

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

A Computational Chemistry Laboratory Notebook

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Instructor Key

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.^{4-13,27} 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 publications⁵⁻¹³ for such suggestions. For good reviews of DFT, you can read refs. 6, 27, 28 or 29.

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 2001.³⁰ 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^{5-13,25,27,28} 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	LSDA	LSDA	GGA	GGA	GGA
Functional	M06-L	M11-L	MN15-L	SCAN	B97M-V
Form	mGGA	mGGA	mGGA	mGGA	mGGA
Functional	B3LYP	B3PW91	M05-2X	M06	M06-2X
Form	H-GGA	H-GGA	H-mGGA	H-mGGA	H-mGGA
Functional	M06-HF	M11*	MN15	PBE0	ωB97M-V*
Form	H-mGGA	H-mGGA	H-mGGA	H-GGA	H-mGGA

* To be more specific, M11 and ωB97M-V are range-separated hybrid mGGAs.

Experiment 1: Applying DFT to Organic Chemistry – Part A.

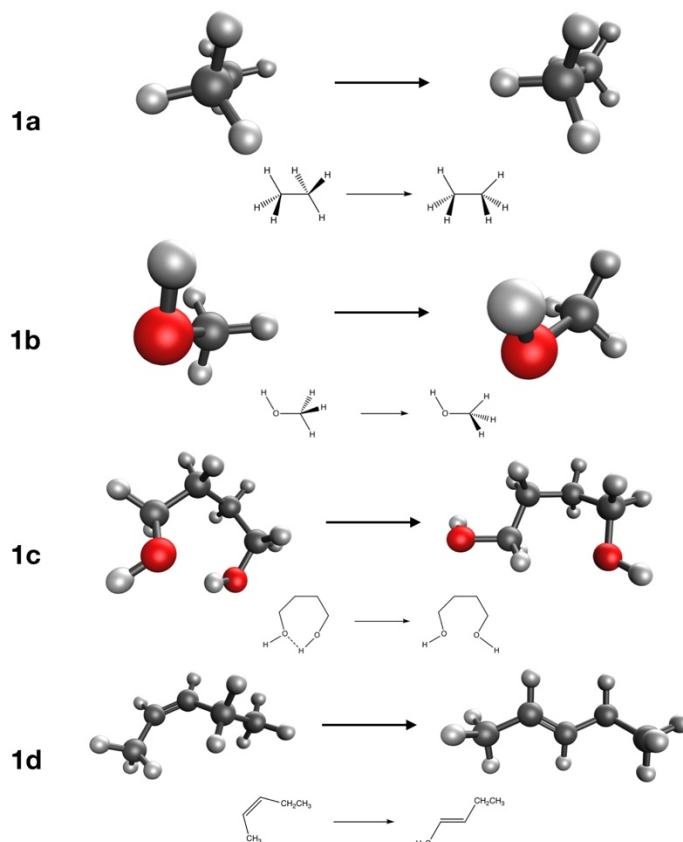


Figure 1 Reactions studied in Experiment 1. Rotational barrier of ethane (**1a**) and methanol (**1b**). Conformational change in two isomers of butane-1,4-diol (**1c**). Cis-trans isomerization reaction of pent-2-ene (**1d**). The carbon atoms are black, the oxygen atoms are red, and the hydrogen atoms 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 BUT14DIOL⁴⁷ and FH51⁴⁸ subsets of the GMTKN55 database.⁵

The κ functional approximations we suggest to use are: SPW92^{33,34} (if not available, use SVWN5^{14,33}), BP86,^{15,19} BLYP,^{15,16} B3LYP,¹⁴⁻¹⁸ B3LYP-D3(BJ),^{14-18,35} B3PW91,^{15,17,34,36} PBE,³⁷ PBE-D3(BJ),^{35,37} PBE0,³⁸ M06-2X,³⁹ M11,⁴⁰ SCAN⁴¹ (if not available, use TPSS)⁴², MN15,⁹ B97M-V^{21,43} (if not available, use MN15-L⁸), ω B97M-V^{20,21} (if not available, use ω B97X-D)⁴⁴ and the Hartree-Fock (HF)⁴⁵ method. The basis set you should use is def2-QZVP.⁴⁶ 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 $|\epsilon|$ with respect to the reference data as the difference:

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

Report them in the same table that collects the results.

Problems:

- 1) Which functional has the most negative error?
1a) BLYP/M11; 1b) M11; 1c) HF; 1d) HF
- 2) Which functional has the most positive error?
1a) HF; 1b) B97M-V; 1c) SPW92; 1d) SPW92
- 3) Which functional is the best performer for each reaction?
1a) M06-2X; 1b) PBE0/BLYP; 1c) PBE0; 1d) M06-2X
- 4) Which functional is the best overall?
M06-2X and PBE0
- 5) Are there functionals that perform badly for these reactions?
Besides HF and SPW92, PBE-D3(BJ) and BLYP.
- 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	B3LYP	B3LYP-D3(BJ)	B3PW91
Total time	~21 min	37 min 13 sec	37 min 13 sec	24 min 26 sec
	M06-2X	MN15	B97M-V	
Total time	23 min 26 sec	30 min	~28 min	

As this table shows, the B3LYP functional takes as much time as –if not slightly longer than– the other hybrid functional, exemplified in this case by the MN15 and M06-2X. We also see that adding the -D3 correction does not impact the performance of the functionals in terms of computational timing. The local functionals, namely SPW92 and B97M-V, take less than a hybrid in general.

Experiment 2: Applying DFT to Organic Chemistry – Part B.

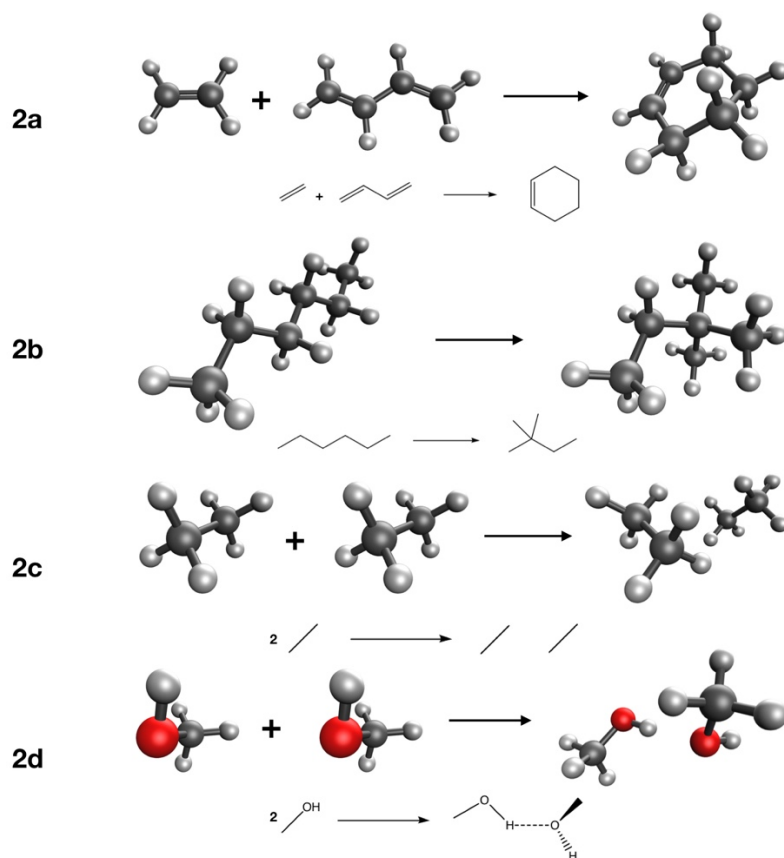


Figure 2 Reactions studied in the Experiment 2. Diels-Alder reaction of ethene and butadiene (**2a**). Isomerization of n-hexane to neo-hexane (**2b**). Formation of the ethene (**2c**) and the methanol (**2d**) dimers. The carbon atoms are black, the oxygen atoms are red, and the hydrogen atoms are 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^{5,49,50} and ADIM6^{5,51} subsets of the GMTKN55 database,⁵ and the AlkIsomer11^{52,53} and S66^{54,55} subsets of the MGCD84 database.⁶

