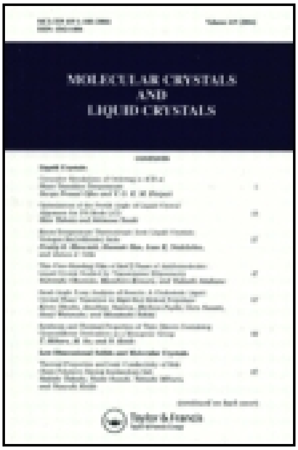

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Rotational Isomeric State and Lattice Model Simulations of the Orientational Behaviour of Hydrocarbon Chains Tethered to an Impenetrable Interface

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Rotational Isomeric State and Lattice Model Simulations of the Orientational Behaviour of Hydrocarbon Chains Tethered to an Impenetrable Interface

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The Rotational Isomeric State description of the conformational behaviour of hydrocarbon chains and their Knight's Gambit Lattice representation are shown to provide the same picture of the orientational order of an isolated chain tethered to an impenetrable interface. The experimental order parameter profile can be reproduced both by subjecting the chain to a mean field potential and by confining it within a cylinder with rigid walls. The chain undertakes conformations containing loops and this is enhanced by the introduction of a *cis* double bond in the middle of the chain. A hydrocarbon chain containing a bulky pentagon corresponding to a nitroxide group, exhibits sowewhat higher order parameters, particularly for those atoms close to the label. This finding indicates that the low orientational order reported by fatty acids labelled at the 12 positions, reflects interactions of the spin label with the surrounding rather than an intrinsic change in the conformational behaviour.

Keywords: Rotational isomeric state; Monte Carlo dynamics; orienting potential; hydrocarbon chain

INTRODUCTION

Much research effort has been expended in the past on studies of the orientational behaviour of hydrocarbon chains in the lamellar phases of

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*Corresponding author.

soap and lipid molecules [1–3]. To this end, the chains were either deuterated or labelled with paramagnetic nitroxide groups. The orientation of the C—D bond or the nitroxide spin labelled in the system is characterized in terms of the order parameter $\langle P_2 \rangle$, being the ensemble average of the second order Legendre polynomial. These order parameters are easily obtained from the spacings of the ^{2}H-NMR or ESR spectral lines [4–6]. The quantitative analysis of the order parameters in terms of the conformational behaviour of the chains is hampered by the multiplicity of internal motions and requires computer simulation methods such as Molecular or Brownian dynamics [7, 8]. However, the computer simulations can be speeded up considerably on using Lattice Dynamics techniques for multichain systems [9], or by simply mimicking the effects of the surroundings on the behaviour of a representative chain in the system by an orienting, the so-called Marcelja, potential [10, 11]. The simplicity of the latter approach is particularly appealing, since it allows the investigation of the effect of the introduction of a double bond or a nitroxide group into the chain structure.

The variation of the order parameters along the length of the chain, its order parameter profile, has been found to be different in ^{2}H-NMR and ESR experiments [4–6]. The NMR profile decreases slowly along the chain and in many instances is characterized by a plateau in the middle of the chain. In particular, the order parameter of the C—D bond of the 12th atom is still significant, while a nitroxide group attached to the same atom reports an order parameter very close to zero. As the effects of chain deuteration are considered to be marginal, certainly compared to the introduction of a bulky nitroxide group, the fidelity of the ESR results has been called into question [12]. It has been forcefully argued that the bulky nitroxide spin label causes major changes in the conformational behaviour of the chain. This point of view was challenged recently by a Lattice Dynamics study [13], which indicated that the order parameter profile of a chain containing an enlarged atom is not significantly different from that of a hydrocarbon chain in a multichain system.

Here we report a computer simulation study of the orientational behaviour of an isolated hydrocarbon chain tethered to an impenetrable interface using the Rotational Isomeric State (RIS) [14] and Lattice Dynamics models. In particular, we re-examine the perturbations caused to the conformational and orientational behaviour of the chain arising from labelling with a nitroxide group. We shall show that both computer models yield similar pictures of the orientational behaviour of saturated and *cis* unsaturated chains. Much insight is obtained from the variation of the order parameter $\langle P_1 \rangle \equiv \langle \cos\beta \rangle$ of chain segments, rather than the experimentally accessible $\langle P_2 \rangle \equiv \langle 3\cos^2\beta - 1 \rangle /2$. We find in agreement with the multichain study using Lattice Dynamics techniques, that the order parameter profile of nitroxide-labelled chains is similar to that of polymethylene chains. This indicates that the solution to the discrepancy between the ^{2}H-NMR and ESR data must be sought in other effects, such as the explicit interaction of the nitroxide group with its surroundings in the bilayer.

