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Excited States of DNA Base Pairs Using Long-Range Corrected Time-Dependent Density Functional Theory

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In this work, we present a study of the excitation energies of adenine, cytosine, guanine, thymine, and the adenine-thymine (AT) and guanine-cytosine (GC) base pairs using long-range corrected (LC) density functional theory. We compare three recent LC functionals, BNL, CAM-B3LYP, and LC-PBE0, with B3LYP and coupled cluster results from the literature. We find that the best overall performance is for the BNL functional based on LDA. However, in order to achieve this good agreement, a smaller attenuation parameter is needed, which leads to nonoptimum performance for ground-state properties. B3LYP, on the other hand, severely underestimates the charge-transfer (CT) transitions in the base pairs. Surprisingly, we also find that the CAM-B3LYP functional also underestimates the CT excitation energy for the GC base pair but correctly describes the AT base pair. This illustrates the importance of retaining the full long-range exact exchange even at distances as short as that of the DNA base pairs. The worst overall performance is obtained with the LC-PBE0 functional, which overestimates the excitations for the individual bases as well as the base pairs. It is therefore crucial to strike a good balance between the amount of local and long-range exact exchange. Thus, this work highlights the difficulties in obtained LC functionals, which provides a good description of both ground- and excited-state properties.

Introduction

Understanding the optical properties of chromophores in biological systems is of fundamental importance for elucidating light-induced processes in life science as well as developing efficient biolabels.[1−8] Fluorescence, for example, is a dominant detection method in life science research and enables scientists to localize proteins to subcellular structures.[2−4] Elucidating the molecular basis for photosynthesis becomes increasingly important as we seek to develop new approaches for efficient solar power capture.[7−9] Knowledge of the photophysical properties of DNA is of fundamental importance for understanding radiation-induced damage of DNA.[5,6] Advances in quantum chemistry methods have enabled accurate calculations of the optical properties of the individual DNA bases.[10−13] However, a complete understanding of the optical properties of the nucleic acids in DNA is complicated due to tautomerization, the surrounding environment, as well as base pairing and stacking.

The very high computational demands of the most accurate quantum chemistry methods prohibits their use for large systems such as DNA. Therefore, it is of fundamental importance to extend the use of quantum chemical methods to treat large systems containing many atoms. A method which has attracted considerable interest is time-dependent density functional theory (TDDFT).[14−18] However, a lingering problem is that the results are dependent on the exchange−correlation functionals. It is well-known that conventional TDDFT has certain categoric failures such as describing polarizabilities of larger extended systems[19,20] and charge-transfer excitations between weakly interacting systems.[21] Recently, progress has been made with the introduction of so-called long-range corrected (LC) functionals.[22−25] These functionals are based on the separation of the Coulomb operator into long- and short-range parts and show great promise for correctly describing the excited states of large molecules.

In this paper, we present a study of the excitation energies of adenine, cytosine, guanine, thymine, and the adenine-thymine (AT) and guanine-cytosine (GC) base pairs using long-range corrected (LC) density functional theory. We will be comparing three recently proposed LC functionals, BNL,[25] CAM-B3LYP,[24] and LC-PBE0,[26] on how they describe the excitation energies of the individual bases and the base pairs.

Theory

In the LC approach, the electron repulsion is separated into long- and short-range parts as

$$\frac{1}{r_{12}} = \frac{1 - [\alpha + \beta \operatorname{erf}(\mu r_{12})]}{r_{12}} + \frac{\alpha + \beta \operatorname{erf}(\mu r_{12})}{r_{12}} \quad (1)$$

where α and β are constants satisfying the relations $0 \le \alpha \le 1$, $0 \le \beta \le 1$, and $0 \le \alpha + \beta \le 1$ and μ is the attenuation or

