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THEORETICAL INVESTIGATION OF
MODEL-POLYMERS FOR EUMELANINS.
II. ISOLATED DEFECTS

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Abstract

We investigate here defects in initially ordered polymers of 5,6-indolequinone, in one or other redox form. The defects studied include aggregation of the carboxyl radical into one skeleton monomer, the aggregation of a host monomer in a lateral misplaced position, and faults in the polymerization sequencing. Our study is carried out, as in the first article I, through Hückel π -electron theory, and results are compared to the perfect structures in I. Our results indicate that the end-type defect suggested as an electron capture center in I is not deactivated by these other structural defects, and that new capture centers might be introduced that could also be responsible for the acceptor behavior of melanins.

1-Introduction

There is great scientific interest in *eumelanin*, the active material of the pigment present in the epithelial tissue as well as in the substantia nigra of the brain of man. Due to the occurrence of melanin-disturbing processes in some pathologies such as Parkinson's disease⁽¹⁾ the medical applications derived from a proper understanding of eumelanins could be very important.

Apart from the direct medical or technological interest, eumelanins appear to be unique biological compounds in that disorder is seemingly present:

(i) Chemical analysis indicate that the active material is mostly composed⁽²⁾ of molecules of 5,6-indolequinone (IQ see Fig.1) or one of the reduced forms semiquinone (SQ) and hydroquinone (5,6-dihydroxyindole, HQ). These units are the result of⁽²⁾ *in vivo* enzymatic processing of tyrosine, or *in vitro* self-oxidation of dopa (dioxypheylalanine). However, both residual precursors and intermediate products are still present in the final product. Also, there are indications that molecules are arranged in linear-chain polymers; the fragments found,⁽³⁾ however, do not indicate a preferential bonding direction or polymerization path and we are thus led to picture a *disordered polymer*.

(ii) Electron paramagnetic resonance experiments (EPR) always detect⁽⁴⁾ a *stable concentration of unpaired electrons* (spin 1/2) with free-radicals in melanin samples, either natural or synthetic, with spin-density localization over one or two monomers. While the spin concentration is independent of temperature for solid-phase samples, it does show a small increase with temperature for solution-phase samples.^(4a,5)

(iii) Structural investigations of solid-phase samples using X-ray diffraction⁽⁶⁾ point to a *stacking arrangement of planar pieces* (with an interplanar separation of $\approx 3.4 \text{ \AA}$) with no long-range order. Experimental evidence for semiconducting behavior comes from analysis of optical data, all samples

presenting⁽⁷⁾ a *structureless absorption spectrum with threshold* around 1.5 eV and sometimes a shoulder at ≈ 3.4 eV. Time-dependent current-vs-voltage measurements in hydrated melanin pressed pellets indicate⁽⁸⁾ a thermal threshold-switching effect, typical of *amorphous materials*.

The experimental evidences are thus consistent with a model picturing eumelanin as a polymer mostly constituted of IQ units (or one of the reduced forms), irregularly arranged and presenting the behavior of an amorphous semiconductor.

In our previous paper⁽⁹⁾, to which we will henceforward refer as I, we studied the electronic structure of four special ordered polymers of SQ (plus the corresponding polymers of IQ and HQ). The chosen polymers are built assuming planar arrangement with uniform bonding between units, following one of the polymerization directions suggested by dimers # 1 to # 4 in Fig. 1, and the calculations are performed using the simple Hückel π -electron theory. Our results indicate that these polymers present semiconducting characteristics in the infinite-chain limit. We have shown further that amorphous characteristics could be obtained for these highly ordered polymers, once we take into account the finiteness of the individual chains.

We found that for most finite chains the lowest unoccupied molecular orbital (LUMO) and/or the highest occupied molecular orbital (HOMO) show a high charge concentration over one or two monomers (molecular units) at the chain ends. Picturing the pigment (or solid pellets) as a dense packing of long finite chains, and neglecting inter-chain coupling effects, the material would show semiconducting behavior with band edges roughly defined by the infinite-chain limit. The chain-ends would act as localized defects⁽¹⁰⁾, introducing deep states in the gap, or creating localized band-tails.

