

Chemical Reactivity Theory Applied to the Calculation of the Local Reactivity Descriptors of a Colored Maillard Reaction Product

Abstract

This computational study assessed ten density functionals that include CAM-B3LYP, LC- ω PBE, M11, M11L, MN12L, MN12SX, N12, N12SX, ω B97X, and ω B97XD related to the Def2TZVP basis set together with the SMD solvation model. These are assessed in calculating the molecular properties and structure of the PPA molecule in water. The chemical reactivity descriptors for the systems are calculated via the Conceptual Density Functional Theory. The choice of active sites applicable to nucleophilic, electrophilic as well as radical attacks is made by linking them with Fukui functions indices, electrophilic Parr functions, and condensed dual descriptor $\Delta f(r)$. The predicted maximum absorption wavelength tends to be considerably accurate relative to the experimental value. The study found the MN12SX and N12SX density functionals to be the most appropriate in predicting the chemical reactivity of this molecule.

Keywords: PPA; Conceptual DFT; Chemical Reactivity Theory; Parr Function; Maximum Absorption Wavelength

1 Introduction

Visual color in processed foods is largely due to colored products of Maillard or nonenzymic browning reactions. In spite of the longstanding aesthetic and practical interest in Maillard derived food coloring materials, relatively little is known about the chemical structures responsible for visual color [1].

These chemical structures are known as Colored Maillard Reaction Products and can be isolated at intermediate stages during the melanoidins formation process.

Besides their interest as dye molecules which may be useful as food additives, but also as dyes for dye-sensitized solar cells (DSSC), these compounds have also antioxidant capabilities. Thus, they are amenable to be studied by analyzing their molecular reactivity properties.

One of these isolated molecules is called PPA (or 4-(dicarboxymethyl)-5-(2, 3-dihydroxy propyl)-pyrrolo[3, 2-b]pyrrole-2-carboxaldehyde) [2] which has interesting properties as a colored compound and fluorescent dye and we believe that it could be of interest to study its molecular reactivity by using the ideas of Conceptual DFT, in the same way of our previous works [3–33].

Thus, in this computational study we will assess ten density functionals in calculating the molecular properties and structure of the PPA intermediate melanoidin pigment in water. Following the same ideas of previous works, we will consider fixed RSH functional instead of the optimally-tuned RSH density functionals that have attained great success [34–53].

2 Theoretical Background

The theoretical background of this study is similar to the previous conducted research presented [3–33], and will be shown here for complete purposes, because this research is a component of a major project that it is in progress.

If we consider the KID procedure presented in our previous works together with a finite difference approximation, then the global reactivity descriptors can be written as:

$$\text{Electronegativity} \quad \chi = -\frac{1}{2}(I + A) \approx \frac{1}{2}(\epsilon_L + \epsilon_H) \quad [54]$$

$$\text{Global Hardness} \quad \eta = (I - A) \approx (\epsilon_L - \epsilon_H) \quad [54]$$

$$\text{Electrophilicity} \quad \omega = \frac{\mu^2}{2\eta} = \frac{(I+A)^2}{4(I-A)} \approx \frac{(\epsilon_L + \epsilon_H)^2}{4(\epsilon_L - \epsilon_H)} \quad [55]$$

$$\text{Electrodonating Power} \quad \omega^- = \frac{(3I+A)^2}{16(I-A)} \approx \frac{(3\epsilon_H + \epsilon_L)^2}{16\eta} \quad [56]$$

$$\text{Electroaccepting Power} \quad \omega^+ = \frac{(I+3A)^2}{16(I-A)} \approx \frac{(\epsilon_H + 3\epsilon_L)^2}{16\eta} \quad [56]$$

$$\text{Net electrophilicity} \quad \Delta\omega^\pm = \omega^+ - (-\omega^-) = \omega^+ + \omega^- \quad [57]$$

where ϵ_H and ϵ_L are the energies of the highest occupied and the lowest unoccupied molecular orbitals (HOMO and LUMO), respectively.

