions.

	SPW92 (SVWN5)	BP86	B3LYP	PBE	PBE0
def2-SVPD					
def2-TZVPD					
def2-QZVPD					

	M06-2X	SCAN (TPSS)	B97M-V (MN15-L)	ω B97M-V	HF
def2-SVPD					
def2-TZVPD					
def2-QZVPD					

Problems:

- 1) Do you see trends that are similar to those in point 1 of Experiment 4a?

- 2) Do you think adding diffuse functions helps for this particular system?

- 3) For what chemical species do you think we need diffuse functions the most?

Tip: When performing calculations, errors arise from different sources. At this point, you might have already realized that each basis set carries an error due to the fact that it is a truncated expansion. This error is called “Basis Set Incompleteness Error”, or BSIE (computational chemists love acronyms). In order to minimize the impact that BSIE has on the final results, you should perform calculations with the largest basis set that you can afford. Another way to express this idea is to say that you want to minimize the error associated with the basis set, so that the error arising from the *xc* functional is always the largest.

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Experiment 5: Basis Set Superposition Error.

The BSIE is not the only error that affects calculations with a small basis. When studying systems bound through non-covalent interactions another error arises, called “Basis Set Superposition Error”, or BSSE. The reason why results might be affected by the BSSE is simple and it can be explained by the fact that the calculation on the bounded system might benefit from a higher number of basis functions than the calculation on the two monomers. This happens because in the bound system the basis functions of monomer A can also partially describe monomer B, and vice-versa. Obviously, these extra contributions are absent in the separate calculations that are performed on the monomers. As pointed out by van Duijneveldt and co-workers,⁷³ this is problematic only when calculating the binding energies, while it might be even beneficial if the energy of the bound system only is of interest.

One approximate method to solve this problem is the counterpoise (CP) correction method of Boys and Bernardi.⁷⁴ In this scheme, slightly modified calculations are performed to calculate the energies of the monomers, in which the basis functions of the other monomer are included, but without its atoms.⁷⁵ The so-called “ghost functions” that the dimer benefits from, are now specifically accounted for in the calculations of both monomers. It is important to notice that this method involves a choice in how the complex is divided into different fragments. This represents an important limitation, since the way we can divide a complex into fragments is not unique, especially when we deal with intramolecular BSSE.⁷⁶ Extremizing this procedure, and considering each atom as a fragment, yields to methods such as the CP^{aa} of Galano and Alvarez-Idaboy⁷⁷ or the ACP(x) correction of Jensen.⁷⁸ Kruse and Grimme, instead, introduced the geometric counterpoise (gCP)⁷⁶ as a simple way to correct both the intermolecular and intramolecular BSSE using the geometry of the molecule alone. We will not explore these methods, but we will limit ourselves to the original Boys and Bernardi CP method.

When it comes to intermolecular BSSE, like in the case of the HCl dimer also used for the previous experiment,^{15,68-71} a simple way to divide the dimer into two monomers suggests itself. You will apply the CP correction to this system using all the functionals,^{8,21-28,31-33,35-41} and basis sets^{42,72} that you have already used in Experiments 4a and 4b. As for experiments 4a and 4b, if some of the def2 basis sets are not defined, use the Dunning basis sets instead.⁷²

Problems:

- 1) Once you put the results in the following table, do you see an improvement in the results? Compare them with the tables from the previous experiments.

CP corrected	SPW92 (SVWN5)	BP86	B3LYP	PBE	PBE0
def2-SVP					
def2-TZVP					
def2-QZVP					
CP corrected	M06-2X	SCAN (TPSS)	B97M-V (MN15-L)	ωB97M-V	HF
def2-SVP					
def2-TZVP					
def2-QZVP					

CP corrected	SPW92 (SVWN5)	BP86	B3LYP	PBE	PBE0
def2-SVPD					
def2-TZVPD					
def2-QZVPD					
CP corrected	M06-2X	SCAN (TPSS)	B97M-V (MN15-L)	ω B97M-V	HF
def2-SVPD					
def2-TZVPD					
def2-QZVPD					

2) If you notice an improvement, where is it? In other words, what basis sets benefit most from the CP correction?

3) Are there any functionals that do not benefit at all from the CP correction?

4) Do you think it would be a good idea to also add the -D3 correction together with the CP correction? Before answering this question, re-run your calculations with B3LYP-D3(BJ) and PBE-D3(BJ).

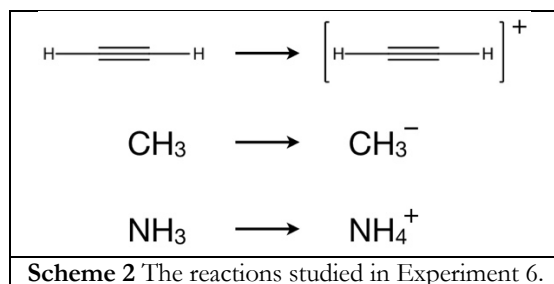
Tip: If you answer yes to question, then you should know that there are some cases for which the validity of the CP is still under debate in the computational chemistry community.^{73,77-83} The simple CP correction is in fact reported to overcorrect results.^{77,78} Hence, you should not assume that the CP correction solves all of your problems, but it surely does for small basis sets, for which it should always be used. In general, however, a better strategy is to use a basis set that is close to the basis set limit, since both BSSE and BSIE will be minimized. Grimme, Goerigk and co-workers,⁶⁰ as well as Mardirossian and Head-Gordon³⁹ have effectively used segmented polarized quadruple- ζ basis sets for exactly this purpose.

