

Chapter 8

The continuous model of the lipidic bilayer

The lipidic molecules are formed by a head with hydrophilic properties to which two hydrocarbon chains (fat acids) with hydrophobic properties are tied. In a lipid dispersion in water, one of the stable states is that of a bilayer formed by two neighboring lipidic monolayers. The hydrophobic chains of each monolayer are directed toward the interior of the bilayer, so that the exterior surfaces of the bilayer are formed by the hydrophilic heads. So, the bilayer separates two volumes of water by the hydrophobic region from its interior. In spite of the fact that the magnitude order of the bilayer thickness is that of the molecules length, however many of its properties can be described by the properties of an elastic membrane and using the macroscopic methods of the continuum mechanics [6]. Because of the complexity of this corpuscular system the usual methods of the statistical mechanics do not allow to prove that the continuous approach is appropriate. We will show that, using the coarse-grained average defined in chapter 4 and the local equilibrium hypothesis, we can obtain the continuous models of the lipidic bilayer.

We model the hydrophilic head of the lipidic molecule by a material point of mass m and a position given by the coordinates (x_i, y_i, z_i) . We simplify the lipidic molecule structure considering that a single hydrophobic chain, not two, corresponds to each head. The chains are modeled as filiform bars of mass M , length L and direction given by the unit vector \mathbf{l}_i with the initial point at the head of the molecule and pointing in direction of the other end of the chain. The hydrocarbon chains flexibility is essential to many of the lipidic bilayer properties (for example the phase transitions) but we shall neglect them in order to not complicate too much the microscopic structure. We consider that the water molecules are material points of mass

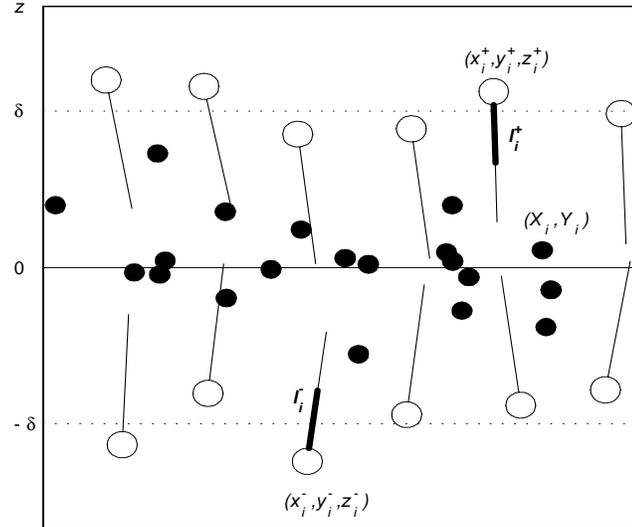


Figure 8.1: The lipidic bilayer structure.

m_a with their position given by the coordinates (X_i, Y_i, Z_i) . We neglect the electrostatic phenomena, i.e. the permanent electric dipoles of the water molecules and of the lipidic molecules heads.

We consider only the processes which leave the bilayer near its equilibrium state. We denote by 2δ the average thickness of the bilayer, so that at equilibrium the hydrophilic heads are on two parallel planes $z = \pm\delta$. The two monolayers stretch laterally to the infinite and the average number of lipidic molecules on the unit surface (the superficial concentration) at equilibrium is n_o . For temperatures high enough, each of the lipidic monolayers behaves like a two-dimensional liquid, the lipidic molecules being in permanent thermal motion, without passing from a side to the other. Some of the water molecules penetrate into the bilayer interior. When the water molecules from the inside are in dynamic equilibrium with those from outside, we denote by c_o their concentration on the surface unit. In figure 8.1 we have the simplified geometry of the bilayer in a plane section.

Due to the two-dimensional geometry of the bilayer we can consider that we have only two spatial coordinates x and y . All the definitions and relations in chapter 4 are still valid if the sphere $S(\mathbf{r}, a)$ is transformed into the disk of center $\mathbf{r}(x, y)$, and the volume of sphere \mathcal{V} , into the circle surface πa^2 . We

denote by φ^\pm all the physical quantities referring to the lipidic molecules, as the molecules are on the superior side ($z = +\delta$) or the inferior side ($z = -\delta$). The lipidic molecules position is given by the two-dimensional position vectors $\mathbf{r}_i^\pm(x_i^\pm, y_i^\pm)$. The coarse-grained averages $\langle\varphi^\pm\rangle$, which we denote by $\langle\varphi\rangle^\pm$, become densities on the unit surface. Then the discrete analogue of the balance equation (4.24) for an arbitrary microscopic quantity φ^\pm , reads

$$\partial_t\langle\varphi\rangle^\pm + \partial_x\langle\varphi\dot{x}\rangle^\pm + \partial_y\langle\varphi\dot{y}\rangle^\pm = \langle\dot{\varphi}\rangle^\pm, \quad (8.1)$$

where the generation term is missing since the lipidic molecules can not leave the monolayer where they belong.