We are thus able to obtain the amorphous characteristics of eumelanins from ordered polymers with overall π -electron delocalization. Since it is often postulated however that some

degree of actual disorder is found in synthetic and probably in biological samples, it is natural to ask if the properties found for ordered polymers can still be obtained when disorder is present. As a first approach to disorder we investigate in this paper the influence of some simple defects on the electronic structure of the polymers studied in I.

2. Method

We use the approach of Hückel π -electron theory⁽¹¹⁾, within the same parametrization used in I. As discussed there, there is enough justification for neglecting σ -symmetry electronic density; however, we are not able to discuss total energies and other properties which depend on the explicit inclusion of all electrons.

In I we investigated both finite and infinite ordered structures following the polymerization directions suggested by dimers 1 to 4 in Fig. 1, and allowing only uniform bonding between units. We concluded that the behavior of the π -electronic structure (such as charge distribution within a typical "cell" or monomer, and energy level spectra) stabilizes after a critical size is reached. This critical size may vary from ≈ 6 to 10 monomers and at this point, using the results for the infinite periodic chains, we can distinguish clearly which effects come from the "bulk" and which come from the finiteness of the polymers (end-effects).

In order to simulate defects in these polymers we use thus chains with nine or ten monomeric units, into which we insert a "defect cell". Results may then be compared to the reference "perfect" polymers discussed in I, and the influence of defects evaluated straightforwardly.

We may class defects as *native* or "intrinsic", or as *impurities* or "extrinsic". An impurity would be a different molecule (a precursor or intermediate product) introduced in the quinoid skeleton either "substitutionally" (replacing a quinoid unit in the linear chain) or through lateral aggregation. We study here (see scheme in Fig. 2a) the effect of substitutional

introduction of DHIC (dihydroxyindole-2-carboxylic acid), an intermediate product in the Raper-Mason⁽¹²⁾ oxidative sequence. We remark that this defect could also be regarded as lateral incorporation of the impurity radical carboxyl (COOH) into site 2 of any redox form of the chains. Other impurities such as tyrosine or dopa, though equally important, form open (non-cyclic) structures so the use of HT is not indicated. We remark that due to the finiteness of actual chains, results might depend on whether the impurity is introduced in the middle of a chain (far from an ending), or exactly at a chain end, where it would probably interfere with existing end-type defects. Accordingly, we have studied for each structure the introduction of the carboxylic impurity at the first, central and last cells.

Native defects may be introduced in different ways, and correspond to a fault in the ordering of the linear chain without the occurrence of any alien unit (even the redox form is maintained). The chain-end itself might be an example, which we investigated in I. We could also have in this class an additional "misplaced" unit bonded to a "regular" skeleton unit through any of the free bonding sites. The possibility of aggregation of molecules to the melanin macromolecule, with no noticeable effects on its spacial structure, is suggested by X-ray measurements.⁽⁶⁾ Here we study this lateral aggregation, but only when it occurs through a 2×2 bond, as shown in Fig. 2b. This choice was based firstly on the evidence for a fair percentage of type-5-dimers (see Fig. 1) as residues⁽¹³⁾ in chemical analyses of eumelanins; furthermore, results⁽¹⁴⁾ with the MNDO technique (Modified Neglect of Diatomic Overlap) indeed point to the stability of these dimers. We even suggested in I that these dimers could work as anchors or seeds. In this case also the position of the defect along the chain might be of relevance, and we proceeded as for the carboxyl radical.

Another native defect which we study here and might easily be introduced in a polymer during growth is the presence of a 2×2

bond somewhere within a differently bonded chain. We might imagine, if type-5 dimers work as polymer seeds, that after this dimer is formed polymerization could proceed along another direction on both sides of the seed. The seed would remain embedded in the final product, as shown schematically in Fig. 2c. For this study we place the defect just in the middle of the chain.