Similarly to Experiment 1, you will use the following functionals: SPW92^{33,34} (or SVWN5^{14,33}), BP86,^{15,19} BLYP,^{15,16} B3LYP,¹⁴⁻¹⁸ B3LYP-D3(BJ),^{14-18,35} B3PW91,^{15,17,34,36} PBE,³⁷ PBE-D3(BJ),^{35,37} PBE0,³⁸ M06-2X,³⁹ M11,⁴⁰ SCAN⁴¹ (or TPSS⁴²), MN15,⁹ B97M-V^{21,43} (or MN15-L⁸), ω B97M-V^{20,21} (or ω B97X-D)⁴⁴ and the Hartree-Fock (HF)⁴⁵ method. The basis set you should use is the def2-QZVP.⁴⁶ 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?
2a) PBE0 (and SPW92); 2b) MN15/SPW92; 2c) B3PW91; 2d) B3PW91
- 2) Which functional has the most positive error?
2a) BLYP; 2b) BLYP (and HF); 2c) MN15 (and SPW92); 2d) BP86/BLYP
- 3) Which functional is the best performer for each reaction?
2a) M11; 2b) M06-2X; 2c) B3LYP-D3(BJ); 2d) B3LYP-D3(BJ)
- 4) Which functional is the best overall?
M06-2X
- 5) Are there functionals that perform badly for these reactions?
Besides HF and SPW92, BLYP and B3LYP.
- 7) 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	B3LYP	B3LYP-D3(BJ)	B3PW91
Total time	~25 min	~37 min	~43 min	57 min 37 sec
	M06-2X	MN15	B97M-V	
Total time	47 min 30 sec	~40 min	~32 min	

As this table shows, the B3LYP functional takes as much time as the other hybrid functional, exemplified in this case by the MN15 and M06-2X. We also see that adding the -D3 correction does not impact the performance of the functionals in terms of computational timing. The local functionals, namely SPW92 and B97M-V, take less than a hybrid in general.

- 6) Do the functionals that include -D3 corrections perform better than the corresponding uncorrected ones?
The dispersion-corrected versions of both B3LYP and PBE are always better than the respective uncorrected versions. We go from an average of 4.51 kcal/mol (B3LYP) and 1.83 kcal/mol (PBE) to 1.78 kcal/mol (B3LYP-D3(BJ)) and 0.47 kcal/mol (PBE-D3(BJ))

Experiment 3: Difficult Cases for DFT.

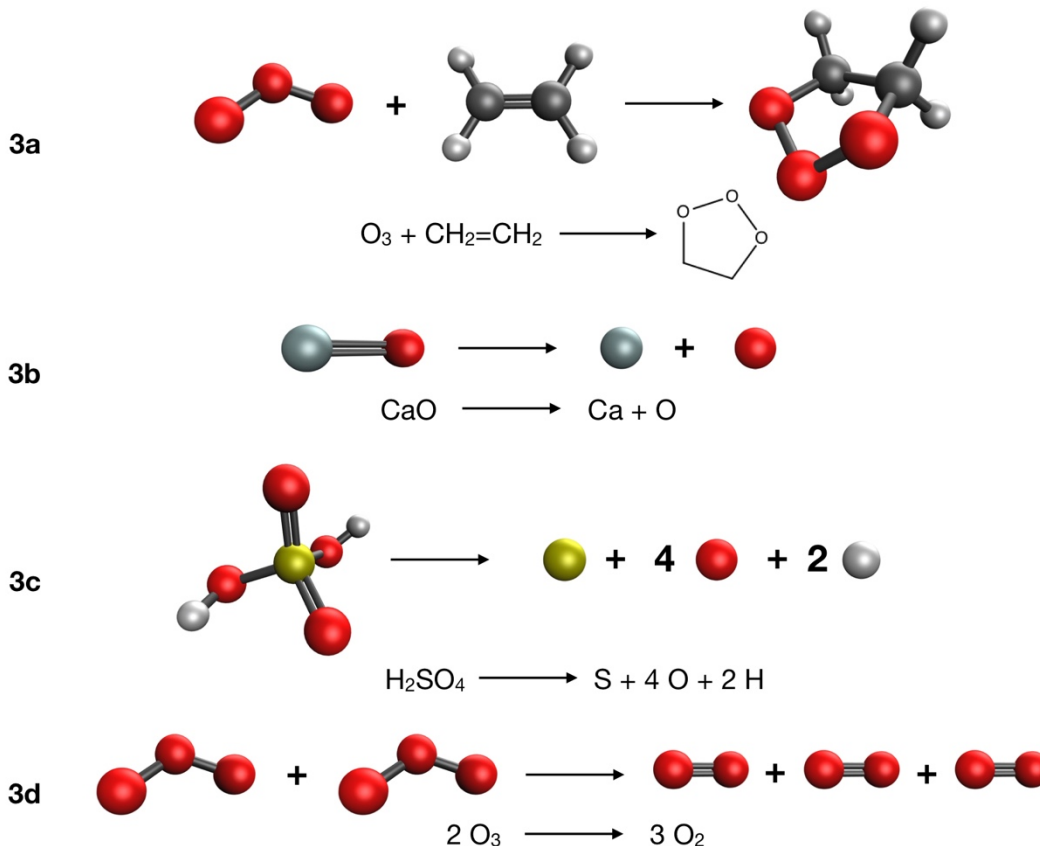


Figure 3 Reactions studied in Experiment 3. The ozonolysis reaction (**3a**), the dissociation of the CaO bond (**3b**), the atomization reaction of sulfuric acid (**3c**), and the conversion of ozone to oxygen (**3d**). The carbon atoms are black, the oxygen atoms are red, the hydrogen atoms are white, 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^{5,31,39,49,56} subset of the GMTKN55 database,⁵ while the second and the third one come from the MR-MGM-BE4⁵⁷ and DC9^{28,58} subsets of the Minnesota 2015B database.⁹ The last reaction has been obtained combining two datapoints of the W4-17 database.⁵⁹ 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^{33,34} (or SVWN5^{14,33}), BP86,^{15,19} BLYP,^{15,16} B3LYP,¹⁴⁻¹⁸ B3LYP-D3(BJ),^{14-18,35} B3PW91,^{15,17,34,36} PBE,³⁷ PBE-D3(BJ),^{35,37} PBE0,³⁸ M06-

2X,³⁹ M11,⁴⁰ SCAN⁴¹ (or TPSS)⁴², MN15,⁹ B97M-V^{21,43} (or MN15-L⁸), ω B97M-V^{20,21} (or ω B97X-D)⁴⁴ and the Hartree-Fock (HF).⁴⁵ The basis set you should use is def2-QZVP,⁴⁶ 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:

- Which functional has the most negative error?
3a) M06-2X; 3b) HF/M06-2X; 3c) B3LYP/HF; 3d) PBE0/SPW92/HF
- Which functional has the most positive error?
3a) HF/BLYP; 3b) SVWN5/PBE/PBE-D3/BP86; 3c) SVWN5; 3d) PBE/BP86
- Which functional is the best performer for each reaction?
3a) B3PW91/B97M-V; 3b) MN15/ ω B97M-V; 3c) SCAN/MN15; 3d) PBE-D3(BJ)/B3LYP-D3(BJ)
- Which functional is the best overall?
MN15
- Are there functionals that perform badly for these reactions?
Besides HF and SPW92, PBE and BP86.
- 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	B3LYP	B3LYP-D3(BJ)	B3PW91
Total time	~4 min	6 min 6 sec	7 min 21 sec	5 min 16 sec
	MN15	B97M-V	M06-2X	
Total time	5 min 36 sec	~5 min	5 min 43 sec	

As this table shows, the B3LYP functional takes as much time as the other hybrid functional, exemplified in this case by the MN15 and M06-2X. We also see that adding the -D3 correction does not impact the performance of the functionals in terms of computational timing. The local functionals, namely SPW92 and B97M-V, take less than a hybrid in general.

- Do the D3-corrected functionals perform better or worse than the respective uncorrected ones?
The dispersion-corrected versions of both B3LYP and PBE are always better than the respective uncorrected versions. We go from an average of 6.05 kcal/mol (B3LYP) and 7.80 kcal/mol (PBE) to 3.00 kcal/mol (B3LYP-D3(BJ)) and 5.00 kcal/mol (PBE-D3(BJ)).

