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Association probabilities between the single-chain amphiphiles into a binary mixture in plan monolayers (II)

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A test system of homologous binary mixtures of single-chain amphiphiles was considered. The dependence of the association probabilities on the hydrophobic chain length, and on the dipole moment of the shorter chain component when the longer chain component has a low dipole moment, was studied. The free-end effect of each hydrophobic chain on the association probability was also analysed. Generally, both the shorter chain end effect and the longer chain end effect on the association process are independent of their own initial chain length, but are dependent on the chain length of the other component and dipole moment. The changes in every association probability produced by the addition of one methylene group to the shorter chain and to the longer chain are unequal and opposite. For this reason the efficiency ratios were defined and analysed. The thermotropic behaviour of lipid mixtures can be related to association processes.

Introduction

It is well known that phospholipids have been assigned essentially a structural role in biological membrane with modulating effect on their functions. The cell membranes contain more than one type of phospholipid as well as lysophospholipid [1], so it is possible that the multicomponent composition of the lipid matrix explains the structural and functional properties of plasma membranes [2]. This is the reason for which many experimental studies on monolayers and bilayers achieved from binary mixtures have been undertaken. The structure of monolayers formed by mixing two different fatty acid salts was investigated by an X-ray method [3]. It was found that binary mixture compounds may be in a single completely mixed phase or in two separate coexisting phases, depending on the chain length, headgroup and mixing ratio of the two components [4].

The formation of microclusters, separated by microinterfaces was observed in some experimental studies on binary mixtures of synthetic lipids [5]. These experimental results may be explained by the existence of a selective association process between the mixture components. A quantitative analysis of the association process has been provided by the calculation of association probabilities [6].

Polar lipid molecules have an interesting structural property: the hydrophobic and hydrophilic region are completely separated. This property determines the organization of amphiphiles, dissolved in polar solvent, into supermolecular aggregates [7,8] having an internal order like liquid crystals [9,10].

Lysophospholipids have been implicated in a variety of physiological processes [11]. A mixture of single-chain amphiphiles can form a bilayer type of organization even though the individual components form micelles in an aqueous phase. Therefore, it is of great interest to study the properties of the mixtures of single-chain amphiphiles and, in this respect, the association probabilities would be worth much more attention.

Materials and Methods

In this work, a binary mixture of single-chain amphiphiles was characterized by the physical properties of its components (the hydrophobic chain length, N, the cross-section area, a, and dipole moment p of the polar headgroup) and the mole fraction x of one of the two mixed components. The chain length was given by the number of carbon atoms contained therein. In this paper the notations referring to the shorter chain component were identified by the index '1'. The index '2' was used to mark the longer chain component from the binary mixture. Two neighbouring amphiphiles interact through van der Waals dispersion forces between their

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hydrophobic chains and through electric forces between the dipole moments of their polar groups. The polar groups are neutral from the electric point of view and their dipoles are parallel to the aggregate surface, which is true for the single chain amphiphiles. In a binary mixture it is possible to find pairs of two shorter chain molecules, or of two longer chain molecules, or of different chain molecules.

The interaction energies for formation of these pairs are different from one another. This is the reason for which the selective association in a binary mixture is possible and the association probabilities were defined.

In a mixture formed by two different components mixed in molar fractions x_1, x_2 ($x_1 + x_2 = 1$), the probabilities for the formation of the three possible pairs were calculated from the following relations [6]:

$$P_{11} = x_1^2 e_1 / \left(x_1^2 e_1 + x_2^2 e_2 + x_1 x_2 \right) \tag{1}$$

$$P_{12} = x_1 x_2 / \left(x_1^2 e_1 + x_2^2 e_2 + x_1 x_2 \right) \tag{2}$$

$$P_{22} = x_2^2 e_2 / \left(x_1^2 e_1 + x_2^2 e_2 + x_1 x_2 \right) \tag{3}$$

with the following notations:

$$e_1 = \exp(-(U_{12} - U_{11})/RT);$$

$$e_2 = \exp(-(U_{12} - U_{22})/RT) \tag{4}$$

$$U_{11} = -\left(p_1^2 N_A / \left(4\pi\epsilon (2r_1)^3 \right) + W_{11} \right) \tag{5}$$

$$U_{12} = -\left(p_1 p_2 N_A / \left(4\pi\epsilon (r_1 + r_2)^3 \right) + W_{12} \right) \tag{6}$$

$$U_{22} = -\left(p_2^2 N_A / \left(4\pi\epsilon (2r_2)^3 \right) + W_{22} \right) \tag{7}$$

where p_1 and p_2 are the electric dipole moments, r_1 and r_2 are the hexagon apothems whose surface areas are equal to the head-groups' cross-section areas. N_A is Avogadro's number, R the universal gas constant and T the absolute temperature. U_{11}, U_{12} and U_{22} are the molar energies of interaction between two neighbouring molecules of the same type (U_{11}, U_{22}) or of a different type (U_{12}). The first term of Eqns. 5–7 is associated with dipole–dipole interaction and the second to van der Waals dispersion interaction between hydrophobic chains of a molecule pair.