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TABLE 1: Different Functionals Implemented

name	K_σ	E_c	α	β	μ
BNL[25]	0.9 × LDA	LYP	0	1	0.30
CAM-B3LYP[24]	B88	0.81 × LYP + 0.19 × VWN5	0.19	0.46	0.33
LC-PBE0[26]	PBE	PBE	0.25	0.75	0.30

range separation parameter. With this, the exchange energy E_x can be partitioned into short- and long-range components, respectively.

$$E_{xc}^{LC} = E_x^{sr} + E_x^{lr} \quad (2)$$

We have implemented the general approach by Hirao and coworkers[22] in a development version of the NWChem program package[27] and have recently used it to study the low-lying excited states of the zinc porphyrin molecule in aqueous solution[28] and the optical spectra of TCF chromophores.[29] In the LC approach, the short-range part is treated with traditional DFT as

$$E_x^{sr} = (1 - \alpha)E_x^{GGA} + \frac{4\beta}{3}\sum_\sigma \int \rho_\sigma^{4/3} K_\sigma a_\sigma \left[\sqrt{\pi}\,\mathrm{erf}\left(\frac{1}{2a_\sigma}\right) + 2a_\sigma(b_\sigma - c_\sigma)\right]\mathrm{d}r \quad (3)$$

where a_σ, b_σ, and c_σ are given by

$$a_\sigma = \frac{\mu K_\sigma^{1/2}}{6\sqrt{\pi}\rho_\sigma^{1/3}} \quad (4)$$

$$b_\sigma = \exp\left(-\frac{1}{4a_\sigma^2}\right) - 1 \quad (5)$$

$$c_\sigma = 2a_\sigma^2 b_\sigma + \frac{1}{2} \quad (6)$$

and K_σ is defined by the standard exchange energy

$$E_x = -\frac{1}{2}\sum_\sigma \int \rho_\sigma^{4/3} K_\sigma \mathrm{d}r \quad (7)$$

This definition of the range-separated functional is based on the LDA exchange hole and generalized to other functionals by a semiempirical modification of the Fermi momentum.[22] Recently, new promising modified exchange holes suitable for constructing range-separated functionals have been presented.[30,31] The first and second derivatives, which are needed for the calculations of TDDFT excitation energies, were implemented following the approach presented by Salek and Hesselman.[32] The long-range component is treated with exact exchange as

$$E_x^{lr} = \alpha E_x - \frac{\beta}{2}\sum_\sigma \sum_{ij} \int\int \psi_{i\sigma}(r_1)\psi_{j\sigma}(r_1)\frac{\mathrm{erf}(\mu r_{12})}{r_{12}}\psi_{i\sigma}(r_2)\psi_{j\sigma}(r_2)\mathrm{d}r_1\mathrm{d}r_2 \quad (8)$$

It can be shown that for large μ, the theory becomes more HF-like and behaves more pure-DFT-like for small μ. A crucial issue in the construction of LC functionals is the choice of the parameters α, β, and μ. We have implemented general short-range versions of the LDA, Becke88, and PBE exchange functionals, which allows us to construct several LC functionals. The parameters for the different functionals tested in this work together with their corresponding correlation parts are tabulated in Table 1. Note that for the BNL functional, we use a smaller value of μ than that originally presented since this value was found to give better excitation energies. This new value is consistent with recently published values for describing CT excitations.[33]

Since the long-range part of LC functionals has to be calculated explicitly, the two-electron integrals have to be handled carefully. The attenuation just affects the exchange; therefore, these interactions have to be treated separately from the pure Coulomb interactions. In our implementation in NWChem, we have implemented two approaches to deal with this. In the first approach, we perform all of the integral evaluations in the conventional way using the direct method, where all of the integrals (with and without attenuation) are recomputed on the fly. The second approach involves utilizing the well-known Dunlap[34] charge fitting method to deal with Coulomb interactions, and the exchange contribution (including the attenuation) is treated in the conventional manner. Our charge fitting approach is implemented along the lines of the von Arnim and Ahlrichs implementation.[35] The Coulomb contribution with this approach is evaluated using three-center integrals. In this paper, we only report results using the former.

