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A cura di F. Conti e S. Vallerga

A STUDY ON THE PHASE DIAGRAMS OF TWO-COMPONENT PHOSPHOLIPID BILAYERS; PHOSPHATIDYLCHOLINE (PC)/ PHOSPHATIDYLETHANOLAMINE (PE) MIXTURES.

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*Abstract – To calculate the phase diagrams
of PC/PE mixtures, a generalization of the
Priest (1) phenomenological model has been
used. A new excess free energy term in the
state function has been proposed to con-
sider the two-component phospholipid
bilayers where both the chain lenghts and
the polar heads of the components can be
different.
With this proposed state function, the
phase diagrams of different experimentally
studied PC/PE mixtures have been construc-
ted. Complete miscibility was obtained
when the components had the same chain
lenght. $L_E > L_C$ gave a peritectic system
while for $L_E < L_C$ an eutectic system was
originated.
Experimental data from different sources
were compared to the theoretical
calculations.*

Introduction – The lipid composition of
biological membranes is complex. This could
be connected with the necessity to provide
the correct micro-environment for the
membrane-bound proteins.
At the moment little is known about the
physiological meaning of the different
head groups of the phospholipids and their
mixing behaviour.
Considering that the phase properties and
the function of the lipid membranes are
directly related, we have developed a model
to study the phase transition properties
of a two-component system where both the
chain lenght and the polar heads of the
components can be different. Based on
Landau phenomehological theory (2) of phase
transition, a simple model for binary
mixtures of lecithin (PC) homologues, when
the lipid components have the same head

group but the chain lenghts are different,
has been developed by Priest (1). The model
contains only two parameters which can be
fitted independently.
Starting from this model we have determined
the parameters for one component bilayers of
PE homologues and taking into consideration
the hydrogen bondings between the polar
heads of PE molecules , a new excess free
energy term in the state function of binary
mixtures was constructed.

Theory – The free energy function of PC/PE
binary mixtures has been considered similar
to that of two-component lecithin bilayers
(eq. 18, Ref. 1). Thus,

$$\frac{G(X_E,S)}{2RT} = X_E \frac{F_E(S)}{RT} + (1-X_E)\frac{F_C(S)}{RT} +$$

$$+ \frac{1}{2} X_E \ln X_E + \frac{1}{2}(1-X_E)\ln(1-X_E) +$$

$$+ \Delta U \cdot X_E + \frac{(\sigma|\Delta L| + \gamma)}{RT}(\frac{1}{2} - S)X_E \cdot$$

$$\cdot (1 - X_E) \qquad\qquad - 1 -$$

where $\Delta L = L_E - L_C$ and X_E is the mole frac-
tion of PE component. The first two terms re-
present the free energy functions of one-
component PE and PC bilayers respectively
(3) while the third and fourth terms are the
entropy of mixing. The difference in chemical
potential (ΔU) between the two components of
the mixture is also considered and the last
term account for the experimental fact that
PC/PE mixtures of same lenght components are
not ideal ones, i.e. the excess free energy
does not vanish when $\Delta L = 0$.
As it has been previously shown (3), the
excess free energy reflects the difference
of the nearest neighbour interaction ener-
gies between the same and different components.

$\sigma \left| \Delta U \right| (1/2 - S)$ and $\gamma (1/2 - S)$ represent the interaction energy differences as a consequence of the different chain lenghts and that of the different polar heads respectively.

Results and discussion. - The model para- meter values employed in the calculations of the phasediagrams are collected in TAB.1. Those concerning PE homologues were deter- mined with the same procedure used by Priest (1) for lecithin molecules. By means of the state function -L-, the phase diagrams of different PC/PE mixtures have been determined. To obtain the points of the solidus and liquidus curves at a given temperature, one has to find out the value or the values of ΔU where two or three minima of the state function become global ones and X_E values belonging to these minima determine the points of the phase diagram.

When $L_E = L_C$ there are two minima. The first is the PE rich gel minimum at large X_E value and $S = 0$, the second is the PC rich liquid crystalline minimum at a smaller value of the mole fraction.

The phase diagrams of DMPC/DMPE and DPPC/ DPPE mixtures are represented in Fig. 1 and Fig. 2 respectively.
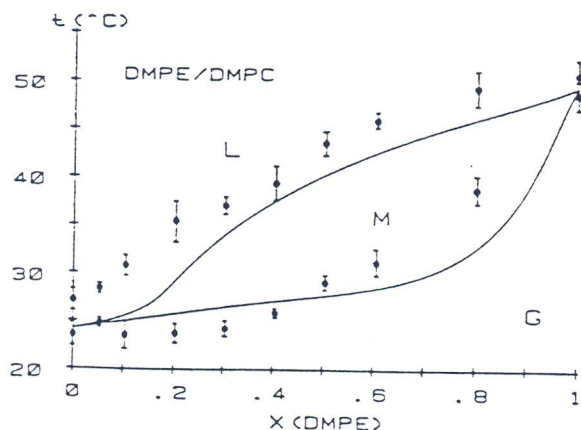
is above the liquidus curve while the gel phase is below the solidus line. Between these two lines PC rich liquid crystalline phase coexists in equilibrium with the PE rich gel phase; this is the mixed phase region.
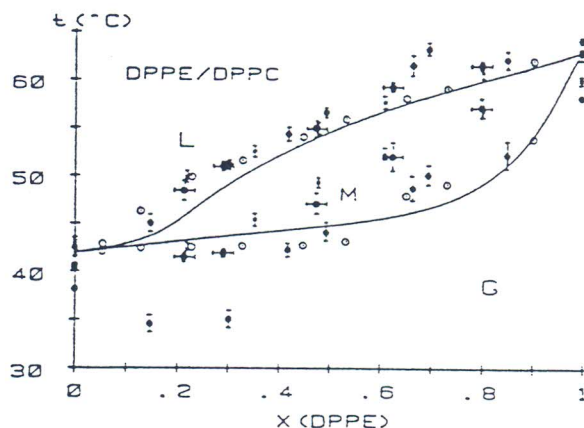

Fig. 2 - DPPC/DPPE mixture phase diagram. Solid curves are the model results. Experimental data: DSC, (● o), (4,6); ESR, ■, (7); fluoroscence, x, (8).