A different polymerization fault could occur through a sudden change of polymerization path. That is, a chain growing through uniform bonding in direction # A (e.g. # 1 with 3×7 and 4×6 bonds) abruptly deviates to direction # B (e.g. # 2, lacking the bond through the oxygen) and continues onwards with uniform bonding in the new direction. This defect is similar to a junction A/B between two distinct materials, since we know that band structure characteristics depend on polymerization direction. We point out, however, that A/B and B/A junctions (see Fig. 2d and e) might present different features, and so we investigated both cases for every pair of chains. Here we again place the defect or junction in the middle of the chain.

We present in the following section selected results for defects of the kind discussed above. Structure #4, as discussed in I, leads to states with very small coupling between units, so effects of impurities or even junction effects should not be relevant; it does not allow, furthermore, for introduction of DHIC as an impurity. Accordingly, we have chosen to implant defects in chains #1 to #3 only.

3-Results and Discussion

We start the discussion by the DHIC impurity, first analysing the effect of appending the COOH radical into site 2 of the isolated molecules IQ, SQ and HQ. We find that the π -electron spectrum is affected in very similar ways for any redox form of the molecules: two occupied states are introduced in the lower half of the band of occupied levels, which are highly concentrated on the radical atoms; and an empty state is placed close to the second

unoccupied state of the indole molecules, so that a strong perturbation of the charge density follows for these unoccupied states, but with little effect on the energy or of the LUMO itself.

This is shown in Fig. 3, where we plot results for the energy levels of the isolated monomers (column *m*) and of the finite polymers studied in I (columns #1 to #3), around the gap region of the infinite chains; results for the band structure of each infinite polymer are also shown as boxes superimposed on the data for the corresponding finite structure (from tables I-I and I-III). In the same figure we enter (column *r*) the energy levels obtained for the isolated molecules with the COOH radical (DHIC in the H form), and the smallness of the perturbation on the LUMO energy is clearly seen.

As may be anticipated from these results, the radical "portion" of the impurity molecules plays no relevant role in the definition of the states close to the band edges. In analysing Fig. 3, we should keep in mind that the LUMO of the impurity molecules is very similar to that of the host molecules, since little charge is projected over the COOH radical. However, small perturbations can be seen for some of the structures. We discuss first the H1 case, for which we do not have end-type defects in the case of the ideal polymer. We show in Fig. 4a the local density of states (LDOS) over the first cell (monomer) of the ideal chain; in parts *b* and *c* we show the LDOS for the first cell of the perturbed chain, which is in this case the impurity cell, separated in the amplitude over the indole atoms in *b* and the amplitude specifically over the COOH radical in *c*. It may be seen that the impurity brings an empty state into the gap, very close to the conduction band minimum, which is quite localised in the impurity cell but not specifically over the radical (the LDOS over the radical also shows a peak at the impurity level energy, indicating it participates in the binding process). The presence of the impurity forces thus localization of the LUMO without introduction of deep defects, and causes just a band-tailing effect. Visible in

Fig. 4c are also the occupied states introduced in the lower half of the valence band. Very similar results are obtained if the defect is placed in the middle or last cells for this chain, and we conclude that the perturbation in the electronic structure is rather small. Similar effects are seen in the case of S2 (middle and last cells), S3 (last cell) and H3 (middle cell). For the remaining structures the perturbation is still smaller, no state is introduced in the gap of I structures (other than the existing end defect). The effect in the vibrational spectrum would undoubtedly be stronger.

We pass now to the results for the lateral aggregation of a host molecule through site 2 of a skeleton unit as in Fig 2b. As said in the introduction, this defect could also be viewed as a #5 dimer acting as a substitutional impurity (the polymer seed). Accordingly, we enter also in Fig. 3 the results for the corresponding dimers (column *d5*).

Analysing the energy location of the LUMO of the dimer relative to the band edges for the different polymers, we may expect now stronger effects on the electronic structure: for instance, for I structures we might expect a midgap acceptor level, and the same effect for the S1 chain. This defect level is in fact obtained but not in every case. For the I3 chain the level is introduced at 0.16 β , already closer to the conduction band than might be anticipated, and only when the impurity is appended to the last cell of the chain (in the opposite end, thus, to the acceptor end-defect cell); the state shows charge highly localised over both cells, the skeleton and the aggregated cell, indicating that the interpretation of the defect as a dimer impurity is appropriate. A very interesting case is that of the S1 structure, for which the end-defect already introduces a midgap level quite close, in energy, to the new defect level. What we observe is that, as shown in Fig. 5a-c, both levels remain extremely localised over the corresponding defect cells, so that there is almost no defect interaction over a distance of only four cells.

