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Lipids lateral diffusion study associated with structural changes in cytoplasmic membranes

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Motivation and Aim: To date, it has been experimentally established that the diffusion of lipids in cytoplasmic membranes is complex. There are several qualitatively different types of lipid diffusion: (slowed, confined, simple-Brownian, directed and hop diffusion) [1]. This paper presents a model of lipid diffusion in heterogeneous native cytoplasmic membranes. It has been shown that the appearance of various types of lipid diffusion mentioned above is associated with structural changes in cytoplasmic membranes [2–5].
Methods and Algorithms: A model of an infinite flat layer with an inhomogeneous, periodic diffusion coefficient is considered. Two cases were studied – one and two sublattices of harmonic dependences of the diffusion coefficient *D* on the coordinate: $D = D_0 - D_1 cos(k_0 x) cos(k_0 y)$ and $D = D_0 - \tilde{D}_1 cos\left(k_0 x\right) cos\left(k_0 y\right) - \tilde{D}_2 cos\left(k_2 x\right) cos\left(k_2 y\right)$ where $D_0, \tilde{D}_1, \tilde{D}_2$ are the first, second and third diffusion coefficients respectively, λ_1 = 100 nm is the distance between the nearest membrane proteins that have slightly changed their conformational state, λ_2 is the distance between the nearest membrane proteins that have greatly changed their conformational state $k_0 = 2\pi/\lambda_1, k_2 = 2\pi/\lambda_2$. The diffusion equations for the Ψ distribution function of lipids in an inhomogeneous membrane $\frac{\partial \Psi}{\partial t} = \frac{\partial}{\partial x}\left(D\left(x,y\right)\frac{\partial \Psi\left(x,y,t\right)}{\partial x}\right) + \frac{\partial}{\partial y}\left(D\left(x,y\right)\frac{\partial \Psi\left(x,y,t\right)}{\partial y}\right)$ have been solved by the Fourier transform method. An analytical analysis of the solution is given.
Results: It is analytically shown that there is an advection-diffusion mode for these models. The alternating modes of nonlinear diffusion and joint advection-diffusion are analytically shown. It is shown that from zero to sometime t_0, nonlinear diffusion is observed, then there comes a period of advection-diffusion, then again a period of nonlinear diffusion, etc. In the experiment, this is not always observed in the form of hop diffusion. When the drift during advection is less than the dispersion, the advection of lipids is not visible against the background of their chaotic thermal motion; the trajectory of lipids in the membrane corresponds to nonlinear diffusion. Analytically, criteria have been obtained, under which the advection of lipids can be observed in the experiment. It is analytically shown that lipid advection is not observed in the case of a single lattice of inhomogeneity's, since the coefficient of membrane inhomogeneity $\beta = D_1/D_0$ must be very high ($\beta > 0.8$), which is rarely performed in an experiment. At lower values of the lattice inhomogeneity coefficient, β advection will not be visible against the background of chaotic thermal motion of the lipid.

In the second case, when the membrane proteins associated with the spectrin-actin-ankyrin network change their conformation in different ways, they attract the lipids surrounding them in different ways. The protein-lipid domains formed in this case will be different, the density of the lipid bilayer can be represented as the superposition of two or more sublattices of inhomogeneous lipid density on top of each other, it is shown that the nature of lipid diffusion remains qualitatively the same, as for the model with a single inhomogeneity lattice. But in this case, hop diffusion can already be observed, in which nonlinear diffusion is replaced by periods of advection-diffusion. Advection is local in membrane, concentrated near protein-lipid domains, in which the increase in lipid density is greatest. The average displacement of particles during advection is higher for molecules that started from the region of lipid-lipid interactions. Analytically, a criterion has been obtained, under which hop diffusion can be observed in the experiment:

$$\frac{\left(\beta_2+\beta_3 q\right)^2}{\beta_2+\beta_3 q^2} \geq 4\left(1-\beta_2-\beta_3\right)$$

where $\beta_2=\tilde{D}_1 / D_0$ is the second lattice inhomogeneity coefficient, the third lattice inhomogeneity coefficient $\beta_3=\tilde{D}_2 / D_0$ and the ratio of the wave numbers of the two sublattices $q=k_2 / k_0$.

Conclusion: This model explains well on a qualitative level the experimental results of measuring the movement of lipids in the cytoplasmic membrane. It has been shown that the lateral diffusion of lipids in the cytoplasmic membrane is determined by structural changes in the membrane, the appearance or disappearance of a stationary periodic network of protein-lipid domains associated with the cytoskeleton.

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