THEORETICAL MODELS

RIS Model

The model aliphatic chain has 16 carbon atoms, i.e. 14 CH_2—CH_2 rotating bonds. The rotation of the methyl group is not considered explicity. The chain is tethered to an impenetrable surface to take into account the presence of the monolayer or bilayer structure. In the latter systems the first atom is not anchored to a rigid support, but to a diffuse interface. We have here simulated this mobility by adding two virtual bonds at the beginning of the chain, C_{-1}—C_0 and C_0—C_1 in Figure 1. Thus, the real chain starts from atom 1 and has 16 degrees of freedom.

The torsional potential has three inequivalent minima, corresponding to the *gauche*$_-$, *trans* and *gauche*$_+$ states, respectively with energies of 1.3, 0, 1.3 kT units. In the Rotational Isomeric State (RIS) approximations [11, 14] only the stable states, corresponding to the minima of the torsional potential, determine the conformation of the chain. Thus, in our case the aliphatic chain has 3^{16} possible conformers. However, excluded volume interactions, the so-called pentane effect, reduce the effective number of configurations entering the calculation of chain properties. Thus if adjacent bonds undertake a g_-g_+ or g_+g_- conformations or the distance between the center of any pair of atoms is less than two van der Waal radii, the chain conformation is rejected. The bond length C—C is taken to be 0.153 nm, the valence

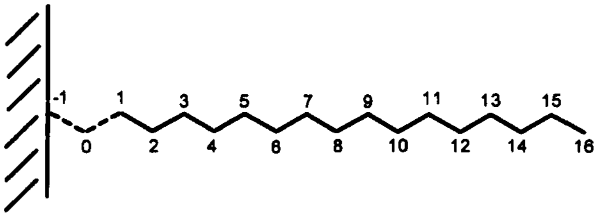

FIGURE 1 Schematic drawing of a saturated hydrocarbon chain tethered to an impenetrable interface.

angle, C—C—C, as 109.4° and the van der Waals radius of the united atom as 0.1 nm.

We shall furthermore consider a hydrocarbon chain with a *cis* double bond at the 9-10 position, Figure 2. The bond angles C—C=C and C=C—C of this rigid structure are 120° and the C—H bond lies on the double bond plane. The torsional potential about the single bond adjacent to a double bond is assumed to exhibit minima at angles of $-60°, 0°, 60°$ with the energies 1.3, 0, 1.3 kT units respectively [15].

Finally, we shall address the question of the perturbation in the conformational behaviour of the chain by a covalently bound nitroxide spin label. The spin lable is mimicked as a regular pentagon of 4 van der Waals spheres of radius 0.1 nm attached to atoms 5 or 12 of the chain, Figure 3. We shall only consider the effects of the excluded volume interactions of the

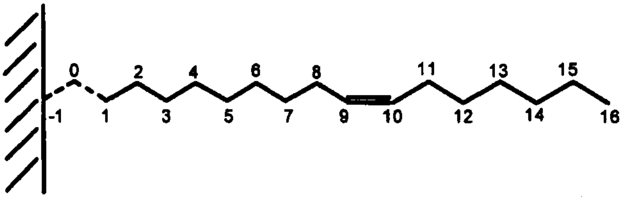

FIGURE 2 Schematic drawing of a hydrocarbon chain containing a *cis* double bond at the 9-10 position, tethered to an impenetrable interface.