Applying the same ideas, the definitions for the local reactivity descriptors are:

$$\text{Nucleophilic Fukui Function} \quad f^+(\mathbf{r}) = \rho_{N+1}(\mathbf{r}) - \rho_N(\mathbf{r}) \quad [54]$$

$$\text{Electrophilic Fukui Function} \quad f^-(\mathbf{r}) = \rho_N(\mathbf{r}) - \rho_{N-1}(\mathbf{r}) \quad [54]$$

$$\text{Dual Descriptor} \quad \Delta f(\mathbf{r}) = \left(\frac{\partial f(\mathbf{r})}{\partial N} \right)_{v(\mathbf{r})} \quad [58]$$

$$\text{Nucleophilic Parr Function} \quad P^-(\mathbf{r}) = \rho_s^{rc}(\mathbf{r}) \quad [59]$$

$$\text{Electrophilic Parr Function} \quad P^+(\mathbf{r}) = \rho_s^{ra}(\mathbf{r}) \quad [59]$$

where $\rho_{N+1}(\mathbf{r})$, $\rho_N(\mathbf{r})$, and $\rho_{N-1}(\mathbf{r})$ are the electronic densities at point $\mathbf{r}$ for the system with $N + 1$, N , and $N - 1$ electrons, respectively, and $\rho_s^{rc}(\mathbf{r})$ and $\rho_s^{ra}(\mathbf{r})$ are related to the atomic spin density (ASD) at the $\mathbf{r}$ atom of the radical cation or anion of a given molecule, respectively [60].

3 Settings and Computational Methods

Following the lines of our previous work, the computational studies were performed with the Gaussian 09 [61] series of programs with density functional methods as implemented in the computational package. The basis set used in this work was Def2SVP for geometry optimization and frequencies, while Def2TZVP was considered for the calculation of the electronic properties [62, 63]. All the calculations were performed in the presence of water as the solvent by doing Integral Equation Formalism-Polarized Continuum Model (IEF-PCM) computations according to the Solvation Model Density (SMD) solvation model [64].

For the calculation of the molecular structure and properties of the studied systems, we have chosen ten density functionals which are known to consistently provide satisfactory results for several structural and thermodynamic properties:

CAM-B3LYP	Long-range-corrected B3LYP by the CAM method	[65]
LC- ω PBE	Long-range-corrected ω PBE density functional	[66]
M11	Range-separated hybrid meta-GGA	[67]
M11L	Dual-range local meta-GGA	[68]
MN12L	Nonseparable local meta-NGA	[69]
MN12SX	Range-separated hybrid nonseparable meta-NGA	[70]
N12	Nonseparable local NGA	[71]
N12SX	Range-separated hybrid NGA	[70]
ω B97X	Long-range corrected density functional	[72]
ω B97XD	ω B97X version including empirical dispersion	[73]

In these functionals, GGA stands for generalized gradient approximation (in which the density functional depends on the up and down spin densities and their reduced gradient) and NGA stands for nonseparable gradient approximation (in which the density functional depends on the up/down spin densities and their reduced gradient, and also adopts a nonseparable form).

4 Results and Discussion

The molecular structure of the PPA molecule was taken from PubChem (<https://pubchem.ncbi.nlm.nih.gov>), a website that acts as the public repository for information pertaining chemical substances together with the biological activities they are associated with. The molecular structure with IUPAC Name for PPA includes 1,4-(dicarboxymethyl)-5-(2, 3-dihydroxy propyl)-pyrrolo[3, 2-b]pyrrole-2-carboxaldehyde [2]. The pre-optimization of the systems was done using random sampling that involved molecular mechanics techniques and inclusion of the various torsional angles via the general MMFF94 force field [74–78] through the Marvin View 17.15 program that constitutes an advanced chemical viewer suited to multiple and single chemical queries, structures and reactions (<https://www.chemaxon.com>). After wards, the structure that the resultant lower-energy conformer assumed for this molecule was reoptimized using the ten density functionals mentioned in the previous section together with the Def2SVP basis set as well as the SMD solvation model using water as the solvent.

