MELTING ENTROPY AND STRUCTURE OF ALIPHATIC CHAINS IN MONO AND BILAYERS

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Received 21 September 1973

1. Introduction

We have recently calculated [1, 2] some structural properties of aliphatic chains mono or bilayer. These calculations were based on the existence of rotation isomers and of interactions between chains (WIRI model). The properties studied were the melting entropy of satured chains, the thickness and birefringence of the layer, and the order parameter of spin labels fixed on the chains.

We report here the results of calculations made with longer chains, with 14 to 22 carbon atoms. There are the lengths of chain which usually exist in phospholipids of biological membranes. We have been able to calculate the mean structural properties of a hexane layer by determining at first the statistical weights of all the conformations of the two chains [2]. This calculation becomes impossible when the chains have more than 12 carbon atoms. The number of conformations is then too large (more than 10^6 conformations for a single chain containing 16 carbon atoms). For long chains, a statistical method of conformational analysis is to be used [3]. This was done previously by Whittington and Chapman [4], using a two dimensional model cruder than ours. The statistical method we have used is due to Metropolis et al. [5]. It was applied for the first time to the conformational analysis of polymers by Verdier and Stockmayer [6]. Following this method, the set of accepted conformations is assimilated to the space of the states of a Markovian chain. The passage from one state to another is effected by modifying the local conformations of a few bonds in the chain [7]. These deformations are effected at random, but taking into account the intra and intercatenary interactions, and steric hindrance (overlaping of the atoms with the wall of the hexagonal cell which encloses the two chains) [2]. (See fig. 1). For any molecular property G and for any sample of size M thus obtained, we have:

$$G = \lim_{M\to\infty} \frac{1}{M} \sum_{t=1}^{M} G(\mu_t)$$

$<G>$ is the mean of G and μ_t is the t^{th} conformation of the sample. When M is sufficiently large,

$$\frac{1}{M} \sum_{t=1}^{M} G(\mu_t)$$

provides a good estimation of $< G >$. The precision obviously depends on M.

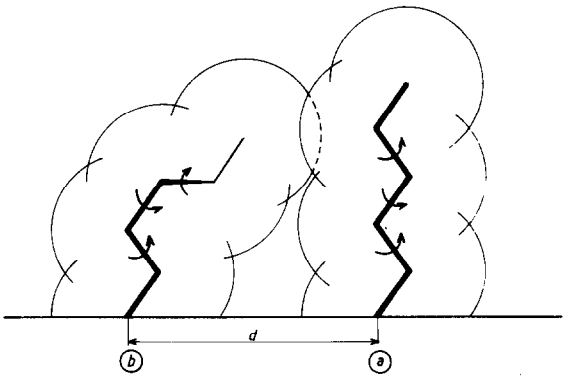

Fig. 1. Distance d between the two chains a and b (WIRI model) see ref. [2].

2. Results and discussion

Philips et al. [8] have studied the melting of saturated chains of synthetic phospholipids with a differential scanning calorimeter. They thus determined the melting entropy of these chains in function of their number of carbon atoms, and in two different states of hydration (see fig. 2). This melting entropy, ΔS_m, is equal to the difference in conformational entropy of the chains in the crystallized state and in the fluid phase, which is a liquid crystal:

$$\Delta S_{melting} = S_{liquid\ crystal} - S_{crystal}$$

In the crystalline phase, all the chains have the completely stretched conformation. Their conformational entropy is thus zero, ($S_{crystal} = 0$). On the other hand, in liquid crystal, gauche conformations are possible; greater is the distance $d_{l.c.}$ between the chains [2], the more numerous are these conformations (see fig. 1). We can calculate the conformational entropy in function of d, with the help of the WIRI model, and thus the melting entropy:

$$\Delta S_{melting} = S(d_{l.c.})$$

We have calculated the conformational entropy of chain layers versus d for n = 14 to 22 carbon atoms. Fig. 3 shows for palmitic chains (n = 16) the variation of conformational entropy S. The evolution of S in function of d is analogous to that previously obtained, with hexane chains [2]. This entropy vanishes when d is less than 4.8 Å. This distance is that of the chains, in the crystallized state [9, 10]. It also corresponds in our calculations to the minimal intra and intermolecular interaction energy. As soon as the chains are slightly displaced from their equilibrium position in the crystal, numerous gauche conformations become possible, and the entropy S increases rapidly. The existence of flat points on the curve is due i) to the quantification of the rotation around the carbon–carbon bonds, ii) to the interaction of the two chains with the hexagonal cell which simulated the presence of other molecules [2] (see fig. 1).

We have shown in fig. 2 the theoretical values of $S(d)$ and thus of $\Delta S_{melting}$ for chains with 14 to 22 carbon atoms.

Comparison with the experimental values of Phillips et al. [8] shows that i) the calculated melting entropy varies linearly in function of n, as the experimental entropy, ii) that it is possible to obtain agreement between the experimental and calculated values. The distance between the chains would be $d_{l.c.}$ = 4.9–5.0 Å after melting, when the phospholipids are

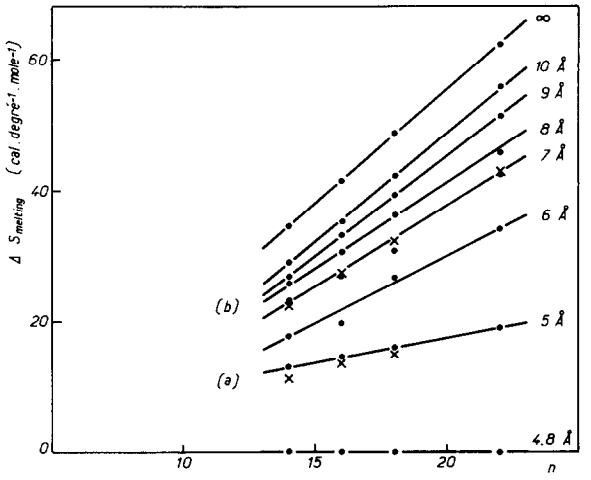

Fig. 2. Theoretical melting entropy (•) of aliphatic chains in terms of the number n of carbon atoms (n = 14, 16, 18, 22), and of the distance $d_{l.c.}$ in the fluid phase. The experimental results (X) are those of ref. [10] (a = monohydrate; b, maximum hydration).