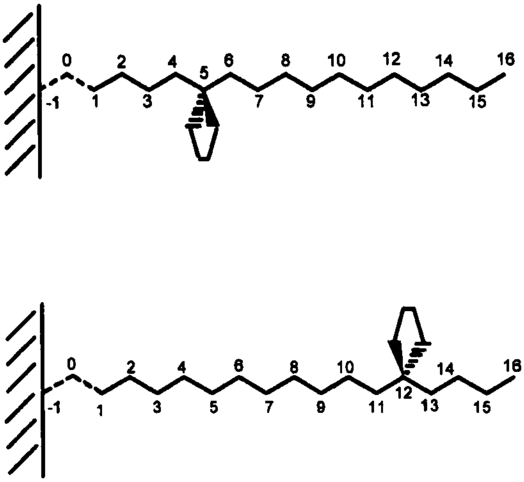

FIGURE 3 Schematic drawing of a saturated hydrocarbon chain labelled at atoms 5 (top) and 12 (bottom) with a pentagon, tethered to an impenetrable interface.

spin label with the atoms of the chain. Moreover, we shall constrain the bonds C_4—C_5 or C_{11}—C_{12} to be in the *trans* conformation so as to account for the strong steric hindrance involved in the displacement of the pentagon.

Knight's Gambit Lattice Representation

This representation had been discussed in detail previously [9, 16] and only the salient points will be summarized here. The hydrocarbon chain is confined to a cubic lattice. The centres of the atoms are separated by a distance of $\sqrt{5}$, and the C—C bonds are formed by the 24 vectors of the type $\{\pm 2, \pm 1, 0\}$. One lattice unit thus corresponds to a distance of 0.069 nm. The bond vectors are chosen from this basis set under the condition that the distance R_{13} between atoms i and $i+2$ lies in the interval $\sqrt{10} \leqslant R_{13} \leqslant \sqrt{18}$. This means that the valence angle, C—C—C, varies between 90° and 143°. This Chess Knight Gambit representation leads to multiple dihedral conformational states about each C—C bond. In the spirit of the RIS the continuous torsional potential about the C—C bond, is replaced by symmetric square-wells representing the *trans* and two *gauche* states. The width of the wells is chosen so that each of the effective t, g_+ and g_- states contains the same number of dihedral conformations. The *trans* and *gauche* states have energies of 0 kT and 1.3 kT respectively and the height of the barries between them is taken to be 3.3 kT. The barrier corresponding to the *cis* state has a height of 8.6 kT.

The representation of the *cis* double bond segment on the lattice is chosen so as to reproduce its rigid planar configuration. 48 distinct triplet vector combinations taken from the basis vector set were found to satisfy this condition. Again a square-well representation was used for the continuous torsional potential about the single bonds adjacent to the double bond. The potential minima were taken to be at 0° and ±60° and the energies were taken as 1.45 kT and 0 kT respectively.

Excluded volume effects were implemented by considering each atom in the chain to be represented as a sphere of radius 2.1 lattice units, 0.155 nm. Chain configurations in which beads separated by more than three bonds came closer together than twice the sphere radius were rejected. The first atoms, atom 0, of the chain was moreover rigidly attached to an impenetrable surface. The anchoring of atom 0 to the surface severely restricts the torsional motion about the first bond, and in order to mimic the behaviour of real chains in monolayer and bilayer structures, we shall consider the chain to consist of atoms 1 to 15.

In analogy with the RIS simulation above, the nitroxide spin label was represented as a regular pentagon attached to atom 5 or 12 of the model chain and with each of the four atoms having an excluded volume radius of 2.1 lattice units.

Different configurations of the model chains were generated by executing local structural arrangements involving the simultaneous transfer of a pair of adjacent atoms, $—C_1—C_2—$, to different lattice sites. As the chain segment is uniquely characterized by the triplet of lattice vectors assigned to the bonds, the moves are described simply as random interchanges between vector triplets. The possible interchanges are generated subject to the condition that the bond lengths remain constant and stored in a lookup table prior to the simulation. The last bond of the chain is allowed to undertake random orientations.

The local conformational moves for chain segments spanning the *cis* double bond are formulated under the constraint that the four bead segment $—C_2—C_3{=}C_4—C_5—$ forms a rigid entity. Consequently, the constituent beads, C_2 to C_5, can only be displaced to different lattice sites by a large scale collective move. This is achieved most simply by the execution of translationally asymmetric collective four bead moves involving segments of the type $—C_1—C_2—C_3{=}C_4—$ or $—C_3{=}C_4—C_5—C_6—$. These are characterized by the set of five bond vectors and the random interchanges between the sets are again implemented using lookup tables.