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Experiment 6: Review of Modern Basis Sets.



Now that you are familiar with what basis sets are, you can apply this knowledge to chemical reactions. In particular, you are going to analyze the effect of adding diffuse functions when studying the proton affinity of ammonia, the ionization potential of acetylene and the electron affinity of the CH_3 radical. Despite their small size, these species can still be used to demonstrate good computational practices in the analysis of anions and cations. The proton affinity of ammonia comes from the PA8^{15,84} subset of the Minnesota 2015B⁹ database, while the reaction of acetylene comes from the G21IP⁸⁵ subset and the electron affinity of the methyl radical comes from the G21EA⁸⁵ subset of the GMTKN55⁵ database. The reference values are 211.90 kcal/mol for the NH_3 proton affinity, 264.60 kcal/mol for the acetylene ionization potential, and 1.20 kcal/mol for the electron affinity of the methyl radical.

The functionals that you will use are the usual: SPW92^{21,22} (or SVWN5^{21,23}), BP86,^{24,25} B3LYP,^{23,24,26-28} PBE,³¹ PBE0,³² M06-2X,³³ SCAN³⁵ (or TPSS)³⁶, B97M-V^{37,38} (or MN15-L⁸), ω B97M-V^{38,39} (or ω B97X-D)⁴⁰ and the Hartree-Fock (HF)⁴¹ method. For this experiment, you are going to use the Ahlrichs' basis sets,⁴² or alternatively the Dunning's ones.⁷² You should run calculations with the def2-SVP, def2-SVPD, def2-TZVP, def2-TZVPD, def2-QZVP, and def2-QZVPD (cc-pVDZ, aug-cc-pVDZ, cc-pVTZ, aug-cc-pVTZ, cc-pVQZ, and aug-cc-pVQZ). As usual, collect all the results, i.e. unsigned errors, in the tables below.

IP of HCCH	def2-SVP	def2-SVPD	def2-TZVP	def2-TZVPD	def2-QZVP	def2-QZVPD
SPW92 (SVWN5)						
BP86						
PBE						
SCAN						
B97M-V (MN15-L)						
PBE0						
M06-2X						
B3LYP						

ω B97M-V (ω B97X-D)						
HF						

EA of CH ₃ [·]	def2-SVP	def2-SVPD	def2-TZVP	def2-TZVPD	def2-QZVP	def2-QZVPD
SPW92 (SVWN5)						
BP86						
PBE						
SCAN						
B97M-V (MN15-L)						
PBE0						
M06-2X						
B3LYP						
ω B97M-V (ω B97X-D)						
HF						

PA of NH ₃	def2-SVP	def2-SVPD	def2-TZVP	def2-TZVPD	def2-QZVP	def2-QZVPD
SPW92 (SVWN5)						
BP86						
PBE						
SCAN						
B97M-V (MN15-L)						
PBE0						
M06-2X						
B3LYP						

ωB97M-V (ωB97X-D)						
HF						

Problems:

- 1) Which functional is the best choice with the def2-nZVP family of basis set?
 - Ionization potential of acetylene: _____
 - Electron affinity of CH₃: _____
 - Proton affinity of ammonia: _____

- 2) Compare the results reported above with those obtained with the def2-nZVPD basis sets. Do the results get better or worse, on average?
 - Ionization potential of acetylene: _____
 - Electron affinity of CH₃: _____
 - Proton affinity of ammonia: _____

- 3) Based on the results that you collected above, do you think we need diffuse functions when studying cations? What about for anions?

- 4) Go back to Experiment 4b, question 3. What answer did you give there?

- 5) The results obtained with small basis sets for cations benefit from the addition of diffuse functions. This seems to be in contradiction with the previous points/experiments. Where do you think this reduction in errors come from?

Tip: The take-home message of these first six experiments is that you should rely on the literature to stay up to date with the recent method development in DFT. Modern functionals like those optimized by Mardirossian and Head-Gordon³⁷⁻³⁹ or the latest Minnesota functionals like MN15⁹ are guaranteed to be robust and highly transferable, and their results can be trusted over a broad spectrum of chemical properties. When coupled with a large basis set, or a small basis set and the CP correction, they deliver good results for several systems. The choice of a basis set should not be underestimated either. We recommend basis sets that are designed for DFT calculations, like those introduced by Ahlrichs⁴² or Jensen,⁸⁶ over the Dunning or Pople⁸⁷ basis sets. The Ahlrichs' basis sets have the additional advantage of being defined for most of the periodic table too (all elements up to Rn).

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Experiment 7: Why is the B3LYP/6-31G* Level of Theory so Successful?

