Polymerization of 5,6-indolequinone: A view into the band structure of melanins

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We present for the first time a study of finite and infinite polymers of 5,6-indolequinone. We show that the band structure of the infinite polymer presents semiconductor characteristics, and that the intrinsic paramagnetism of eumelanin can be modeled through electron trapping at deep "end-effect" defects.

I. INTRODUCTION

In the last three decades an impressive amount of experimental data on the behavior of melanins has been collected,[1] and the most accepted model, derived on a phenomenological basis, pictures the pigment as an amorphous semiconductor.[2-5] It is established that eumelanin is a copolymerization of the products of oxidation of tyrosine,[6-9] extending in three dimensions to form an amorphous compound.[10] The unit 5,6-indolequinone is the abundant species and is mostly supposed to constitute the skeleton of the compound in one or the other redox form. The semiconductor model proposed in 1960 by Longuet-Higgins[11] based on earlier suggestions of a polymeric structure for melanins received strong support from the work of Pullman and Pullman in 1961.[12] In this pioneering study, which we will refer to as PP in the remainder of this work, the authors apply the molecular orbital theory in its most simplified version—the Hückel π-electron theory (HT)—to the 5,6-indolequinone molecule and one particular dimer, shown in Fig. 1.

The main results presented in PP concern the electronic structure of the dimer: contrary to the monomer, the dimer lowest unoccupied molecular orbital (LUMO) has a bonding character (although small); furthermore, the energy difference between the LUMO and the highest occupied molecular orbital (HOMO) is quite small. These results led the authors to predict that these characteristics should extend to the infinite polymer, in which case we would have a small-gap linear semiconductor, with the lowest conduction band of bonding character. The electron–acceptor properties of melanins and the semiconducting properties[2-5] would then be reasonably explained.

Objections to the "conjugated polymer" model came from magnetic resonance data.[13] It is a well known fact that melanins present a stable "free-radical" EPR (electron paramagnetic resonance) signal, and the analysis of this signal[13,14] indicates that the unpaired spins are localized over one or at most two monomeric units or single molecules. This is in clear contradiction with a model of itinerant spins on extended band states, so an alternative view of highly disordered unconjugated polymers developed.

Other polymerization models than the one studied in PP have been proposed[5,7,15] and results indeed point to the coexistence of several different dimerizations (notably a C_2–C_2

bond between units[7]). The polymerization mechanism and consequently the polymeric structure of the melanins is, however, not properly understood. The work of Pullman and Pullman remained the only theoretical calculation directly related to the band structure of melanins.

Here we present the first study of infinite indolequinone polymers. In this paper we explore the possibilities of the dimerization proposed in PP, within the simple HT keeping the same parametrization used in the original work. We show that, although the predictions in PP are not fulfilled, several interesting features can be discussed that relate well to the properties of eumelanin.

II. ELECTRONIC STRUCTURE RESULTS

We start with the 5,6-indolequinone (IQ) molecule and the reduced forms semi- (SQ) and hidroquinone (HQ). The first feature we mention is that, while the IQ and HQ do not present bonding LUMOs, this characteristic is already present for the SQ, as we show in Table I. We note that the infinite polymer resulting from this particular dimerization can be thought of as descending either from the IQ or the SQ: in other words, the bonding character could have been predicted for the dimer if the SQ was considered as one of the monomeric units.

We then build the dimer discussed in PP and successively add monomeric units to form the trimer and so forth. We find that the main characteristics stabilize around the penta- to hexaquinonoid polymers: We consider, for instance, the LUMO energy, the HOMO–LUMO energy difference, and the energy difference between the HOMO and the lowest occupied molecular orbital. These two later quantities would translate into gap value and π-electron valence bandwidth in the infinite chain.

Accordingly, we enter in Table I values for the dimer, the trimer, and the hexapolymer in units of the parameters α
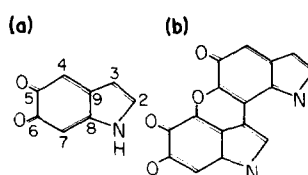

FIG. 1. Schematic representation of (a) the molecule 5,6-indolequinone and (b) the dimer proposed in PP (Ref. 12). The site numbering in (a) is used as reference in the text and in Fig. 2.

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TABLE I. Relevant energies calculated through the Hückel theory for the molecules: 5,6-indolequinone (IQ); 5,6-dihydroxiindole or hydroquinone (HQ); 5-hydroxi 6-indolequinone or semiquinone (SQ); and the finite polymers with 2 (dimer), 3 (trimer), and 6 (hexamer) indolequinone units. The energies are in units of β as in PP (Ref. 12), and refer to LUMO: the lowest unoccupied molecular orbital (LUMO) eigenvalue; LUMO–HOMO: difference in eigenvalues of the LUMO and the highest occupied molecular orbital (HOMO); and HOMO–LMO: difference in eigenvalues of the HOMO and the lowest π-electron eigenvalue.