The analysis of the results obtained in the study aimed at verifying that the KID procedure was fulfilled. On doing it previously, several descriptors associated with the results that HOMO and LUMO calculations obtained are related with results obtained using the vertical I and A following

the Δ SCF procedure. A link exists between the three main descriptors and the simplest conformity to the Koopmans' theorem by linking ϵ_H with -I, ϵ_L with -A, and their behavior in describing the HOMO-LUMO gap as $J_I = |\epsilon_H + E_{gs}(N-1) - E_{gs}(N)|$, $J_A = |\epsilon_L + E_{gs}(N) - E_{gs}(N+1)|$, and $J_{HL} = \sqrt{J_I^2 + J_A^2}$. Notably, the J_A descriptor consists of an approximation that remains valid only when the HOMO that a radical anion has (the SOMO) shares similarity with the LUMO that the neutral system has. Consequently, we decided to design another descriptor Δ SL, to guide in verifying how the approximation is accurate.

The results of the calculation of the electronic energies of the neutral, positive and negative molecular systems (in au) of PPA, the HOMO, LUMO and SOMO orbital energies (also in au), J_I , J_A , J_{HL} and Δ SL descriptors calculated with the ten density functionals and the Def2TZVP basis set using water as a solvent simulated with the SMD parametrization of the IEF-PCM model are presented in Table 1.

Table 1: Electronic energies of the neutral, positive, and negative molecular systems (in au) of Blue-M1, the HOMO, LUMO, and SOMO orbital energies (also in au); and J_I , J_A , J_{HL} , and Δ SL descriptors calculated with the ten density functionals and the Def2TZVP basis set using water as solvent simulated with the SMD parametrization of the IEF-PCM mode

	Eo	E+	E-	HOMO	LUMO	SOMO	J(I)	J(A)	J(HL)	Δ SL
CAM-B3LYP	-1252.9957	-1252.7918	-1253.0679	-0.2560	-0.0185	-0.1258	0.0521	0.0537	0.0748	0.1073
LC- ω BPE	-1252.7608	-1252.5511	-1252.8399	-0.3024	0.0142	-0.1725	0.0927	0.0933	0.1315	0.1867
M11	-1252.9189	-1252.7067	-1252.9944	-0.2955	0.0091	-0.1600	0.0833	0.0846	0.1187	0.1691
M11L	-1252.8535	-1252.6365	-1252.9387	-0.2049	-0.0974	-0.0732	0.0121	0.0122	0.0172	0.0242
MN12L	-1252.4065	-1252.2005	-1252.4758	-0.1949	-0.0796	-0.0601	0.0111	0.0103	0.0151	0.0195
MN12SX	-1252.4724	-1252.2600	-1252.5473	-0.2106	-0.0741	-0.0756	0.0018	0.0008	0.0020	0.0015
N12	-1253.3228	-1253.1301	-1253.3880	-0.1790	-0.0805	-0.0514	0.0137	0.0153	0.0205	0.0291
N12SX	-1252.9644	-1252.7614	-1253.0361	-0.2027	-0.0702	-0.0728	0.0003	0.0015	0.0015	0.0026
ω B97X	-1253.2348	-1253.0288	-1253.3076	-0.2912	0.0131	-0.1590	0.0852	0.0859	0.1210	0.1721
ω B97XD	-1253.1513	-1252.9448	-1253.2243	-0.2789	0.0008	-0.1468	0.0724	0.0738	0.1034	0.1476

As presented in previous works [3–33], we consider four other descriptors that analyze how well the studied density functionals are useful for the prediction of the electronegativity χ , the global hardness η , and the global electrophilicity ω , and for a combination of these Conceptual DFT descriptors, considering only the energies of the HOMO and LUMO or the vertical I and A: $J_\chi = |\chi - \chi_K|$, $J_\eta = |\eta - \eta_K|$, $J_\omega = |\omega - \omega_K|$, and $J_{CDFT} = \sqrt{J_\chi^2 + J_\eta^2 + J_\omega^2}$, where CDFT stands for Conceptual DFT. The results of the calculations of J_χ , J_η , J_ω , and J_{CDFT} for the low-energy conformer of PPA in water are displayed in Table 2.