It was considered that the lipid monolayer is in the gel phase. In other words, the lipid molecules are quite close, so that all C-C bonds in the hydrophobic tails are in the *trans* conformation and the dipoles of two interacting molecules are antiparallel. In the saturated hydrophobic chain the electronic charge is organized in independent subdistributions of atomic dimensions, localized in atoms and bonds. Also, the electron correlation is negligible between distant points of the hydrophobic chain. For these reasons, it is not wrong to accept the assumption of locally additive forces within the limits of second order perturbation theory, so the attraction energy between two neighbouring hydrophobic chains may be obtained by adding all the attraction energies between pairs of attractive centers, one in each chain. At the same time, the distance between the nearest attractive centers is about 7.14 Å (equal to the distance between the axes of two neighbouring molecules with short chains) which is large in comparison with the sizes of the attractive units (atoms, bonds). Therefore, the interaction between two attractive centers in the two hydrophobic chains verifies London's inverse-sixth power distance law ($W = -A/d^6$), where A is equal to $5.6 \cdot 10^3$ Å^6 J kmol^{-1} [12]. The constant A was calculated so that the attractive centers would be found in the middle of C-C bonds, such that one attractive center is equivalent to a methylene group. On the other hand, the distance between the most spaced out attractive centers is shorter than 1000 Å, so that the retardation effects are not taken into account [13]. In the case of saturated paraffin chains, it seems that the assumption of locally additive dispersion forces is good enough [14]. In addition, in our relations with association probabilities, the difference in the interaction energies appears, which causes us to think that non-additivity of the dispersion forces does not modify the results or conclusions of this paper.

As stated above, a binary mixture of single chain amphiphiles is characterized by the values of the following parameters p_1, N_1, a_1, x_1, p_2, N_2, a_2. The test system was composed by 36 binary mixtures. For all selected binary mixtures four of the parameters mentioned above were taken to be constants $a_1 = 40$ Å^2, $p_2 = 5$ D, $a_2 = 60$ Å^2, $x_1 = x_2 = 0.5$. The chains of the mixture components contain an even number of carbon atoms N_1 ($8 \leq N_1 \leq 22$) and N_2 ($10 \leq N_2 \leq 24$). These binary mixtures can be arranged into a matrix in which on the horizontal line there are the homologous mixtures with respect to the longer chain component (the first component is common for the entire homologous set) and on the vertical column there are the homologous mixtures with respect to the shorter chain component (the longer chain is the same). Therefore, if the matrix elements contain two component chain lengths ($N_1 : N_2$), then on the horizontal lines are the binary mixtures with $8 \leq N_1 \leq 22$ and $N_1 + 2 \leq N_2 \leq 24$ and on the vertical columns are the binary mixtures with $10 \leq N_2 \leq 24$ and $8 \leq N_1 \leq N_2 - 2$. Several homologous mixtures were selected from the test system in order to point out the properties of amphiphile binary mixtures.

The shorter chain dipole moment effect on the association probabilities

The association probabilities were calculated for the test system when the low dipole moment was attached to the headgroup of the longer chain component ($p_2 = 5$ D). The dipole moment embedded on the shorter chain component headgroup took the following values: $p_1 = 5, 10, \ldots 45$ D. Unless otherwise stated the dipole moment p_2 is equal to 5 D. In Figs. 1 and 3 we can easily see that the direct association probability P_{11}, decreases (Fig. 1) and P_{22} increases (Fig. 3) when the shorter chain component dipole moment increases, irrespective of the chain lengths of the two components.

For about all binary mixtures, the cross-association probability increases with increasing dipole moment p_1 (Fig. 2), excepting the mixtures formed by two long single chain amphiphiles: 20:24; 22:24.

Every curve is like an increasing sigmoid with different inclinations with respect to the horizontal axis. We remind the reader that in the symmetrical case when the shorter chain component has a low dipole moment ($p_1 = 5$ D), the association probabilities P_{11} and P_{12} increase and P_{22} decreases with an increasing dipole moment p_2 for every mixture of the test system [6]. The results can be summarized as follows:

