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THE INFLUENCE OF AN CHARGE ADMIXTURE ON THE BINDING ENERGY OF AN ELECTRIC DIPOLES SYSTEM SIMULATING THE SURFACE LAYER OF A LIPID MEMBRANE – A COMPUTER MODEL

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The Monte Carlo method was used to investigate the influence of electric charge admixtures on the binding energy of a dipoles system simulating the surface layer of lipid membranes. A system containing 225 dipoles (15x15), which formed a flat rectangular and hexagonal centered matrix, was exposed to simulation. The number of the charges in relation to the number of the dipoles was altered within the range from 0 to 6%, whereas the values of the charges amounted to $Q = +1, +2, +4$, in arbitrary units. The dipoles forming the matrix were 0,3, 0,5, 1, 1,5, 2 nm in length. The simulation was carried out at 300 K. The results of the research point to an occurrence of the extremum of the binding energy for a precisely determined concentration of the charges. The value of the charge, in dependence on the size and dimension of the dipoles, was changing from 1 to 2,5%. Furthermore, it was found that the sizes of the charge, the type of the matrix, as well as the boundary conditions have a considerable influence on the shape of the curves that describe the dependence of the binding energy of a dipoles system on the concentration of admixtures.

Key words: membrane, computer model, ion admixture.

Cell membranes are built from lipids, proteins and water. The quantitative ratio of lipids to proteins amounts, on the average, to 50 particles of lipids per one particle of protein, while water makes for around 20% of the mass of the membrane [11]. Therefore, lipids constitute the considerable majority of the percentage composition of the membranes. Due to the amphiphilic properties, lipid membranes spontaneously form a bilayer in water environment, which is the structural core of the biological membrane. The most numerous lipids occurring in the membranes include phospholipids, and among them – lecithins. The polar head of a particle of lecithin contains a positively charged choline group and a negatively charged phosphate one. The electric charges of these groups are shifted in relation to each other, and because of that the lecithin head makes an electric dipole. It is known from the literature of the subject [1, 2] that the polar heads of membrane lipids form, in the bilayer, hexagonal centered structures, and that the axes of their dipoles are set almost parallel (at 4°) against the surface of the bilayer. The sizes of the polar heads of lecithin amount to about 1nm, the heads being able to freely rotate around the axis which remains perpendicular against the bilayer surface.

The electric interactions in the membrane surface layer have, as it may be supposed, a considerably strong influence on the stability of both the lipid bilayer and the whole cell membrane. The structure of the membrane in this area is the stiffest (the least fluid). From [3] it follows that electric dipoles of the lipid heads form ferroelectric domains that are separated by dynamic defects. The domain structure of the polar heads orders the setting of hydrocarbon chains neighboring on them. The ordering extends up to the 9th carbon in the chain. Charge admixtures, interacting with dipoles which form the surface layer of the membrane (at low concentrations), stiffen its structure (increase the binding energy), yet – after exceeding the given concentration – they weaken the energy (increase the fluidity of the membrane) [7, 8].

The aim of the present paper was to investigate the influence of charge admixtures on the binding energy of the system of dipoles simulating the membrane surface layer in dependence on the concentration of the admixture, the length of dipoles and the geometry of distribution of their symmetry centers (a hexagonal centered or rectangular matrix), as well as to investigate the influence of boundary conditions of the above-mentioned matrixes on the binding energy of the system. In both matrixes each dipole had a determined location, but was able to rotate freely around the axis set perpendicular against the matrix surface [4, 5].

The physical model of the surface layer of the membrane presented in this paper was thoroughly described in earlier works [4, 9, 10]. Therefore, we have presented here only a shortened description containing its basic assumptions.