Table 2: J_χ , J_η , J_ω , and J_{CDFT} for the PPA molecule in water

	J_χ	J_η	J_ω	J_{CDFT}
CAM-B3LYP	0.0008	0.1058	0.0327	0.1107
LC- ω BPE	0.0003	0.1860	0.0470	0.1919
M11	0.0007	0.1679	0.0420	0.1731
M11L	0.0001	0.0243	0.0196	0.0313
MN12L	0.0004	0.0214	0.0124	0.0247
MN12SX	0.0013	0.0010	0.0008	0.0018
N12	0.0008	0.0290	0.0202	0.0354
N12SX	0.0009	0.0012	0.0016	0.0022
ω B97X	0.0004	0.1711	0.0412	0.1760
ω B97XD	0.0007	0.1462	0.0386	0.1512

As Tables 1 and 2 provide, the KID procedure applies accurately from MN12SX and N12SX density functionals that are range-separated hybrid meta-NGA as well as range-separated hybrid NGA density functionals respectively. In fact, the values of J_I , J_A , and J_{HL} are actually not zero. Nevertheless, the results tend to be impressive especially for the MN12SX density functional. As well, the ΔSL descriptor reaches the minimum values when MN12SX and N12SX density functionals are used in the calculations. This implies that there are sufficient justifications to assume that the LUMO of the neutral approximates the electron affinity. The same density functionals follow the KID procedure in the rest of the descriptors such as J_X , J_η , J_ω , and J_{CDFT} .

In the past, various TDDFT studies of molecules of different size have used optimally-tuned RSH density functionals with great success [34–53]. The considerable success of the approach is however undermined by the issue of the tuning optimization being system dependent. Therefore, focus should be on establishing the effectiveness of the behaviors of the fixed RSH density functionals in describing the excitation characteristics. In his works, Becke has recently mentioned that the adiabatic connection and the ideas of Hohenberg, Kohn, and Sham apply only to electronic ground states is a common misconception [79]. Furthermore, consistent with Baerends et al., KS model is not appreciated for being superior because of its lowest excitation energy in molecules. Physically, it amounts to an excitation of the KS system rather than electron addition as would be the case in Hartree-Fock. Thus, it can be effectively be used as a measure of the optical gap and is an effective approximation to the gap (in molecules) [80]. In their conclusion, van Meer et al. advanced that the HOMO-LUMO gap associated with the KS model tends to be an approximation of the lowest excitation energy, a desirable characteristic with no concerns regarding it [81].

In this work, the calculation of the maximum wavelength absorption of the PPA molecule in water involved conducting ground state calculations with the mentioned ten density functionals at the same level of model chemistry and theory and determining the HOMO-LUMO gap as well as TDDFT calculations. Figure 1 provide an illustration that compares graphically the results involved in the ground-state approximation derived from the HOMO-LUMO gap together with TDDFT results and the experimental value of 348 nm in water. A similar comparison is shown in Table 3.