The B3LYP^{23,24,26-28} functional and the 6-31G* basis set of Pople and co-workers⁸⁷ is the *de facto* standard method in the organic chemistry community. This functional is based on the three-parameter hybrid scheme that Becke introduced in 1993.²⁷ The originally proposed three-parameter functional used his 1988 exchange functional²⁴ in conjunction with the correlation functional of Perdew and Wang (PW91).^{22,30} B3LYP was introduced one year later by Frisch and co-workers by replacing PW91 with the LYP functional,²⁶ since the latter provided better results in a computational study of circular dichroism spectra.²⁸ The B3LYP functional became more popular than B3PW91, even though the performances and theoretical foundations for both functionals are almost identical. The 6-31G* basis set is a double- ζ split-valence polarized basis set,⁸⁷ and as such, it contains a reasonably moderate amount of basis functions. Its usage with B3LYP became popular in the 1990s and early 2000s because they allowed calculations on relatively large molecules that are relevant to organic chemistry, with performances drastically superior to previously available methods, such as semi-empirical and Hartree–Fock. However, in light of the increased computational capabilities of computers in the last two decades, the usage of a double- ζ basis set in a research setting is sometimes dangerous, as we also saw in the previous three experiments. In this experiment, you will test the B3LYP functional with several different double- ζ polarized basis sets in order to understand why the B3LYP/6-31G* level of theory is so “special”. Namely, the basis sets that we suggest are: 6-31G*, cc-pVDZ,⁷² def2-SVP,⁴² and pc-1⁸⁶ (if this one is not available use def2-SV(P), the smallest of the Ahlrichs basis sets). The systems that you run the calculations on are those of Experiment 1,^{5,19,20} 2^{5,6,43-49} and 3.^{5,15,33,43,50-54} You should then report the results in a table, together with the results obtained in Experiments 1-3 with the def2-QZVP basis set. Remember to report together with the calculated value also the error with respect to the reference, as shown in Experiment 1.

Problems:

- 1) Choose one of the molecules. How many basis functions do the different basis set have?

Molecule	6-31G*	def2-SVP	cc-pVDZ	pc-1 or def2-SV(P)
Basis functions (#)				

- 2) Which basis set gives the smallest absolute error for the molecules in Experiment 1?
-

- 3) Which basis set gives the smallest absolute error for the molecules in Experiment 2?
-

- 4) Which basis set gives the smallest absolute error for the molecules in Experiment 3?
-

- 5) Which basis set gives the smallest absolute error overall?

-
- 6) Now re-do all the calculations using the B3LYP-D3(BJ)^{23,24,26-29} with the same small basis sets. What happens to the results? Do they get better?
-
-

- 7) Try one of the other functionals with the 6-31G* basis set. Do you observe the same trends?
-
-

- 8) Compare now the results of B3LYP/def2-QZVP with the results of B3LYP/6-31G*, and for B3LYP-D3(BJ)/def2-QZVP and B3LYP-D3(BJ)/6-31G*. Do you see anything strange?
-
-
-

Tip: This experiment confirms that the B3LYP/6-31G* level of theory is so good because it benefits from a fortuitous error cancellation.⁶⁰ The theory suggests that the error made using a functional with a smaller basis set should always be larger than the error made using a larger one. The fact that this expectation is not met by B3LYP/6-31G* when compared to B3LYP/def2-QZVP is worrisome, since it underlines a fortuitous cancellation of errors. Such error cancellation, however, might have an unpredictable behavior: sometimes it can work in your favor—as for the reactions in Experiment 2—, but sometimes it can work against you—as for the reactions in Experiment 3. The 6-31G* basis set does not make the B3LYP functional better, nor more physically sound. Instead of trying to understand which chemical problems can be solved by B3LYP/6-31G*, we suggest start moving away from it, and start using a more modern functional with a predictable behavior with respect to the basis set. If this is not possible due to limited computational capabilities, then more appropriate corrections—as those suggested by Kruse, Goerigk and Grimme—should be put in place with the help of an expert. In 2012, Cohen, Mori-Sánchez and Yang said that uniformly performing better than B3LYP was still a challenge for κ functional approximations.⁵⁶ Recent reviews in the field proved that this is no longer true,^{6,14-16} and we feel that the real challenge is to get rid of B3LYP/6-31G* altogether. As Kruse, Goerigk and Grimme said, we do not expect this to happen anytime soon.

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Experiment 8: Integration Grids 1: The Argon Dimer.

For this experiment, you are going to analyze a subtle issue that might potentially affect the results of every exchange–correlation functional. Kohn–Sham (KS)⁸⁸ DFT necessitates the usage of a real-space grid for the evaluation of the exchange–correlation integrals. Most software use a grid construction algorithm first introduced by Becke in 1988.⁸⁹ In practice, the integrals are calculated as weighted sums over a finite amount of grid points generally defined on the surface of a sphere. The “thickness” of these grids is usually represented by the corresponding number of radial and angular points. The choice of the grid can significantly affect the computed results, as shown for instance by Wheeler and Houk⁹⁰ for the M06 family³³ of the Minnesota functionals, and by Mardirossian and Head-Gordon^{4,91} for two generations of Minnesota functionals developed between 2006 and 2016. They also point out that meta-GGA functionals usually require finer grids than GGA functionals.

The issue of choosing the most appropriate integration grid is often overlooked, and many computational practitioners are unaware of it. Relying on the default settings of quantum chemistry programs is not a good idea, even if some developers implemented variable grid requirements that depend on the chosen functional.⁹² For this experiment, you are going to study the dissociation curve of the argon dimer. Geometries for these systems come from the RG10⁹³ subset of the MGCDB84 database.⁶ The distance between the two argon atoms varies between 3.0 and 6.0 Ångström. The reference data (kcal/mol) are reported in the following table.