Overall Problems for Experiments 1-3:

- 1) Which functional or method is the best overall performer?
The best overall performer is MN15, followed by B97M-V and ω B97M-V.
- 2) Which functional or method is the worst overall performer?
The worst overall performers are PBE, BP86 and BLYP (besides HF and SPW92).
- 3) Is B3LYP faster than other functionals/methods?
B3LYP is a hybrid GGA functional. For this reason, it is going to be more expensive than any local (GGA or mGGA) functional because it is a hybrid. However, if we take other hybrids into account, their computational time is comparable. We believe that it is better to spend a little more computational time to have a better accuracy than to save time and get less accurate results
- 4) Do you think that adding the -D3 correction helps? For which reactions?
Despite being designed to address dispersion interactions, the -D3 correction helps in all the reactions analyzed in the previous experiments since the magnitude of the error decreases.

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,^{70,71} which have been developed in the past sixty years by different computational chemists. Head-Gordon and co-workers⁷² found that the most cost-effective basis sets for DFT belong to the Ahlrichs’ family.⁴⁶ We will analyze their performance for the dissociation reaction of the HCl dimer, coming from the NCCE23^{28,73-76} 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^{33,34} (or SVWN5^{14,33}), BP86,^{15,19} B3LYP,¹⁴⁻¹⁸ PBE,³⁷ PBE0,³⁸ M06-2X,³⁹ SCAN⁴¹ (or TPSS⁴²), B97M-V^{21,43} (or MN15-L⁸), ω B97M-V^{20,21} (or ω B97X-D)⁴⁴ and the Hartree-Fock (HF)⁴⁵ method. For now, we only use the def2-SVP, def2-TZVP and def2-QZVP basis sets.⁴⁶ 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 sets⁷⁷ instead. However, keep in mind that they are optimized for correlated wave-function calculations,⁷⁷ 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	BP86	B3LYP	PBE	PBE0
def2-SVP	3.75	0.99	1.19	1.90	1.43
def2-TZVP	2.08	0.52	0.45	0.33	0.02
def2-QZVP	1.88	0.78	0.75	0.03	0.23
	M06-2X	SCAN	B97M-V	ω B97M-V	HF
def2-SVP	1.36	1.43	1.54	1.79	0.30
def2-TZVP	0.15	0.25	0.39	0.16	1.67
def2-QZVP	0.28	0.17	0.14	0.12	1.84

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?

For some functionals like B97M-V or ω B97M-V, the magnitude of the error decreases when going from double- to a quadruple- ζ basis set. The Minnesota functionals usually work best with a triple- ζ basis set. The HF method has an unpredictable behavior.

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

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

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

PBE, SCAN, B97M-V and ω B97M-V with a quadruple- ζ basis set.

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 sets⁴⁶ (or the aug-cc-pVDZ, aug-cc-pVTZ, and aug-cc-pVQZ basis sets).⁷⁷ Report the absolute errors in the table below, and then answer the following questions.

	SPW92	BP86	B3LYP	PBE	PBE0
def2-SVPD	2.51	0.30	0.20	0.62	0.38
def2-TZVPD	1.96	0.73	0.73	0.05	0.21
def2-QZVPD	1.84	0.84	0.81	0.03	0.28
	M06-2X	SCAN	B97M-V	ω B97M-V	HF
def2-SVPD	0.36	0.65	0.69	0.44	1.24
def2-TZVPD	0.23	0.18	0.21	0.09	1.80
def2-QZVPD	0.32	0.15	0.11	0.18	1.86

Problems:

- 1) Do you see trends that are similar to those in point 1 of Experiment 4a?
Yes, the general trends are the same.
- 2) Do you think adding diffuse functions helps for this particular system?
We can identify three cases: First, well-behaved functionals like B97M-V always benefit from adding diffuse functions; second, functionals like BP86 or M06-2X benefit but only with a double- ζ basis set, probably because of the increased number of basis functions; third, adding diffuse functions with the HF method is always detrimental.
- 3) For what chemical species do you think we need diffuse functions the most?
Anions, since they have an electron density that decays slowly, extending far away from the nuclei.

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,⁷⁸ 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.⁷⁹ 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.⁸⁰ 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.⁸¹ Extremizing this procedure, and considering each atom as a fragment, yields to methods such as the CP^{aa} of Galano and Alvarez-Idaboy⁸² or the ACP(x) correction of Jensen.⁸³ Kruse and Grimme, instead, introduced the geometric counterpoise (gCP)⁸¹ 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,^{28,73-76} 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,^{14-21,33,34,37-39,41-45} and basis sets^{46,77} 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.⁷⁷

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	BP86	B3LYP	PBE	PBE0
def2-SVP	2.17	0.40	0.31	0.43	0.19
def2-TZVP	1.77	0.79	0.74	0.02	0.26
def2-QZVP	1.81	0.83	0.81	0.04	0.28
CP corrected	M06-2X	SCAN	B97M-V	ωB97M-V	HF
def2-SVP	0.14	0.28	0.39	0.29	1.37
def2-TZVP	0.38	0.03	0.15	0.15	1.85
def2-QZVP	0.33	0.13	0.10	0.18	1.86
CP corrected	SPW92	BP86	B3LYP	PBE	PBE0
def2-SVPD	1.93	0.79	0.69	0.10	0.12
def2-TZVPD	1.80	0.85	0.84	0.06	0.31

def2-QZVPD	1.83	0.84	0.82	0.04	0.28
CP corrected	M06-2X	SCAN	B97M-V	ω B97M-V	HF
def2-SVPD	0.11	0.19	0.19	0.02	1.68
def2-TZVPD	0.37	0.09	0.12	0.19	1.90
def2-QZVPD	0.33	0.15	0.10	0.18	1.87

The calculated results get better for small basis sets, which is when the counterpoise correction works best. This is true for all the functionals, but it is not for the HF method. In this latter case, the results get always worse.

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

The largest magnitude for the CP corrections is obtained with double- ζ basis sets, both augmented and non-augmented. The effect is negligible for quadruple- ζ basis sets.

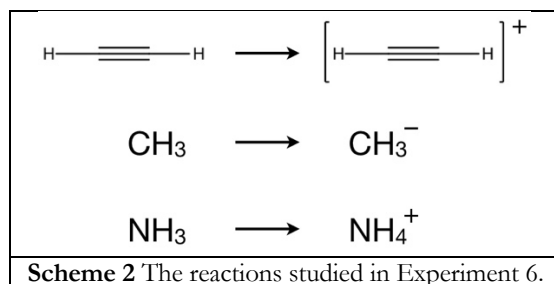
- 3) Are there any functionals that do not benefit at all from the CP correction?

The only method that doesn't benefit from the CP correction is HF.

- 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).

Yes, it would be a good idea because they correct for different errors.

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^{28,89} subset of the Minnesota 2015B⁹ database, while the reaction of acetylene comes from the G21IP⁹⁰ subset and the electron affinity of the methyl radical comes from the G21EA⁹⁰ 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^{33,34} (or SVWN5^{14,33}), BP86,^{15,19} B3LYP,¹⁴⁻¹⁸ PBE,³⁷ PBE0,³⁸ M06-2X,³⁹ SCAN⁴¹ (or TPSS⁴²), B97M-V^{21,43} (or MN15-L⁸), ω B97M-V^{20,21} (or ω B97X-D)⁴⁴ and Hartree-Fock (HF).⁴⁵ For this experiment, you are going to use the Ahlrichs' basis sets,⁴⁶ or alternatively the Dunning's ones.⁷⁷ 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)	1.23	2.60	2.92	3.03	3.42	3.43
BP86	4.64	3.57	3.50	3.38	3.08	3.07
PBE	6.40	5.23	5.25	5.08	4.83	4.80
SCAN	8.89	8.54	8.91	8.82	8.68	8.67
B97M-V (MN15-L)	7.46	6.82	8.27	8.05	7.85	7.84
PBE0	7.06	6.46	6.96	6.84	6.66	6.65
M06-2X	5.51	5.03	4.73	4.67	4.25	4.25
B3LYP	6.37	5.10	5.11	4.97	4.68	4.67

ω B97M-V (ωB97X-D)	7.47	6.56	6.69	6.59	6.42	6.41
HF	36.84	37.03	38.67	38.62	38.62	38.63

EA of CH ₃ [•]	def2-SVP	def2-SVPD	def2-TZVP	def2-TZVPD	def2-QZVP	def2-QZVPD
SPW92 (SVWN5)	16.11	0.84	0.82	3.87	3.70	4.75
BP86	18.77	3.06	4.72	0.29	0.40	0.52
PBE	21.65	6.16	8.01	3.25	3.44	2.38
SCAN	25.95	12.37	13.67	9.96	9.88	9.14
B97M-V (MN15-L)	19.55	6.49	9.01	4.12	4.48	3.46
PBE0	23.33	9.93	11.23	7.39	7.45	6.63
M06-2X	20.70	7.57	8.12	5.02	4.63	3.77
B3LYP	21.38	6.35	8.09	3.81	3.97	3.02
ω B97M-V (ωB97X-D)	21.14	6.35	7.96	4.11	4.27	3.47
HF	51.06	40.58	41.51	38.61	38.63	38.02