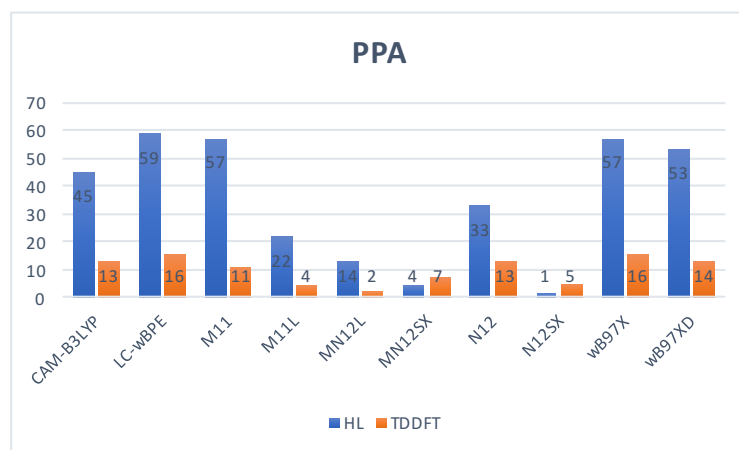


Figure 1: A graphical comparison of the results for the calculation of the λ_{max} of the PPA molecule between the HOMO-LUMO gap prediction, TDDFT values, and experimental data

Table 3: Maximum wavelength absorption (λ_{max}) of the PPA molecule calculated from the HOMO-LUMO gap and from TDDFT results in comparison with the experimental value

	λ_{max} (HL)	Δ (HL)	λ_{max} (TDDFT)	Δ (TDDFT)
CAM-B3LYP	192	156	303	45
LC- ω BPE	144	204	294	54
M11	150	198	309	39
M11L	424	76	362	14
MN12L	395	47	340	8
MN12SX	334	14	323	25
N12	463	115	393	45
N12SX	344	4	330	18
ω B97X	150	198	293	55
ω B97XD	163	185	301	47

Having verified that the MN12SX/Def2TZVP model chemistry is a good choice for the calculation of the global reactivity descriptors and the prediction of the maximum absorption wavelength from the ground state calculation of the HOMO and LUMO, we now present the optimized molecular structure of PPA in water in Figure 2. Meanwhile, the calculated bond lengths and bond angles are shown in Tables 4 and 5.

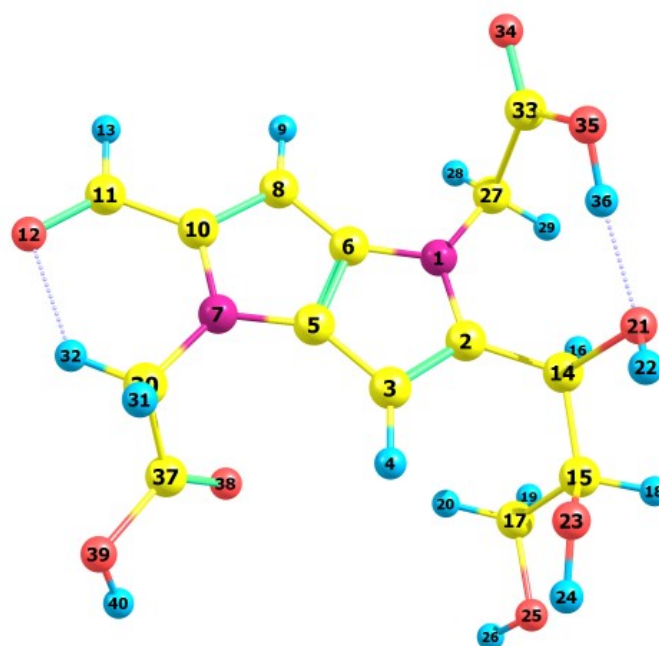


Figure 2: A schematic representation of the optimized structure of the PPA molecule calculated with the MN12SX density functional showing the numbering of the atoms

Table 4: Calculated bond lengths (in Å) of the PPA molecule with the MN12SX density functional using water as the solvent simulated with the SMD solvation model

