Gas molecules could be transferred through the lipid bilayer by kinks-solitons

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Abstract. A hypothesis on the transfer of gas molecules through erythrocyte membrane by kink-solitons is discussed. Earlier it was supposed that gas molecules could be transferred through the lipid bilayer by kinks. It is accepted that kinks can emerge due to thermal vibrations. However, it remained unclear how the chaotic thermal vibrations can generate kinks moving along a hydrocarbon chain. According to the proposed hypothesis, kink-solitons appear under the simultaneous action of compressive lateral mechanical stresses and straining longitudinal mechanical stresses in the membrane. Compressive lateral stresses should have a certain value. This model explains a sharp increase in gas permeability of the membrane that occurs when erythrocyte passes through a microcapillary network, which is accompanied by substantially increased compressive lateral mechanical stresses.

1. Introduction

The transfer of gas molecules (O₂, CO, CO₂, NH₄) through erythrocyte membranes is an important physiological process. It was established experimentally that permeability of erythrocyte membrane to gas molecules is not lower than permeability of a water layer of the same thickness [1]. This is very strange because viscosity of the lipid bilayer, which constitutes a large part of the erythrocyte membrane surface, ranges from 10 to 60 cSt, while that of water is equal to 1 cSt. According to the Stokes-Einstein formula for the diffusion coefficient D, diffusion resistance of the lipid bilayer should also be higher than the corresponding value for the same water layer. This agrees with the measurements of oxygen molecule permeability through artificial monolayer lipid membranes. Permeability of such membranes was found to be much lower as compared to a water layer of the same thickness [2]. Presumably, the main flow of oxygen molecules in the membrane passes through membrane proteins. It was supposed that gases are transferred through erythrocyte membranes by aquaporin AQP1 proteins. Aquaporins are considered to be the proteins of water channels. By now, aquaporins transporting CO, CO₂, O₂ and NH₄ have also been found [3]. They facilitate the diffusion of gases through membranes.

A facilitated diffusion of gases is necessary for saturation of erythrocyte hemoglobin with oxygen in the capillaries of human lungs. In a quarter of a second, approximately one third of the oxygen transferred by erythrocyte penetrates into its cytoplasm [4]. There is another problem with gas exchange in the cardiovascular system. When erythrocytes move in arteries and veins, gas exchange is undesirable. It should occur when erythrocytes are passing through microcapillaries in tissues and through the lung alveoli. Otherwise, oxygen in the bloodstream increases the concentration of reactive
oxygen species (ROS), thus enhancing lipid peroxidation (leading to oxidative stress (OS)) in cell membranes of blood vessel walls. What is the mechanism of gas exchange control? In our opinion, one of the mechanisms can be related to the effect of mechanical stresses in erythrocyte membrane on permeability of the lipid bilayer to gas molecules.

The field of mechanical stresses in the biomembrane [5, 6] affects the function of membrane proteins [7, 8]. Mechanical stresses in membranes affect some functions of erythrocytes, for example, the erythrocyte ability to twist when passing through microcapillaries [9–11]. Mechanical stresses in membranes are affected by exogenous and endogenous factors, for example, hormones [12, 13], nanoparticles [14, 15], and blood plasma proteins [16].

The transfer of oxygen and carbon dioxide through native erythrocyte membrane differs from the passive gas diffusion through artificial lipid bilayers. The main distinction is that the erythrocyte cytoplasmic membrane contains proteins connected to a cytoskeleton. The cytoskeleton prevents expanding or contracting of the membrane, thus increasing its internal mechanical stresses. Changes in the conformation of such membrane proteins also create mechanical stresses in erythrocyte membrane. The general principle that native erythrocyte membrane in the bloodstream under physiological parameters undergoes a structural transition has earlier been established experimentally in vitro. Slight changes in the blood pH, concentration of hormones and temperature sharply alter the conformation of biomembranes and their functions by changing the field of mechanical stresses in biomembrane [12, 13]. We think that mechanical stresses can affect the gas permeability of biomembrane. This is another manifestation of the general principle.

Earlier it was supposed that diffusion of gases in the lipid bilayer can occur via kinks running along the hydrocarbon chains of phospholipids and moving gas molecules by their bends [17]. The mechanism underlying the appearance of such kinks was not considered. It is not clear how the appearance of kinks in the hydrocarbon chain is synchronized to move gas molecules along the chain. In our opinion, gas molecules can be transferred through the lipid bilayer not by any kinks, but rather by kink-solitons. The energy of kink solitons is generated under mechanical lateral compression of erythrocyte membrane when erythrocyte passes through microcapillary bloodstream and lung alveoli. This mechanism is discussed in our work.