PA of NH ₃	def2-SVP	def2-SVPD	def2-TZVP	def2-TZVPD	def2-QZVP	def2-QZVPD
SPW92 (SVWN5)	2.37	5.43	4.02	5.44	4.95	5.26
BP86	5.49	1.20	0.32	0.94	0.43	0.69
PBE	5.41	1.43	0.17	1.33	0.75	1.09
SCAN	6.07	0.36	1.54	0.50	1.07	0.87
B97M-V (MN15-L)	4.24	1.10	0.58	0.77	0.18	0.04
PBE0	6.44	0.70	1.95	0.78	1.30	1.07
M06-2X	3.77	1.88	1.22	2.17	1.91	2.11
B3LYP	5.44	1.22	0.32	0.94	0.35	0.61

ω B97M-V (ωB97X-D)	3.16	3.34	1.68	2.89	2.24	2.51
HF	7.64	3.42	4.19	3.50	4.05	3.94

Problems:

- 1) Which functional is the best choice with the def2-nZVP family of basis set?

See details in the table below.

- Ionization potential of acetylene: **SPW92 and BP86**
- Electron affinity of CH₃: **SPW92 and BP86**
- Proton affinity of ammonia **varies**

IP of HCCH	Functional	EA of CH ₃ [·]	Functional	PA of NH ₃	Functional
def2-SVP	SPW92	def2-SVP	SPW92	def2-SVP	SPW92
def2-SVPD	SPW92	def2-SVPD	SPW92	def2-SVPD	SCAN
def2-TZVP	SPW92	def2-TZVP	SPW92	def2-TZVP	PBE
def2-TZVPD	SPW92	def2-TZVPD	BP86	def2-TZVPD	SCAN
def2-QZVP	BP86	def2-QZVP	BP86	def2-QZVP	B97M-V
def2-QZVPD	BP86	def2-QZVPD	BP86	def2-QZVPD	B97M-V

- 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: **The results always get better.**
- Electron affinity of CH₃: **The results always get better.**
- Proton affinity of ammonia: **The results get better for the basis sets of double- ζ quality, but they get worse for triple- and quadruple- ζ .**

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

We do not need diffuse functions when studying cations, as shown by the results of the proton affinity of ammonia. These results consistently get worse by adding augmented functions, so their usage is not recommended for these chemical species. In the case of the ionization potential of acetylene, augmenting the basis sets resulted in small improvements that can be attributed to the fact that the functionals benefit from having more basis functions available. In these cases, however, it is preferable to provide the additional basis functions by increasing the size of the basis set, rather than using diffuse functions. For anions, instead, we need an augmented basis set to appropriately describe the electron density in regions far away from the nuclei. The electron distribution of an anion is more “spread out” than the electron density of a neutral species. If we exclude the behavior of SPW92, the results for the electron affinity always get better, no matter the size of the basis set.

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

Hopefully, it was already correctly identified that anions need augmented basis sets, while cations do not.

- 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?

The calculation of the IP of acetylene always benefits from the availability of more basis functions. The number of basis functions for acetylene with the def2-SVP, def2-TZVP and def2-QZVP basis sets is 38, 74, and 174 respectively. For the same molecule, the def2-SVPD, def2-TZVPD and def2-QZVPD have 56, 92, and 192 basis functions respectively. When we increase the size of the basis set, we roughly double the amount of basis functions, while when we add diffuse functions we increase the number of basis functions by only about a half. Therefore, in general, it is better to increase the number of basis functions by increasing the basis set size rather than by adding diffuse functions.

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

The B3LYP¹⁴⁻¹⁸ functional and the 6-31G* basis set of Pople and co-workers⁹² 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 1993.¹⁷ The originally proposed three-parameter functional used his 1988 exchange functional¹⁵ in conjunction with the correlation functional of Perdew and Wang (PW91).³⁴ B3LYP was introduced one year later by Frisch and co-workers by replacing PW91 with the LYP functional,¹⁶ since the latter provided better results in a computational study of circular dichroism spectra.¹⁸ 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,⁹² 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,⁷⁷ def2-SVP,⁴⁶ and pc-1⁹¹ (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,^{5,47,48} 2^{5,6,49-55} and 3.^{5,28,31,39,49,56-59} 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?
We chose the hexane molecule from the AlkIsomer11 geometries. Note that def2-SV(P) has 112 basis functions.

Molecule	6-31G*	def2-SVP	cc-pVDZ	pc-1
Basis functions (#)	118	154	154	154

- 2) Which basis set gives the smallest absolute error for the molecules in Experiment 1?
The pc-1 basis set gives the smallest error.
- 3) Which basis set gives the smallest absolute error for the molecules in Experiment 2?
The 6-31G* basis set gives the smallest error.
- 4) Which basis set gives the smallest absolute error for the molecules in Experiment 3?
The def2-SVP basis set gives the smallest error.
- 5) Which basis set gives the smallest absolute error overall?
The def2-SVP basis set gives the smallest error overall.
- 6) Now re-do all the calculations using the B3LYP-D3(BJ)^{14-18,35} with the same small basis sets. What happens to the results? Do they get better?

With the B3LYP-D3(BJ) functional, the results get better for the molecules in Experiments 2 and 3. For Experiment 1, the results are on average slightly worse (only 0.07 kcal/mol, which is totally negligible) than those obtained with the uncorrected B3LYP functional. Overall, the -D3 correction makes the results better by 0.86 kcal/mol.

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

We tried the ω B97M-V functional, and we reported the results in the Excel spreadsheet. Since 6-31G* is a double- ζ basis set, the results obtained with it are always worse than the results obtained with the def2-QZVP basis set. We only found two exceptions, which have to be attributed more to random cancellation of errors rather than to a better performance of the 6-31G* basis set.

- 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?

A well-behaved functional like ω B97M-V shows that the magnitude of the error decreases with increasing basis set size. This is what we expect. We observe this behavior with B3LYP and B3LYP-D3(BJ) in Experiments 1 and 3. In fact, the average error of the quadruple- ζ results is always lower than the error obtained with 6-31G*, as expected. However, for the molecules in Experiment 2, B3LYP/6-31G* and B3LYP-D3(BJ)/6-31G* give lower errors than the respective quadruple- ζ results, and this is due to error cancellation. The behavior of error cancellation, unfortunately, is completely unpredictable. In some cases, such as in Experiment 2, it can be useful (take a look at the Diels-Alder reaction), while in some others (look at the bond dissociation energy of CaO, or the atomization energy of H₂SO₄) it is catastrophic. There is no way to predict beforehand whether error cancellation will work in your favor or against you.

Experiment 8: Integration Grids 1: The Argon Dimer.

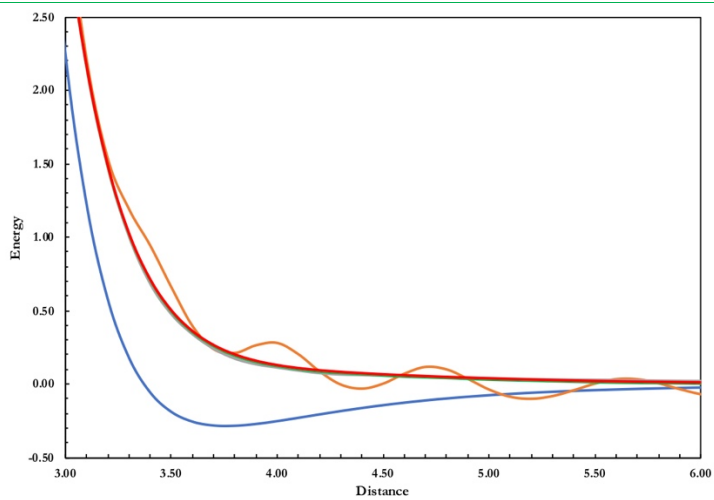
For this experiment, you are going to analyze a subtle issue that might potentially affect the results of every exchange–correlation functional. Kohn–Sham (KS)⁶⁰ DFT necessitates the usage of a real-space grid for the evaluation of the exchange–correlation integrals. Most software use a grid construction algorithm first introduced by Becke in 1988.⁹³ 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 Houk⁹⁴ for the M06 family³⁹ of the Minnesota functionals, and by Mardirossian and Head-Gordon^{4,95} 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.⁹⁶ For this experiment, you are going to study the dissociation curve of the argon dimer. Geometries for these systems come from the RG10⁹⁷ 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.