Molecule	IQ	HQ	SQ	Dimer	Trimer	Hexamer
LUMO ($\times 10^{-2}\beta$)	-18.767	-98.973	5.664	5.061	5.167	5.166
LUMO–HOMO (β)	0.514	1.378	0.334	0.221	0.212	0.211
HOMO–LMO (β)	2.957	2.238	2.677	2.927	2.976	3.006

and β.[12] We note that the "gap" value for the hexapolymer differs only slightly from the result for the dimer, and the bonding character of the LUMO is maintained. The "valence bandwidth" increases also very slightly. The charge density (as inferred from total charges and bond orders) at an internal "cell" or monomeric unit stabilizes also around the penta- to hexapolymer at the values shown in Fig. 2(a).

Still using the same parametrization, we introduce translation symmetry to build an ideal infinite chain of indolequinone units following this particular dimerization as polymerization direction. The resulting energy bands are shown in Fig. 3, and were calculated for 1500 k points uniformly spaced over the unidimensional Brillouin zone.

We see that the energy bands show a reasonably well defined dispersion, with a gap of 0.4 β ($\sim$0.5 eV) and bandwidth of 3.01 β ($\sim$4.06 eV): These results are the first theoretical confirmation of the probable semiconducting properties of indolequinone polymers.

If we compare the total "charge distribution" for the unit cell of the infinite chain, shown in Fig. 2(b), with the charge distribution of an internal cell of the hexapolymer [Fig. 2(a)] we verify that at this level of approximation, the

central portion of the finite chain is already effectively analogous to the infinite chain.

The striking result, however, is that the lowest conduction band (dashed line) is nonbonding, contrary to the predictions in PP. In fact, the gap increases from $\sim$0.2 β (the HOMO–LUMO energy difference in the finite polymer) to $\sim$0.4 β in the infinite chain.

We are led hence to analyze more carefully the partial charge density for the molecular orbitals in the neighborhood of the gap in the finite chains. We find that the LUMO of the finite polymers (from three units on) consistently shows more than 70% of charge concentrated on a single monomeric unit at one end of the chain, as shown in Fig. 2(c). In other words, *the bonding character of the LUMO is a typical "end effect," clearly not extendable to infinite chains.*

III. DISCUSSION

When modeling melanins, we must keep in mind that the pigment (either natural or synthetic) presents amorphous characteristics. The study of ideal infinite polymers may constitute, however, a first approximation to the actual

(a) HEXAPOLYMER: INTERNAL CELL

	All occupied states	
N C$_2$	0.648	
C$_2$ C$_3$	0.612	
C$_3$ C$_9$	0.451	C$_3$ C$_7'$ 0.490
C$_9$ C$_4$	0.615	C$_9$ C$_8$ 0.520
C$_4$ C$_5$	0.296	C$_4$ O$_6'$ 0.489
C$_5$ C$_6$	0.341	C$_5$ O$_5$ 0.841
C$_6$ C$_7$	0.645	C$_6$ O$_6$ 0.406
C$_7$ C$_8$	0.434	C$_7$ C$_3''$ 0.490
		O$_6$ C$_4''$ 0.489

(b) INFINITE CHAIN: UNIT CELL

	All occupied states	
N C$_2$	0.649	
C$_2$ C$_3$	0.612	
C$_3$ C$_9$	0.451	C$_3$ C$_7'$ 0.491
C$_9$ C$_4$	0.615	C$_9$ C$_8$ 0.520
C$_4$ C$_5$	0.290	C$_4$ O$_6'$ 0.489
C$_5$ C$_6$	0.341	C$_5$ O$_5$ 0.842
C$_6$ C$_7$	0.645	C$_6$ O$_6$ 0.406
C$_7$ C$_8$	0.435	C$_7$ C$_3''$ = C$_3$ C$_7'$
		O$_6$ C$_4''$ = C$_4$ O$_6'$