The attempted move of the beads is accepted with a probability P given by the symmetric scheme

$$P = \frac{\exp(-E_{new}/kT)}{\exp(-E_{old}/kT) + \exp(-E_{new}/kT)}$$

The Mean Field Potential

The mean field potential [10, 11] will be taken to act so as to orient the C—D bonds in a direction parallel to the impenetrable surface when the chain is in its all-trans conformation. Effectively this means that the chord vector of atom i, the vector joining atoms $i-1$ and $i+1$, is made to align along the normal to the surface, the director. We shall thus consider the potential to act on the individual chord vectors and the total energy of the chain to be the sum of the contributions from every atom in the chain:

$$U = -\varepsilon \sum_i (3\cos^2\beta_i - 1)/2$$

where β_i is the angle between the chord and the director axis and ε is a positive parameter determining the strength of the potential. With this definition the potential energy for a chord is lowest for $\beta_i = 0$ with $U_i = -\varepsilon$, and assumes the highest value $U_i = \varepsilon/2$ for $\beta_i = \pi/2$.

RESULTS AND DISCUSSION

The RIS and Knight's Gambit Lattice representation of the hydrocarbon chain were used to simulate the profile of the order parameter S_{CD} observed experimentally for perdeuterated potassium palminate chains [17]. The simulations were carried out on varying only the strength of the mean field orienting potential ε. The best fits, Figure 4, were obtained for the RIS model with $\varepsilon = 0.125$ and for the Lattice model with $\varepsilon = 0.12$. We note that these values for the orienting potential are specific for our choice of the energy of the *gauche* state. We cannot rule out other combinations of the two parameters for describing the same data.

The quality of the fit is good, though both models yielded systematic deviations along the length of the chain. This is particularly noticeable towards the terminal end of the chain, where consistently higher values for

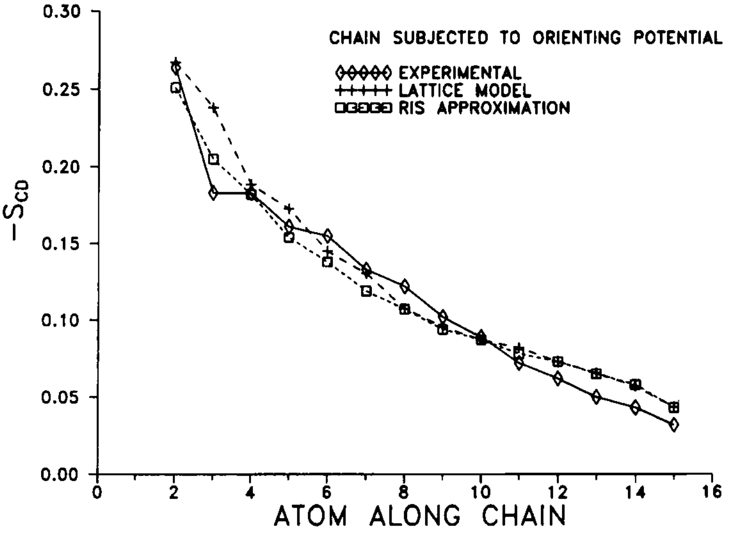

FIGURE 4 The order parameter profile of the C—D bonds observed experimentally [-◇-] for a perdeuterated K-palmitate chain and those simulated with the RIS approximation [+] and the Lattice model [□] using a P_2 orienting potential.

the order parameters are found. The form of the order parameter profile turns out to be inherent to the use of a P_2 orienting potential. The fitting procedure essentially involves the search of a compromise between the undershoot in the middle of the chain and the overshoot towards its free end. The finding that both models require virtually the same strength of the orienting potential is not fortuitous. It simply reflects the fact that the C—D bonds can only undertake a limited range of angles relative to the normal to the surface. While the exact values differ for both models, their distribution in space is similar.