2. Results and discussion

Erythrocytes can twist into cylinders when passing through microcapillaries. This increases longitudinal mechanical tensile stresses G in plasmatic membranes of erythrocytes and mechanical compressive stresses P that are perpendicular to the membrane plane. In this work, it will be demonstrated that the indicated processes raise the formation frequency of the kinks that push oxygen or carbon dioxide molecules through the membrane. Kinks acquire properties of the solitons running along hydrocarbon chains of a phospholipid molecule and pushing gas molecules. The transfer of gas molecules by kink solitons takes place in the tension zones of the lipid bilayer.

Following [18], let us consider the region of hydrocarbon chain of a phospholipid molecule with saturated bonds. Figure 1 displays the region of such hydrocarbon chain. Let us numerate each carbon atom: i is the number of a group of CH2 atoms, $\theta_i$ is the valence angle, and $\phi_i$ is the angle of internal rotation. Bond lengths and valence angles $\theta_i$ remain constant (figure 1). Conformation of the polymer molecule is determined by the angles of rotation around C-C bonds, or internal rotation angles $\phi_i$. These are the angles between two planes formed by the pairs of $i - 1$, i and i, i + 1 bonds.

In the trans conformation, all angles are equal to zero, and the hydrocarbon chain is a linear structure (figure 2a) [19]. Figure 2a displays the side view of the double hydrocarbon tails of phospholipid molecules in the trans configuration. Figure 2b displays the tails of phospholipid molecules during the passage of an erythrocyte through a microcapillary. Under the action of mechanical compression stress P and longitudinal tensile stress G, the hydrocarbon tail loses stability, its links begin to rotate, and a kink-soliton is formed in it. As a result of the compression of the membrane, its thickness decreases by h.
Figure 1. The region of hydrocarbon chain with saturated bonds: $i$ – the number of a group of CH$_2$ atoms, $\theta_i$ – the valence angle and $\varphi_i$ – the internal rotation angle.

Figure 2. a) The side view of the double hydrocarbon tails of phospholipid molecules in biomembrane, which are in the trans configuration. b) When the membrane passes through microcapillary, it is subjected to lateral mechanical compressive stress $P$ and longitudinal mechanical tensile stress $G$. The distance between adjacent double hydrocarbon chains increases, and force acts on each CH$_2$ group of the chain to turn it around the C-C bond by a certain internal rotation angle $\varphi_i$.

The kink-soliton moves by simultaneously rotating two CH$_2$ – groups no. $i$ and $i + 1$ around the instantaneous axis of rotation OA by the angle $\Psi_i$ (figure 3).

The equation of motion relative to the axis OA for a group of three links adjacent to the CH$_2$-group no. $i$, has the form:

$$ J \frac{\partial^2 \Psi_i}{\partial t^2} = N_{i1} + N_{i2} \tag{1} $$

where $J$ is the moment of inertia of atomic groups no. $i$ and $i+1$; $N_{i1}$ is the moment of forces created by the interaction of adjacent hydrocarbon chains; $N_{i2}$ is the moment of forces generated due to rotation of the atomic group around C-C bond. Let us consider the expressions for moments of forces $N_{i1}$, $N_{i2}$.
Figure 3. The kink moves by simultaneously rotating two CH$_2$ – groups no. $i$ and $i + 1$ around the instantaneous axis of rotation OA by the angle $\Psi_i$.

If the lipid bilayer does not have tension regions, the double hydrocarbon tails of phospholipid molecules in biomembrane are completely in the trans configuration (figure 2a). Hydrocarbon chains are located at equal distances from each other. The interaction forces between the adjacent tails balance one another. When erythrocyte passes through microcapillary, its membrane experiences lateral mechanical compressive stress $P$ and longitudinal mechanical tensile stress $G$. Figure 2b shows the tails of phospholipid molecules in the erythrocyte passing through microcapillary. Due to compression, the membrane thickness decreases by $h$, and a kink is formed in the hydrocarbon tail. The distance between double hydrocarbon chains of adjacent phospholipid molecules increases (figure 2b); therewith, the distance between two chains of one phospholipid molecule does not increase. In the plane going through double chains of one phospholipid molecule, a balance of the interaction forces between chains of adjacent phospholipids is disturbed, and force acts on each CH$_2$ group of the chain to turn this group around the C-C bond by a certain angle of internal rotation $\Psi_i$ (figures 3, 4). Figure 4 shows three successive positions of CH$_2$ groups no. $i$ and $i + 1$ upon turning axis OA to angle $\Psi_i$. In trans configuration $\Psi_i = 0$, while in gauche(+)-trans-gauche(-) configuration $\Psi_i = \pi$. In the top view of a phospholipid molecule, the dark point is the head of a phospholipid. One can see in figure 4 that the moment of forces generated by the interaction of adjacent hydrocarbon chains $N_{i1}$ reaches a maximum at $\Psi_i = \pi/4; 3\pi/4; 5\pi/4; 7\pi/4$ and is equal to zero at $\Psi_i = 0; \pi/2; \pi; 3\pi/4$. Indeed, at $\Psi_i = 0$ or $\pi$ the arm of force $\vec{F}$ is equal to zero. At $\Psi_i = \pi/2$ or $3\pi/2$ the force $\vec{F}$ is zero. Moment of forces $N_{i1}$ can be presented as $N_{i1} = -K_F \cdot \sin^2 \Psi_i$, where $K_F = \text{const}$.