(c) HEXAPOLYMER: END CELL

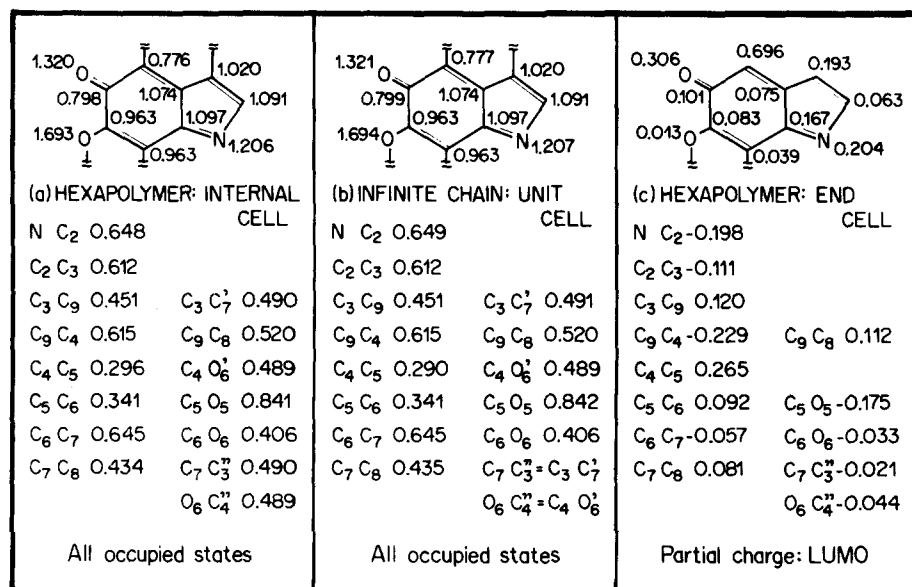|	Partial charge: LUMO	
N C$_2$	-0.198	
C$_2$ C$_3$	-0.111	
C$_3$ C$_9$	0.120	
C$_9$ C$_4$	-0.229	C$_9$ C$_8$ 0.112
C$_4$ C$_5$	0.265	
C$_5$ C$_6$	0.092	C$_5$ O$_5$ -0.175
C$_6$ C$_7$	-0.057	C$_6$ O$_6$ -0.033
C$_7$ C$_8$	0.081	C$_7$ C$_3''$ -0.021
		O$_6$ C$_4''$ -0.044

FIG. 2. Results for the charge distribution (in electrons) obtained through Hückel theory in this work. (a) All occupied states of the internal cell of hexapolymer; (b) all occupied states of the unit cell of infinite polymer; (c) LUMO of the end cell of hexapolymer. The total charges per atom are placed directly in the figure, and bond orders are listed below each case, with atom numbers as in Fig. 1. We remark that in (c) the charge over the whole polymer sums two electrons.
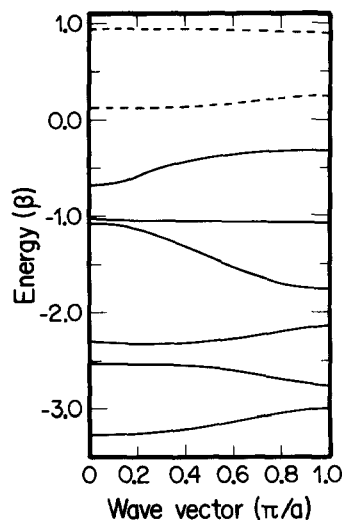
FIG. 3. Energy bands obtained through Hückel theory for the infinite indolequinone polymer based on the dimerization proposed in PP (Ref. 12). Energies are in terms of the parameter β; the zero in the scale corresponds to $E = \alpha$. Occupied bands in solid lines, unoccupied bands in dashed lines.
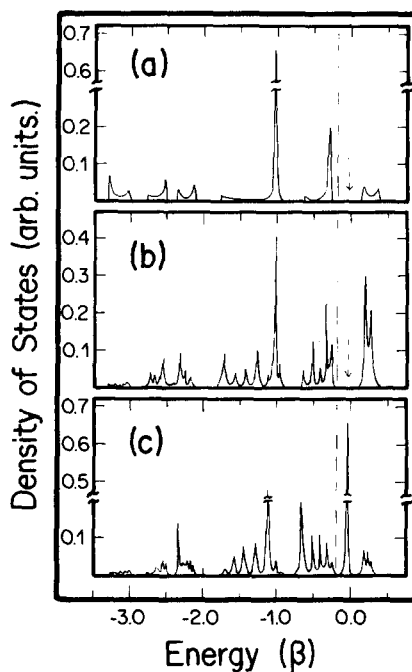

FIG. 4. Density of states (DOS) obtained through Hückel theory for (a) the unit cell of infinite polymer; (b) local DOS for the internal cell of hexapolymer; and (c) local DOS for the end cell of hexapolymer. For the hexapolymer, the (discrete) spectrum was Lorentzian enveloped and weighted to reproduce the DOS localized over the specific cell or monomeric unit. Dashed line separates occupied from unoccupied states. Arrows in (a) and (b) indicate location of the defect level seen in (c).

compound and, as such, yield informations on the nature of the effects to be expected. The model we explore in this work, based on a single polymerization path, already points to the soundness of the semiconducting-polymer approach.