Computational Details

All of the calculations were performed using a development version of the NWChem computational chemistry package[27] developed at the Pacific Northwest National Laboratory. This suite of programs has been designed to provide the capability to run large scientific molecular simulations on massively parallel and scalable computers. The gas-phase geometries were taken from ref 36, where they were optimized using BP86 and a large STO basis set and shown to be in good agreement with MP2 benchmark results. It is well-established that the bases in the gas phase are slightly nonplanar, where the two hydrogens on the amino group are out of the ring plane.[37,38] The base pairs were optimized using C_s symmetry.[36] The excited-state calculations using the various functionals reported in this paper were performed using the cc-pVTZ basis set. Although this basis set is not large enough to correctly describe high-lying Rydberg states,[10] it accurately describes the lowest excited states of the individual bases and the base pairs. All of the excitation energies were calculated using the TDDFT module in NWChem.

Results

Lowest Excitations in the Individual Bases. The lowest excitation energies and oscillators strengths, *f*, for adenine, thymine, guanine, and cytosine calculated using the different functionals are presented in Table 2. Since most experimental data for the absorption spectra of the bases refer to solution-phase measurements, we will compare our results with theoreti-

TABLE 2: Lowest Vertical Excitation Energies (in eV) and Oscillator Strengths (*f*) for the Individual Bases

	B3LYP		BNL		CAM-B3LYP		LC-PBE0		CC2[a]	
state	E_{ex}	f	E_{ex}	f	E_{ex}	f	E_{ex}	f	E_{ex}	f
					Adenine					
n → π^*	4.939	0.0041	5.033	0.00027	5.335	0.08962	5.581	0.03591	5.12	0.007
π → π^*	5.015	0.18169	5.398	0.19037	5.353	0.17731	5.559	0.24523	5.25	0.302
π → π^*	5.265	0.04745	5.446	0.10467	5.449	0.01939	5.638	0.03724	5.25	0.302
					Thymine					
n → π^*	4.712	0.00001	4.928	0.00000	5.071	0.00000	5.267	0.00000	4.82	0.000
π → π^*	4.992	0.12960	5.158	0.15997	5.243	0.18045	5.422	0.21264	5.20	0.182
					Guanine					
π → π^*	4.857	0.14177	5.132	0.14940	5.103	0.15699	5.299	0.16394	4.98	0.132
π → π^*	5.215	0.18200	5.677	0.30672	5.608	0.29402	5.887	0.35759	5.47	0.179
					Cytosine					
π → π^*	4.631	0.03826	4.891	0.06025	4.936	0.06448	5.144	0.08217	4.66	0.052
n → π^*	4.737	0.00089	5.013	0.00134	5.232	0.00149	5.475	0.00160	4.87	0.002

[a] Results from ref 10 using the aug-cc-pVTZ basis set.

TABLE 3: Lowest Vertical Excitation Energies (in eV) and Oscillator Strengths (*f*) for the AT and GC Base Pairs

	B3LYP		BNL		CAM-B3LYP		LC-PBE0		Litt.
state	E_{ex}	f	E_{ex}	f	E_{ex}	f	E_{ex}	f	E_{ex}
				AT base pair					
Thy n → π^*	4.816	0.00003	5.098	0.00003	5.246	0.00003	5.486	0.00003	4.94[a]
Ade n → π^*	5.139	0.00014	5.275	0.00017	5.571	0.00022	5.825	0.00027	5.54[a]
Thy π → π^*	4.892	0.17017	5.073	0.13946	5.157	0.18225	5.339	0.19705	5.21[a]
Ade π → π^*	4.949	0.13758	5.387	0.24809	5.301	0.21911	5.554	0.23141	5.40[a]
Ade π → π^*	5.199	0.07865	5.315	0.10749	5.358	0.09770	5.532	0.14180	5.47[a]
Ade π → Thy π^*	4.224	0.00260	6.251	0.02868	5.803	0.00548	6.724	0.02247	6.04[a]
				GC Base Pair					
Cyt n → π^*	4.754	0.00016	5.426	0.00081	5.643	0.00081	5.988	0.00114	4.25[b]
Gua π → π^*	4.603	0.00789	4.988	0.07508	5.112	0.06266	5.203	0.09634	4.67[b]
Cyt π → π^*	4.854	0.03884	5.124	0.09382	5.188	0.10188	5.385	0.14109	
Gua π → π^*	4.781	0.09392	5.581	0.44980	5.524	0.41152	5.793	0.47955	
Gua π → Cyt π^*	3.307	0.00177	5.598	0.01581	4.8561	0.03388	6.201	0.01066	4.75[b]