Table 1 Reference values in kcal/mol for the argon dimer given the Ar-Ar distance in Å.					
Distance	Energy	Distance	Energy	Distance	Energy
3.0	2.24	4.0	-0.25	5.0	-0.08
3.1	1.21	4.1	-0.23	5.1	-0.07
3.2	0.57	4.2	-0.21	5.2	-0.06
3.3	0.18	4.3	-0.18	5.3	-0.05
3.4	-0.06	4.4	-0.16	5.4	-0.05
3.5	-0.19	4.5	-0.14	5.5	-0.04
3.6	-0.26	4.6	-0.13	5.6	-0.04
3.7	-0.28	4.7	-0.11	5.7	-0.03
3.8	-0.28	4.8	-0.10	5.8	-0.03
3.9	-0.27	4.9	-0.09	5.9	-0.03
				6.0	-0.02

We suggest using the following functionals: B3LYP,^{23,24,26-28} B3LYP-D3(BJ),^{23,24,26-29} M05-2X,⁹⁴ M06-L,⁹⁵ M06-HF,⁹⁶ M11,³⁴ M11-L,⁹⁷ MN15-L,⁸ PBE³¹ and ω B97M-V^{38,39} (or ω B97X-D)⁴⁰. As usual, feel free to add any functionals you like. The basis set of choice is def2-QZVP⁴² for all calculations. We will try different grid options: SG1 (if available), (75,302), (99,590) and (175,974). These grids correspond to the SG1, Fine, UltraFine and SuperFine grids in Gaussian, and can be requested with the keyword XCGRID in Q-Chem.

When presenting the results, try to use a dissociation plot like the one reported in **figure 4** for the VSXC functional.⁹⁸ Before generating the graphs, collect all the results in a table formatted like **Table 2** in the next page.

Functional:		VSXC		Grid:	
Distance	Energy	Distance	Energy	Distance	SG1
3.0	2.33	4.1	-0.18	5.2	-0.12
3.1	0.71	4.2	-0.04	5.3	-0.09
3.2	-0.63	4.3	-0.17	5.4	-0.05
3.3	-1.04	4.4	-0.20	5.5	-0.01
3.4	-0.53	4.5	-0.13	5.6	0.01
3.5	-0.18	4.6	-0.18	5.7	0.02
3.6	-0.50	4.7	-0.24	5.8	-0.01
3.7	-0.81	4.8	-0.08	5.9	-0.06
3.8	-0.69	4.9	0.00	6.0	-0.10
3.9	-0.66	5.0	-0.06		
4.0	-0.58	5.1	-0.12		

Table 2: Data used to generate the SG1 curve in **figure 4**. The energy is reported in kcal/mol, while the distance is in Å.

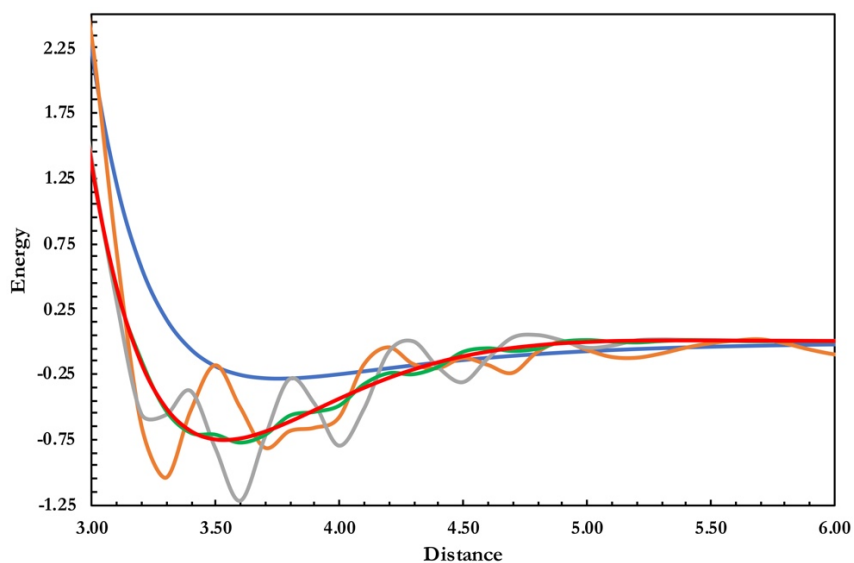


Figure 4 Behavior of the VSXC functional in the description of the Ar dimer with different integration grids: SG1 (orange curve), (75,302) (gray curve), (99,590) (green curve), (175,974) (red curve). The reference curve is reported in blue. The energy is in kcal/mol, while the distance is in Å.

Problems:

1) Can you find any problematic functionals?

2) Why do you observe several minima and maxima in these curves? Do you think they might be unphysical?

3) Compare the results obtained using the grid having the smallest and the one with the largest number of points. Which functionals are well converged with respect to these grids?

4) What are the minimum grid requirements for the tested functionals?

5) Did you notice any difference in the time needed for the calculations? Collect the results in a table and plot the time needed and the grid size in a graph. How noticeable is the time increase?

6) Given the results that you collected, which grid(s) would you recommend?

7) Does the HF method suffer from this problem? Why?