We treat the water molecules from the bilayer inside in the same two-dimensional geometry, their position being given by the vector $\mathbf{R}_i(X_i, Y_i)$. The information given by the coordinate Z_i is neglected and the coarse-grained averages $\langle\varphi\rangle$ for the microscopic quantities attached to the water molecules are averages on the bilayer thickness too. Then the relation (4.24) reads

$$\partial_t\langle\varphi\rangle + \partial_x\langle\varphi\dot{X}\rangle + \partial_y\langle\varphi\dot{Y}\rangle = \langle\dot{\varphi}\rangle + \langle\partial_t\varphi\rangle_g, \quad (8.2)$$

where the generation term describes the water molecules possibility to enter or leave the bilayer inside.

The relation (8.1) can be written for $\varphi^\pm = 1^\pm, \mathbf{r}_i^\pm, z^\pm, \dot{\mathbf{r}}_i^\pm, \dot{z}^\pm, \mathbf{l}_i^\pm, \dot{\mathbf{l}}_i^\pm$, i.e. for 22 physical quantities and the relation (8.2) for $\varphi = 1, X, Y$ i.e. for other 3 additional physical quantities. In all it results 25 de relations between 81 coarse-grained averages. The next step is the choice of the averaging parameters a and τ such that the local equilibrium principle should be satisfied, as discussed in chapter 1. Thus, all the coarse-grained averages become usual continuous fields and $81-25=66$ constitutive relations are needed. As the bilayer microscopic structure is very complex, the form of the constitutive relations depends on the magnitude of parameters a and τ . This is due to the fact that a and τ define the space-time scale of the phenomena that by coarse-grained averaging are maintained in the resulting continuous description. By this averaging the processes with smaller space-time scale are eliminated. For example in the mechanical model of the lipidic molecules we have neglected the carbon chains flexibility and then it is necessary that $\tau > 10^{-10}$ s for the chains conformation fluctuations not to influence the coarse-grained averages [6]. If the processes taking place at the space-time scale given by a and τ satisfy the local equilibrium principle, then the usual balance equations are obtained.

In this stage of the continuous modeling of the lipidic bilayer, we have to evaluate the amount and the quality of the available information on the average behavior, characteristic to the macroscopic motion, of the microscopic

components. At the present time the measurement of the physical properties of the lipidic bilayers (NMR, RES, electronic microscopy, etc.) make possible the study of the behavior of individual lipidic molecules or of groups of several molecules. Furthermore, the numerical simulations through molecular dynamics produce results in accordance with the experimental measurements [72], [58]. The information obtained represents the motion of each molecule, which allows us to obtain, by statistical averagings, the average behavior of the molecules needed for the constitutive relations.

We also notice that when there exist very many constitutive relations (in our case 66) it is possible that some of them to be ignored. Therefore an other advantage of the relations (8.1) and (8.2) is the fact that they form a frame in which every continuous field necessary to be expressed by a constitutive relation appears. Thus, to choose a particular constitutive relation or to neglect a field, we are compelled to make explicit hypotheses and approximations, which leads to a more coherent and rigorous microscopic model. To keep the presentation uncomplicated we choose a simple phenomenon to be modeled continuously. The thermal fluctuations of the lipidic bilayer shape have been used to explain some properties of the bilayer [26]. Lately it has been proved theoretically and experimentally that they strongly influence the mechanical properties of the bilayer in the equilibrium state [6], [53], [37], and [25]. First we have to choose the averaging parameters a and τ that by coarse-grained averaging render evident this phenomenon. We are interested in the fluctuations to which several lipidic molecules participate, knowing that in average a surface of $50\text{-}100 \text{ \AA}^2$ is occupied by a molecule. That is why we choose $a \sim 50 \text{ \AA}$. The capillary waves at the free surface of the water with the wave length of de 50 \AA have a period of approximate 10^{-11} s . Since the two lipidic monolayers which form the bilayer are situated on the free surfaces of the two volumes of water separated by the bilayer, their fluctuations are characterized by this time interval. So we have to choose $\tau \sim 10^{-11} \text{ s}$. Such a small value τ does not satisfy any more the averaging condition of the fluctuations of the carbon chains configurations. However, to keep the discussion uncomplicated we shall ignore in the following the chains flexibility, so the equations we will obtain, exemplify only the continuous description.