[a] Results from ref 40 using CC2/TZVP. [b] Results from ref 13 using CASPT2.

cal results obtained using high-level ab initio methods CC2/aug-cc-pVTZ.[10] These results were shown to be in good agreement with CASPT2 as well as experimental results.[10,11] The errors in these calculations are expected to be in the range of 0.1−0.3 eV.[10,11] Results obtained using CC2/aug-cc-pVTZ show that the lowest transition for adenine is an n−π^* transition located at 5.12 eV (f = 0.007) followed by two degenerate π−π^* transitions at 5.25 eV (f = 0.302).[10] For thymine, CC2/aug-cc-pVTZ predicts the lowest transition to be an n−π^* transition located at 4.82 eV (f = 0.000). The strong π−π^* transition is found at 5.20 eV (f = 0.182). The lowest two transitions for guanine are found by CC2/aug-cc-pVTZ to be at 4.98 (f = 0.132) and 5.08 eV (f = 0.028). For guanine, the second excitation has a strong Rydberg character and is therefore not captured correctly by the basis set used in this work. However, a strong transition for guanine is found at 5.47 eV (f = 0.179), with which we will compare. CC2/aug-cc-pVTZ predicts the two lowest transitions to be at 4.66 (f = 0.052) and 4.87 eV (f = 0.002) for cytosine. We find good agreement between the B3LYP and BNL results, with an average deviation of 0.14 and 0.15 eV, respectively, for the nine transitions studied. Both of these functionals show good agreement with respect to both the order of the transitions as well as the oscillator strengths. CAM-B3LYP shows a slightly higher average deviation of 0.19 eV, whereas the average deviation for LC-PBE0 is the highest at 0.41 eV. It is striking that the LC-PBE0 functional shows the largest deviations because its base functional PBE0 is often considered to give very good excitation energies.[39] The fact that the two LC-functionals based on global hybrids, that is, B3LYP and PBE0, show the largest deviations illustrates the importance of carefully balancing the amount of local exact exchange in conjunction with the attenuation.

Lowest Excitations in the Base Pairs. The lowest excitation energies and oscillator strengths, f, for the AT and GC base pairs calculated using the different functionals are collected in Table 3. Due to the size of the base pairs, most calculations have been performed at the TDDFT level of theory.[41−43] A recent study using CC2 for the AT base pair found that the lowest transition is localized on the thymine base at 4.93 eV and that the CT transition lies higher in energy at 6.04 eV.[40] These results were obtained without the use of extra diffuse functions and thus expected to be too high by about 0.1 eV. TDDFT using the LC-ωPBE functionals was shown to be in good agreement, whereas PBE0 predicted a much lower CT excitation energy.[40] For the AT base pair, we found good agreement between the results calculated using BNL and CAM-B3LYP and the CC2 results, with average deviations of 0.16 and 0.14 eV, respectively. LC-PBE0 shows larger deviations; however, the trend is similar to what we found for the individual bases, where most excitations were overestimated as compared with CC2. The B3LYP functional showed the largest average deviation of 0.56 eV due to the underestimation of the CT transition, which the functional predicts to be the lowest transition. This is illustrated in Figure 1, where we plot the HOMO and LUMO of the AT base pairs as obtained using B3LYP and CAM-B3LYP. We see that B3LYP predicts that

