Fundamental building blocks of eumelanins: electronic properties of indolequinone-dimers.

K. Bochenek and E. Gudowska–Nowak

Marian Smoluchowski Institute of Physics, Jagellonian University, Kraków, Poland

Abstract

We present results from the theoretical INDO calculations of the electronic structure for stacked eumelanins’ monomers. As basic indolic components of the eumelanin structure 5,6-dihydroxyindole (DHI or HQ) and its oxidized forms (SQ and IQ) were chosen. The results reveal dependency of electronic properties of such aggregates on monomers’ redox states. They point out also a tendency to localize an extra charge on one of dimer’s subunits that could be suggestive of an electron hopping as a model mechanism for the electron transfer in eumelanins.

1 Introduction

Melanin is a photoactive biopolymer [1], a common biological pigment responsible for much of coloration observed in nature. Despite its ubiquity, documented photoprotective [2,3] character, reported photosensitizing activity [4,5] and otherwise hypothesized multifunctionality of the pigment in animals and humans [1,6], neither the size nor the structure of the fundamental molecular unit of the melanins has been well understood yet. Black eumelanins are composed of indolic units derived from the oxidation of tyrosine: among those 5,6-dihydroxyindole (DHI or HQ) together with their oxidized forms (indole-5,6-quinone (IQ)) and semiquinone (SQ) and 5,6-dihydroxyindole-2-carboxylic acid (DHICA) are usually accepted [1,2,4,7,8] as main components of natural eumelanins and their synthetic analogues. Photoreactivity, ability to bind transition metal ions, redox properties and presence of persistent free radical centers in the pigment structure are usually mentioned as main features of eumelanins [2], although their biological significance is still unclear.

X-ray diffraction measurements of dried synthetic pigments have led to a model that pictures eumelanin [7,8,9,10] as a \( \pi \) - stack of crosslinked planar oligomeric structures with a spacing of \( \approx 3.4 \text{Å} \). Such a \( \pi \)-conjugated, randomly arranged heteropolymer system could be responsible for intrinsic semiconductivity of eume-
The eumelanins’ monomers, as well as their dimers and polymers have been subject to theoretical studies in the framework of Hückel theory [11,12,13] that have supported the hypothesis of eumelanins as semiconductors. A further investigation along those lines has been performed for the charged monomers [14] where the stability of charged HQ, SQ and IQ was investigated. Following that study all monomers have been concluded to be strong electron acceptors (in the decreasing order from SQ to IQ to HQ). Elucidation of the spectral properties of synthetic eumelanins has been also addressed [14,15] pointing out consequences of the assumed random organisation of the polymer that explains well experimental absorption spectra of synthetic eumelanins.

The aim of the present study is to examine electronic properties: orbital- and charge-localization of stacked eumelanins’ monomers forming an "indolic sandwich" with a characteristic separation distance of about 3 Å. Two parallel, mostly planar monomers (Figure 1) laying one above the other are chosen as a main unit for modelling. A few assemblies in which one of the monomers has been rotated or moved apart have been also examined checking for the effect of conformational variations on formation of a stable dimeric unit.

Natural eumelanins are built of both DHI and DHICA [6] monomers but it is possible to prepare synthetic material as pure DHI– or DHICA–melanin [10]. In this respect, the article focuses on a distinct class of synthetic eumelanins discussing properties of simple DHIs aggregates only.

2 Methods

Since experimental data on the geometry of the monomers are not available, the model structures have been created in the InsightII/MSI module [16] and geometrically optimized by use of the consistent valence forcefield (CVFF) [16] until the demanded convergence in energy has been achieved (the maximum derivative less than 0.0001 kcal mol$^{-1}$ Å$^{-1}$). Coordinates of such monomers have been used as input data for semiempirical INDO calculations [17]. Ground electronic states of the neutral charged molecules, as well as of the negatively charged molecules from
wich one H$^+$ ion was removed (the number of electrons remains the same), have been obtained as closed-shell molecular orbital wave functions in the Hartree-Fock (RHF) framework. For molecules with an extra electron or without one electron Unrestricted Hartree-Fock (UHF) method has been used. For molecules without hydrogen ion the first excited states were calculated by configuration interactions (CI) among configurations generated as single excitations from RHF ground state. The CI method included the highest 10(20) occupied and lowest 10(20) unoccupied molecular orbitals for the monomers(dimers). At the first step, the calculations have been performed for each monomer (HQ, IQ and SQ) and then for the aggregates built of two stacked monomers (HH, II, SS, SH, HI, IS). For simplicity, we adopt here a notation where HH, II, SH, etc. stand for dimers of HQ-HQ, IQ-IQ and SQ-HQ, respectively. The distance between molecules has been controlled within the range 2.86-4.12Å by a translation (a shift in the z-coordinate) of all atoms forming a displaced monomer in the pair. In order to test whether the mirror symmetry of dimer coordinates in HH, II and SS assemblies does not generate special results in the INDO runs, model HQ-HQ aggregates were built in which one monomer has been optimized with the CVFF and the second with a slightly different version of the consistent valence forcefield [16] intended for application to polymers and organic materials (PCFF). Such a procedure breaks the symmetry of the aggregate producing nevertheless fully agreeable INDO results for both HQ$_{pcff}$-HQ$_{cfvv}$ and HQ$_{cfvv}$-HQ$_{cfvv}$ sets of data. To check for localization of the HOMO and LUMO orbitals a simple routine has been undertaken: In the LCAO framework each molecular orbital ($\psi_i$) is composed as a linear combination of atomic orbitals ($\phi_k$) $\psi_i = \sum_k c_{ik} \phi_k$. The ratio of the sum of squared coefficients $c_{ik}^2$ over atomic orbitals of one of the monomers to the relevant sum for all atoms in a dimer has been assumed to be a measure of the localization of the $i$-th molecular orbital:

