

Cooperative Dynamics of Quasi-1D Lipid Structures and Lateral Transport in Biological Membranes

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Abstract. A model for the dynamics of quasi-1D lipid structures in biological membranes is proposed. The model takes into account interactions between the lipid heads and hydro-carbon chains, the description of their relaxation dynamics being based on the phenomenological Ginzburg-Landau approach. It is shown that in lateral linear structures of lipids, a soliton-like excitation can propagate with constant velocity. The latter in turn may provide for lateral transport of matter and for membrane conformation changes.

Key words: Membranes — Solitons — Lateral transport — 1D-structures

Introduction

Traditional approaches to description of biological membranes as mechanically passive systems in thermodynamic equilibrium are not always adequate. Cell membrane is a boundary structure that provides for irreversible processes of energy and mass exchange between the cell and its environment. During last few years a special role of quasi-1D structures of biosystems in long-distance transfers of energy, mass and information has been revealed in a number of investigations (Bishop and Schneider 1978, Collins 1983, Davydov 1984, Hianik and Vozár 1985, Scott and Davydov 1985, Bolterauer et al 1991, Hianik et al 1996). Many phenomena in cell behavior such as differentiation, aggregation into colonies, growth control, effects of hormones and poisons, allosteric effects, etc involve membranes and are

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cooperative. A detailed knowledge of possible characteristics of collective behavior of quasi-1D structures in multicomponent bilayer lipid membranes is therefore important.

Biological membranes are known to be dynamic cooperative systems (Aloia 1983, Rubin 1987). Both biological and artificial membranes have two basic states: rigid gel, or 2D crystalline state, and melted, or liquid crystalline state. The gel-liquid crystalline transition corresponds to the lipid molecules' conformation changing from totally *trans*- to a chaotic one. The transition temperature depends on lipid composition of the bilayer (Aloia 1983, Rubin 1987), and the average membrane surface area per molecule increases during the transition from 0.48 to 0.58 nm².

Under quasi-1D structures we understand linear arrays of acyl chains of lipids (cf. Fig. 1), linear defects of the bilayer structure, and boundaries of domains formed during lateral separation of lipids in the bilayer formation process. Such structures were found in biological membranes with the help of X-ray diffraction and electron microscopy (Aloia 1983). Their existence was also confirmed by computer modeling (Goltsov 1994).

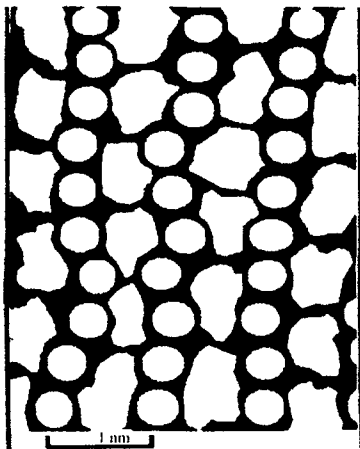


Figure 1. One possible model of a mixed phase of phospholipid and cholesterol (circles represent acyl chains that form linear structures) (Aloia 1983).

In this paper, some theoretical concepts of cooperative processes in quasi-1D lateral structures of multicomponent lipid membranes are developed. The membrane is viewed as being built of two subsystems: lipid heads (LH), and lipid tails (LT). In such a two-component structure, collective excitations are considered that can mediate long-distance interactions between membrane-bound macromolecules.

Dynamics of LH and LT subsystems interaction

Phase transitions in lipids are accompanied by conformation changes of their molecules. Lipids melting may be considered as a conformation change as it corresponds to rotational isomerization of the lipid molecules. The energy level difference of gosh- and trans-conformations is small (2–3 kJ/mol) in comparison with the energy barrier between them (12–17 kJ/mol).