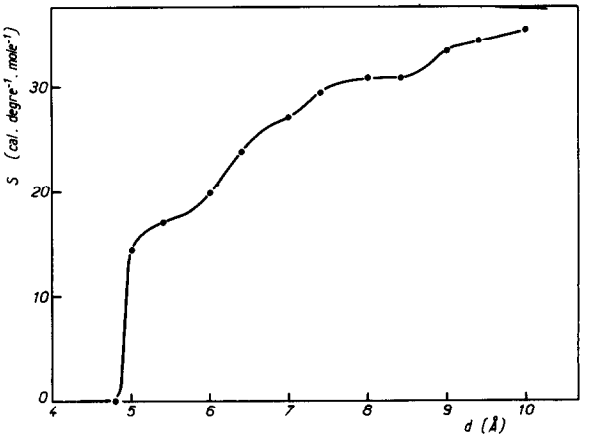

Fig. 3. Conformational molar entropy of a palmitic chain monolayer (16 carbon atoms). The maximum value of S is obtained when interchain distance in infinite (WIRI model is then identical to RI one: see ref. [2] and [11]).

monohydrated (case a), or approximately 7 Å when the layer is hydrated to a maximum (case b). In the first case (a) melting would appear to be accompanied by a very slight increase in the interchain distance ($d_{c.}$ = 4.8 Å in the crystal). This very slight enhancement may be explained by the simple increase in the thermic agitation of the molecules around melting temperature. On the other hand, in the second case (b) the distance would appear to increase considerably (4.8–7 Å). The disorder caused by the important hydration of the polar heads could be the cause for this much more greater distance after melting. One must note, moreover, that this distance of 7 Å corresponds to the maximum distance between chains, when the two ester functions of the phospholipid are in stretched conformation. One must not, however, attach too much importance to the theoretical value of $d_{l.c.}$ for two reasons: i) the interaction between the two chains of a phospholipid molecule and the neighbouring molecules is represented by a hexagonal box. This cage, which is too stiff, reduces the number of gauche conformations possible for a given distance d; ii) the two chains are assumed to be in the same plane when all stretched (see fig. 1). Until now, there is no experiment which allows determination of the true orientation of the two chains. These two remarks lead to the conclusion that the distances $d_{l.c.}$ found may be slightly higher than the true distances.

Theory also makes possible to foresee a reduction in the thickness of the bimolecular layer after melting [2]. We have calculated this decrease of the thickness, $\Delta e = -6$ Å, in the case of palmitic chains (n = 16). In a first approximation, we have neglected the interactions between the two monomolecular layers on the bilayer. Experiments on the membranes of *Mycoplasma laidlawii* [10] have shown a decrease of the membrane thickness after the melting of the chains. These membranes were greatly enriched with dipalmitoyl lecithin. The reduction observed by X-ray diffraction is $\Delta e = -8$ Å. The agreement between the theoretical and experimental values of Δe is thus satisfactory.

3. Conclusion

We have been able to calculate theoretically two very different structural properties of aliphatic bimolecular layers: the melting entropy of saturated chains and the variation in thickness of the bilayer during melting. The agreement with the experiment is very satisfactory, although the model used is very crude. We nonetheless take into account two fundamental structural properties of these chains: their intra- and intermolecular interactions. That is certainly the reason for this agreement with the experiment.

We shall demonstrate in a further article that it is also possible to study theoretically other structural properties of aliphatic layers, such as the pressure of monomolecular film.

References

[1] Belle, J. and Bothorel, P. (1972) Compt. Rendue 275, 355.
[2] Bothorel, P., Belle, J. and Lemaire, B., Chem. Phys. Lipids. 000.
[3] Lemaire, B. and Fourche, G. (1971) Compt. Rendue 272, 1071; J. Polymer Sci. (in press).
[4] Whittington, S.G. and Chapman, D. (1966) Trans. Faraday Soc. 62, 3319.
[5] Metropolis, N., Rosenbluth, A.W., Rosenbluth, M.N., Teller, A.H. and Teller, E. (1953) J. Chem. Phys., 21, 1087.
[6] Verdier, P.H. and Stockmayer, W.H. (1962) J. Chem. Phys., 36, 227.
[7] Monnerie, L. and Geny, F. (1969) J. Chem. Phys. 66, 1691.
[8] Phillips, M.C., Williams, R.M. and Chapman, D. (1969) Chem. Phys. Lipids 3, 234.
[9] Luzzati, V. (1968) in: Biological membranes (Chapman, D. ed.) p. 104, Academic Press, London, New York.
[10] Engelman, D.M. (1971) J. Mol. Biol. 58, 153.
[11] Bothorel, P. Lussan, C., Lemaire, B. and Belle, J. (1972) Compt. Rendue 274, 1541.