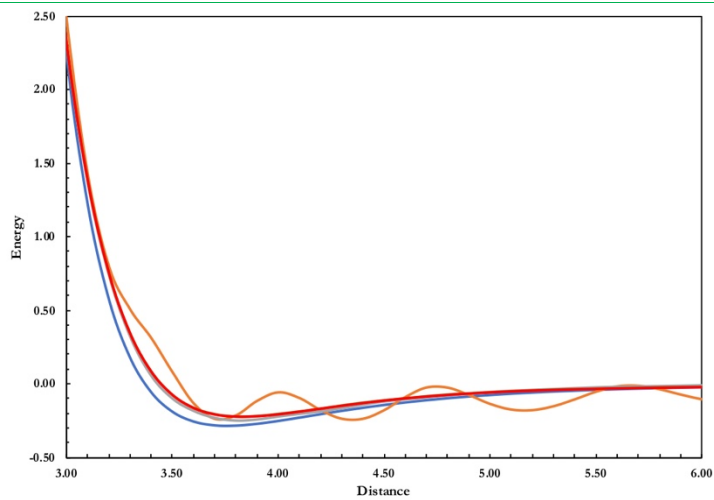
Table 1 Reference values in kcal/mol for the argon dimer given the Ar-Ar distance in Å.					
Distance	Energy	Distance	Energy	Distance	Energy
3.0	2.24	4.0	-0.25	5.0	-0.08
3.1	1.21	4.1	-0.23	5.1	-0.07
3.2	0.57	4.2	-0.21	5.2	-0.06
3.3	0.18	4.3	-0.18	5.3	-0.05
3.4	-0.06	4.4	-0.16	5.4	-0.05
3.5	-0.19	4.5	-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,¹⁴⁻¹⁸ B3LYP-D3(BJ),^{14-18,35} M05-2X,⁹⁸ M06-L,⁹⁹ M06-HF,¹⁰⁰ M11,⁴⁰ M11-L,¹⁰¹ MN15-L,⁸ PBE³⁷ and ω B97M-V^{20,21} (or ω B97X-D)⁴⁴. As usual, feel free to add any functionals you like. The basis set of choice is def2-QZVP⁴⁶ 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.

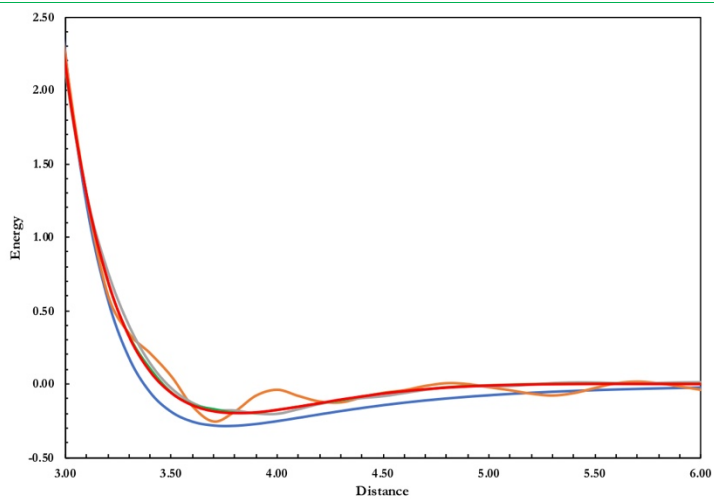
When presenting the results, try to use a dissociation plot like the one reported in **figure 4** for the VSEX functional.¹⁰² Before generating the graphs, collect all the results in a table formatted like **Table 2** in the next page.



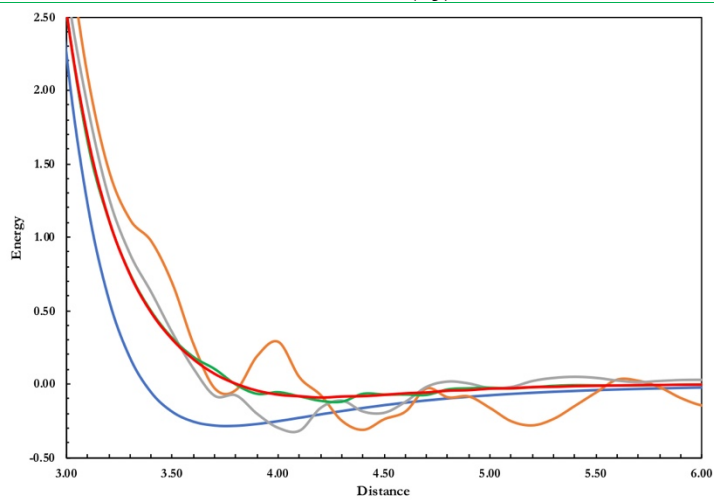
B3LYP



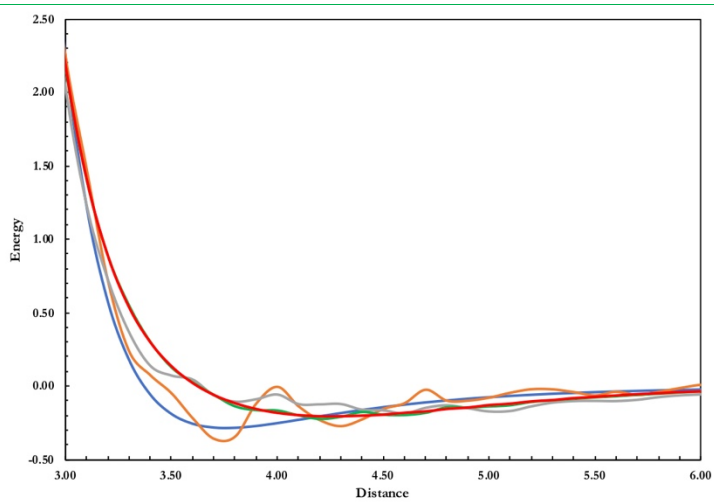
B3LYP-D3(BJ)