Figure 4. Three consecutive positions of three links of the hydrocarbon chain when they rotate around the axis OA. When $\Psi_i = 0$ and $\pi$, force F tends to rotate two CH$_2$ – groups no. $i$ and $i + 1$ around the instantaneous axis of rotation OA. When $\Psi_i = \pi/2$ or $3\pi/2$ force F is zero.

The moment of forces $N_{i2}$ is created by the interaction of atomic group no. $i$ with adjacent atomic groups no. $i-1$ and atomic group no. $i+1$ with adjacent atomic groups no. $i+2$ (figure 3). It arises because of the barrier in the energy of interaction of neighboring atomic CH$_2$ groups, which appears when these groups rotate around C–C bonds. Conformations with $\Psi_i = 0$ and $\Psi_i = \pi$ are separated by the energy barrier with a height of about 12.5 kJ/mol [20]. The barrier arises as a result of the steric repulsion of closely spaced valence unbonded hydrogen atoms of the adjacent CH$_2$ groups. The energy minimum is carried out if two pairs of hydrogen atoms of neighboring CH$_2$ groups are in the crossed state ($\Psi_i = 0$ or $\pi$), and the maximum corresponds to the darkened conformations ($\Psi_i = \pi/2$ or $3\pi/2$). Thus, $N_{i2} = 2K_T \cdot \sin^2 \Psi_i$. 

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We complete the passage to the limit in equation (1), as in [18]. The OX axis should be directed along the hydrocarbon tails. The equation of motion, which determines the conformational dynamics of the chain, is obtained from (1) in the continual approximation (sine-Gordon equation):

\[ J \frac{\partial^2 \Psi}{\partial t^2} - (2K_T - K_F) \cdot \sin 2\Psi = 0 \]  

(2)

A solution is found as a function \( f \) of variable \( \xi = x \pm V \cdot t \), where \( x \) is the coordinate of OX axis directed along hydrocarbon chain, \( V \) is the kink-soliton velocity, and \( t \) is the time. The substitution in equation (2) and transformations give:

\[ \frac{JV^2}{2} \left( \frac{\partial f}{\partial \xi} \right)^2 + \left( \frac{2K_T - K_F}{2} \right) \cdot \cos 2f = W \]  

(3)

where \( W \) is the soliton energy. This is the equation of an oscillator moving in a potential well \( U(f) = 0.5(2K_T - K_F)\cdot \cos 2f \). At \( W < -0.5(2K_T - K_F) \) the equation does not have a solution, whereas at \( -0.5(2K_T - K_F) < W < 0.5(2K_T - K_F) \) the oscillator generates periodic vibrations in a potential well. At \( W = 0.5(2K_T - K_F) \) the solution describes an isolated perturbation tending to constant values at infinity: \( \lim_{\xi \to \pm \infty} f(\xi) = \text{const} \). In this case, a solution of equation (3) is as follows [18]:

\[ \operatorname{tg} \left( \frac{f}{2} \right) = \exp \left\{ V \cdot (\xi \pm \xi_0) \right\} \]

(4)

where \( \gamma = \frac{4W}{J \cdot V^2} \cdot \xi_0 = \text{const} \).

Figure 5 displays the dependence of \( f \) on \( (x-V\cdot t) \).

For the appearance of kink-solitons, the work \( A \) of pressure \( P \) compressing the membrane in the transverse direction must be equal to the energy of the kink-soliton \( W \) and the kinetic energy carried by the kink soliton gas molecule with mass \( m \). The phospholipid transverse to the plane of the membrane by pressure \( P \) is compressed by \( \Delta \), then the phospholipid is flattened back, and a kink-soliton runs along it.