Furthermore, even when the defect is introduced in the last cell of the chain (where the end-defect is located) the interaction between the defects is such that two deep acceptor levels appear in the gap. A similar effect is seen for the H1 structure. Systematically for aggregation in any region of the polymer, the defect introduces an acceptor level with high charge localization, that appears now, however, close to the conduction band of the chain; the energy of the defect level is hardly changed in this case from the energy of the LUMO of the dimer.

The effectiveness of #5 dimers in playing the role of capture centers is met again when we analyse the results of introducing this 2×2 bond in the middle of the chains, right along the π -electron delocalization path as indicated in Fig. 2c. We now obtain the expected strong perturbations in the electronic structure, with introduction of deep levels for the chains I2, I3 and S1; and localised "band tail" states for chains S2 and S3. Again for the S1 chain the end-defect is not affected, and the new state is introduced only slightly higher in energy and spatially localised over the dimer seed; as shown in Fig. 5d, there is also a perturbation at the top of the valence band in this case, an effect that is seen for the other S chains and could be inferred from Fig. 3b. For the H structures we obtain strong perturbative effects, with acceptors introduced in the upper half of the band gap for H1 and H2 (localised over the dimer in this latter case); our results cannot be regarded as definitive, however, since these H forms require longer chains to stabilize (as described in I) and the length used here, 5 cells on each side of the seed, is probably too short.

We come now to the analysis of the last type of defect investigated here, the sudden change of polymerization direction along a chain. As remarked in the previous section, we obtain the characteristic electronic structure of a junction between two different materials (except for the case I3/I2 which we discuss below); for instance in the cases S1/S2 and S2/S1 the "conduction

band edge" is spatially defined by the polymerization sequence on each side of the junction. The end-defect of the S1 structure in particular is not affected in the case of the S2/S1 junction, and, more striking, does not seem to be affected in the S1/S2 case either, in spite of the fact that it is localised exactly at the polymerization fault: the lack of the bond through the oxygen atom is enough to concentrate charge in an unoccupied state (which is now higher than the first empty state of the neighboring S2 cells, as is expected from Fig. 3b) that is not seen in the neighboring S1 cells. Only in the case of the I3/I2 junction a distinctive effect is observed, in that the electronic structure is completely altered. Among all chains considered in this work, I3 is the only one to present the energy difference for the LUMO and HOMO almost zero; each of these states is highly localised, but over opposite ends of the chain. When we join the last cell of I3 with the first cell of I2 we are "forcing into contact" the donor end-defect (HOMO) of I3 and the acceptor end-defect of I2 (LUMO). This interaction causes a complete redistribution of the electronic structure, extending well into both sides of the junction, which has the net effect of filling the energy gap with new states.

With the exception of the I3/I2 junction, then, we may say that changes of polymerization path do not introduce new (in character) defect states that could act as capture centers; on the other hand, this polymerization fault does not seem to deactivate existing centers.

4-Summary and Conclusions

Recalling the conclusions drawn in Ref. 10 and in I for melanin granules or pellets in the solid state we could picture the closely packed chains as an amorphous semiconductor with bands roughly defined by the infinite chains (boxes in Fig. 3). The existence of defects with deep states in the gap, and associated with high charge localization, permits us to explain the

electron-acceptor behavior of this hypothetical melanin: an electron injected at the surface of the pigment would be captured and remain trapped at such defects, producing the observed⁽⁸⁾ magnetic signal. A second electron captured at the same center would have its ionization energy (to the conduction band) much diminished due to electron-electron repulsion effects, and would be easily transferable to another (empty) defect center through the itinerant states of the band. The spin concentration should be roughly independent of temperature⁽⁵⁾, since the isolated trapped electrons, responsible for the $S=1/2$ signal, should not be thermally released at reasonable temperature; very few defects would be doubly occupied ($S=0$), however these defects could be ionized giving rise to a very slight increase in spin concentration with temperature.