The LT-subsystem dynamics may be described with the use of Ginsburg-Landau hamiltonian (Bolterauer et al 1991). At the same time phase transitions in lipids may be described in terms of the Landau phenomenological theory (Ginsburg and Landau 1950). Any general approach to such transitions always includes some kind of order parameter η which takes non-zero values only in the ordered phase. Then, the free energy of the system $F(\eta, T)$ near the transition point may be spread into power series

$$F(\eta, T) = \Phi(\eta) = a_0 + a_1\eta + \frac{a_2}{2}\eta^2 - \frac{a_3}{3}\eta^3 + \frac{a_4}{4}\eta^4 \quad (1)$$

where coefficients a_0, \dots, a_4 may be found from the dependence of T_c and η on lateral pressure p (Rubin 1987). The order parameter is defined as (Rubin 1987)

$$\eta = (S_F - S)/(S_F - S_G), \quad (2)$$

where S_F and S_G are surface areas per molecule in liquid crystalline and gel states. The surface area per molecule in the real state of a lipid is S , and it increases with the transition of the lipid molecules from the trans-state into a disordered one.

Further elaboration of this approach was used for the modeling of the system parameters influence on the phase transition characteristics. For example it could be shown, that the phase transition temperature strongly depends on parameters affecting the LH-system charge (i.e. pH, ionic strength, adsorption of ions, etc.) in the case of charged lipids, whereas there is no such dependence for zwitterionic lipids. Therefore, the correct description of phase transitions in LT-subsystem must include interactions between the LT- and the LH-subsystems.

These interactions may be accounted for by proper choice of the free energy terms. The Ginsburg-Landau free energy of an LT-system interacting with an LH-system may be presented as the sum (approximated by an integral) of individual molecules contributions. Interaction between adjacent molecules taken into account, the corresponding functional is

$$F(\eta, \rho, T) = \frac{1}{a} \int dx \left[\Phi(\eta) + \frac{\gamma}{2} (\nabla\eta)^2 \right], \quad (3)$$

where x is the molecule coordinate. With the use of appropriate scaling and displacement of the coordinate system origin it is possible to substitute coordinates

for new ones $(\tilde{\eta}, \tilde{F})$ so that

$$\tilde{F}_0(\tilde{\eta}, \rho, T) = \frac{1}{a} \int dx \left[\lambda \tilde{\eta} - \frac{\alpha}{2} \tilde{\eta}^2 + \frac{\beta}{4} \tilde{\eta}^4 + \frac{\gamma}{2} (\nabla \tilde{\eta})^2 \right], \quad (4)$$

where $\lambda = p(S_F - S_G)$, p stands for lateral pressure, $\alpha = \alpha_0(T_c - T)$, α_0 and β are positive and in practice do not depend on temperature, γ is diffusion coefficient for the order parameter. The new variable, $\tilde{\eta}$, depends linearly on the old variable, η

The free energy in (4) has one minimum if $\left(\frac{\alpha^3}{27} + \frac{\lambda^2}{4}\right) > 0$, and two minima corresponding to gosh- and trans-conformations of the lipid molecules if $\left(\frac{\alpha^3}{27} + \frac{\lambda^2}{4}\right) < 0$. From the relaxation equation for the order parameter $\tilde{\eta}$ (Haken 1978)

$$\tilde{\eta}_t = -\frac{\delta \tilde{F}(\tilde{\eta}, T)}{\delta \tilde{\eta}}, \quad (5)$$

it is possible to derive the time-dependent Ginzburg-Landau equation

$$\tilde{\eta}_t = -\lambda + \alpha \tilde{\eta} - \beta \tilde{\eta}^3 + \gamma \tilde{\eta}_{xx}, \quad (6)$$

which describes spatio-temporal changes of the order parameter in the LH-system

Displacement of LH from equilibrium may be obtained from the energy operator for a chain of LH

$$H = \frac{1}{a} \int dx \left[\frac{m}{2} (\rho_t^2 + \Omega_0^2 \rho^2 + V_0^2 \rho_x^2) \right], \quad (7)$$

where m is the LH mass, $V_0 = a\Omega_1$, Ω_0 and Ω_1 are the characteristic frequencies of the LH-grid. The dynamic equation corresponding to this operator is

$$m\rho_{tt} + m\Omega_0^2\rho - mV_0^2\rho_{xx} = 0 \quad (8)$$

In the presence of particles and external fields with which the LH interact Eq (8) should contain additional terms describing viscous friction and other interactions

$$m\rho_{tt} + m\Omega_0^2\rho - m\Gamma\rho_t - mV_0^2\rho_{xx} = f \quad (9)$$

Thus, the dynamics of the LH chain changes. We will confine ourselves to two limit cases of extremely low and extremely high friction