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Experiment 9: Integration Grids 2: The Case of But-2-yne.

In a recent publication,⁹⁹ Bootsma and Wheeler found out that some functionals are sensitive to the choice of integration grid not only for electronic energies,^{4,90,91} but also for thermochemical properties like entropies and Gibbs' free energies. They reported five different reactions, and in this experiment, we will focus on the first reaction they reported: the isomerization reaction of butadiene to but-2-yne. The calculations that you are going to perform only involve but-2-yne and its thermochemical properties. To set up this experiment, you will use the B97-D GGA functional⁵⁷ and the def2-TZVP basis set.⁴² You should use four integration grids: the pruned SG1 grid, the (75,302), (99,590), and (175,974) Lebedev grids. The last three correspond to the Fine, UltraFine, and SuperFine grid in Gaussian, respectively. Since you need to calculate the thermodynamic properties of the molecule, you should set up a frequency calculation. Please note that the frequency calculation will also give the SCF electronic energy. No geometry optimization is required.

Problems:

- 1) Take a look at the geometries with a molecular visualization program. Are the molecules the same? What changes do you notice?

- 2) Collect the electronic energies of the molecules. How do they look like?

- 3) Analyze the smallest frequency of the molecules. Are the molecules at their minima, transition structures, or else?

- 4) How much did the computational timing increase when going from the SG1 to the (175,974) grid?

- 5) What conclusion can you draw from this experiment? Is there a recommended integration grid?

- 6) Re-run this experiment using the “NoSymm” keyword in Gaussian/Q-Chem (or the equivalent for your program of choice). Do you notice any difference?
-
-

- 7) Try one functional of your choice. Is it affected by the same issue?
-
-

- 8) Do you think that this issue affects all functionals, or only some of them?
-
-

Tip: The issue of the integration grids is subtle, and it is impossible to know in advance which molecules—or which functionals—might be affected. The (99,590) integration grid represents the minimum requirement that allows us to obtain reliable results without a substantial increase in the computational time. Bootsma and Wheeler also showed that the integration grids are not invariant with respect to the rotation of the molecule. To avoid this issue, quantum chemistry programs rotate the input geometry into the so-called “standard orientation” by default, and then they rotate it back before the results are presented. The Gaussian keyword “NoSymm”, or the equivalent “SYMMETRY=FALSE” in Q-Chem avoid this procedure. As a general guideline, beginner practitioners should avoid the use of symmetry, because it might lead to numerical problems, convergence to constrained molecular structures, or other inconveniences. However, if symmetry is necessary for cost reduction, seeking help from an expert is highly recommended.

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Experiment 10: Stability Analysis and Transition Metals.

You should already be familiar with the fact that the coefficients of the basis functions in the final Kohn–Sham orbitals are obtained in the self-consistent field (SCF) procedure. Once this procedure converges, the energy is invariant with respect to unitary transformations of such orbitals. The final single-particle wave functions are obtained as a product of the molecular orbitals and a function that depends on the spin coordinate. Before starting a calculation, we implicitly impose a constraint on the shape of the single-particle wave function, by choosing either a restricted or an unrestricted Kohn–Sham framework. Other constraints might be imposed as well during the SCF procedure. In other words, the SCF procedure is performing a search in a constrained space, and such searches are not always guaranteed to converge to the global minimum, especially for systems with almost-degenerate low-lying states. To confirm that the final result of a Kohn–Sham SCF calculation is indeed the global minimum solution, we need to perform a stability analysis. This procedure usually involves the calculations of the second derivatives of the wavefunction, and hence is as costly as a frequency calculation. A good description of the stability analysis procedure is found in ref. 100.

For this experiment, you will use the usual functionals: SPW92^{21,22} (or SVWN5^{21,23}), BP86,^{24,25} B3LYP,^{23,24,26-28} PBE,³¹ PBE0,³² M06-2X,³³ SCAN³⁵ (or TPSS)³⁶, B97M-V^{37,38} (or MN15-L⁸), ω B97M-V^{38,39} (or ω B97X-D)⁴⁰ and the Hartree-Fock (HF)⁴¹ with the def2-QZVP basis set.⁴²

You will perform calculations for the excitation energies of two atoms, namely Fe and Ru⁺. The reference values are 34.32 kcal/mol for Fe, and 21.96 kcal/mol for Ru⁺. The data come from the 3dAEE8¹⁰¹⁻¹⁰³ and 4dAEE5¹⁰⁴ subsets of the Minnesota 2015B⁹ database. You should perform two sets of experiments: in the first, you calculate the excitation energy from calculation without using the stability analysis. In the second, you should repeat the calculations with the stability analysis and reoptimize the wave function if instabilities are found (Stable=Opt keyword in Gaussian). As usual, calculate the errors between your results and the reference value.

Problems:

- 1) Compare the errors results: do you think you need the stability analysis?

- 2) How does the HF method perform? Why do you think it performs this way?

- 3) Which functional would you recommend in this case?

- 4) Re-run the calculations for the reactions in Experiments 3 and 7 including the stability analysis. Do you notice any changes?

Tip: This fairly simple example shows that performing calculations involving transition metals is not an easy task. Even for a reaction involving only atomic species, the results might show very large errors, and in extreme cases¹⁰⁵ it is not straightforward to understand which functionals give the right results. As a general advice, it is always a good idea to perform the stability analysis of the final solution, and it is mandatory for systems with low-lying states, such as transition metals, and even more so if a small basis set is used. Seeking help from a theoretician in these problematic cases is always recommended.