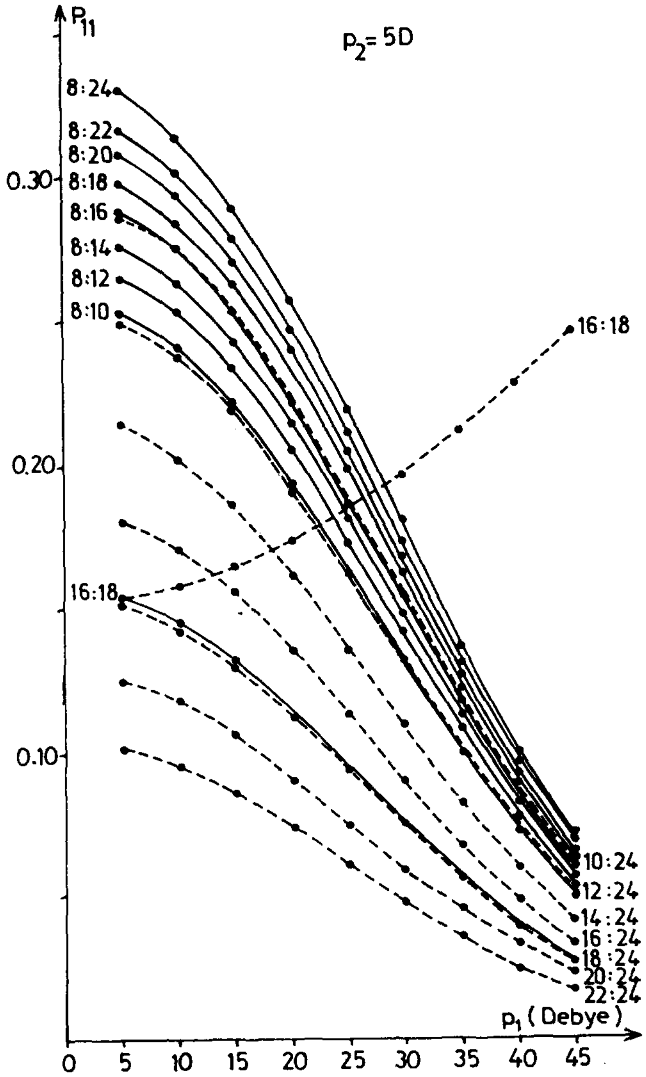

Fig. 1. The variation of self-association probability of two short hydrophobic chain molecules, P_{11}, as a function of the electric dipole moment of the first component for two series of homologous binary mixtures.

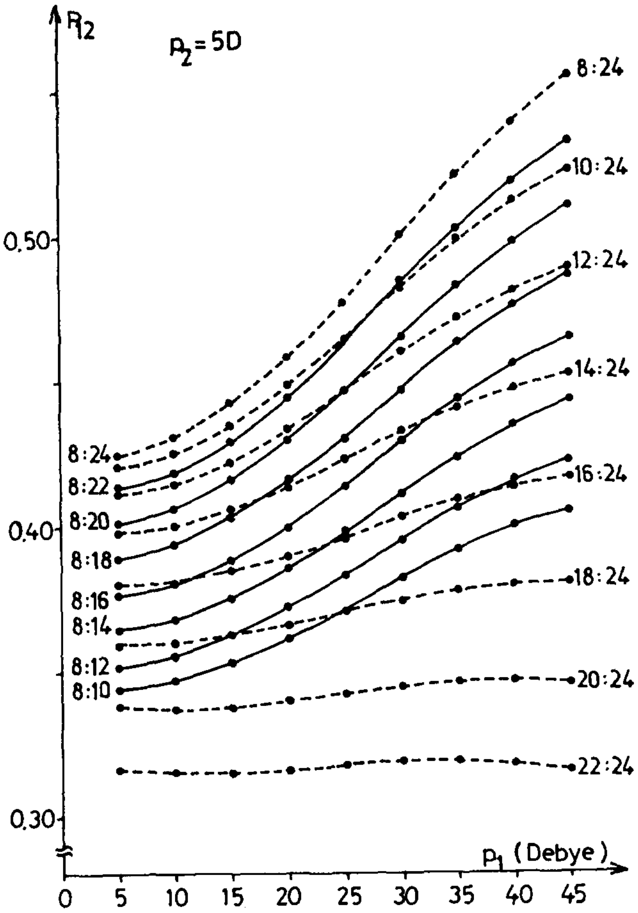

Fig. 2. The variation of cross-association probability P_{12}, against the electric dipole moment of the first component for two series of homologous binary mixtures.

$p_1 = 5$ D and p_2 increases $\Rightarrow P_{11}$ increases,

P_{12} increases, P_{22} decreases

$p_2 = 5$ D and p_1 increases $\Rightarrow P_{11}$ decreases,

P_{12} decreases, P_{22} increases

for almost all binary mixtures analysed here, except for those specified in the case of P_{12}.

Therefore, the dipole moment interchange between binary mixture components has an opposite effect on the direct association probabilities P_{11} and P_{22} with respect to their monotonic properties. More generally, we can also say that the increase in the dipole moment of one component inhibits direct association but stimulates the direct association of the other component which has a small dipole moment. For any given binary mixture, the curves corresponding to each association probability in the two cases ($p_1 = 5$ D, p_2 is variable; $p_2 = 5$ D and p_1 is variable) starts from the same point $p_1 = p_2 = 5$ D (see Figs. 1, 3). Therefore, for every binary mixture, we can write the following inequalities for P_{11} and P_{22} as functions of p_1 and p_2:

$$P_{11}\,(p_1)_{p_2=5} \leq P_{11}\,(p_2)_{p_1=5} \quad \text{and}$$

$$P_{22}\,(p_1)_{p_2=5} \geq P_{22}\,(p_2)_{p_1=5}$$

In order to demonstrate this statement, we have drawn the association probability P_{11} (Fig. 1) and P_{22} (Fig. 3) versus p_2 when $p_1 = 5$ D (the dotted curves) for the binary mixture 16:18. It was found that the association probabilities as a function of p_1 are fitted very well by a three-degree polinomial function for each binary mixture for the case when $p_2 = 5$ D. The particular points coordinates of fitting curves appear in Table I. An oscillating feature of each association probability must be mentioned. It is interesting that all three association probabilities have their extremum values and inflexion point for about constant values of dipole moment p_1, which are not modified too much by the increase of acyl chain length. For instance, all association probabilities show their inflexion point for about $p_1 = 30$ D. The first derivative of the association probabilities may be understood as a reaction speed (sensibility) of the binary system to the change of dipole moment produced on each association. In this effect, both the direct association of longer chain molecules and cross association are very sensitive, while the direct association of shorter chain molecules is less sensitive to the change of dipole moment p_1 around 30 D. The changes of dipole moment p_1 around values for which the association probabilities take their extremum values are not perceptible by the binary system.