Interestingly, we were able to reproduce the experimental order parameter profile by confining the carbon atoms of a free chain within a cylinder of radius 1.15 nm for the RIS model and 1.13 nm for the Lattice model, Figure 5. This indicates that the effects of the packing constrains on a hydrocarbon chain in a bilayer system can also be mimicked by forcing it to undertake a simple geometric shape on average. The latter finding underpins the shape concept introduced to account for the polymorphism of lipid molecules [18].

Further insights into the behaviour of the chain can be obtained by considering the order parameter profile of the chord vector joining atoms $i-1$ and $i+1$ along the length of the chain. In particular we shall consider the order parameter $\langle P_1 \rangle$, Figures 6 and 7. This order parameter varies

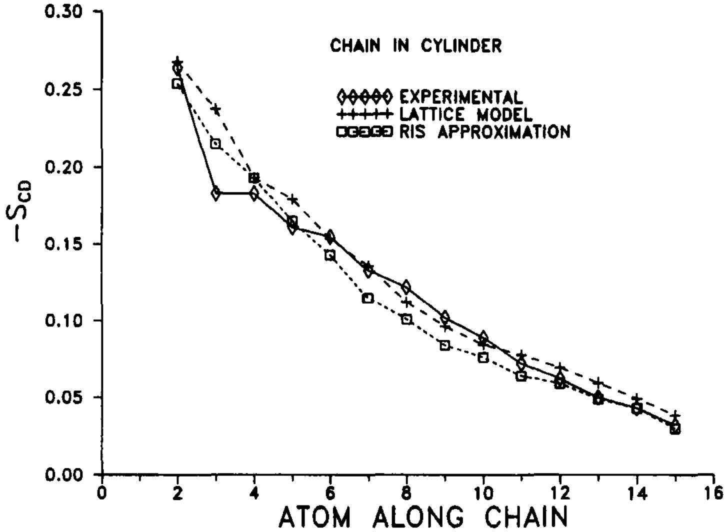

FIGURE 5 The order parameter profile of the C—D bonds observed experimentally [-◊-] for a perdeuterated K-palmitate chain and those simulated with the RIS approximation [+] and the Lattice model [□] on confining the chain to lie within a cylinder with rigid walls.

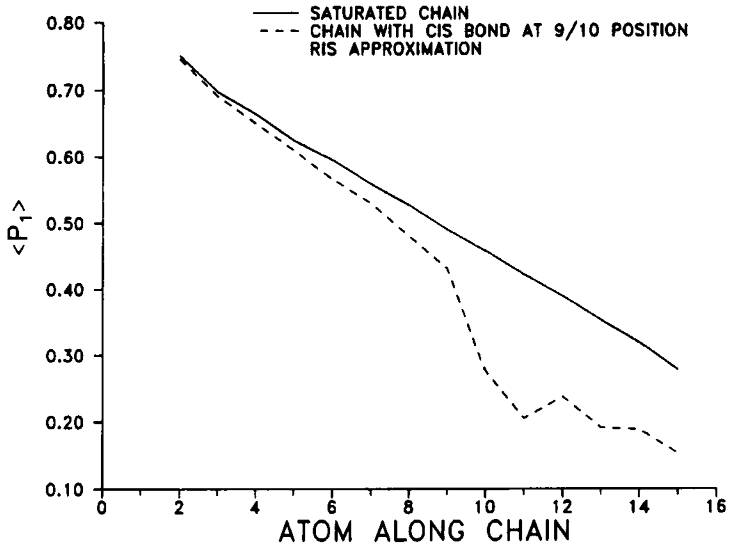

FIGURE 6 The profile of the order parameter $\langle P_1 \rangle = \langle \cos\beta \rangle$ for the chord vector (see text) simulated with the RIS approximation using an orienting potential ($\varepsilon = 0.12$) for the saturated polymethylene chain and a chain containing a *cis* unsaturated bond at the 9/10 position.