Hamiltonian of a system of electric dipoles which are free to rotate around their own symmetry axes can be described with the equation:

$$H = H_1(L) + H_2(\varphi). \quad (1)$$

The first term of the Hamiltonian:

$$H_1 = \sum_{i=1}^N \frac{L_i^2}{2I}, \quad (2)$$

presents the kinetic energy of the system which depends on angular momenta L_i of individual dipoles with their moments of inertia I . The second term:

$$H_2 = \frac{e^2}{4\pi\epsilon_0\epsilon_r} \sum_{i<j}^N \left(\frac{1}{|r_{ij} + a_j - a_i|} - \frac{1}{|r_{ij} - a_j - a_i|} + \frac{1}{|r_{ij} - a_j + a_i|} - \frac{1}{|r_{ij} + a_j + a_i|} \right), \quad (3)$$

describes the potential energy of the system which depends on the spatial orientation of individual dipoles enforced by angles φ_i between the distinguished axis of the system and the direction of the dipole. Vectors r_{ij} are lattice vectors (connecting two lattice points) calculated with the inclusion of conditions of periodicity of the lattice, while vectors $a_i = [a \cos(\varphi_i), a \sin(\varphi_i)]$ point to the location of a positive dipole charge against its center. Any microstate of the system is determined through enforcing angular momenta of individual dipoles L_1, L_2, \dots, L_N and angles $\varphi_1, \varphi_2, \dots, \varphi_N$ (N – number of dipoles in the system). The space of states of the system is then $2N$ dimensional. Through notation of the volume element of this space by $d^N L d^N \varphi$ we can write the statistic sum of the system under consideration (Z) in the following way:

$$Z = \frac{1}{h^N} \int d^N L d^N \varphi \exp \left[-\frac{H(L, \varphi)}{kT} \right]. \quad (4)$$

The above sum can be presented as a product $Z = JQ$, where

$$J = \frac{1}{h^N} \int d^N L \exp \left[-\sum_{(i)} \frac{L_i^2}{2IkT} \right] = \left(\frac{2\pi IkT}{h^2} \right)^{\frac{N}{2}}, \text{ and } Q = \int d^N \varphi \exp \left[-\frac{H_2(\varphi)}{kT} \right]. \quad (5)$$

The first of the integrals in equation (5) was calculated analytically (Gauss integral). The second integral, because of the complexity of the interactions, was calculated by means of the numerical method.

The internal energy of the dipole system U equals the value of mean total energy and is expressed by the formula:

$$U = \langle H \rangle = \frac{\frac{1}{h^N} \int d^N L d^N \varphi H(L, \varphi) \exp[-\beta H(L, \varphi)]}{Z} = -\frac{Z'}{Z}, \quad (6)$$

where

$$\beta = \frac{1}{kT}, \quad Z' = \frac{\partial Z}{\partial \beta}.$$

Since $Z = JQ$, then

$$U = -\frac{Z'}{Z} = -\frac{(JQ)'}{JQ} = -\frac{J'}{J} - \frac{Q'}{Q} = \frac{1}{2} NkT + \langle H_2 \rangle. \quad (7)$$

In equation (7), the mean value of potential energy of the dipole system was denoted by $\langle H_2 \rangle$.

$$\langle H_2 \rangle = -\frac{Q'}{Q} = \frac{\int d^N \varphi H_2(\varphi) \exp[-\beta H_2(\varphi)]}{\int d^N \varphi \exp[-\beta H_2(\varphi)]}. \quad (8)$$

The mean value of potential energy $\langle H_2 \rangle$ was determined in the process of computer simulation through generating a sequence of system states (Markov's chain) that corresponds to the balance distribution in the canonical ensemble for the set temperature T . In order to generate such a chain Metropolis's method [6] was made use of. Elements of the sequence are formed by a random change in the current state of inclination angle of individual dipoles (the first state was also chosen at random). The probability of transition of dipoles from the current state φ to the new one φ' is given by the equation:

$$P(\varphi \rightarrow \varphi') = \begin{cases} 1, & \text{for } \Delta H_2 = H_2(\varphi') - H_2(\varphi) < 0 \\ \exp \left[-\frac{\Delta H_2}{kT} \right], & \text{otherwise} \end{cases}. \quad (9)$$

If the energy of the new state is smaller than that of the current state, then it is this former state that becomes accepted as a new current state. If the new state leads to a rise in energy, it is accepted with probability determined by Boltzmann distribution (9).