The chain length's effect on association probabilities

In order to see the chain-length effect of every component on the association probabilities, two series of homologous binary mixtures were considered with respect to each component. The common component of all binary mixtures belonging to a series has its chain length equal to $N_1 = 8$ carbon atoms ($N_2 = 10; 12; \ldots; 24$) and of the other series one has its chain length equal to $N_2 = 24$ carbon atoms ($N_1 = 8; 10; \ldots; 22$). The association probabilities calculated in this case as functions of dipole moment p_1 ($p_2 = 5$ D) are depicted in Figs. 1–3, for all these binary mixtures. Analysing the order of the curves for P_{11}, P_{12}, P_{22} corresponding to the binary mixtures from each of the two series, we can conclude that:

$N_1 =$ ct. and N_2 increases $\Rightarrow P_{11}$ increases;

P_{12} increases; P_{22} decreases

$N_2 =$ ct. and N_1 increases $\Rightarrow P_{11}$ decreases;

P_{12} decreases; P_{22} increases.

This conclusion also applies when $p_1 = 5$ D and p_2 is variable, so the interchange of dipole moments between the two components of a binary mixture does not change the hydrophobic chain-length's effect on the association probabilities.

In Figs. 4–6 the association probabilities are presented with respect to the chain length of one component when the hydrophobic chain of the other compo-

TABLE I

The particular points' coordinates of three degree polinomial functions fitting the association probabilities, for some suggesting binary mixtures AMP = $(P_{\max} - P_{\min})/2$.

	$N_1 : N_2$	$p_{1\max}$	$P_{\max}$	$p_{1\min}$	$P_{\min}$	$p_{1\inf}$	$P_{\inf}$	AMP
P_{11}	8:10	2.22	0.2544	54.40	0.0308	28.30	0.1426	0.1118
	8:18	2.37	0.2986	55.75	0.0342	29.24	0.1663	0.1322
	8:24	3.00	0.3257	56.80	0.0350	29.90	0.1804	0.1453
	16:24	1.68	0.1832	52.88	0.0233	27.28	0.1033	0.0800
	20:24	1.05	0.1271	51.82	0.0717	26.43	0.0717	0.0554
P_{12}	8:10	49.50	0.4075	5.04	0.3449	27.28	0.3762	0.0313
	8:18	52.02	0.4935	4.53	0.3897	28.28	0.4416	0.0519
	8:24	53.76	0.5659	4.32	0.4252	29.04	0.4955	0.0704
	16:24	50.58	0.4203	5.20	0.3809	27.89	0.4006	0.0197
	20:24	41.03	0.3468	9.97	0.3374	25.50	0.3422	0.0004
P_{22}	8:10	56.05	0.5606	0.75	0.3998	28.40	0.4802	0.0805
	8:18	61.56	0.4809	0.43	0.3108	30.98	0.3958	0.0850
	8:24	61.71	0.4037	1.07	0.2482	31.39	0.3759	0.0777
	16:24	57.63	0.5655	−1.43	0.4332	28.10	0.4994	0.662
	20:24	56.76	0.6643	−2.78	0.53.14	27.00	0.5873	0.0560