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Experiment 11: Different flavors of partial atomic charges

There are many different computational schemes that allow the computation of atomic charges. The simplest one was introduced by Robert Mulliken in the 1950s,¹⁰⁶ and it is based on an atomic partitioning of the wave function. In other words, charges are computed according to the contribution that the different atomic orbitals give to the total wave function. Other orbital-based schemes are the one introduced by Löwdin,¹⁰⁷ or the Natural Population Analysis (NPA) of Weinhold and co-workers.¹⁰⁸ An alternative scheme, called ChelPG,¹⁰⁹ computes the atomic charges from a calculated electrostatic potential instead.

In this experiment, you will calculate the atomic charges for a few organic molecules—namely methane, water, ammonia, ammonium, formic acid, and O₂—using the Mulliken and ChelPG schemes. The Mulliken charges are computed by default at the end of every calculation by most software. Hence only the ChelPG keyword is usually required to calculate both type of charges. We suggest using the following functionals: SPW92^{21,22} (or SVWN5^{21,23}), B3LYP,^{23,24,26-28} PBE,³¹ SCAN³⁵ (or TPSS)³⁶, MN15,⁹ B97M-V^{37,38} (if not available, use MN15-L⁸), ωB97M-V^{38,39} (if not available, use ωB97X-D)⁴⁰ and the Hartree-Fock (HF)⁴¹ method. As for the previous experiments, you will use the def2-SVP, def2-SVPD, def2-TZVP, def2-TZVPD, def2-QZVP, def2-QZVPD basis sets⁴² (or alternatively the cc-pVDZ, aug-cc-pVDZ, cc-pVTZ, aug-cc-pVTZ, cc-pVQZ, and aug-cc-pVQZ basis sets⁷² if the Ahlrichs are not available). In this case, we do not have reference values, but we suggest comparing the Mulliken and ChelPG results for each molecule as a function of the different basis sets.

Problems:

- 1) What is the behavior of the Mulliken charges when the basis set size increases? Do they converge to a specific value?

- 2) What is the behavior of the ChelPG charges when the basis set size increases? Do they converge to a specific value?

- 3) Compare the values of the Mulliken charges and the values of the ChelPG charges. Do they agree with each other? Which one is more stable with respect to the basis set size?

- 4) Do different functionals give the same values of atomic charges?

5) How can you use this information when studying a chemical reaction?

6) Do these results meet your expectations?

Tip: The goal of this experiment is to show you that the computation of atomic charges, despite being conceptually very simple, is not univocal. There is no simple way to discern methods that are “right” from methods that are “wrong”. The computed charges are merely a computational object, and as such they cannot be compared to experimentally observed values. Moreover, even comparing the data obtained with different functionals and basis sets does not help, since there is not a clear convergence pattern. Other theoretical limitations of partial atomic charges methods should always be kept in mind as well. For example, the Mulliken scheme suffers from a remarkable basis set dependence—as shown by this experiment—which is less severe in the ChelPG scheme. However, even this method is not immune from drawbacks.^{110,111} One can still make a meaningful use of atomic charges provided that they are calculated using the same method and used cautiously. Specifically, computed charges can be used to understand the effect of a substituent, or a group of substituents, on a molecule. Expert advice is once again recommended for complicated cases.

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Experiment 12: Orbitals meaning and usage.

Part A: The concept of (de)localization.

The concept of orbital is present in every area of chemistry, with a special place in organic and inorganic chemistry. In the context of computational chemistry, orbitals are described using basis sets, which define the atomic orbitals used in the construction of the many-electron wavefunction of the molecule under investigation. The orbitals resulting from a HF calculation are called canonical orbitals, and these are the ones the students are going to plot using either IQMol¹ or GaussView.² We can also call what we get at the end of a DFT calculation canonical orbitals, but we have to keep in mind that HF and KS orbitals are different because their theoretical frameworks are different. In other words, canonical implies that the orbitals represent the converged eigenfunctions of the HF or KS equations. There has been a lot of discussion in the literature whether the canonical orbitals are localized or delocalized.¹¹² With this experiment, we want to show that there is no difference between the two. We suggest using the HF⁴¹ method, and one functional of choice among the ones used throughout the rest of this notebook. We suggest the def2-SVP basis set,⁴² and we will analyze the orbitals of benzene. First run the calculations as you did before and save all the files generated from them. Then, re-run the calculations using the Boys localization scheme,¹¹³ which is one of many different frameworks used to localize the orbitals.^{113,114} If you are using Q-Chem, note that the program saves both the delocalized and localized orbitals at the same time when using the BOYSCALC=2 keyword, so you do not have to run the calculations twice. When discussing the results, report pictures of the orbitals, and try to answer the following questions (and those in Part B) in the form of a short essay (~300 words). Plot the orbitals from 19 to 22 (the Lowest Unoccupied Molecular Orbital, or LUMO).

Problems:

Try to answer these questions when writing your essay.

- 1) Compare the delocalized and the localized orbitals. Are they different, or are they the same? What changes do you notice?
- 2) How does the LUMO look like?
- 3) Are the HF and DFT orbitals similar or different from each other? If so, to what extent?