The research was conducted for a system of $15 \times 15 = 225$ dipoles admixed with point positive charges of different sizes $Q=1$, $Q=2$, $Q=4$ (in arbitrary units). The concentrations of the charges, in relation to the number of dipoles, was being changed within 0 to 6%. The dipoles were arranged in a flat hexagonal centered or rectangular matrix and were able to rotate around their own immovable axes set perpendicular against the matrix surface. The distances between the centers of the dipoles were twice

the dipoles length. The sizes of the dipoles were being changed within the range between 0,3 and 2 nm. The investigation was carried out for temperature equal to 300 K.

The computer simulation was begun with drawing, at random, a dipoles distribution (randomized distribution) and a location of admixtures which were substituted for the dipoles. Thus, the total number of elements in the matrix was constant, amounting to 225. At the first stage of the simulation, the potential energy of the system was calculated in a randomized state. Then, through a series of simulation-related steps the system aimed to reach the state of equilibrium, for which the energy obtained the lowest value. After the state of equilibrium settled down, the energy of the system oscillated (due to the temperature) around the mean energy, whose value was accepted as the final energy of the simulation. The measurements were taken ten times for each parameter and the final results were averaged. The computer-based investigation was conducted for two types of interactions between the components of the system: the first – non-periodical interactions – taking into account the boundary conditions of the matrix restricted by the number of dipoles, whereas the other – periodical interactions, where the matrix did not have the boundaries.

Fig. 1, 2, 3 A and B show the dependence of the relative potential energy E/E_0 of the dipoles system on the concentration of the charge $Q=1$ (Fig. 1), $Q=2$ (Fig. 2), $Q=4$ (Fig. 3), dipoles length, the geometry of the matrix and the type of boundary interactions (periodical and non-periodical).

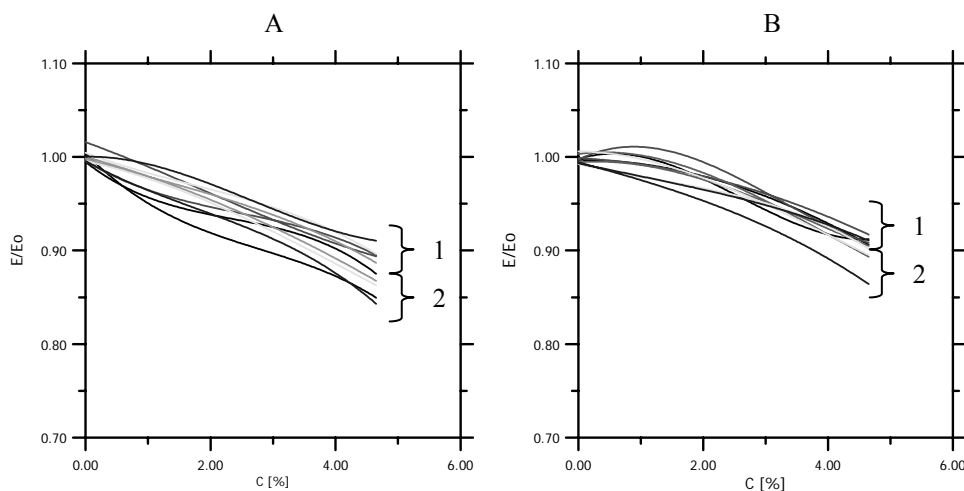


Fig. 1. Dependence of the relative potential energy (E/E_0) of a system of dipoles for the rectangular matrix (A) and hexagonally centered (B) one on the concentration of the charge $Q=1$. The family of curves (1) represents the energy of the dipoles system for non-periodical interactions, while the family of curves (2) – for periodical interactions. The sizes of the dipoles in both families had the values 0,3, 0,5, 1, 1,5 and 2 nm