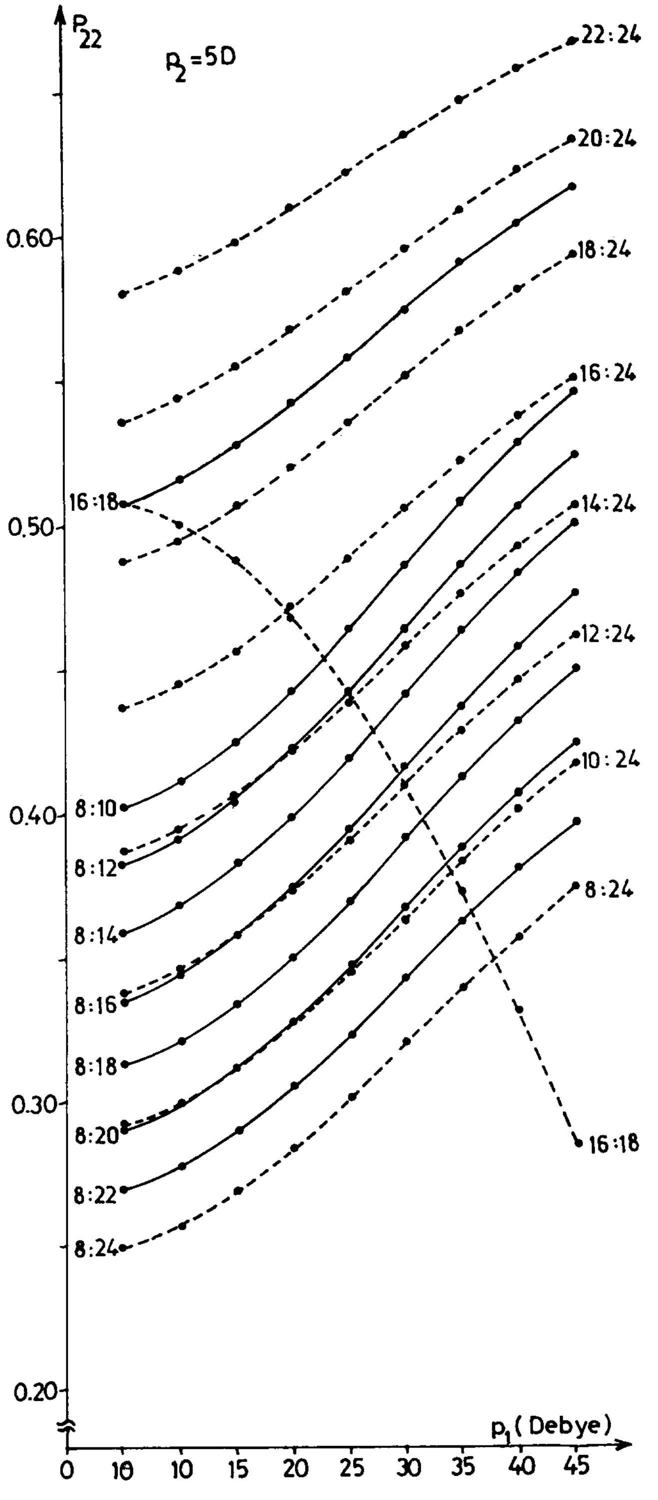

Fig. 3. The variation of self-association probability of two long hydrophobic chain molecules, P_{22}, as a function of the electric dipole moment of the first component. In Figs. 1–3, at the end of each curve the mixture compounds for which it was drawn are indicated. The second component has low dipole moment ($p_2 = 5$ D). Also $x_1 = x_2 = 0.5$.

nent remains unchanged. From these figures one can see more about the association dependence on chain length.

These plots represent a better confirmation of the monotonic properties of the association probabilities with respect to chain lengths of the binary mixture components. In this effect, we can say that all association probabilities depend linearly (or about linearly) on the acyl chain length of each component, excepting the cross association P_{12} dependence on the shorter chain length when $p_1 = p_2 = 5$ D and $N_2 = 24$ (* curve on Fig. 5). On the other hand, the slope of such graphic representations is equal to the contribution to the association probabilities of one methylene group adding to the short or long chain. In Table II, the slopes of all the plots are given from Figs. 4–6, except one, fitted by a right line.

Owing to the fact that the end methyl group of the hydrophobic chain was substituted for a methylene group, we can consider that the change of the association probabilities produced by the increase of one

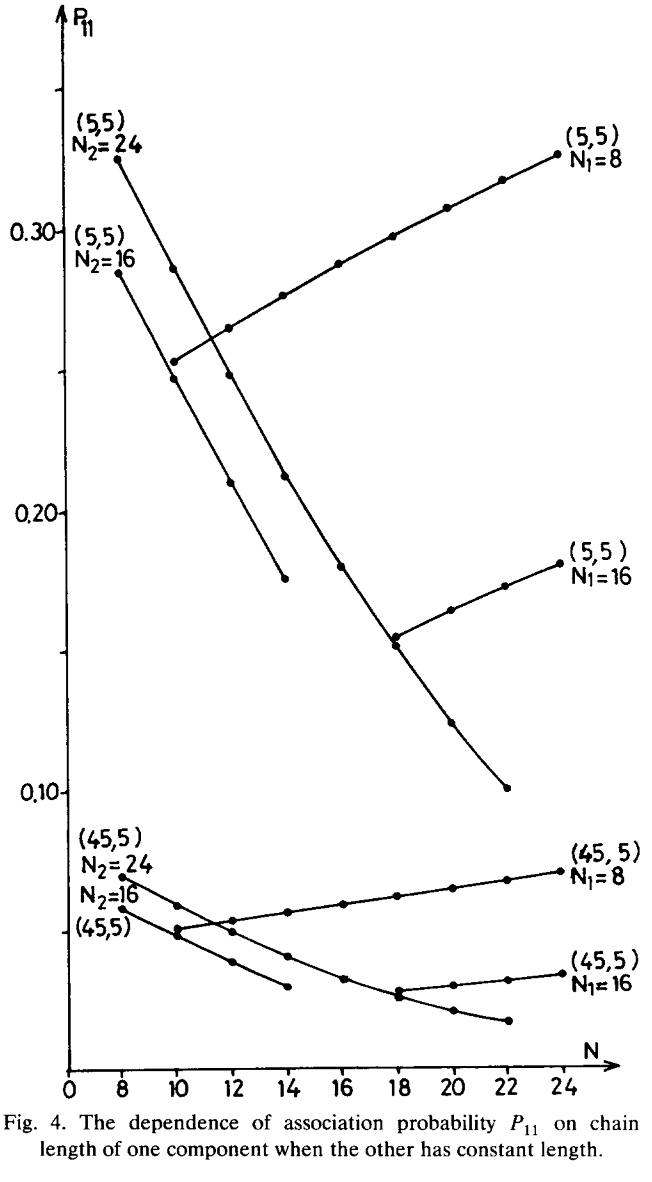

Fig. 4. The dependence of association probability P_{11} on chain length of one component when the other has constant length.