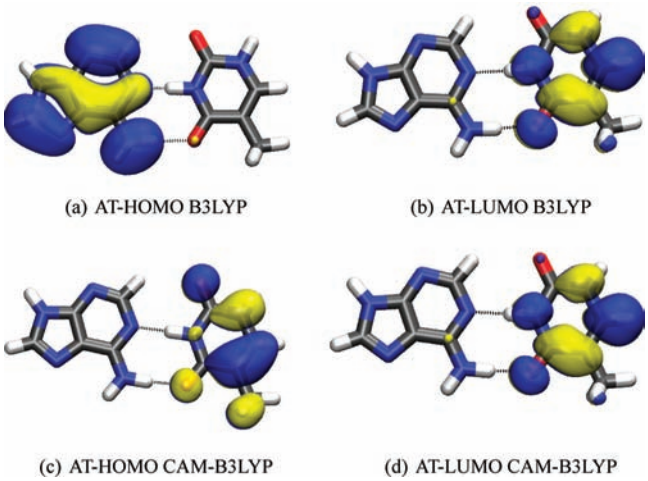

Figure 1. HOMO and LUMO orbitals calculated using B3LYP and CAM-B3LYP. The figure was prepared using VMD.[44]

the HOMO is located on adenine and the LUMO on thymine, whereas CAM-B3LYP (and the other LC functionals) correctly predicts that both orbitals are located on the thymine unit. Thus, the wrong result predicted by B3LYP is due to an underestimation of the highest occupied adenine orbital relative to the thymine in the base pair. For the GC base pair, CASPT2 calculations[13] show that the lowest transition is localized on the guanine base at 4.25 eV, followed by a transition at 4.67 eV located at the cysteine base, and that the CT transition is found at 4.75 eV. These results are lower than what we find most likely due to a limited active space in the CASPT2 calculations since the transitions for the individual bases are also lower than our results and the CC2 results. However, the results clearly show that the lowest excitation is a $\pi-\pi^*$ transition located on guanine. B3LYP wrongly predicts that the first excitation is a CT transition between the bases. Interestingly enough, CAM-B3LYP also predicts the lowest transition to be a CT transition, whereas the two LC functionals with 100% long-range exact exchange predicts this transition to lie much higher in energy. This clearly illustrates the importance of the long-range exchange for correctly describing CT excitations even when the molecules are fairly close.

We find that only BNL using a smaller value for μ was able to correctly describe the excitation energies of both the individual bases and the base pairs. However, the smaller attenuation parameter used in the BNL functional will lead to worse results for ground-state properties. This is in agreement with the recent work of Rohrdanz and Herbert,[45] where they found it difficult to obtain a good description of both ground-state and excited-state properties using the model of Hirao and co-workers.[22] Although, LC functionals based on the new exchange hole of Scuseria and co-workers[31] were later shown to be able to simultaneously describe ground- and exited-state properties. A different approach has been suggested by Baer and co-workers, where they "tune" the attenuation parameter based on first-principles to obtain a molecule-specific value.[33]

Conclusions

In this paper, we have presented a study of the excitation energies of adenine, cytosine, guanine, thymine, and the adenine-thymine (AT) and guanine-cytosine (GC) base pairs using long-range corrected (LC) density functional theory. We compared three recent LC functionals, BNL, CAM-B3LYP, and LC-PBE0, with B3LYP and coupled cluster results from the literature. We found that the best overall performance is for the BNL functional based on the LDA functional with a smaller attenuation parameter. B3LYP severely underestimates the CT transition in the base pairs. Surprisingly, the CAM-B3LYP functional also underestimates the CT excitation energy for the GC base pair but correctly describes the AT base pair. This illustrates the importance of retaining the full long-range exact exchange even at distances as short as hydrogen bonds. The worst performance was obtained with the LC-PBE0 functional, which overestimated the excitations for both the individual bases as well as the base pairs. Thus, this work highlights the difficulties in obtained LC functionals, which provides a good description of both ground- and excited-state properties.

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