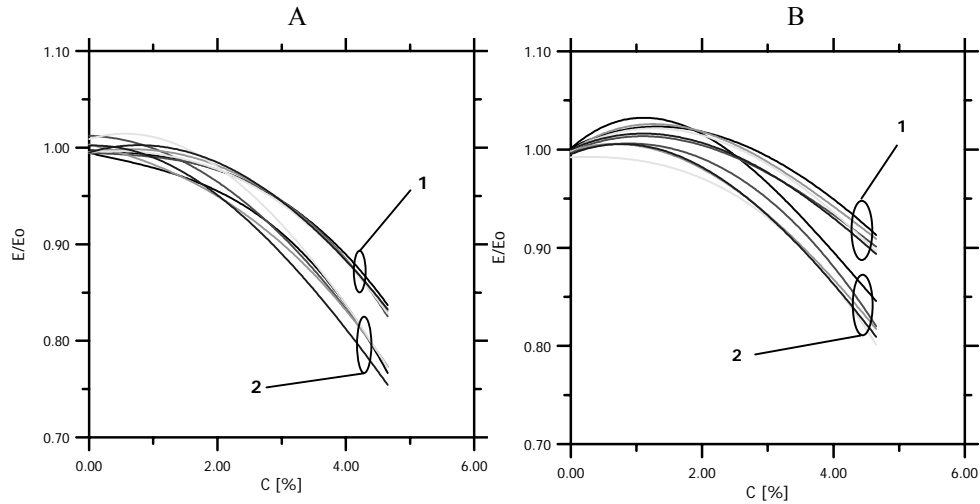


Fig. 2. Dependence of the relative potential energy (E/E_0) of a system of dipoles for the rectangular matrix (A) and hexagonally centered (B) one on the concentration of the charge $Q=2$. The family of curves (1) represents the energy of the dipoles system for non-periodical interactions, while the family of curves (2) – for periodical interactions. The sizes of the dipoles in both families had the values 0,3, 0,5, 1, 1,5 and 2 nm

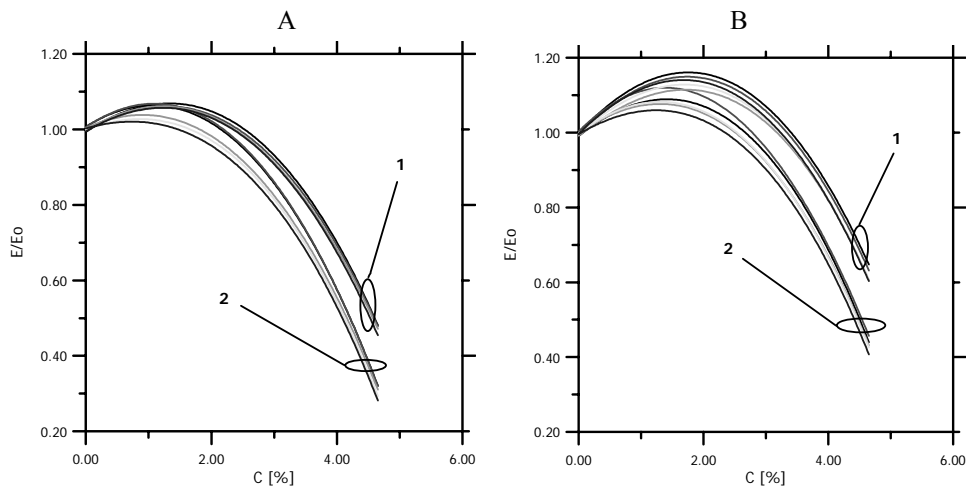


Fig. 3. Dependence of the relative potential energy (E/E_0) of a system of dipoles for the rectangular matrix (A) and hexagonally centered (B) one on the concentration of the charge $Q=4$. The family of curves (1) represents the energy of the dipoles system for non-periodical interactions, while the family of curves (2) – for periodical interactions. The sizes of the dipoles in both families had the values 0,3, 0,5, 1, 1,5 and 2 nm