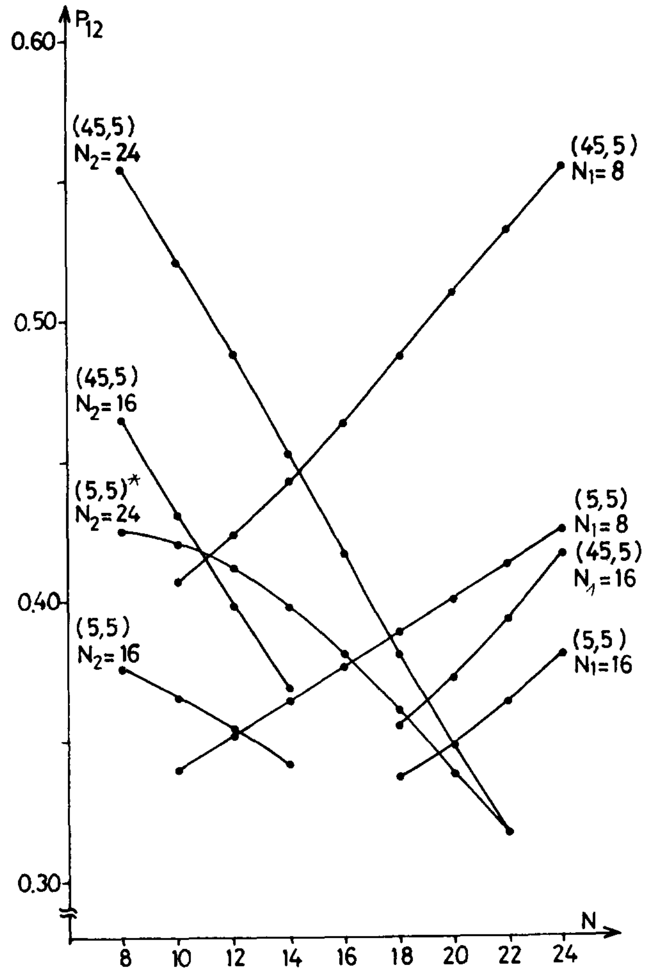

Fig. 5. The cross-association probability, P_{12}, against the chain length of one of the two components when the other chain is constant.

chain with a methylene group is a chain-end effect. Analysing Figs. 4–6 and the data given in Table II we can reach the following conclusions:

(i) From the linear dependence of the association probabilities on the longer chain length it can be concluded that the longer chain-end effect is independent of its initial length. This conclusion does not apply to the cross association probability P_{12} in the case of binary systems in which the first component has longer length (in our case $N_1 = 16$), when P_{12} is not a linear function of N_2. Also, the longer chain free-end effect is only slightly influenced by the shorter hydrophobic chain-length increase from 8 to 16 carbon atoms, irrespective of the dipole moments. For the same dipole moment values, the curves for these series of mixtures are parallel.

(ii) The shorter chain-end effect depends on its initial length in the case of the association probability P_{11} for all values of the dipole moment p_1 and only for low values of p_1 in the case of the cross association P_{12} (* curve on Fig. 5). Excepting the latter case, the shorter chain-end effect is independent of longer chain length, irrespective of dipole moment p_1.

(iii) The dipole moment p_1 increase influences on the end-effect methylene group contributions is as fol-

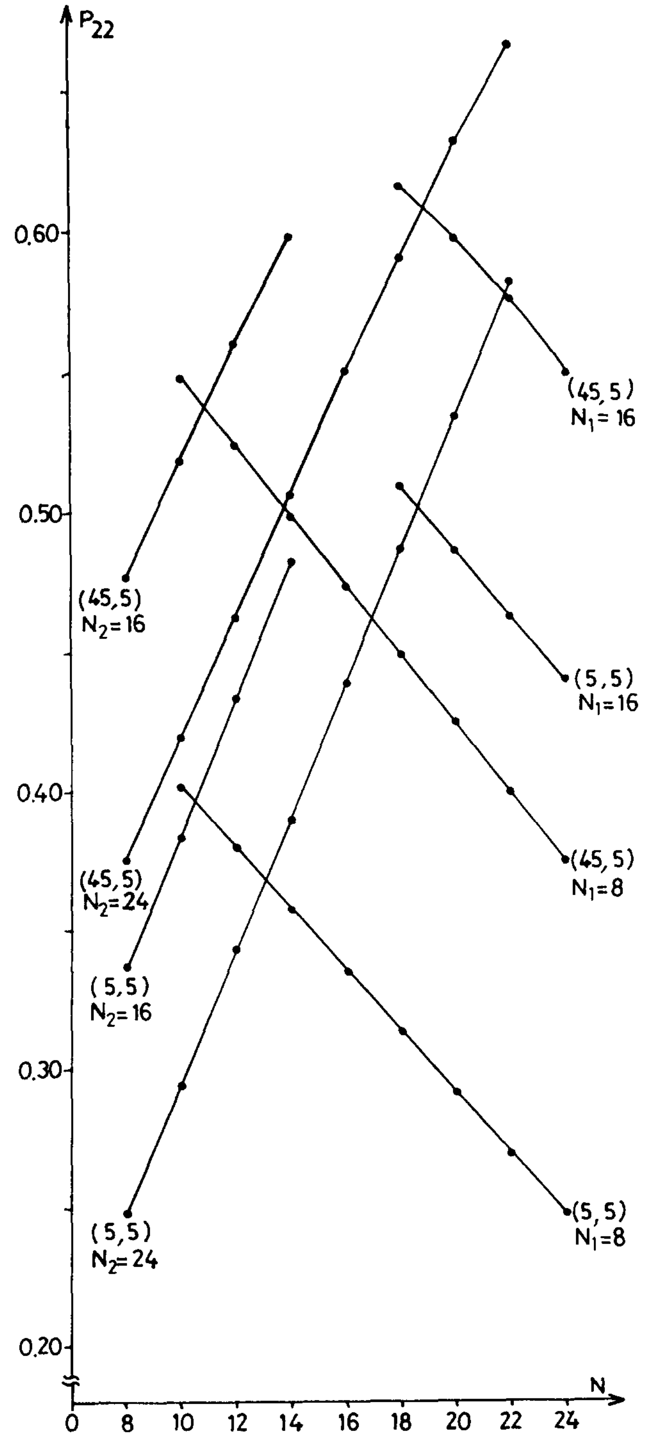

Fig. 6. The dependence of association probability, P_{22}, on the chain length of one of the two components when the other has constant length. In Figs. 4–6, at the end of each line is written the dipole moment (p_1, p_2) and the length of the hydrophobic chain which remained unmodified. On the horizontal axis, $N = N_1$ when N_2 is constant and inverse.