A more complex situation is obtained when $L_E > L_C$. In the (X_E, G) plane local minima are three: a liquid crystalline, a PC rich gel and a PE rich gel minimum.

At P (in Fig. 3 for DMPC/DPPE mixture) all three phases coexist in equilibrium. In the MG (mixed gel) region the two gel phases co- exist in equilibrium.
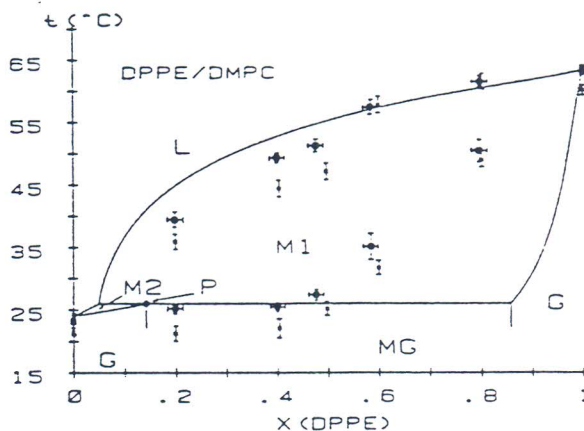

Fig. 1 - Calculated phase diagram of binary mix- tures of DMPC and DMPE. DSC experimental data (6)

The upper curves of phase diagrams are the liquidus and the lower ones are the solidus lines. The liquid crystalline phase

Fig.3 - Phase diagram for DMPC/DPPE mixture. Experimental data: ESR, ■, (7); fluorescence, x, (8).

In the M1 region a PC rich liquid crystal- line phase coexists with a PE rich gel phase while in M2 a PC rich crystalline

phase coexists with a PC rich gel phase. Also in the cases where $L_E < L_C$ there are three important local minima. The phase diagrams of DPPC/DMPE and DSPC/DMPE mixtures are represented in Fig. 4 and 5 respectively.
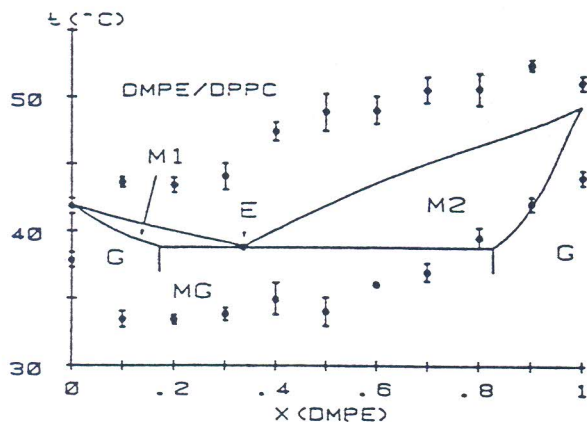

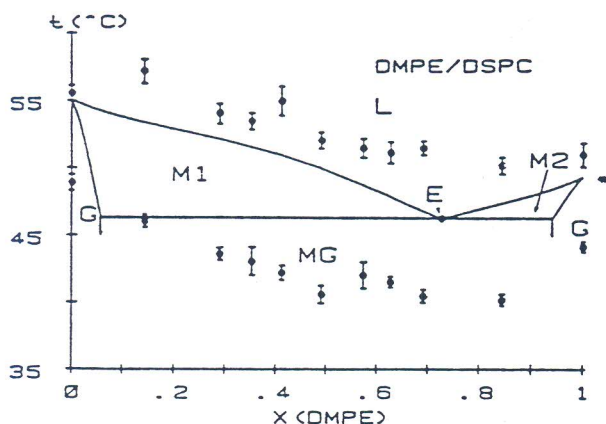Fig. 4 – Phase diagram for the binary mixture DPPC/DMPE. DSC experimental data (4).

Fig. 5 – Phase diagram for the binary mixture DSPC/DMPE. DSC experimental data (4)

These systems are eutectic mixtures as was also concluded by Blume and Ackermann (4) analyzing their calorimetric data. The obtained results indicate that, depending on the chain lenght differences, three types of PC/PE mixed systems can be differentiated as summarized in Tab. II. The calculated liquidus curves fit quite well the available experimental data. For the solidus curves the agreement is good only for calorimetric data.

Table I. Model parameter values for phosphatidylcholine and phosphatidylethanolamine homologues.

P i	Z_i/R	W_i/R	σ/R	γ/R
	°K	°K	°K	°K
P C	-275.1	-1085	125	0
P E	-188.3	-1117.8	125	500

Table II

L_C	L_E	Mixtures	Results
14	14	DMPC/DMPE	complete miscibility
16	16	DPPC/DPPE	complete miscibility
14	16	DMPC/DPPE	peritectic system
16	14	DPPC/DMPE	eutectic system
18	14	DSPC/DMPE	eutectic system

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Abbreviations: DPPC, L-α-dipalmitoylphosphatidylcholine; DMPC, L-α-dimyristoylphosphatidylcholine; DSPC, L-α-distearoyl-phosphatidylcholine; DPPE, L-α-dipalmitoylphosphatidylethanolamine; DMPE, L-α-dimiristoylphosphatidylethanolamine.