$$\text{orbital localization} = \frac{\sum_{\text{one monomer}} c_{ik}^2}{\sum_{\text{both monomers}} c_{ik}^2}$$  \hspace{1cm} (1)

Based on the density matrix, all charges and their distributions have been calculated according to the Mulliken population analysis.

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1 Our test calculations have revealed that expansion of the CI basis to more than 20 highest occupied nad 20 lowest unoccupied orbitals does not change significantly neither the values of estimated excitation energies nor the main contributions $c_{ik}$ to the molecular orbitals of the dimer.
3 Results

3.1 Neutral dimers

In the absence of any extra charge both monomers remain neutral for all distances reported in this study. The biggest value for charge separation has been observed for SQ-HQ set at the distance \( \approx 2.86 \text{ Å} \) (charge 0.26 and -0.26 respectively). The degree of orbital localization as defined above is displayed in Figure 2 and 3.

The results of the analysis are displayed as HOMO (LUMO) localization for HQ monomer in the sets of HS, IH dimers and as HOMO (LUMO) localization for SQ monomer in the IS dimers, respectively. By inspection of Figure 2 one can deduce that in the case of symmetrical assemblies HOMO is delocalized even at relatively large separations of monomers. This tendency remains also unchanged for HQ_{ccff}-HQ_{pcff} sets, for which the spatial symmetry of coordinates is broken. At extremal intermolecular distances (\( \approx 10 \text{ Å} \)) the HOMO orbital becomes localized on one of

\[^2\] Intermolecular distances have been defined as distances between the mean planes located on all atoms of the separated monomers.
Figure 3. Localization of the LUMO orbital on the neutral charged aggregates. Data points displayed for the HQ monomer in the case of HI, SH dimers and for the SQ monomer in the case of SI dimers.

| HI       | SH       | IS       |
|----------|----------|----------|
| $H_I HOMO - 1 \approx IQ_{HOMO}$ | $SH_{HOMO - 1} \approx SQ_{HOMO}$ | $IS_{HOMO - 1} \approx IQ_{HOMO}$ |
| $H_I HOMO \approx HQ_{HOMO}$ | $SH_{HOMO} \approx HQ_{HOMO}$  | $IS_{HOMO} \approx SQ_{HOMO}$  |
| $H_I LUMO \approx IQ_{LUMO}$ | $SH_{LUMO} \approx SQ_{LUMO}$  | $IS_{LUMO} \approx SQ_{LUMO}$  |
| $H_I LUMO + 1 \approx HQ_{LUMO}$ | $SH_{LUMO + 1} \approx HQ_{LUMO}$ | $IS_{LUMO + 1} \approx IQ_{LUMO}$ |

Table 1
Structure of the two highest occupied and two lowest unoccupied molecular orbitals of the indolic sandwich at 4.12 Å intermolecular separation.

the monomers that has been examined for both HQ_{cvff-HQ_{pcff}} and HQ_{cvff-HQ_{cvff}} dimers sets. However, the delocalization decreases faster with increasing distance when the mixed sets of dimers (SH, HI, IS) are analyzed. Distances of about 3.28-3.7 Å seem to be "transition distances": If the monomers are closer to each other, they behave as supermolecule, if they are farther apart, they become two separated molecules.