![Graph](image-url)

**Figure 5.** The solution of (4) at \( \sqrt{\gamma} = V = 1 \) 

h is the kink width.
Work A on squeezing one phospholipid is transferred to the kink-soliton. \[ A = \frac{E_{\perp} \cdot S \cdot \Delta^2}{2L}, \] where \( S \) is the cross-sectional area of the phospholipid, \( L \) is the membrane thickness, \( E_{\perp} \) is the Young's modulus of transverse compression (figure 2b). In addition, the width of the kink should have a certain value, equal to \( h \) (figure 5). At this distance, the angle of rotation \( \Psi \) changes from \( \pi/8 \) to \( 3\pi/8 \). We write these conditions:

\[
W = \frac{2K_F - K_E}{2L}
\]

\[
A = \frac{E_{\perp} \cdot S \cdot \Delta^2}{2L} = W + \frac{mV^2}{2}
\]

\[
V^2 = \frac{4W}{J} \cdot \left( \frac{h}{1,014} \right)^2
\]

Let us estimate the speed of movement of the kink-soliton \( V \) and the critical compression of the phospholipid \( \Delta \) from (5). To do this, we make the estimates of the constants \( K_F, K_T \). The force \( F = E_{\|} \cdot e \cdot S \), that tends to turn the \( \text{CH}_2 \) – groups no. \( i \) and \( i + 1 \) around the axis OA through a certain rotation angle \( \Psi_i \) (figure 3, 4) is estimated using the Young modulus of the longitudinal extension \( E_{\|} \) of biomembranes, \( S_1 \) is the area occupied by two \( \text{CH}_2 \) – groups, \( e \) is the relative elongation of the membrane. Then, for the moment of force \( N_{i1} \), created by the interaction of neighboring hydrocarbon chains, the constant \( K_F = F \cdot e \), where \( e \) is the length of the C–C bond. Let us assume that \( E_{\|} = 5 \cdot 10^8 \text{ N/m}^2, e = 0.01, S_1 = 0.098 \text{ nm}^2 \) \( [20] \), we obtain \( K_F = 0.972 \cdot 10^{-22} \text{ N} \cdot \text{m} \). The KT constant is determined by the energy barrier, \( K_T = 2.080 \cdot 10^{-20} \text{ N} \cdot \text{m} \). For the C–C bond, the polarizability is \( \beta = 1.25 \cdot 10^{-30} \text{ m}^3 \) \( [20] \). The energy of a kink-soliton is \( W = 2.075 \cdot 10^{-20} \text{ J} \), the velocity of a kink-soliton is \( V = 1092 \text{ m/s} \). The magnitude of the critical compression of the phospholipid \( \Delta = 1.827 \text{ nm} \).

When red blood cells pass through arteries and veins, whose diameter is larger than the size of red blood cells, longitudinal mechanical compressive stresses prevail in the erythrocyte membranes \( [12, 13] \). There are no conditions for the formation of kink solitons. The permeability of the membrane for gas molecules is low. To pass through the microcapillary bed, where the diameter of the microcapillaries is less than the diameter of the red blood cells, the red blood cell must curl into a cylindrical tube. The erythrocyte membrane begins to act transverse compression \( P \) and the longitudinal mechanical tension \( G \) (figure 2). In addition, contractions of smooth muscle cells of microcapillaries occur with great frequency, resulting in radial mechanical movements of the walls of microvessels \( [21] \). The conditions for membrane compression to the critical value \( \Delta \) from (5) arise, kink-solitons start moving along the hydrocarbon tails of phospholipids, moving the gas molecules with their bends. The permeability of the erythrocyte membrane increases dramatically.

**Conclusion**

Erythrocyte membrane is involved in the regulation of gas exchange between cell and its environment. One of the control methods can be the effect of mechanical stresses in the membrane on permeability of the lipid bilayer to gas molecules. This is achieved using kink-solitons moving along the hydrocarbon tails of phospholipids. Kink-solitons emerge if a combination of the external lateral compression \( P \) and the longitudinal mechanical tensile \( G \) occurs there. Such a combination appears only when erythrocyte passes through microcapillaries in tissues and through the lung alveoli. This mechanism reduces the oxygen amount penetrating into the bloodstream in other regions of the cardiovascular system. This decreases the blood concentration of reactive oxygen species (ROS), thus suppressing lipid peroxidation (leading to oxidative stress (OS)) in cell membranes of blood vessel walls.
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