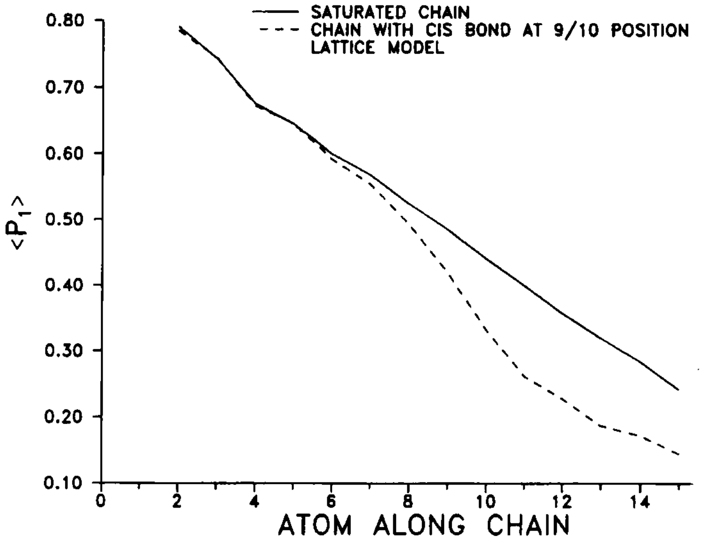

FIGURE 7 The profile of the order parameter $\langle P_1 \rangle = \langle \cos\beta \rangle$ for the chord vector (see text) simulated with the Lattice model using an orienting potential ($\varepsilon = 0.125$) for the saturated polymethylene chain and a chain containing a *cis* unsaturated bond at the 9/10 position.

between 1 for a perfect alignment of the vector along the normal to the surface, $\beta = 0$, to 0.5 for a uniform distribution over the angular range between parallel and perpendicular alignments, $0 \leqslant \beta \leqslant \pi/2$. Values lower than 0.5 are only obtained if the vector can access larger orientations, where it points towards the surface rather than away from it, $\pi \geqslant \beta \geqslant \pi/2$. It can be clearly seen from Figures 6 and 7 for a chain in a mean field potential that the order parameter profile is larger than 0.5 only for atoms near the fixed end of the chain and decreases significantly below this value for atoms near the free end. A similar profile is observed for a chain confined in a cylinder. This shows that the chain undertakes a significant number of conformations containing loops. It is important to note here that loop formation is consistent with the P_2 mean field potential, which is symmetric about $\beta = \pi/2$. The formation of loops is furthermore reflected in the broad distribution in the position of the last atom of the chain above the impenetrable surface, Figure 8. It can be seen that the terminal atom has a significant probability of reaching the surface. We note that the differences in the maximal extension of the chain between the two models is due to the fact that the RIS chain contains two virtual atoms tethered to the interface, while the Lattice chain has only one.

We shall now address the question as to how far the introduction of a rigid *cis* double bond segment at the 9–10 position affects the conformational

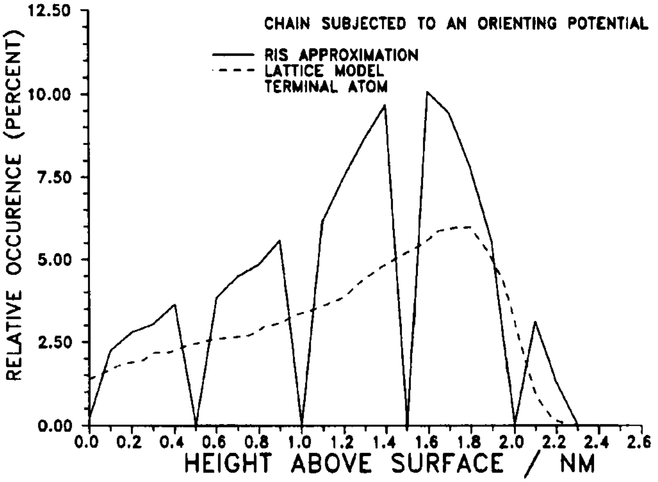

FIGURE 8 The distribution of the height above the impenetrable surface of the terminal atom of a saturated chain obtained from simulations using a P_2 orienting potential with the RIS approximation ($\varepsilon = 0.12$) and Lattice model ($\varepsilon = 0.125$).

behaviour of the chain. The same strengths of the orienting potential and radii of the cylinders were used as for the simulations of the saturated chains. The order parameter profiles of the C—D vectors for a chain in a mean field potential obtained from the RIS and Lattice models are shown in Figures 9 and 10 respectively. Similar profiles are found for chains confined