Bond	Distance	Bond	Distance	Bond	Distance	Bond	Distance
R(1-2)	1.389	R(7-30)	1.438	R(15-23)	1.445	R(30-32)	1.116
R(1-6)	1.383	R(8-9)	1.094	R(17-19)	1.122	R(30-37)	1.514
R(1-27)	1.442	R(8-10)	1.409	R(17-20)	1.117	R(33-34)	1.216
R(2-3)	1.394	R(10-11)	1.455	R(17-25)	1.438	R(33-35)	1.366
R(2-14)	1.508	R(11-12)	1.227	R(21-22)	0.987	R(35-36)	1.002
R(3-4)	1.093	R(11-13)	1.143	R(23-24)	0.985	R(37-38)	1.219
R(3-5)	1.421	R(14-15)	1.529	R(25-26)	0.980	R(37-39)	1.383
R(5-6)	1.406	R(14-16)	1.124	R(27-28)	1.110	R(39-40)	0.982
R(5-7)	1.371	R(14-21)	1.466	R(27-29)	1.110	R(12-32)	1.961
R(6-8)	1.408	R(15-17)	1.526	R(27-33)	1.542	R(21-36)	1.741
R(7-10)	1.394	R(15-18)	1.129	R(30-31)	1.118		

Table 5: Calculated bond angles (in $^{\circ}$) of the PPA molecule with the MN12SX density functional using water as the solvent simulated with the SMD solvation model

Bond	Angle	Bond	Angle	Bond	Angle	Bond	Angle
A(2-1-6)	108.1	A(5-6-8)	108.8	A(14-15-18)	108.0	A(27-33-34)	122.5
A(2-1-27)	127.3	A(5-7-10)	108.3	A(14-15-23)	108.0	A(27-33-35)	115.4
A(1-2-3)	110.0	A(5-7-30)	126.0	A(16-14-21)	106.6	A(31-30-32)	107.3
A(1-2-14)	120.8	A(6-8-9)	128.7	A(14-21-22)	105.1	A(31-30-37)	108.9
A(6-1-27)	124.4	A(6-8-10)	105.6	A(14-21-36)	110.0	A(32-30-37)	110.5
A(1-6-5)	107.8	A(10-7-30)	125.6	A(17-15-18)	108.6	A(30-32-12)	134.3
A(1-6-8)	143.4	A(7-10-8)	109.2	A(17-15-23)	109.5	A(30-37-38)	126.5
A(1-27-28)	109.3	A(7-10-11)	124.0	A(15-17-19)	110.3	A(30-37-39)	113.0
A(1-27-29)	109.5	A(7-30-31)	110.7	A(15-17-20)	111.5	A(34-33-35)	122.2
A(1-27-33)	111.1	A(7-30-32)	107.8	A(15-17-25)	107.1	A(33-35-36)	111.6
A(3-2-14)	129.2	A(7-30-37)	111.7	A(18-15-23)	108.6	A(35-36-21)	174.1
A(2-3-4)	125.9	A(9-8-10)	125.7	A(15-23-24)	105.5	A(38-37-39)	120.5
A(2-3-5)	105.7	A(8-10-11)	126.8	A(19-17-20)	107.5	A(37-39-40)	107.8
A(2-14-15)	114.9	A(10-11-12)	124.7	A(19-17-25)	110.3		
A(2-14-16)	109.9	A(10-11-13)	114.2	A(20-17-25)	110.0		
A(2-14-21)	108.6	A(12-11-13)	121.1	A(17-25-26)	107.9		
A(4-3-5)	128.4	A(11-12-32)	103.0	A(22-21-36)	111.9		
A(3-5-6)	108.5	A(15-14-16)	109.2	A(28-27-29)	107.8		
A(3-5-7)	143.5	A(15-14-21)	107.3	A(28-27-33)	109.2		
A(6-5-7)	108.0	A(14-15-17)	114.0	A(29-27-33)	109.8		

As a summary of the previous results, the global reactivity descriptors for the PPA molecule calculated with the MN12SX/Def2TZVP model chemistry in water are presented in Table 6.