For solution samples, on the other hand, the chains behave as isolated molecules whence double occupation of defects levels is more probable (without the semiconducting media to control the "Fermi level") and we may now expect increased temperature dependence for the spin concentration: each doubly negative molecules ($S=0$) may thermally release one electron to the aqueous media, activating the magnetic signal ($S=1/2$).

In our previous works⁽⁹⁻¹⁰⁾ we suggested these defects could be introduced by the physical ending of the chains. Here, proceeding with the systematic study of polymers of 5,6-indolequinone initiated in I, we introduced isolated defects in the finite chains, and also investigated changes in the polymerization direction along a finite chain. This study in finite polymers is validated by our previous investigation of "perfect" finite and infinite chains, which allows us to identify new states introduced by the defects.

Among the defects studied here, the incorporation of the carboxyl radical into site 2 of skeleton molecules is the one to induce less perturbation, indicating that a fair amount of this impurity could indeed be present in actual melanin samples, as

recently suggested⁽¹⁵⁾; the energetic cost to decarboxylate the molecules would thus appear to be the relevant quantity in this case. The sudden deviation in the polymerization sequence, with a single exception, also does not affect the electronic structure of the compound in a significant way, except maybe in introducing more end-like defects. When we come to the #5 dimer impurity however, involving the 2×2 bond, we see in the gap region of most structures the appearance of deep localised states that are intrinsically new states.

This effect offers an alternative to the introduction of localised electron traps other than the actual breaking of a chain: these dimer impurities would effectively enhance the capture processes, without in any way altering the main electronic structure of the polymer.

The model we suggested in I for eumelanins, of a mostly ordered polymer of one or other redox form of indolequinone, densely packed in the solid state, with structural defects of limited order acting as electron-capture centers or introducing amorphous-like band-tail states, stands strongly reinforced by this study of localised defects. These polymers demonstrate a remarkable stability, as regards electronic structure characteristics, against structural defects. On the other hand, defects that do induce strong perturbations may perform the same function, namely trap electrons gained by the pigment from neighbor donor molecules which could degrade the biological environment.

The results presented here were obtained from a model that, although closer to the presumedly disordered natural pigment than the model used in I, is still pertinent to models for defects in ordered compounds. In the next article in this series we will use a powerful technique for the study of long-range disorder in finite chains⁽¹⁶⁾, which will allow us to investigate defect interaction and other typical disorder effects in indolequinone chains.

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Figure Captions

Fig. 1) Scheme of the molecules 5,6-indolequinone (IQ), semiquinone (SQ), and 5,6 dihydroxyindole or hydroquinone (HQ); also the polymerization directions studied in this series of articles, represented by the dimers.

Fig. 2) Schematic representation of the defects studied in this work: a) Aggregation of the carboxyl radical COOH into site 2 of a regular skeleton unit; b) lateral aggregation of an identical molecule into site 2 of a regular skeleton unit; c) substitutional (embedded) #5 dimer (impurity or single polymerization fault); d,e) deviation of polymerization direction or junctions A/B and B/A.

Fig. 3) Energy level scheme for relevant systems around the gap region of the infinite polymers studied here. a) Indolequinone I forms; b) Semiquinone S forms; c) Hydroquinone H forms. The first column of each portion concerns the isolated monomer (m); the middle columns to the finite (horizontal lines) and infinite (boxes) chains, labeled according to polymerization direction following the notation of Fig. 1; the column marked r refers to the isolated molecules with incorporation of the carboxyl radical COOH through site 2; and in the column marked d5 we enter results for the isolated #5 dimers. Solid lines indicate occupied states, dashed lines unoccupied states. Results in units of β , the resonance energy, and the zero of the scale is in each case at $E=\alpha$ (see Ref. 11).