Part B: Comparing the HOMO of an anion with the LUMO of the respective neutral molecule.

In this second part of the experiment, we will compare the LUMO of benzene with the HOMO (Highest Occupied Molecular Orbital) of the benzene anion. We will use the same geometry but remember to change charge and spin in the input file. Keep using the HF⁴¹ method, and the functional you chose for Part A. We will use the def2-SVP basis set.⁴² First run the calculations as you did before and save all the files generated from them. Then, re-run the calculations using the Boys localization scheme,¹¹³ which is one of many different frameworks used to localize the orbitals.^{113,114} If you are using Q-Chem, note that the program saves both the delocalized and localized orbitals at the same time when using the BOYSCALC=2 keyword, so you do not have to run the calculations twice. When discussing the results, report pictures of the orbitals, and try to answer the following questions (and those of Part A) in the form of a short essay (~300 words). Plot the orbitals from 19 to 22.

Problems:

Try to answer these questions when writing your essay.

- 1) Compare the delocalized and the localized orbitals. Are they different, or are they the same? What changes do you notice?

- 2) Are the HF and DFT orbitals similar or different from each other? If so, to what extent?
- 3) Compare the HOMO of the anion with the LUMO of the neutral species. Do you see any difference? Which one do you think is better as a representation of the LUMO of benzene? (Hint: which one is optimized, and which one is not optimized in a calculation?)

Tip: The main message of this experiment is that orbitals are mere mathematical objects, and their shape, size or color have no physical or chemical meaning.¹¹⁵ In addition, the canonical orbitals have no special value besides being the orbitals that minimize the energy in a HF calculation, or provide the best density in a DFT one.

Practice comment: The canonical orbitals are obtained as solutions of the SCF procedure, and their most remarkable property is that the energy is invariant with respect to any small changes in the orbitals. This means that once we have the canonical orbitals, the energy of the system does not change, since it is made stationary by the SCF procedure. As a consequence, we can manipulate the orbitals as much as we want provided that we *only* rotate them, i.e. we do not change the angles or the distance between the atoms. In other words, we are not changing the space spanned by these orbitals when we perform these rotations, which are called unitary transformations. This means that the canonical orbitals are invariant with respect to them, and it is because of this property that we can localize the delocalized canonical orbitals, and vice-versa. For this reason, the canonical orbitals “are not unique, and no particular significance can be given to a particular set”,¹¹⁶ and this applies to occupied and unoccupied orbitals in HF and DFT. With this experiment, we showed that the energy does not change if we change the spatial orientation of the orbitals, or if we make them localized through the procedure introduced by Boys.¹¹³ In addition, it is important to keep in mind that only the occupied orbitals are optimized in the SCF cycle, while the unoccupied, or virtual, orbitals are just symmetrized combinations of the basis functions used in the calculation. As a consequence, the LUMO and all the other virtual orbitals have no meaning. All of this implies that showing canonical orbitals’ pictures or claiming that it is possible to observe orbitals¹¹⁷ is meaningless.^{112,115}

We also showed that if you want to study the LUMO of a neutral molecule, you should run calculations on the anion instead. In fact, the LUMO in the neutral molecule becomes the HOMO in the anion, and as such it is optimized in the SCF cycle. In other words, the true shape of the LUMO of the neutral molecule can be established by running calculations on the anion of the same molecule at the same geometry. In this way, the orbitals are optimized in the SCF cycle, instead of being left as virtual obtained as symmetrized eigenfunctions.

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Experiment 13: Required corrections to compare with experimental values.

This experiment analyzes the outcome of two bond dissociation reactions from the Minnesota 2015B database.⁹ One comes from the SR-MGN-BE107 subset,^{15,94,118} the other from the SR-TM-BE17^{15,97,119-121} subset. In addition, you will also examine some total atomization energies from the W4-11 subset¹²² of the GMTKN55 database.⁵

First, you are going to analyze the dissociation of the C–O bond in *tert*-butyl alcohol to give the *tert*-butyl radical and the OH radical. The reference energy for this reaction is 115.02 kcal/mol. In the second case, you will take into account the FeCl¹²¹ molecule, and its dissociation into atomic chlorine and iron. The reference electronic energy for its dissociation is 78.5 kcal/mol.

Do not forget to use stability analysis for both cases. Remember also to use at least the (99,590) grid, and the def2-QZVP basis set.⁴² When it comes to functionals, we suggest using the MN15-L,⁸ MN15,⁹ B3LYP^{23,24,26-28} and PBE³¹ functionals, and the HF method.⁴¹ Before answering the questions below, we suggest you collect the data and put them in a table, including the calculated results and the error calculated with respect to the reference energy.

Problems for *tert*-butyl alcohol.

- 1) Which functional is the best? Which one is the worst?

- 2) How does the HF method perform? Are you surprised?

- 3) Try the B3LYP functional with the 6-31G* basis set of Pople.⁸⁷ Do you see any improvement? Where do you think this improvement come from?

Problems for FeCl.

- 1) Which functional is the best performer?

- 2) How does the HF method perform? Are you surprised?

- 3) Go on the Nist Webbook of Chemistry Website and look for the enthalpy of formation in the gas phase of FeCl. How much is it, in kcal/mol? Do you see any difference with the reference data that you are using?