Table 6: Global reactivity descriptors for the PPA molecule with the MN12SX density functional using water as the solvent simulated with the SMD solvation model

Electronegativity (χ)	Chemical Hardness (η)	Electrophilicity (ω)
3.8733	3.7142	2.0197
Electrodonating Power (ω^-)	Electroaccepting Power (ω^+)	Net Electrophilicity ($\Delta\omega^\pm$)
3.6505	2.2387	5.8892

The calculations of the condensed Fukui functions and dual descriptor are done by using the Chemcraft molecular analysis program to extract the Mulliken and NPA atomic charges [82] beginning with single-point energy calculations involving the MN12SX density functional that uses the Def2TZVP basis set in line with the SMD solvation model, and water utilized as the solvent.

Considering the potential application the PPA molecule as an antioxidant, it is of interest to get insight into the active sites for radical attack. A graphical representation of the radical Fukui function f^0 calculated with the MN12SX/Def2TZVP model chemistry in water is presented in Figure 3.

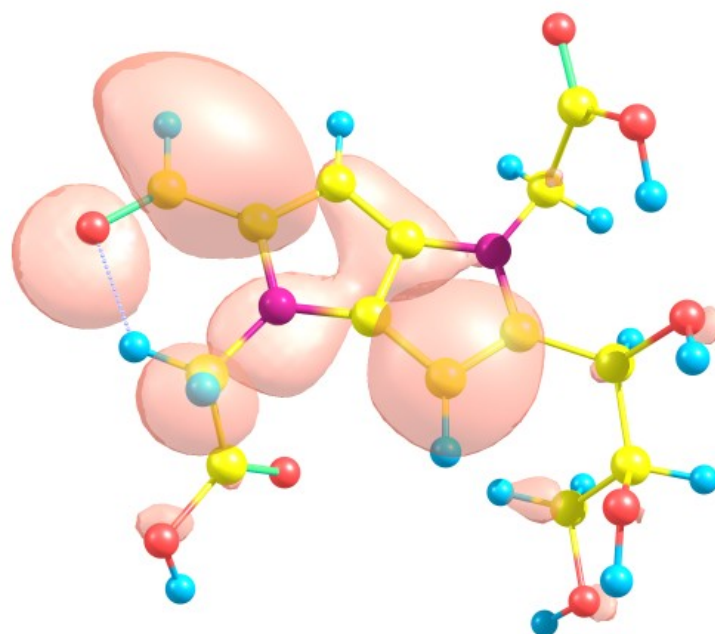


Figure 3: A graphical representation of the radical Fukui function f^0 of the PPA molecule calculated with the MN12SX/Def2TZVP model chemistry in water

The condensed electrophilic and nucleophilic Parr functions P_k^+ and P_k^- over the atoms of the PPA molecule in water have been calculated by extracting the Mulliken and Hirshfeld (or CM5) atomic charges using the Chemcraft molecular analysis program [82] starting from single-point energy calculations of the ionic species with the MN12SX density functional using the Def2TZVP basis set in the presence of the solvent according to the SMD solvation model.

The results for the condensed dual descriptor calculated with Mulliken atomic charges Δf_k (M), with NPA atomic charges Δf_k (N), the electrophilic and nucleophilic Parr functions with Mulliken atomic spin densities P_k^+ (M) and P_k^- (M), and the electrophilic and nucleophilic Parr functions with Hirshfeld (or CM5) atomic spin densities P_k^+ (H) and P_k^- (H) are displayed in Table 7 for the PPA molecule in water.

Table 7: The condensed dual descriptor calculated with Mulliken atomic charges Δf_k (M) and with NPA atomic charges Δf_k (N), electrophilic and nucleophilic Parr functions with Mulliken atomic spin densities P_k^+ (M) and P_k^- (M), and electrophilic and nucleophilic Parr functions with Hirshfeld (or CM5) atomic spin densities P_k^+ (H) and P_k^- (H) for the PPA molecule