To make the model more realistic, we should consider the effect of disorder which we may introduce, still very simply, by viewing the pigment as composed of arrays of very long but finite chains. If we discard chain–chain interaction (in the sense of assuming that the general features of the band structure, e.g., band edges, are not seriously affected) we may consider the chain ends as defects in an otherwise ordered compound.

We present in Fig. 4(a) the density of states (DOS) of the infinite chain, where the well-defined gap around $E = \alpha$ (zero in the scale of the figure) is seen. We compare this DOS with the local DOS (LDOS) in Fig. 4(b) at the internal cell of the hexapolymer investigated above, to show the similarity of the curves already at this length (six units) of chain; this LDOS is obtained through Lorentzian enveloping of the weighted spectrum. In Fig. 4(c) we plot the LDOS at the end cell of the hexapolymer (the "defect" cell): We clearly see the introduction of a deep midgap defect level, empty in the neutral charge state, and thus able to accept two electrons. This is a very localized defect state, no trace of it is found already at the neighboring cell.

A possible mechanism for the electron–acceptor behavior of this hypothetical melanin could be the following: As an electron is injected at the surface of the pigment through, e.g., interaction with a donor molecule,[16] it enters the conduction band and travels until it is captured at a defect. Considering the charge localization and midgap location of the energy level, the electrons remain trapped (stabilized) at the defect centers.

The adding of a second electron to the same defect center would be accompanied by an increase in the level energy due to electron–electron repulsion which, again considering the localization of the state, could be quite sizeable placing the level close to the conduction band. Hence, the second electron would be easily excitable to an itinerant state (leaving behind an unpaired spin) to be trapped at an empty defect state elsewhere. The magnitude of the "intrinsic" para-

magnetism would then be governed by the ratio of available electrons to defect density, and the spin concentration should be roughly independent of temperature (in a Curie–Weiss fashion) for high defect-density compounds where the Fermi energy would be "pinned" to the first-electron level. This case correlates approximately to dense packing of finite (20 to 30 monomeric units) chains as in solid melanin pellets or powders, where indeed this behavior is detected.[13]

For highly hydrated compounds or for solutions, where the interaction between chains is smaller, we may speculate that the polymers will behave more like isolated molecules so the probability of occurrence of doubly occupied end-type states, with net spin $S = 0$, is increased. In this case, we may expect a slight increase in paramagnetism with temperature[14] upon thermal emission of the second electron, without in any way altering the molecular structure of the compound.

We draw attention to the fact that, *while the magnetically active electron is in our model actually localized over a single monomeric unit, the model is still based on an unsaturated polymer with a highly delocalized π-electron system*, as can be seen from the well-defined dispersion of the bands. These results would seem to account for both the postulated semiconducting properties of melanins (such as energy dispersion through photon–phonon coupling) and the neutralization of citotoxic free radicals.

IV. SUMMARY AND CONCLUSIONS

We present for the first time a semiconducting-polymer model for melanins based on actual band-structure calcula-

tions. Using an extremely simple model, we are able to explain some of the properties of the pigment such as the stabilization of free radicals (or unpaired electrons) through electron trapping at deep defect states, and the behavior of paramagnetism with temperature.

We must remark that the model presented here is still a crude approximation, on several accounts. (i) The calculation technique used is a simple π-electron method. The complexity of the problem precludes the use of *ab initio* or even sophisticated semiempirical techniques, however, the σ-electronic structure will have to be analyzed. The use of the extended Hückel theory must depend, on the other hand, on reliable geometries[17] which are not available at present; furthermore, the use of a single parametrization procedure is very helpful when trying to analyze trends in behavior of different polymers. (ii) We study a single polymerization path, while other paths are probably favored energetically since this particular dimer is not found as an abudant residue. Our choice is, we feel, historically justified, for continuing the work first proposed in PP. (iii) Only one type of defect is investigated—the end-effect defect—and we do not introduce defect interaction or any other disorder effect. (iv) Finally, we disregard interchain coupling.

Further studies in these directions are under way. Considering the simplicity of the model used here and the quality of results, we feel a study of polymerization trends should be amply rewarding.

We would also like to stress the significance of our results in what concerns the behavior of polymer edges as "intrinsic defects," which should be further investigated in a wider sense as, in analogy with surface physics, this kind of "border-effect" defects could play a larger role in polymeric biological reactions than hitherto suspected.

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