TABLE II

The slopes of the linear curves from Figs. 4–6

These slopes represents the longer chain free-end effect on the association probabilities

Constant length	P_{11}		P_{12}		P_{22}	
	$p_1 = 5$	$p_1 = 45$	$p_1 = 5$	$p_1 = 45$	$p_1 = 5$	$p_1 = 45$
$N_1 = 8$	1.0230	0.3018	1.1779	2.1588	−2.2017	−2.4755
$N_1 = 16$	0.9057	0.1995	1.4649	2.0261	−2.3059	−2.2335
$N_2 = 16$	−3.7271	−0.7689	−1.1926	−3.4457	4.9199	4.2256
$N_2 = 24$	−3.2062	−0.9224	*	−3.2131	4.8031	4.1355

* This case corresponds to the indicated curve in Fig. 5.

lows: it is decreased for P_{11} and P_{22} and increased for P_{12}. This is true for both the hydrophobic chains.

There is an exception to this rule: the longer chain end effect on the association probability P_{22} increases as the dipole moment p_1 increases when the first component has a small hydrophobic chain (here $N_1 = 8$).

The increase of the dipole moment p_1 influences much more the end effect in the case of the shorter chain component than in the case of the longer chain component, especially for P_{11} and P_{12}.

It is interesting to observe that, regarding P_{12}, the longer chain end effect dependence on its initial length is cancelled by the increase of the dipole moment p_1 from 5 D to 45 D (Fig. 5, * marked curve).

The dependence of the end effect on dipole moment p_1 together with its own initial length influence on it (when it exists) explains why the curves corresponding to every series of binary mixtures from Fig. 1 are convergent, those from Fig. 2 are divergent and those from Fig. 3 are parallel.

Efficiency ratios

Taking into account that the end effect, with respect to the two hydrophobic chains, on each association probability is opposed (see Table III), it is normal to introduce the methylene group efficiency ratio. This was defined in Ref. 6 as the ratio of the methylene group's number added to the shorter chain and those which must be added to the longer chain so that the association probability does not change. This is a mean efficiency ratio for entire homologous series.

There is an efficiency ratio for each association probability. On the other hand, as we have already mentioned, both the end effects owing to each of the two chains depend on at least one of the following parameters: the length of one chain, the length of the other chain and dipole moment p_1.

It can be concluded that it is more useful to define efficiency ratios for each binary mixture. For example, let us consider a binary mixture given by the hydrophobic chain lengths of its components (N_1, N_2) and the association probability P_{ij}. For the binary mixture (N_1

TABLE III

The efficiency ratios, calculated for two homologous series of binary mixtures

The dipole moment of the short-chain component takes two very different values; $p_1 = 5$ D and 45 D.

$N_1 : N_2$	$p_1 = p_2 = 5$ D			$p_1 = 45$ D; $p_2 = 5$ D		
	K_{11}	K_{12}	K_{22}	K_{11}	K_{12}	K_{22}
8:12	0.2533	1.5425	0.4582	0.2952	0.7612	0.6415
8:14	0.2641	1.1623	0.4503	0.3121	0.7045	0.6137
8:16	0.2747	0.9877	0.4475	0.3272	0.6719	0.5986
8:18	0.2852	0.8871	0.4478	0.3431	0.6517	0.5905
8:20	0.2961	0.8211	0.4501	0.3593	0.6385	0.5862
8:22	0.3074	0.7739	0.4537	0.3757	0.6296	0.5816
	$\frac{1}{4} \leq K_{11} \leq \frac{1}{3}$	$\frac{3}{4} \leq K_{12} \leq \frac{3}{2}$	$K_{22} \approx \frac{1}{2}$	$\frac{1}{4} \leq K_{11} \leq \frac{2}{5}$	$\frac{2}{3} \leq K_{12} \leq \frac{3}{4}$	$K_{22} \approx \frac{2}{3}$
8:22	0.3074	0.7739	0.4537	0.3757	0.6296	0.5816
10:22	0.3046	0.8467	0.4747	0.3432	0.6356	0.5768
12:22	0.2973	0.9073	0.4907	0.3095	0.6326	0.5681
14:22	0.2860	0.9487	0.4939	0.2785	0.6190	0.5512
16:22	0.2719	0.9624	0.4885	0.2837	0.5909	0.5248
18:22	0.2560	0.9370	0.4696	0.2207	0.5503	0.4661
	$\frac{1}{4} \leq K_{11} \leq \frac{1}{3}$	$\frac{3}{4} \leq K_{12} \leq 1$	$K_{22} \approx \frac{1}{2}$	$\frac{2}{5} \leq K_{11} \leq \frac{1}{5}$	$K_{12} \approx \frac{2}{3}$	$\frac{1}{2} \leq K_{22} \leq \frac{2}{3}$

$+ 2, N_2$) the association probability is $P_{ij} + |\Delta P_{ij}|$ and for the homologous binary mixture (N_1, $N_2 + \Delta N_2$) the association probability must be equal to $P_{ij} - |\Delta P_{ij}|$. Then the efficiency ratio is:

$$K_{ij} = \frac{2}{\Delta N_2}$$

Here, ij is equal to 11, 12, 22 – the indices of association probabilities. For the binary mixtures (N_1, N_2) and ($N_1 + 2$, $N_2 + \Delta N_2$), the association probability P_{ij} must be approximately equal. All binary mixtures for which one of the three association probabilities remains unchanged are equivalent with respect to that association probability.