In the first case, ($\Gamma \rightarrow 0$) in the absence of interaction between LH and LT ($f = 0$) equation (9) describes longitudinal (acoustic) waves with the dispersion

$$\Omega^2(\vec{q}) = \Omega_o^2 + V_0^2 q^2 \quad (10)$$

The other case, ($\Gamma \gg 0$) corresponds to a chain of weakly interacting particles, their motion caused by external forces being overdamped

$$m\Omega_0^2\rho - m\Gamma\rho_t = f. \quad (11)$$

Interaction of LT with polar groups undergoing displacement ρ as a result of conformational changes in LT system may be written as:

$$W = \frac{1}{a} \int \chi\rho\nabla\tilde{\eta}dx. \quad (12)$$

Then, the force with which LT acts on polar groups is

$$f = -\chi\nabla\tilde{\eta}, \quad (13)$$

where the interaction constant χ in general case depends on the surroundings of the membrane.

Substituting (13) into Eq. (9) when $\Gamma \rightarrow 0$, and into Eq. (11) we obtain equations of motion for the LH chain which interacts with the LT system both for free (no friction) and overdamped cases.

In the absence of friction, most interesting is the case of constant propagation velocity, $V = V_0$. We obtain from (9)

$$\rho = -\frac{\chi}{m\Omega_0^2}\nabla\eta, \quad (14)$$

i.e. the polar groups displacement is completely defined by the order parameter changes. In the case of overdamped motion of polar groups as defined by Eq.(11) this relationship also holds under condition that

$$\frac{\Omega_0^2}{\Gamma\alpha} \gg 1. \quad (15)$$

The meaning of (15) is that the LH system characteristic time $\tau_\rho = \Gamma/\Omega_0^2$ must be much smaller than the LT system time constant $\tau_\eta = \alpha^{-1}$. At this kind of "adiabatic approximation" $\rho_t = 0$, which leads to (14). It should be noted that the closer T to T_c , the better this approximation.

The Ginsburg-Landau free energy \tilde{F} for the system of LT interacting with LH can be written down as the sum of free energy F_0 of LT subsystem without interaction with LH (4) and the energy W of LT interacting with polar groups (12). Then, from (12) with (14) taken into account we get

$$\tilde{F}(\tilde{\eta}, \rho, T) = F_0 + W = \frac{1}{a} \int dx \left[\lambda\tilde{\eta} - \frac{\alpha}{2}\tilde{\eta}^2 + \frac{\beta}{4}\tilde{\eta}^4 + \frac{\gamma_0}{2}(\nabla\tilde{\eta})^2 \right], \quad (16)$$

where $\gamma_0 = \gamma \left(1 - \frac{2\chi^2}{m\Omega_0^2\gamma} \right)$

The time-dependent Ginsburg-Landau equation can be obtained by substituting of (16) into (5)

$$\tilde{\eta}_t = -\lambda + \alpha\tilde{\eta} - \beta\tilde{\eta}^3 + \gamma_0\tilde{\eta}_{xx} \quad (17)$$

This equation describes spatio-temporal changes of the order parameter in the LT system interacting with the LH grid when (15) is true. It has steady-state solutions $\tilde{\eta}_i = \tilde{\eta}_0 q_i$ ($i = 1, 2, 3$), where $\tilde{\eta}_0 = \pm\sqrt{\alpha/\beta}$ and q_i are the roots of the polynomial

$$-q + q^3 - Q = (q - q_1)(q - q_2)(q - q_3), \quad (18)$$

with $q_1 < q_2 < q_3$, and $Q = \lambda\sqrt{\beta/\alpha^3} < 2/\sqrt{27} = Q_{\max}$