Additional examination provides further arguments that at large distances ($\approx 4$ Å), the supermolecular structure of dimers breaks down and monomers behave as two weakly interacting molecules. By analyzing the five largest coefficients $c_{ik}$ and the energy of the relevant orbitals we have found that at the distance 4.12 Å HOMO-1/HOMO/LUMO/LUMO+1 aggregates’ orbitals are created of HOMO/LUMO relevant monomers’ orbitals. (see Tab. 1).
When the intermolecular distance decreases, HOMO of the aggregate becomes a mixture of the HOMOs of both monomers. At the same time the HOMO-LUMO gap does not change and remains within the range 0.20-0.22 a.u. for HI and 0.19-0.20 a.u. for SH dimers, respectively. However, in the case of the IS dimers a monotonic decrease in the energy of the HOMO-LUMO gap is registered (from 0.20 a.u. at 4.12 Å to 0.16 at 2.86 Å). Figure 2 comprises also an extra data set for SH dimers: in one case the molecules have been shifted apart preserving the same intermolecular distance - a bigger ring of one molecule was above the smaller ring of the other. In the second case, one of the molecules has been rotated in plane by 90° or 180° (monomers remained parallel). The results indicate that such a variation in the configuration of a dimer changes significantly localization of orbitals, although none persistent tendencies have been observed. In contrast to HOMO, LUMO orbitals reveal lower tendency to delocalization. Only LUMO of the IS aggregate is more delocalized (at small intermolecular distances) than its HOMO.

3.2 Charged dimers

In case of molecules with unchanged number of atoms both, negatively and positively charged assemblies have been examined. Charge localization for symmetrical sets (HH, II, SS) are displayed in the Figure 4. As can be inferred from the latter, an extra charge placed on a dimer is localized on one of the monomers, although as expected, the smaller the distance, the tendency of charge delocalization becomes more noticeable.

For negatively charged heterogeneous assemblies (SH, HI, IS), at all intermolecular distances the charge is localized on the more electron-liked monomer, i.e. (SH)\(^{-}\) results in localization of charge on S monomer, (SH)\(^{-}\) = S\(^{-}\)H and similarly, (HI)\(^{-}\) = H\(^{-}\)I and (IS)\(^{-}\) = IS\(^{-}\).

This finding changes however when a positive charge is taken into account. The molecules are poor electron-donors and our results show that the positive charge becomes localized on one of the monomers without any correlation with distance or monomer’s redox state.

For negatively charged systems the localization of the HOMO orbital has been also examined indicating that the orbitals are restrained exactly to the same monomer as the charge itself.

Similar behavior has been observed for dimers of molecules with a proton removed from the -OH group of one of the constituting monomers (cf. Figures 5, 6).

With the exception of the HS-dimer sets, all HOMOs for deprotonated assemblies are localized on different monomer than the relevant LUMOs (cf. Figures 5, 6). At the same time negative charge is localized on the same monomer as the relevant HOMO of the dimer (Figure 7). The results of our computational analysis point out a persistent tendency for localization of charge/HOMO/LUMO within the studied dimeric assemblies of DHI monomers at the separation exceeding 3.4 Å.
the observation of HOMOs and LUMOs localization in the dimer, we have also examined the structure of first excited states of the assemblies. In most cases, the first excited state of a dimer is composed of its relevant HOMO→LUMO excitation, the apparent exceptions are however HI dimers at 3.00–3.14 Å separation and SH dimers at 3.28 Å separation whose first excited states are mostly composed of the HOMO-1→LUMO transitions. Similarly, the first excited state of the SH dimer at 3.00–3.14Å separation and of the IS dimer at 3.42Å (and more) separation are predominantly formed of the HOMO-1→LUMO and HOMO→LUMO+1 transitions, respectively.

4 Discussion and Summary

The simplest sets of the stacked monomers, building blocks of eumelanin polymers have been examined. Analysis of localization of additional charges and HOMO/LUMO
Figure 5. Localization of the HOMO for assemblies with one proton removed from the -OH group of one of the monomers. Data points are displayed for the monomer without the proton.

Figure 6. Localization of the LUMO for assemblies with one proton removed from the -OH group of one of the monomers. Data points are displayed for the monomer without the proton.

orbitals in an indolic dimer structure has been performed. Charged aggregates have been created either by adding/removing one electron from the neutral dimeric structure, or by deprotonating the -OH group in one of the monomers. Our investigations show that the structure of the frontier orbitals of any particular dimer depends
Figure 7. Charge localization for assemblies with one proton removed from -OH group of one of the monomers. Data for the monomer without the proton.

on redox state of its components as well as on the way the molecule has gained the charge. Heterogeneous structures (SH, HI, IS) tend to behave as two separate molecules even if the distance between the molecules is small. Moreover, negatively charged dimers formed by adding an excessive electron to the neutral aggregate are characterized by the charge localization on a more electron-like monomer. In dimers where one of constituting monomers has been deprotonated, the proton-deficient monomer holds the negative charge independent of the electron-affinity of the neighbouring molecule in the set.