On the basis of the conducted investigations, the following was found:

- The binding energy of systems admixed with ions forms extremums within the range of concentrations between 1–2,5% of ions in relation to the dipoles.
- The larger the admixture charge ceased the higher the value of the extremum.
- The position of the extremum moves towards the higher concentrations together with the value of the admixture charge.
- The dipoles arranged in the hexagonal matrix are far more sensitive to admixtures – the extremums are much clearer than in the case of the rectangular matrix.
- The sizes of the dipoles do not have any significant influence on the shape and height of the extremum of the binding energy.
- For the admixture charges $2Q$ and $4Q$ (Fig. 2 and 3) a clear separation between the families of curves was found: the upper family (1) for non-periodical interactions and the lower one (2) – for periodical interactions.
- The curves representing the binding energy of dipoles of the smallest sizes (0,3 nm) restrict the observed families from the top (correspond to higher values of energy), whereas the longest dipoles (2 nm) restrict these families from the bottom.
- For the admixture charge $1Q$, introduced into the rectangular matrix, no occurrence of the extremum of the binding energy was found.

The value of the charge and the geometry of the matrix had the strongest influence on the shape and the value of the extremum of the binding energy. Sizes of the dipoles only insignificantly affect the position of the extremum, while taking into account the condition of periodicity in boundary interactions influences the position of the extremum to a significant degree. The authors also conducted experimental research into lecithin liposomes, with the use of the ESR technique [7, 8] and found a marked influence of ion admixtures on the fluidity of membranes. The highest stiffening of the membrane was observed for concentrations of the admixture within the range 2–4%, which corresponds well to the presented theoretical model, since – as it can be supposed – the fluidity of the membrane is linked to the binding energy of its surface layer, which is built from electric dipoles. Inclusion, in computer simulations, of the conditions of periodicity of interactions between the components of the system causes lowering of the value of the binding energy in the whole of the range of the investigated admixture concentrations, in comparison with the energy of non-periodical interactions. The effect rises together with the rise in the size of the admixture charge being introduced into the dipoles system and also along with the rise in the admixture concentration. At 4% concentration of admixture charge of $1Q$ the decrease in energy amounted to about 5%, whereas in the case of charges with the value of $4Q$ – to about 25%.

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**ВПЛИВ ЗАРЯДЖЕНИХ ДОМШОК НА ЕНЕРГІЮ ЗВ'ЯЗКУ
ЕЛЕКТРИЧНИХ ДИПОЛЬНИХ СИСТЕМ, ЩО ІМІТУЮТЬ ПОВЕРХНЕВІ
ШАРИ ЛІПІДНИХ МЕМБРАН – КОМП'ЮТЕРНА МОДЕЛЬ**

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З використанням методу Монте-Карло досліджено вплив електрично-заряджених домішок на енергію зв'язку дипольних систем, що імітують поверхневі шари ліпідних мембран. Симульована система складалася з 225 диполів (15×15), які створювали плоску, прямокутну, гексагонально-центровану матрицю. Кількість зарядів відносно кількості диполів змінювалося в рамках від 0 до 6%, тоді як величини зарядів становили $Q = +1, +2, +4$ (у відносних одиницях). Диполі утворювали матриці з лінійними розмірами 0,3; 0,5; 1,0; 1,5; 2,0 нм. Розрахунки виконували за температури 300 К. Результати досліджень свідчать про наявність екстремуму в енергії зв'язку для точно визначеної концентрації зарядів. Величина заряду, залежно від розміру і протяжності диполів, змінювалася від 1 до 2,5%. Окрім того, з'ясовано, що величина заряду, тип матриці, а також граничні умови мають значний вплив на форму кривої, яка описує залежність енергії зв'язку дипольної системи від концентрації домішки.

Ключові слова: мембрана, комп'ютерна модель, іонна домішка.

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