- 4) Given the NIST reference and the electronic energy, do you think you can directly compare the theoretical result with the experimental one? Why?
-
-

We will now turn the attention to the atomization reactions.¹²² Remember that the definition of atomization reaction implies that we decompose the molecule into its constituent atoms (see, for example, reaction **3c** in Experiment 3). You will take into account the H₂ molecule, methane, water, ammonia, and ozone. The reference values (in kcal/mol) are given in the following table (**Table 3**). Note that for the H₂ molecule, the atomization reaction and the bond dissociation reaction are conceptually the same.

We suggest using the same methods used above. Total atomization energies are not very important from the chemical viewpoint, but they are interesting from the computational perspective because they represent a challenge in functional development and because they are a good test of the robustness and reliability of functional approximations. Remember to collect the data in a table before going on and answering the following questions.

Molecule	Reference energy (kcal/mol)
H ₂	109.5
CH ₄	420.4
NH ₃	298.0
H ₂ O	233.0
O ₃	147.4
Table 3 Reference energies for the total atomization energies from the W4-11 subset.	

Problems for the W4-11 subset.

- 1) Which functional is the best? Which one is the worst?
-

- 2) How does the HF method perform? Are you surprised?
-

- 3) In your opinion, what is the reason of the failure of the HF method?
-

- 4) Do you see the same trend in both bond dissociation reactions and atomization reactions?

-
- 5) Can you directly compare the atomization energy with the formation enthalpy of a substance? Why?
-

Practice comment: Bond dissociation energies are ubiquitous in databases,⁵⁻⁹ because it is very important for *xc* functionals to correctly describe them. However, even simple reactions can be tricky: the dissociation of the C–O bond is in principle easy, but it results in two radical molecules whose description is challenging for theoretical methods (remember that in principle KS-DFT is a single-determinant theory like HF). For the dissociation energy of FeCl, the scenario gets even more complicated when heavier elements are involved. Also, remember that there is no simple way to compare the calculated result with the experimental result, as explained by Truhlar and co-workers.^{119,121} Without going into much details, you have to account for different corrections in order to go from the experimental to the purely theoretical value. That is why the direct comparison between the experimental and the computed values is discouraged, unless you seek help from a theoretician. Coming to the last set of reactions, they can be seen as an additional example of why you should rely on more modern functionals. Not only do we need a functional that is capable of describing the molecule in the most appropriate way, but it needs to describe correctly also the atoms, which are a completely different chemical species. The HF method fails to account for electron correlation, and therefore its description of atoms is really bad, which results in high errors. On the other hand, all DFAs account for electron correlation in some approximate way,¹²³⁻¹²⁷ and their results for atoms are better. In general, however, we once again advise non-experts to seek help from a theoretician for such cases.

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Experiment 14: A Collaborative Project.

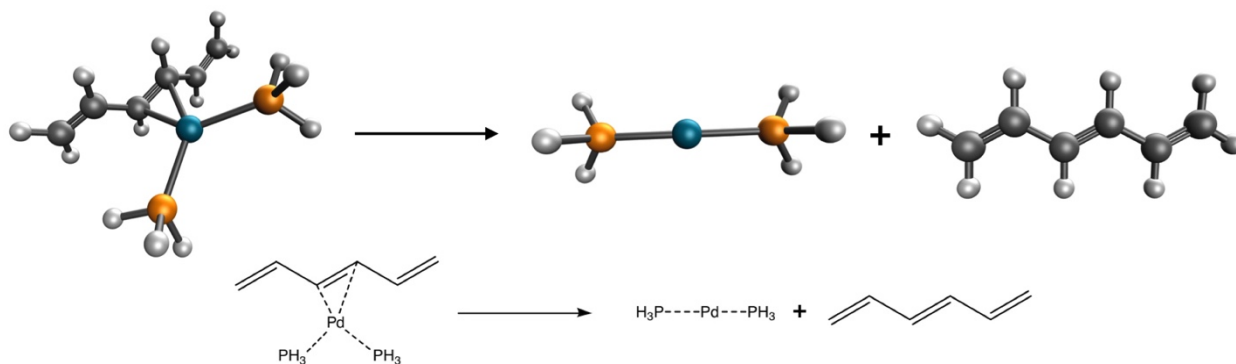


Figure 5 Dissociation reaction of the diphosphinohexatrienepalladium(0) complex. The carbon atoms are black, the phosphorus atoms are orange, the hydrogen atoms are white, the palladium atom is light blue. The dotted lines show dative bonds.

Imagine that somebody in your department is studying the following complex of Pd (these structures are taken from the PdBE2 subset¹²⁰ of the Minnesota 2015B database⁹), and they ask you to calculate the bond dissociation energy for the reaction reported below (**figure 5**). You are now in charge of setting up the calculations. Choose the functional and the basis set you want to use based on the published literature (for instance, look at these recent publications^{5-10,13,15,128,129}), the functionals available to you based on the program you have, and your experience with the previous experiments. Remember also that performing calculations is a compromise between accuracy and computational capabilities.

After you finished all calculations and collected all the results, write a short report (~300 words) indicating the method you adopted and why you chose it. In addition, describe the computational setup appropriately, present the results you obtained, and compare them to the reference value of 16.20 kcal/mol. Do not forget to add a title and an appropriate reference section.

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