From Table III it can be seen that neither chain length nor dipole moment p_1 changes efficiency ratios by very much (excepting, may be, K_{12} for short chain).

The efficiency ratio K_{12} is the most sensitive to both the acyl chain length and dipole moment change. In order to analyse the efficiency ratios, two observations have to be borne in mind: (i) the difference between hydrophobic chain lengths decreases when one methylene unit was added to the shorter chain and increases when it was added to the longer one; (ii) only two of the dispersion interaction energies are modified by the addition of a CH_2 group to one of the two hydrophobic chains (W_{11} and W_{12} or W_{12} and W_{22}) and therefore only two association probabilities will be directly modified. The third one will be modified according to the normalisation equation (Eqn. 3). At the same time, in the cross pairs, a CH_2 methylene group added to the shorter chain interacts with all methylene groups of the longer chain, which are on both sides of the CH_2 unit added to the shorter chain, while a CH_2 added to the longer chain interacts with all the methylene groups of the shorter chain, but these are far away for it. Therefore, the change of interacting energy through van der Waals dispersion forces between two components of different type is more affected when the CH_2 is added to the shorter chain than when it is added to the longer one.

Concluding remarks

Unfortunately, there are no experimental results directly related to the association process in binary mixtures of single-chain amphiphiles; those existing are only the subject of qualitative interpretation.

In fact, the association process in amphiphile binary mixtures cannot be doubted. The association of two single-chain amphiphiles may be considered as a special double-chain lipid with large headgroup and a dipole moment which, sometimes, can be much smaller than each of the two individual dipole moments. These two uncommon types of molecule can participate further on in the association process. It is a possible way by which microclusters, which were already found experimentally [5], appear.

Recently, a collective motion of lipid was demonstrated by transverse deuteron spin relaxation [15]. On the other hand, differential scanning calorimetry (DSC) traces for binary mixtures of single-chain amphiphiles present more than one transition temperature, while the traces for pure single-chain amphiphiles have a single (or at the most, two) transition temperature(s). The transition temperatures can appear because of the three posibilities of association between the components of the binary system. In my opinion, two of these transition temperatures have to increase with the increasing of the acyl chain of each component. These transition temperatures correspond to the pairs which contain the increasing chain amphiphile. The peak areas would also be correlated to the association probabilities.

In this way, it is possible to explain the occurrence of more than one phase transition and the shifting of peaks on thermograms obtained for homologous binary mixtures of fatty acid and lysophosphatidylcoline [16].

Some remarks must be made regarding this work: (i) The relationships from which we have calculated the association probabilities are symmetrical regarding the dipole moment p_1 and p_2. For example, the association probabilities P_{11}, P_{12} and P_{22} from case $p_1 = 5$ D (p_2 is variable) would be identical to P_{22}, P_{12} and P_{11} from the case $p_2 = 5$ D (p_1 is variable), but owing to the fact that their headgroup areas and chains are different, this doesn't really occur. Comparing every pair set of curves corresponding to symmetrical probabilities, it can be appreciated how the difference between headgroups and chain lengths of the two components of each mixture influence the self-association probabilities.

(ii) If the longer chain component has small dipole moment, the association probability P_{11} is very small. Moreover, there are mixtures for which the association probability $P_{12} \simeq 0.5$ and P_{22} is also high; therefore, some of the shorter chain molecules may be 'eliminated' from association 'competition', and it is possible that the binary system can reache a more stable state in which the two components are separated by a region composed by pairs of different associating amphiphiles.

(iii) There are three important facts regarding the cross association probability P_{12}: it has high values, irrespective of the binary mixture composition; it is as high as the difference between the chain length of the components; it has its maximum value when the binary mixture is equimolar [6,16]. On the other hand, the hydrophobic chains of natural phospholipids are unequal, having 14–22 methylene groups [1] and the dipole moment $p > 35$ D [18]. The phospholipids adopt the conformation with the unequal chains even if their chains are equal [19]. Taking into account the large value of the cross association probability P_{12}, one confirms the natural conformation of the phospholipids. Also, the association of different single-chain molecules in binary mixtures can simulate the various two-chain phospholipids [16].

(iv) The selective association between amphiphile molecules gives birth to structural nonhomogeneities with different degrees of stability and is the first cause of the corrugated surface and of the thickness fluctuations in bilayers [20] which can generate the appearance of statistical pores through the lipid bilayers [21].

An interesting remark can be made concerning the existence of lysophospholipid molecules among the phospholipids in the natural membranes. One lysophospholipid molecule can attach to the long or the short acyl chain of the phospholipid (depending on the properties of both phospholipid and lysophospholipid molecules) resulting in a three acyl chain 'pseudomolecule'. The phospholipid dipole moment direction should play an essential role in the formation of such a pseudomolecule.

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