Fig. 4) Local density of states (LDOS) obtained through Hückel π -electron theory for a) the first cell of the "perfect" H1 chain; b) the first cell of the H1 chain, where now we have aggregated the COOH radical, without the contribution from the radical atoms; and c) the contribution from the radical. Energies as in Fig 3; the vertical line separates occupied from unoccupied states.

Fig. 5) Local density of states (LDOS) obtained through Hückel theory for a) the middle cell of the "perfect" S1 structure; b) the middle cell of the S1 structure where now an identical molecule is aggregated through site 2 (the LDOS over the aggregated unit is very similar); c) end cell of the same perturbed structure as in b(very similar to the end cell of the perfect structure, shown in 1); and d) the middle cell of the S1 structure when the bonding sequence is singly deviated to a 2×2 bond, or in other words, when the cell is part of a #5-dimer impurity embedded in the chain. Energies as in Fig. 3. The vertical line separates occupied from unoccupied states in each case.

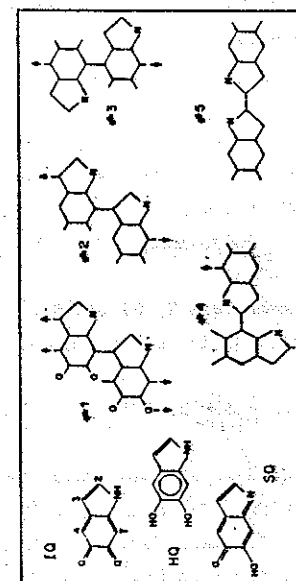


Fig. 1

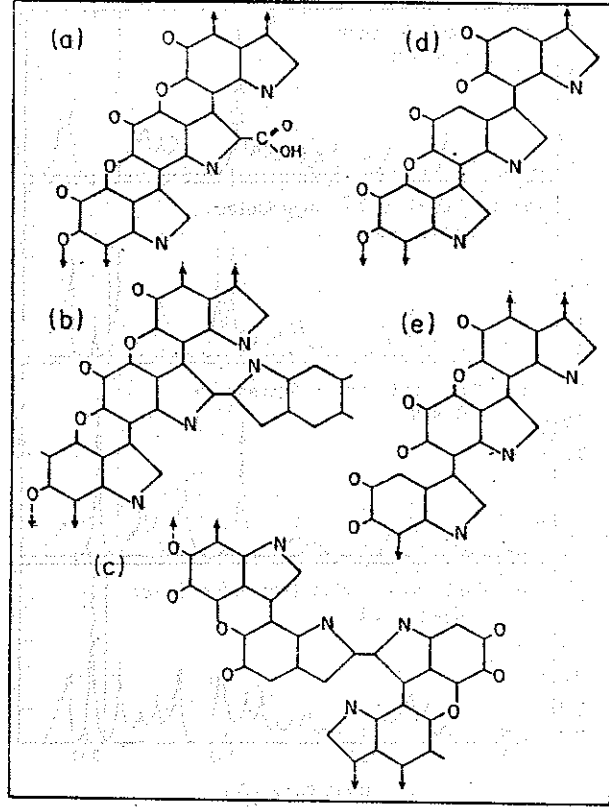


Fig. 2

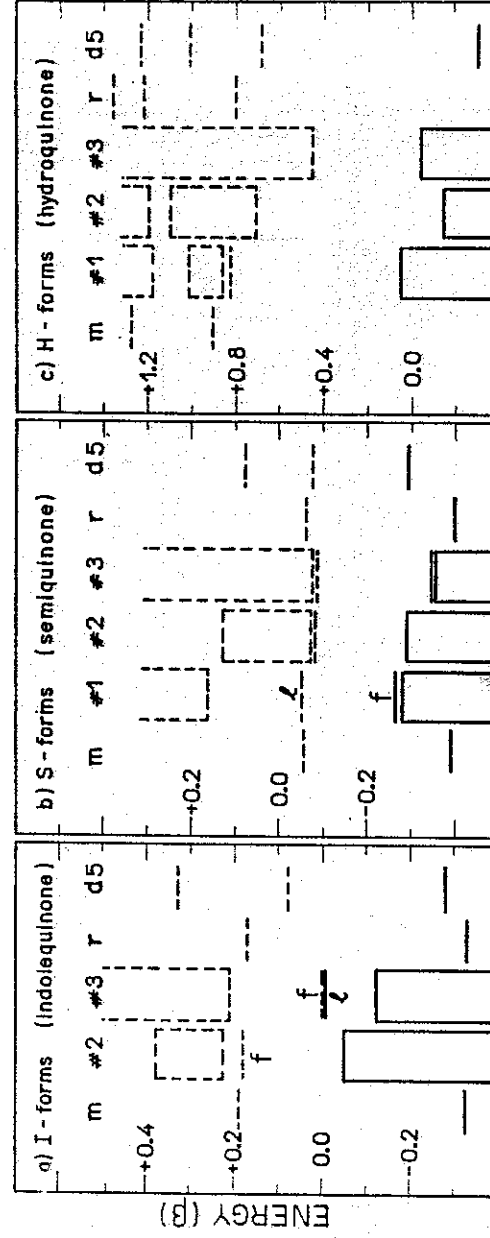


Fig 3

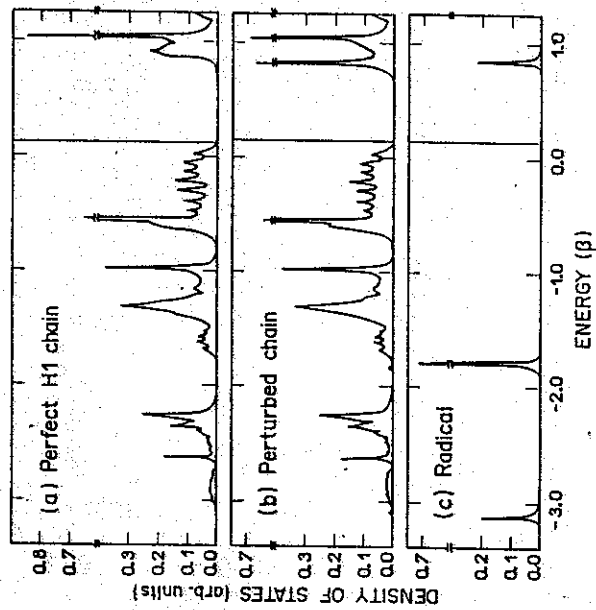


Fig. 4

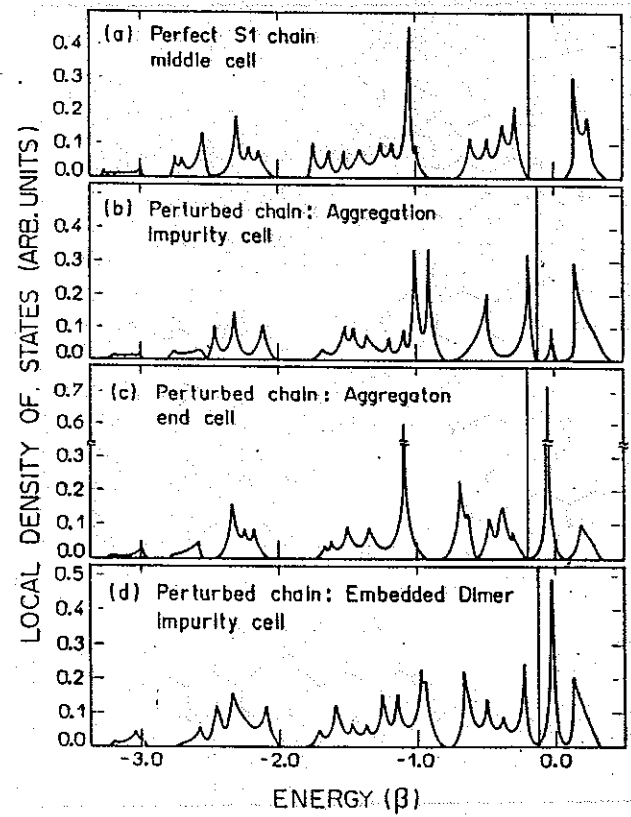


Fig 5