Besides equation (17) possesses a soliton-type equation which corresponds to excitation like a solitary wave of kinks that propagates at a constant speed

$$\tilde{\eta}_{\text{sol}}(r, t) = \tilde{\eta}_1 + \frac{\tilde{\eta}_2 - \tilde{\eta}_1}{1 + \exp\left(\frac{r - Vt}{\Delta}\right)}, \quad (19)$$

where

$$\Delta = \frac{\sqrt{2\gamma_0}}{(\tilde{\eta}_3 - \tilde{\eta}_1)\sqrt{\beta}} \quad (20)$$

defines the soliton's width and consequently its localization

The wave described by (13) has the peculiar feature that it may only have one certain speed at each value of external force, e.g. λ . In particular, when there is no external force ($\lambda = 0$ in our case), solution to equation (19) corresponds to a resting kink. When there is external force the kink moves at a definite speed, otherwise it loses energy and stops because of viscous friction.

A kink moving in the LT-system induces a region of deformation in the LH system which moves together with the kink. The spatio-temporal structure of the defect in the quasi-1D lateral grid of the lipid molecules heads may be found from (14) and (17)

$$\rho_{\text{sol}}(x, T) = -\frac{\lambda(\tilde{\eta}_2 - \tilde{\eta}_1)}{4m\Omega_0^2\Delta} \operatorname{sech}^2\left(\frac{x - Vt}{2\Delta}\right) \quad (21)$$

(see Fig. 2)

At temperatures below T_c both the excitation localization and the speed of its propagation change with T . At temperatures close to T_k which is determined by

$$T_k = T_c - \frac{3}{\alpha_0} \left(\frac{\lambda^2\beta}{4} \right)^{1/3}, \quad (22)$$

the localized state is destroyed

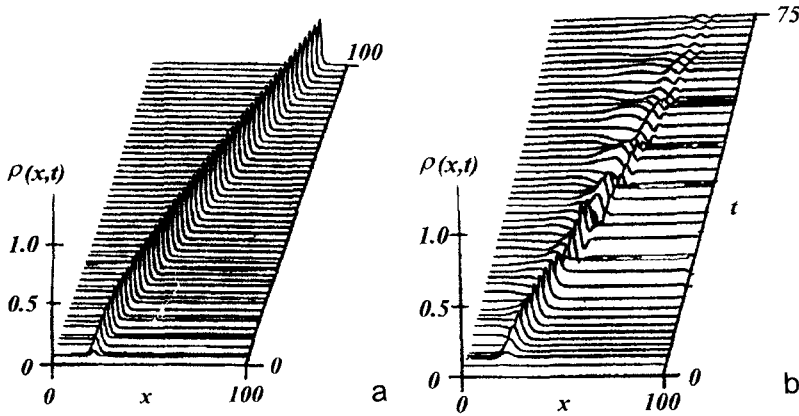


Figure 2. Excitation propagation $\rho = \rho(x, t)$ (a soliton) along a quasi-1D structure in lipid bilayer at different temperatures **a** $T = 0.5 T_c$, **b** $T = 0.84 T_c$. Other parameters and variables are $x = x/a$ $t = \Omega_1 t$, $a = 0.5$ nm $\Omega_1 = 10^{12}$ s $^{-1}$, $\gamma_0 = 2.5 \cdot 10^{-2}$ cm 2 /s

Lateral charge and transport of small molecules by solitons along the quasi-1D structures in membranes