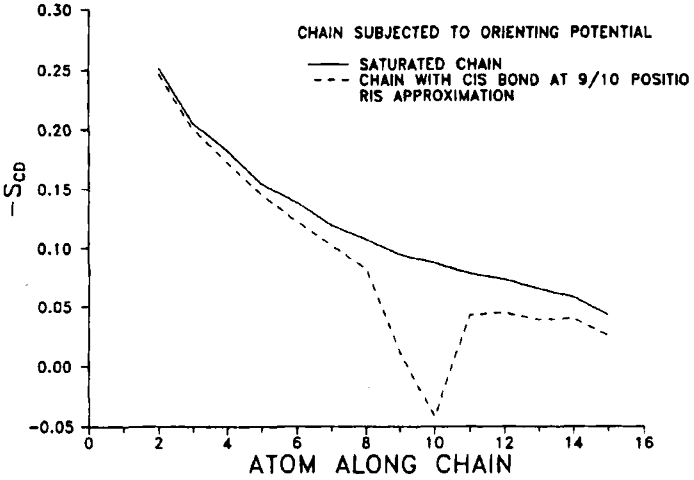

FIGURE 9 The order parameter profile of the C—D bonds for a saturated chain and a chain containing a *cis* unsaturated bond at the 9/10 position simulated with the RIS approximation using the same P_2 orienting potential, $\varepsilon = 0.12$.

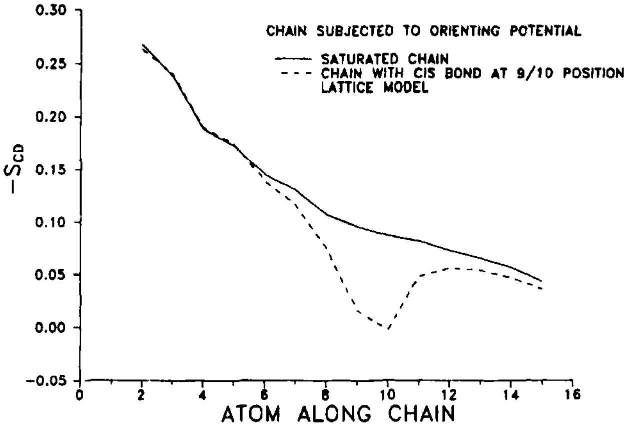

FIGURE 10 The order parameter profile of the C—D bonds for a saturated chain and a chain containing a *cis* unsaturated bond at the 9/10 position simulated with the Lattice model using the same P_2 orienting potential, $\varepsilon = 0.125$.

in a cylinder. Again both models reproduce the experimental observation [19, 20] of a minimum for atom 10 for the *cis* chain. The models indicate a general reduction in the value of the order parameters for the *cis* unsaturated chains. This difference is also found in a more accentuated way in the profile of $\langle P_1 \rangle$ of the chord vectors along the length of the chain, Figures 6 and 7. Both models show that the *cis* unsaturated chain undertakes substantially more conformations containing loops than the saturated chain. The simulations thus indicate that the introduction of a rigid unsaturated segment containing a *cis* double bond causes the chain to become disordered, in agreement with experimental observations [19].

Finally, we have studied the effect on the conformational behaviour of chains labelled with a model spin-label at the 5 and 12 positions. Interestingly, the RIS model reveals that the introduction of the bulky pentagon into the chain structure induces a general increase in the order parameter profile on the C—D bonds, Figure 11, in a chain subjected to the same orienting potential as above. The effect is largest in the segments of the chain closed to the labelled atom and is more significant for labelling at the 5 position than the 12 position. The Lattice model, Figure 12, also yields the same increase in the order parameters for atoms close to the label position, though it predicts a small reduction in the values of the order parameters elsewhere. The same effects are found for the labelled chains confined within a cylinder. Interestingly, the finding of an increase in the order parameter