Because of the value τ , which is too small, the molecules displacements in the bilayer plane are negligible. And similarly the variation of the carbon chains directions. Then we write the relation (8.1) only for $\varphi^\pm = 1^\pm, z^\pm, \dot{z}^\pm$. Since the terms which contain the velocities \dot{x} and \dot{y} are negligible, we obtain the relations

$$\partial_t \langle 1 \rangle^\pm = 0, \quad (8.3)$$

$$\partial_t \langle z \rangle^\pm = \langle \dot{z} \rangle^\pm, \quad (8.4)$$

$$\partial_t \langle \dot{z} \rangle^\pm = \langle \ddot{z} \rangle^\pm. \quad (8.5)$$

The meaning of the first relation is the constancy in time of the lipidic molecules concentration. This is due to the very small time scale of the phenomenon we study. Dividing the relations (8.4) and (8.5) by $\langle 1 \rangle^\pm$, we obtain

$$\partial_t^2 \zeta^\pm = \frac{1}{m+M} f^\pm, \quad (8.6)$$

where $\zeta^\pm = \langle z \rangle^\pm / \langle 1 \rangle^\pm$ is the average coordinate z of the lipidic molecules, i.e. the coordinate of the exterior surfaces of the bilayer, and f^\pm is the average force acting on a lipidic molecule on the normal direction to the bilayer.

For $\varphi = 1$, the relation (8.2) becomes

$$\partial_t c + \partial_x(cU) + \partial_y(cV) = g, \quad (8.7)$$

where $c = \langle 1 \rangle$ is the concentration of the water molecules on the unit surface, $U = \langle \dot{X} \rangle / \langle 1 \rangle$ and $V = \langle \dot{Y} \rangle / \langle 1 \rangle$ are the average velocity components and g is the generation term. For $\varphi = \dot{X}, \dot{Y}$ we obtain

$$\begin{aligned} \partial_t(cU) + \partial_x \langle \dot{X}^2 \rangle + \partial_y \langle \dot{X}\dot{Y} \rangle &= \langle \ddot{X} \rangle, \\ \partial_t(cV) + \partial_x \langle \dot{X}\dot{Y} \rangle + \partial_y \langle \dot{Y}^2 \rangle &= \langle \ddot{Y} \rangle, \end{aligned} \quad (8.8)$$

where we assumed that the generation term vanished since when the water molecules enter the lipidic bilayer or go out from it, their velocity tangent to bilayer is negligible. As the numerical simulations showed, inside the bilayer the lateral pressure p due to the interaction between the carbon chains is of the magnitude order of hundreds of atmospheres [72]. The water molecules have the same pressure and the equations (8.8) can be written

$$\begin{aligned} \partial_t(cU) + \partial_x(cU^2) + \partial_y(cUV) + \partial_x p &= \frac{1}{m_a} F_x, \\ \partial_t(cV) + \partial_x(cUV) + \partial_y(cV^2) + \partial_y p &= \frac{1}{m_a} F_y, \end{aligned} \quad (8.9)$$

where we have neglected the viscosity forces because, due to the small number, the water molecules interact mainly with the carbon chains. Here \mathbf{F} is the average force acting on a water molecule.

In the balance equations (8.6), (8.7), and (8.9) we have 6 fields (f^+, f^-, g, p, F_x, F_y) which have to be expressed with respect to the fields ζ^+, ζ^-, c, U , and V through constitutive relations. The simplest solution is that, on the basis of the available data, hypotheses on the physical quantities on which the 6 fields depend should be made, and assume that near the equilibrium state these dependences are linear. It is obvious that this approach is a first approximation which has to be improved by the information on the real microscopic structure.

We denote by p_o the average lateral pressure in the equilibrium state. The lateral pressure depends on the squeezing degree of the carbon tails and on the water molecules concentration and then a constitutive equation (in first approximation) for p is

$$p = p_o - k_1(\zeta^+ - \zeta^- - 2\delta) + k_2(c - c_o), \quad (8.10)$$

where k_1 and k_2 are positive constants. The generation term g depends on (also in first approximation) the deviation of the water molecules from the equilibrium concentration

$$g = -k_3(c - c_o), \quad (8.11)$$

where k_3 is a positive constant. The interaction forces of the water molecules with the carbon chains are included into the lateral pressure and then

$$F_x = F_y = 0. \quad (8.12)$$

The average force acting on a lipidic molecule is given by two distinct processes. When a monolayer is bending the lateral pressure has the tendency to increase the curvature. If the monolayer does not move much from the plane equilibrium state, the average curvature is proportional to the Laplacian in ζ^\pm . The second process is the interaction of the lipidic molecules with the free surface of the water. The monolayer bending change the lipidic molecules positions and these forces tend to bring them back to the equilibrium position. In the same linear approximation we have

$$f^\pm = \mp k_4 p (\partial_x^2 \zeta^\pm + \partial_y^2 \zeta^\pm) - k_5 (\zeta^\pm \mp \delta) \quad (8.13)$$

where k_4 and k_5 are other two positive constants. The constitutive relations looked for are (8.10)-(8.13). Together with the balance equations (8.6), (8.7), and (8.9), with the initial conditions and the boundary conditions they form altogether the continuous model for thermic fluctuations of the lipidic bilayer surfaces. It is obvious that in this model other hypotheses have to be introduced in order to obtain applicable practical results. However it contains some of the properties specific to the lipidic bilayer.