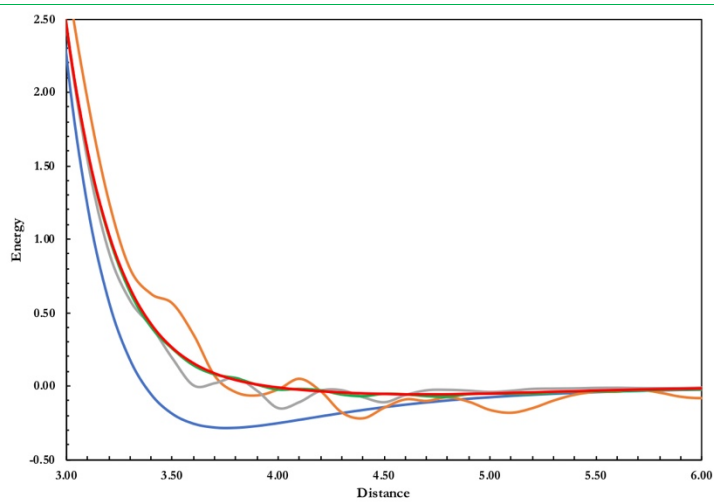
M05-2X



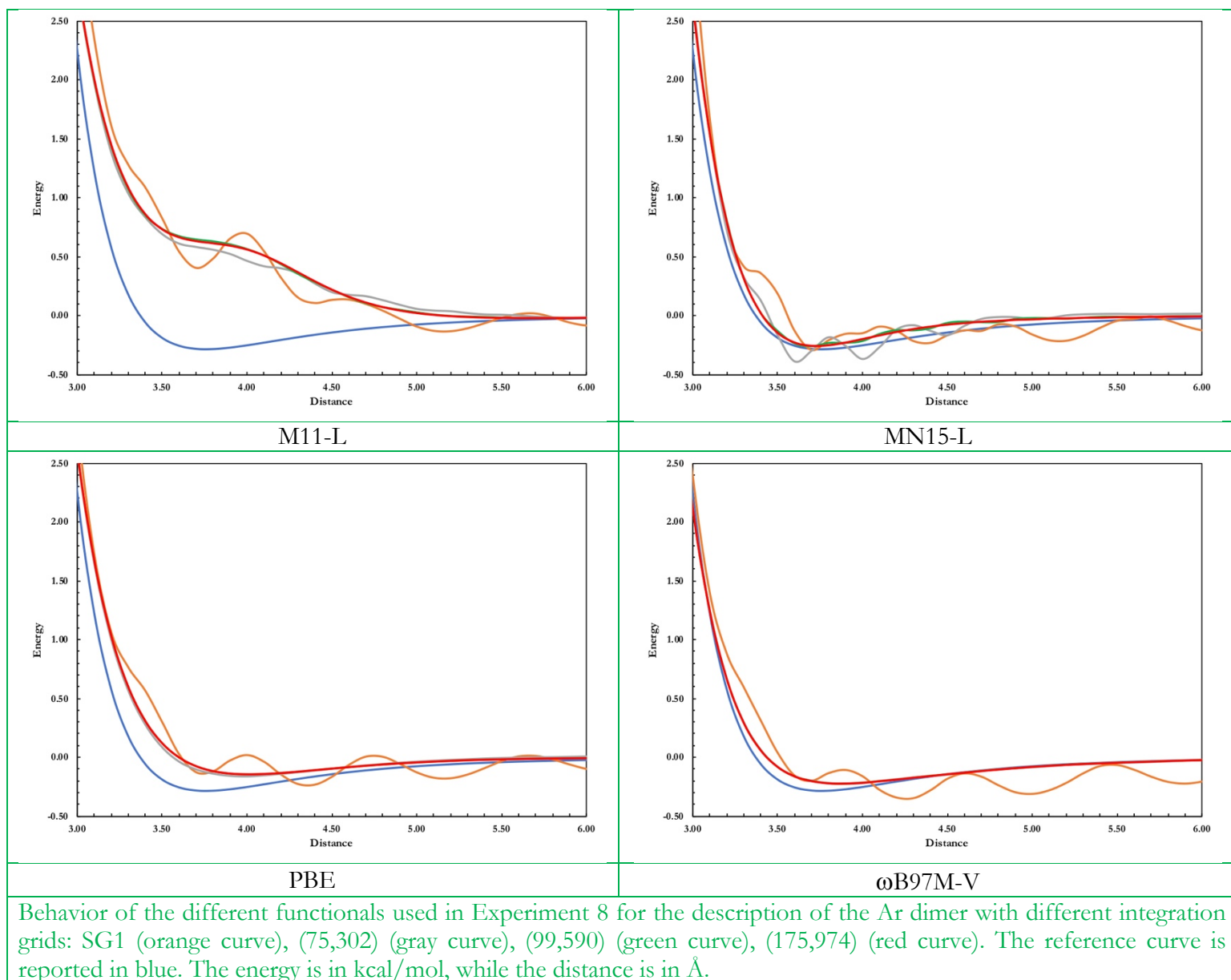
M06-L



M06-HF



M11



Problems:

- 1) Can you find any problematic functionals?
The Minnesota family of functionals is problematic for these molecules. In fact, they are not converged even using the (175,974) grid.
- 2) Why do you observe several minima and maxima in these curves? Do you think they might be unphysical?
The different minima and maxima represent oscillations due to an insufficient description of the atomic space using the different integration grids. Convergence is achieved only with the large (175,974) grid, but in the case of the M11-L functional the dissociation curve is still oscillating. Therefore, we can conclude that they are unphysical artifacts that can be eliminated by using finer grids.

- 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?
B3LYP, B3LYP-D3(BJ), PBE and ω B97M-V are all well converged already when using the (75,302) grid.
- 4) What are the minimum grid requirements for the tested functionals?
Functional dependent. But it is in general better to use at least the (99,590), since most results are converged with this grid.
- 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?
We took the CPU timings for the B3LYP functional as an example. In our run, the calculations with the SG1 grid took about 5 minutes per structure. The (75,302) grid took slightly more, about 5.30 minutes. The (99,590) grid took around 9 minutes, and the (175,974) grid about 21 minutes.
- 6) Given the results that you collected, which grid(s) would you recommend?
We would recommend either the (99,590) or the (175,974) grids. As stated in the answer to question 4, the (99,590) should be the required minimum.
- 7) Does the HF method suffer from this problem? Why?
HF does not suffer from this problem because most software do not use any integration grid for this method. Grids are needed in general only for DFT.

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

In a recent publication,¹⁰³ Bootsma and Wheeler found out that some functionals are sensitive to the choice of integration grid not only for electronic energies,^{94,95} 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 functional⁶³ and the def2-TZVP basis set.⁴⁶ 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?
These geometries are the same, and they differ only by a simple rotation around the three Cartesian axes.
- 2) Collect the electronic energies of the molecules. How do they look like?
The electronic energies are the same (numerical differences between two calculations can appear, but they should be smaller than $10^{-6} E_h$).
- 3) Analyze the smallest frequency of the molecules. Are the molecules at their minima, transition structures, or else?
Depending on the grid and the orientation, the molecules go from being minima (i.e. the eigenvalues of the Hessian matrix are all positive) to transition structures (one negative eigenvalue).
- 4) How much did the computational timing increase when going from the SG1 to the (175,974) grid?
Taking the non-rotated molecule as example, we found that in terms of CPU time the SG1 grid takes about 1.5 minutes per SCF cycle, while the (99,590) grid takes 3 minutes and the (175,974) grid takes 4 minutes. Surprisingly, the (35,702) grid is the fastest, taking less than a minute per SCF cycle.
- 5) What conclusion can you draw from this experiment? Is there a recommended integration grid?
Once again, the minimum recommended grid for all the functionals should be the (99,590), as also suggested in Experiment 8.
- 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?
We did not notice any difference, since we found the same electronic energies also when allowing the use of symmetry to solve the KS equations.
- 7) Try one functional of your choice. Is it affected by the same issue?

We tried many functionals—we report the results obtained with B3LYP-D3(BJ) in the excel results—and apparently, they are not affected by the same issue.

- 8) Do you think that this issue affects all functionals, or only some of them?
This problem might be specific to some functionals only, such as B97-D.

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. 104.

For this experiment, you will use the usual functionals: SPW92^{33,34} (or SVWN5^{14,33}), BP86,^{15,19} B3LYP,¹⁴⁻¹⁸ PBE,³⁷ PBE0,³⁸ M06-2X,³⁹ SCAN⁴¹ (or TPSS)⁴², B97M-V^{21,43} (or MN15-L⁸), ω B97M-V^{20,21} (or ω B97X-D)⁴⁴ and Hartree-Fock (HF),⁴⁵ with the def2-QZVP basis set.⁴⁶ 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 3dAEE8¹⁰⁸⁻¹¹⁰ and 4dAEE5¹¹¹ 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?
Yes, we need the stability analysis. In the most drastic case, we gained a stabilization of 256 kcal/mol.
- 2) How does the HF method perform? Why do you think it performs this way?
The HF method performs very badly for these reactions. Transition metals are likely to need a multi-determinantal description, as well as a method capable of accounting for electron correlation.
- 3) Which functional would you recommend in this case?
The two ionization reactions are actually very hard. It is difficult to give recommendations in such cases.
- 4) Re-run the calculations for the reactions in Experiments 3 and 7 including the stability analysis. Do you notice any changes?
For systems that are not “low gap”, there is essentially no noticeable change. The goal of the stability analysis is to find the most stable wavefunction (under certain constraints), and therefore the lowest energy. If the converged solution is already stable, then its energy would not change. If it is unstable, the stable solution would be lower in energy.

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,¹¹³ 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,¹¹⁴ or the Natural Population Analysis (NPA) of Weinhold and co-workers.¹¹⁵ An alternative scheme, called ChelPG,¹¹⁶ 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: B3LYP,¹⁴⁻¹⁸ B97M-V^{21,43} (or MN15-L⁸), PBE,³⁷ MN15,⁹ SCAN¹⁴¹ (or TPSS⁴²), SPW92^{33,34} (or SVWN5^{14,33}), ωB97M-V^{20,21} (or ωB97X-D)⁴⁴ and the HF method.⁴⁵ As for the previous experiments, you will use the def2-SVP, def2-SVPD, def2-TZVP, def2-TZVPD, def2-QZVP, def2-QZVPD basis sets (or alternatively the cc-pVDZ, aug-cc-pVDZ, cc-pVTZ, aug-cc-pVTZ, cc-pVQZ, and aug-cc-pVQZ if the Ahlrics 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?
The Mulliken charges are known to be unstable with respect to the basis set size. As our results show, they do not 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?
The ChelPG charges are better behaved than the Mulliken ones with respect to the basis set size. While a little oscillatory, they converge to the same 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?
The Mulliken charges exhibit more variability than the ChelPG charges, and they do not converge with the basis set. At the same time, the value of the charge varies heavily with the different basis sets and functionals. In some cases it is so unstable that the charge goes from being negative to being positive, and then negative again. For example, this happens in the description of methane with the MN15 functional. On the other hand, ChelPG charges agree better with each other. They converge with increasing basis set size, and are more independent from functionals and basis sets, since they have about the same value (with minor oscillations). As such, they should be the preferred choice when performing qualitative studies.
- 4) Do different functionals give the same values of atomic charges?
When the ChelPG charges are used, the different functionals give results that are reasonably similar to each other.