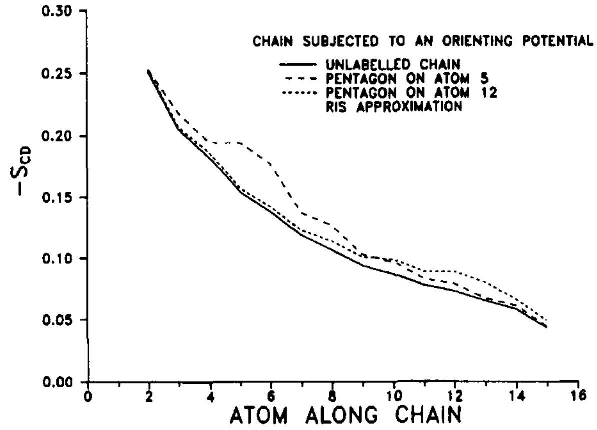

FIGURE 11 The order parameter profile of the C—D bonds for a saturated chain, a chain labelled at the 5 position and the 12 position with a pentagon and a chain labelled at the 12 position with a pentagon simulated with the RIS approximation using the same P_2 orienting potential, $\varepsilon = 0.12$.

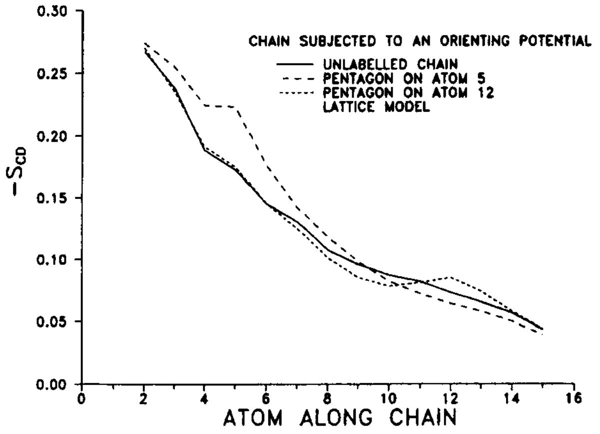

FIGURE 12 The order parameter profile of the C—D bonds for a saturated chain, a chain labelled at the 5 position and the 12 position with a pentagon and a chain labelled at the 12 position with a pentagon simulated with the Lattice model using the same P_2 orienting potential, $\varepsilon = 0.125$.

relative to the unlabelled chain are at odds with the results of ESR experiments [4, 13]. The ESR experiments show that while the order parameter of fatty acid chains labelled at the 5 position is high, chains labelled at the 12 position exhibit a virtually isotropic orientational distribution.

The discrepancy between the order parameter profile of the C—D bonds obtained from ^{2}H-NMR experiments and that found using fatty acid spin-labels has been the subject of intense discussions over the past 20 years [3]. It has been cogently argued that the introduction of a spin-label modifies the conformational behaviour of the hydrocarbon chain to such an extent that it no longer reflects the behaviour of unlabelled chains [12]. On the other hand, recent Lattice Dynamics simulations of lipid bilayers containing fatty acid chains [13], have suggested that the discrepancy arises not from an intrinsic modification of the chain behaviour due to excluded volume effects, but rather to the hydrophilic character of the nitride group that attracts the label towards the aqueous interface. The simulations presented here provide strong evidence refuting the view that spin-labelled chains exhibit a different conformational behaviour than unlabelled chains. They indicate rather, in agreement with the Lattice Dynamics simulations, that labelled chains undertake essentially the same conformations as unlabelled ones. They suggest that the reduction in the orientational order observed in ESR experiments are due to effects arising from the detailed interaction of the nitroxide spin label with its surroundings in the bilayer structure.

CONCLUSIONS

We have here shown that the both the RIS description of the conformational behaviour of hydrocarbon chains and their Knight's Gambit Lattice representation provide the same picture of the orientational order of chains tethered to an impenetrable interface. The experimental order parameter profile can be reproduced by subjecting the chains to a mean field potential and by confining them within a cylinder with rigid walls. The chains show a propensity to undertake conformations containing loops and the formation of loops is enhanced by the introduction of a *cis* double bond in the middle of the chain. Interestingly, we have found that labelling chain atoms with a bulky pentagon corresponding to a nitroxide group, the order parameters of the C—D bonds to increase, particularly for those atoms close to the label. This finding indicates that the low orientational order reported by fatty acids labelled at the 12 positions, cannot be attributed to intrinsic changes in the conformational behaviour of the chains.

Acknowledgments

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