Soliton-like excitations (21) are local displacements of the LHs from the state of equilibrium and local conformation changes in the LT-subsystem. Both perturbations are generated in, and move together along, the quasi-1D membrane structures under proper conditions. Electrons, ions or other ligands interacting with the lipid molecules acquire additional energy (deformation potential)

$$W(x - Vt) = -2\sigma\rho_{\text{sol}}(x - Vt) = -\frac{\sigma\chi(\tilde{\eta}_2 - \tilde{\eta}_1)}{2m\Omega_0^2\Delta} \text{sech}^2\left(\frac{x - Vt}{2\Delta}\right), \quad (23)$$

where σ is the parameter characterizing interaction between the ligand and the deformation of the lipid chain. This energy may provide trapping of small particles and their transfer along with the soliton. The possibility of such a phenomenon has been investigated by Zmuidzinas (1978), Davydov (1984), Kadantsev and Lupichev (1990). The movement of a particle trapped by the soliton is described by Schrodinger equation solution to which for the energy well (23) corresponding to the soliton (21) has been obtained by Landau and Lifshits (Landau and Lifshits 1963). They demonstrated that the energy spectrum of a microparticle in such an energy well is negative, i.e. the surplus particle trapped by the soliton in the lipid chain may only have finite number of energy levels, the lowest of them being

$$E_0 = -\frac{\hbar^2 n_0^2}{4M_T\Delta}, \quad (24)$$

where M_T is the trapped particle effective mass, which depends on the temperature of the LH-chain, and n_0 is defined by:

$$n_0 = \frac{1}{2} \left(\sqrt{1 + \frac{16\sigma\chi\Delta(\tilde{\eta}_2 - \tilde{\eta}_1)M_T}{\hbar^2\Omega_0^2 m}} - 1 \right).$$

Particles trapping and transport by the soliton is only possible when $|E_0| > k_B T$, where k_B is the Boltzmann constant. Thus, the trapping and hauling by solitons in quasi-1D lipid structures of small particles may provide for the lateral transport in cell membranes. The problem of feasibility of the necessary conditions to be investigated separately.

Discussion

This paper is dedicated to theoretical investigation of the cooperative dynamics of quasi-1D lateral structures in multicomponent lipid membranes. The membrane bilayer is represented as consisting of two subsystems, those of lipid tails (LT) and of lipid heads (LH). It was taken into account that the LT-subsystem behavior strongly depends on temperature, and melting of lipids is observed near some critical temperature T_c . The phenomenological Ginsburg-Landau approach widely used to treat critical phenomena in various systems was also used to tackle this problem.

It was shown that, when the two major subsystems interact with each other and with the environment, then in quasi-1D lipid structures of bilayers there may exist excitations of the solitary wave type (with not small magnitudes) moving at constant speed.

For such excitations to exist it is crucial that interactions between lipid molecules comprising the quasi-1D structure be much stronger than interactions with other lipid molecules (“transversal” interactions). Introduction of “transversal” interactions into a computer model of the system results in the excitation “hanging” at the beginning of the chain or becoming quickly disintegrat.

Propagation of a stable soliton-like excitation in the LT-subsystem (a kink) induces a soliton in the LH-subsystem which moves coherently with the kink in the LT-subsystem. The soliton’s speed and the degree of its localization both increase with the increasing temperature but in the presence of even a slight noise at some temperatures close to the melting point, the localized state decays. Local conformation changes in quasi-1D lateral lipid structures of the LH system can provide for additional energy in the interaction of small ligands, both charged and neutral, with the membrane. This may result in the ligand becoming trapped by the soliton with subsequent movement of both of them as a whole. Thus, quasi-1D lipid structures in the membrane may provide for lateral transport of matter and for conformation changes sufficient for sustained long-distance intramembrane interactions.

To a large extent, the effectivity of this transport depends on the degree of the excitation localization and on the velocity of propagation, both of which in turn depend on temperature. The high sensitivity of the lateral transport to temperature, changes in lipid composition of the membrane, and to other conditions requires further investigation.

The described mechanisms in our opinion may be a basis for highly cooperative changes in large areas of the membrane in response to local internal or external stimuli. The developed approach may prove useful in modeling of phenomena such as synchronous changes of membrane bound enzymes or ion channels.

Acknowledgements. This work was made possible partly thanks to the support from ISF and the Russian Government, grants No. MA6000 and MA6300.

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