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

Suppose we are studying a series of benzene derivatives, starting from the unsubstituted compound and then substituting one of the hydrogen atoms with another substituent. A qualitative way to use atomic charges is to understand how the partial charge on the carbon atom that bears the substituent, or how the charge of the whole ring changes with respect to the different substituents. Charges should never be used to make comparisons between different molecules since there is no unique way to partition the molecular charge into atomic contributions in addition to a remarkable functional dependence.

- 6) Do these results meet your expectations?

Overall, the results obtained with ChelPG charges meet our expectations. For example, the charge of the carbon atom is always negative—no matter the functional—in methane, and the hydrogen atoms are always positive. This picture is in agreement with the negative charge of carbon that we would assign if we are labelling the oxidation states of this element. However, it is surprising to see that the charge on nitrogen in ammonium is actually negative, and not positive as suggested by the Lewis structure for this species. The Mulliken charges are less straightforward, and sometimes their values are not in agreement with what we expect. For some functionals, namely B97M-V or MN15, the carbon atom in methane is sometimes positive and sometimes negative, which is counterintuitive. The same happens for the nitrogen atom in ammonia and ammonium, as well as some hydrogen atoms in formic acid.

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.¹¹⁹ With this experiment, we want to show that there is no difference between the two. We suggest using the HF⁴⁵ method, and one functional of choice among the ones used throughout the rest of this notebook. We suggest the def2-SVP basis set,⁴⁶ 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,¹²⁰ which is one of many different frameworks used to localize the orbitals.^{120,121} 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).

Localized and Delocalized Orbitals for Benzene: Similarities and Differences.

We used the molecule of benzene to understand eventual differences and similarities of delocalized and localized orbitals. We used the Boys localization scheme. Using either the HF method or the B3LYP functional and the def2-SVP basis set, we found that localized and delocalized orbitals look different, and we report an example in **figure 1**.

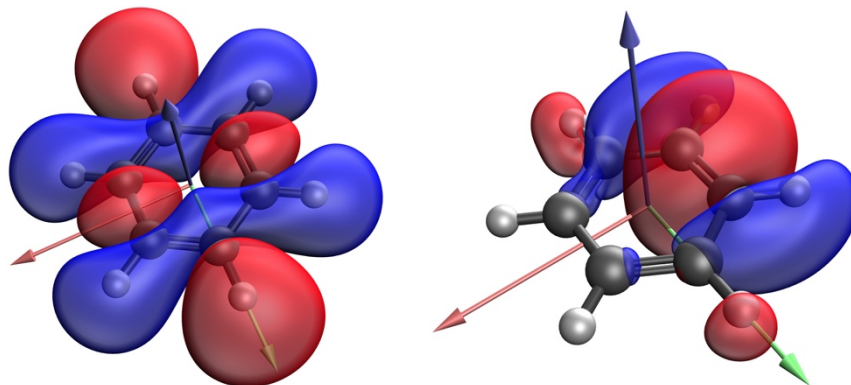


Figure 1: Canonical (left panel) and localized (right panel) orbitals for benzene obtained at the B3LYP/def2-SVP level of theory. The blue color is used when the orbitals have negative sign, while the red one is used for positive sign.

The HOMO of benzene is reported in **figure 2** as calculated with the HF method. The picture on the left shows the delocalized orbital, while the picture on the right depicts the localized one.

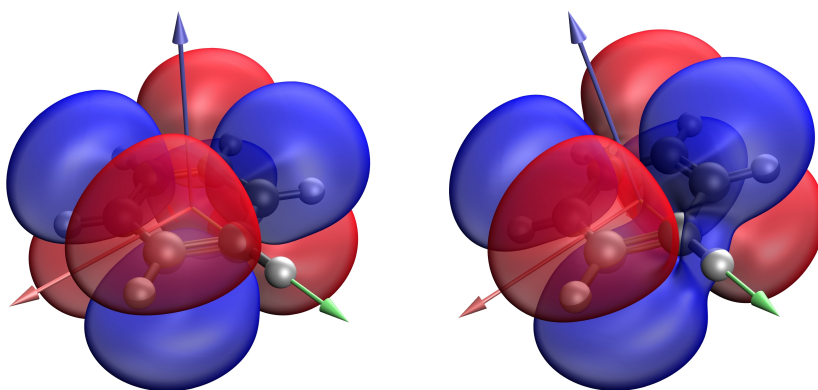


Figure 2: Delocalized LUMO (left panel) and localized LUMO (right panel) for benzene obtained at the HF/def2-SVP level of theory. The green arrow is the x axis, the red one is the y axis, and the blue one is the z axis. The blue color is used when the orbitals have negative sign, while the red one is used for positive sign.

Visual inspection of all the orbitals from 19 to 22 (LUMO) of benzene as obtained with B3LYP and HF shows that the orbitals are similar in shape and size. The delocalized (canonical) molecular orbitals are obtained as a linear combination of atomic orbitals (LCAO), and the coefficients of each atomic orbital are optimized within the SCF cycles. The coefficients that we obtain with B3LYP and HF are different, and so are the orbitals, but a visual inspection is not enough to appreciate this difference.

The same is true also for the orbitals of the benzene anion, with the HF and B3LYP orbitals being very similar to each other. For the anion as well the delocalized and localized orbitals look different. We have to realize though that this difference is only in the representation. In fact, the two sets of orbitals are totally equivalent because they give the same energy. In other words, the energy is stationary with respect to these orbitals. We can imagine many other sets of orbitals that would give the same energy. As a consequence, there is no special value in any of them because the energy would not change, and any localized set is equivalent to the delocalized one.

The LUMO of the anion is of special interest because it gives us an idea on the shape of the LUMO in the neutral molecule. In fact, the 22nd orbital of benzene (the LUMO, shown in **figure 2**) is a virtual orbital, that is obtained simply as a symmetrized combination of atomic orbitals, and it is not optimized in the SCF cycles. However, if we study the 22nd orbital of the anion, it is the HOMO, and as such its coefficients are optimized in the SCF cycles. In this way, we obtain a more meaningful picture of the LUMO for the neutral molecule: it is not a mere artifact, as for the neutral molecule because its coefficients are optimized. In **figure 3**, we show the localized LUMO of benzene and its anion.

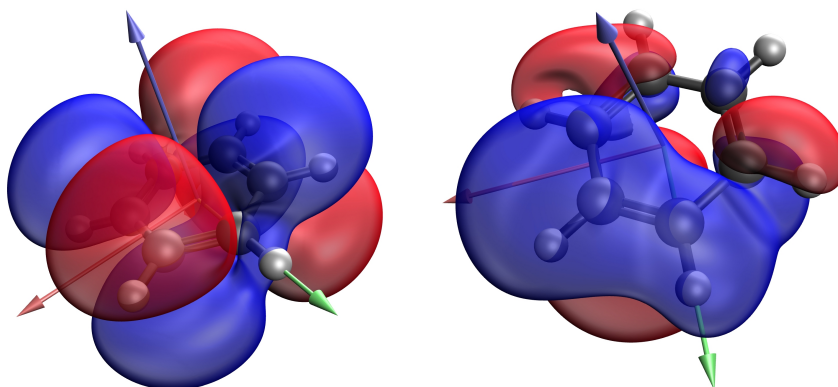


Figure 3: Localized LUMO for benzene (left panel) and localized LUMO for the anion (right panel) calculated at the HF/def2-SVP level of theory. The green arrow is the x axis, the red one is the y axis, and the blue one is the z axis. The blue color is used when the orbitals have negative sign, while the red one is used for positive sign.