Atom	Δf_k (M)	Δf_k (N)	P_k^+ (M)	P_k^- (M)	P_k^+ (H)	P_k^- (H)
1N	-1.64	0.07	0.0163	-0.0012	0.0182	0.0293
2C	-7.68	-6.26	0.1775	0.2903	0.1046	0.1993
3C	-13.84	-9.98	-0.0506	0.1429	0.0011	0.1280
5C	1.21	3.05	0.0913	0.0450	0.0545	0.0661
6C	-8.77	-7.81	-0.0610	0.1338	-0.0047	0.1005
7N	1.14	2.27	0.0768	0.0212	0.0578	0.0395
8C	9.15	9.72	0.2250	0.0014	0.1427	0.0468
10C	-14.47	-16.60	-0.0175	0.3103	0.0499	0.2032
11C	25.42	22.49	0.3447	-0.0648	0.2693	0.0089
12O	9.60	5.00	0.2274	0.1217	0.2227	0.1019
14C	1.12	-1.01	-0.0057	-0.0356	0.0137	0.0100
15C	-0.07	-0.12	0.0010	0.0021	0.0014	0.0015
17C	-0.19	0.03	-0.0016	0.0062	0.0010	0.0055
21O	-0.76	-0.82	0.0089	0.0224	0.0145	0.0221
23O	-0.18	-0.16	0.0006	0.0034	0.0006	0.0032
25O	-0.32	-0.39	0.0005	0.0042	0.0005	0.0041
27C	-0.14	-0.23	-0.0017	0.0001	0.0014	0.0023
30C	-0.03	-0.25	-0.0057	-0.0027	0.0048	0.0024
33C	-0.09	0.07	0.0021	0.0000	0.0015	0.0015
34O	-0.19	-0.58	0.0005	0.0017	0.0006	0.0015
35O	-0.08	-0.31	0.0006	0.0015	0.0006	0.0010
37C	0.07	0.17	0.0028	0.0015	0.0029	0.0014
38O	0.02	0.20	0.0000	-0.0003	0.0005	0.0001
39O	0.00	0.00	0.0006	0.0003	0.0008	0.0003

From the results for the local reactivity descriptors in Table 7, it can be concluded that C11 will be the preferred site for a nucleophilic attack and that this atom will act as an electrophilic species in a chemical reaction. In turn, it can be appreciated that C3 and C10 will be prone to electrophilic attacks and that these atomic sites will act as nucleophilic species in chemical reactions that involve the PPA molecule.

5 Conclusions

Ten fixed RSH density functionals, including CAM-B3LYP, LC- ω PBE, M11, N12, M11L, MN12L, N12SX, MN12SX, ω B97X and ω B97XD, were examined to determine whether they fulfill the empirical

KID procedure. The assessment was conducted by comparing the values from HOMO and LUMO calculations to those generated by the Δ SCF technique for the PPA molecule in water. This is a compound which is of academic as well as industrial interest. The study has observed that the range-separated and hybrid meta-NGA density functionals tend to be the most suited in meeting this goal. Thus, they can be suitable alternatives to density functionals where the behavior of them are optimally tuned using a gap-fitting procedure. They also exhibit the desirable prospect of benefiting future studies aimed at understanding the chemical reactivity of colored melanoidins with larger molecular weights when reducing sugars react with proteins and peptides.

From the results of this work, it becomes evident that it is easy to predict the sites of interaction of the PPA molecule under study. This involves having DFT-based reactivity descriptors, including Parr functions and dual descriptor calculations. Evidently, the descriptors are useful in characterizing and describing the preferred reactive sites. They are also useful in comprehensively explaining the reactivity of the molecules.

Furthermore, it is also possible to predict the maximum absorption wavelength for the PPA in water with considerable accuracy. The prediction involves the MN12SX density functional, beginning with the HOMO-LUMO gap instead of TDDFT calculations. Such a finding is particularly crucial considering the likelihood of it being used to inform the alternative determination method on the color that larger systems such as prosthetic chromophore groups. This becomes necessary in circumstance when it is not possible to carry out TDDFT calculations.

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