Homogeneous sets (HH, II, SS) of monomers show a stronger tendency to create dimers than the respective heterogeneous assemblies and at comparable distances they behave as one supermolecule with its HOMO and LUMO orbitals smeared over the whole structure. Additional charge in this structures becomes, however, located on one monomer only. Similar conclusion can be drawn from the preliminary studies on sets of planar pentameric polymers formed of indolic units, whose structure and absorption properties have been discussed elsewhere [15]. Same analysis performed for neutral and charged assemblies of that type has revealed that also in the pentamers of randomly assembled HQ, IQ and SQ molecules, the excessive charge becomes localized on one of constituing monomers. This result suggests that, in spite of the electron-acceptor properties, the indolic dimers (and most likely, indolequinone polymers, in general) do not stabilize the charge by delocalization over the entire structure, but rather tend to position the charge on one of the composing molecules.

The additional analysis performed on the SH dimer sets with one molecule rotated or translated with respect to another suggests that electronic properties of the complex may strongly depend on its conformation. Nevertheless, if we limit our
considerations to characteristic distances (3.4Å) reported in experimental studies, the aforementioned general conclusions remain valid.

The above findings along with the conclusions recalled from References [12,13,6,2] suggest a highly dynamic picture of hypothetical eumelanins, whose chemical structure has been proven to be composed mainly of DHI molecules in different redox states. The redox state of the melanin units may change spontaneously under the influence of the environment (acidity, exposure to light and oxygen) and their relevant proportion and state of oxidation may vary in time. In agreement with the former theoretical studies [14], our results show high charge localization in basic clusters of eumelanin structure. Given the latter and an apparent localization of the HOMO and LUMO orbitals on one of the monomers in the stack, the electron-acceptor behavior of the melanin can be viewed as a process in which an electron injected (or photogenerated) in the polymer remains trapped or transfers via a hopping mechanism in between the indolic subunits. Moreover, any temporary charge distribution within the eumelanin complex can be altered e.g. in the process of spontaneous HQ→IQ reaction that effectively will also influence structure of frontier orbitals of the aggregate. Discussed from that perspective, eumelanins can be understood as amorphous polymers whose macroscopic electronic properties are essentially ensemble-average of various structures.

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References

[1] G. Prota, Melanin and Melanogenesis, Academic Press: New York, 1992.

[2] T. Sarna, H.M. Swartz, in: J. Nordlund, R. Boissy, V. Hearing, R. King, J-P. Ortonne (Eds.) The Pigmentary System - Physiology and Pathology, Oxford University Press: Oxford, 1998, p. 333.

[3] L. Zeise, M.R. Chedekel, T.B. Fitzpatrick, (Eds.) Melanin: Its Role in Human Photoprotection, Valdenmar Publishing Company, Overland Park, Kansas, 1995.

[4] X. Zhang, C. Erb, J. Flammer and W. Nau, Photochem. Photobiol. 71 (2000) 524.

[5] A. Young, Phys. Med. Biol. 42 (1997), 789.
[6] G. Prota, M. D’Ischia, A. Napolitano, in: J. Nordlund, R. Boissy, V. Hearing, R. King, J-P. Ortonne (Eds.) The Pigmentary System -Physiology and Pathology, Oxford University Press: Oxford, 1998, p. 307.

[7] G.W. Zajac, Biochem. Biophys. Acta 1199 (1994) 271.

[8] J. Cheng, S.C. Moss, M. Eisner, Pigment Cell Res. 7 (1994) 263.

[9] M.A. Rosei, L. Mosca, F. Galluzzi, Synth. Met. 76 (1996) 331.

[10] C.M.R. Clancy, J.D. Simon, Biochemistry 40 (2001) 13353.

[11] B. Pullman, A. Pullman, Quantum Biochemistry, Academic Press: New York, 1965.

[12] D.S. Galvão, M.J. Caldas, J.Chem.Phys. 92 (1990) 2630.

[13] D.S. Galvão, M.J. Caldas, J.Chem.Phys. 93 (1990) 2848.

[14] L.E. Bolivar-Marinez, D.S. Galvão, M.J. Caldas, J.Phys.Chem. 103 (1999) 2993.

[15] K. Bochenek, E. Gudowska-Nowak, submitted to Acta Physica Polonica B.

[16] www.sb.fsu.edu/imb/facilities/software/msi/insight970/

[17] J. Ridley, M. Zerner, Theor. Chem. Acta 72 (1987) 867.