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,^{28,98,125} the other from the SR-TM-BE17^{28,101,126-128} subset. In addition, you will also examine some total atomization energies from the W4-11 subset¹²⁹ 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 FeCl¹²⁸ 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.⁴⁶ When it comes to functionals, we suggest using the MN15-L,⁸ MN15,⁹ B3LYP¹⁴⁻¹⁸ and PBE³⁷ functionals, and the HF method.⁴⁵ 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?
M06-2X is the best, B3LYP is the worst (together with HF).
- 2) How does the HF method perform? Are you surprised?
Unsurprisingly, the HF method is the worst. Since it does not take electron correlation into account, and it is a single-determinant method. HF fails badly in the description of species having a complex electronic structure, or in need of a multi-determinant description. To describe radicals correctly, we need a method capable of accounting for electron correlation, and it is highly likely that we need a multi-determinant method (like CAS-SCF) as well.
- 3) Try the B3LYP functional with the 6-31G* basis set of Pople. Do you see any improvement? Where do you think this improvement come from?
In 5 out of 7 reactions, the 6-31G* basis set gives a better agreement with the calculated result than the def2-QZVP basis set. As shown in Experiment 7, this behavior is due to the error cancellation that occurs between the LYP correlation functional and the 6-31G* basis set. This is further evidence that this behavior is completely unpredictable. We should move away from it, going towards a more physically sound level method.

Problems for FeCl.

- 1) Which functional is the best performer?
M06-2X is (once again) the best performer.
- 2) How does the HF method perform? Are you surprised?
Unsurprisingly, the HF method is the worst once again.
- 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?

The enthalpy of formation of FeCl in the gas phase is 60.0 kcal/mol. It is different than the reference electronic energy reported for this experiment.

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

In general, comparing a calculated value with an experimental one is not a good idea. When we measure an experimental thermodynamic energy like the enthalpy of formation, we are implicitly measuring many different contributions to that energy that are not included in the computational result. The most famous of these contributions is the zero-point energy (ZPE), but there are indeed several others that are mostly due to the ensemble. Smaller effects like spin-orbit couplings, scalar relativistic effects, and Born-Oppenheimer corrections might also be present. In order to compare a calculated result with an experimental one we should also calculate all of these contributions and add them to the computed electronic energy.

We will now turn the attention to the atomization reactions. 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?
B3LYP is the best functional for these reactions, while PBE is the worst.
- 2) How does the HF method perform? Are you surprised?
Unsurprisingly, the HF method performs badly for this set of reactions.

- 3) In your opinion, what is the reason of the failure of the HF method?
As stated in the previous point, the HF method fails because of a bad description of atoms and molecules.
- 4) Do you see the same trend in both bond dissociation reactions and atomization reactions?
Yes, we see the same trend in both sets for almost all functionals. In fact, almost all of them give acceptable results for the small molecules in this set, namely H₂, H₂O, NH₃ and CH₄. The only exception is M06-L, which has the highest average error for these molecules. However, it works better than any other functional for O₃, and it performs acceptably for FeCl, while some of the others (PBE, B3LYP) struggle with these two molecules. None of the functionals taken into account here is acceptable for the dissociation energy of the *t*-butyl alcohol. The overall picture though shows that the MN15 and ω B97M-V functionals are the best performing, closely followed by M06-2X.
- 5) Can you directly compare the atomization energy with the formation enthalpy of a substance? Why?

In addition to what is stated in the answer to question 4 in the previous set of problems, we have to keep in mind that the enthalpy of formation is calculated for elements in their standard state. An isolated atom in the gas phase is never the standard state for atomic species, and therefore we cannot make the direct comparison between atomization energies and enthalpies of formation.

Experiment 14: A Collaborative Project.

We report here an example of how the final report should look like.

Theoretical study of the dissociation energy of a palladium complex.

Palladium is widely used as a catalyst for many chemical processes, like the Heck reaction¹ and the Suzuki-Negishi cross-coupling.^{2,3} Given the ubiquitous nature of these reactions in organic syntheses, understanding and predicting the reactivity of palladium is of capital interest.

Density Functional Theory (DFT)⁴ represents a good compromise between accuracy and computational cost, which makes it easily applicable to medium and large molecules.⁵ The most important challenge that one has to face is the choice of an *exchange correlation* (*xc*) functional. Most functionals give reasonably accurate results for main-group elements, but transition metals still represent a challenge.^{6,7} In light of recent studies,^{6,8} we decided to use the MN15⁸ and MN15-L⁹ functionals of Truhlar and co-workers because of their reliability in both main-group and transition metal chemistry. In addition, we chose the def2-TZVP basis set of Weigend and Ahlrichs¹⁰ because it allowed us to afford calculations without compromising too much the accuracy of the results obtained. We run single-point calculations on the provided geometries, and we performed stability analysis to ensure that the converged wavefunction was stable, allowing symmetry-breaking when necessary. In all calculations, we used the (99,590) Lebedev grid as recommended in the literature.¹¹

The calculated dissociation energy for this compound is 15.59 kcal/mol with the MN15, which is in excellent agreement with the reported value of 16.20 kcal/mol, confirming that the choice of functional and basis set was accurate for the purpose of this reaction. In comparison, the calculated energy is 15.19 kcal/mol with the MN15-L functional—the error with respect to the reference value is 1.01 kcal/mol—showing that both functionals perform well for this reaction, and they both represent a good choice in this case.* As a comparison, the B3LYP¹² functional gives a dissociation energy of 3.27 kcal/mol, underestimating it of about 13 kcal/mol, and performing very poorly.

In conclusion, we calculated the dissociation energy of a palladium complex using three different exchange-correlation functional approximations, namely MN15, MN15-L and B3LYP, and we showed that the two Minnesota functionals described the reaction well, with MN15 being the best choice.

References:

- 1) R. F. Heck *Org. React.*, **1982**, 345–390.
- 2) N. Miyaura, K. Yamada, and A. Suzuki, *Tetrahedron Lett.*, **1979**, 20, 3437–3440.
- 3) A. O. King, N. Okukado, and E. Negishi, *J. Chem. Soc. Chem. Comm.*, **1977**, 683–684.
- 4) W. Kohn, and L. J. Sham, *Phys. Rev.*, **1965**, 140, A1133–A1138; P. Hohenberg, and W. Kohn, *Phys. Rev.*, **1964**, 136, B864–B871; R. G. Parr, W. Yang, *Density Functional Theory of Atoms and Molecules*, 1st edition, Oxford University Press, **1994**.
- 5) H. S. Yu, S. L. Li, and D. G. Truhlar, *J. Chem Phys.*, **2016**, 145, 130901; L. Goerigk, A. Hansen, C. Bauer, S. Ehrlich, A. Najibi, and S. Grimme, *Phys. Chem. Chem. Phys.*, **2017**, 19, 32184–32215.
- 6) B. Chan, P. M. W. Gill, M. Kimura, *J. Chem. Theory Comput.*, **2019**, 15, 3610–3822.
- 7) B. Chan, *J. Phys. Chem. A*, **2019**, 123, 5781–5788; C. J. Cramer, and D. G. Truhlar, *Phys. Chem. Chem. Phys.*, **2009**, 10757–10816.
- 8) H. S. Yu, X. He, S. L. Li and D. G. Truhlar, *Chem. Sci.*, **2016**, 7, 5032–5051.
- 9) H. S. Yu, X. He and D. G. Truhlar, *J. Chem. Theory Comput.*, **2016**, 12, 1280–1293.

- 10) F. Weigend, and R. Ahlrichs, *Phys. Chem. Chem. Phys.*, **2005**, 7, 3297–3305.
- 11) N. Mardirossian, and M. Head-Gordon, *J. Chem. Theory Comput.*, **2016**, 12, 4303–4325.
- 12) S. H. Vosko, L. Wilk, and M. Nusair, *Can. J. Phys.*, 1980, 58, 1200-1211; A. D. Becke, *Phys. Rev. A*, 1988, 38, 3098-3100; C. Lee, W. Yang, and R. G. Parr, *Phys. Rev. B*, 1988, 37, 785-789; A. D. Becke, *J. Chem. Phys.*, 1993, 98, 5648-5652; P. J. Stephens, F. J. Devlin, C. F. Chabalowski, and M. J. Frisch, *J. Phys. Chem.*, 1994, 98, 11623-11627.

* it should be noted that this reaction comes from the training set of MN15 and MN15-L (the database used to develop these functionals). That is why they are so good for this specific reaction.