Human red blood cells′ physiological water exchange with the plasma

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Abstract

In the present paper, fundamental issues related to the mechanisms of human red blood cells' physiological water exchange with the plasma (for the stationary conditions) have been discussed. It has been demonstrated, on the basis of mechanistic transport equations for membrane transport that red blood cells are capable of exchanging considerable amounts of water with the plasma. Water absorption is osmosis-driven, and its removal occurs according to the hydromechanics principle, i.e. is driven by the turgor pressure of red blood cells. This newly-acquired knowledge of these issues may appear highly useful for clinical diagnosis of blood diseases and blood circulation failures.

Key words: human red blood cells, cell membrane, water exchange, cytoplasm, plasma, transport equations.

Introduction

Human red blood cells, like any other living cells of the human body, must continue to exchange water, as well as other solutes, with their surroundings. To be precise, the erythrocytes must absorb water as well as other necessary dissolved substances from the plasma (i.e. their surroundings), and simultaneously remove both water and redundant metabolites. This physiological exchange of water and dissolved substances occurs across the erythrocyte cell membrane, with its active participation. It must be stressed here that the mechanisms of this exchange appear to be highly complex [1-7]. This complexity is markedly heightened by the processes related to erythrocyte participation in the removal of carbon dioxide from the entire body, and the supply of oxygen to all the body's living cells. These very problems appear to be very sophisticated, difficult to investigate and little known.

In the present article, which initiates a certain research cycle concerning these issues, we shall necessarily limit our considerations to the issues of red blood cells' exchange of water only with the plasma. We shall be here interested in the so-called stationary water exchange, i.e. the exchange which occurs with the red blood cells maintaining constant volumes ($V=$const.). This restriction of the research problem results from the fact that the non-stationary exchange ($V\neq$const.) may be explained on the basis of the equations of the Kedem-Katchalsky (KK) thermodynamic formalism [8,9]. However, with the help of these equations, it is not possible to interpret the stationary water exchange [10]. This is caused by the fact that in the KK formalism one does not go into the microscopic structure of porous membranes, whereas real membranes do have specific structures. In fact, the membranes are porous. They have certain pores (channels) which are permeable to water and other solutes. Moreover, porous membranes may be divided into homogeneous and heterogeneous [11-15]. A membrane is homogeneous in terms of transport properties if its pores do not vary in their linear dimensions (cross-section radiuses). A membrane, in turn, whose pores do vary in their linear dimensions, is to be treated as heterogeneous. At this point, it must be explained that cell membranes, erythrocyte cell membranes included, are increasingly perceived as heterogeneous porous structures [16-27]. Under the circumstances, for the purposes of investigation into the stationary physiological water exchange by human red blood cells, the equations of the mechanistic substance transport formalism [11-15] shall be applied. These equations apply unrestrictedly to any porous membranes, both homogenous and heterogeneous ones.

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These mechanistic transport equations have the following forms:

1) $$J_{vM}^{(1)} = L_p \Delta P - L_p \sigma \Delta\Pi$$

2) $$j_{sM} = \omega_d \Delta\Pi + (1-\sigma)\bar{c}_s L_p \Delta P$$

or $$J_{vsM} = \omega_d \bar{V}_s \Delta\Pi + (1-\sigma)\bar{c}_s \bar{V}_s L_p \Delta P$$

where J_{vM} is the volume flow; J_{vsM} and j_{sM} are solute flows; L_p, σ and ω_d are coefficients (of filtration, reflection and diffusion permeability of the solute); ΔP and $\Delta\Pi$ – pressure differences (mechanical and osmotic); $\bar{c}_s \approx 0.5(C_1+C_2)$ – mean concentration of the concentrations C_1 and C_2; $\bar{V}$ is the solute molar volume.

The flow J_{vM} is given by the formula:

(3) $$J_{vM} = J_{va} + J_{vb}$$

while (4) $$J_{va} = L_{pa}\Delta P - L_{pa}\Delta\Pi,$$

(5) $$J_{vb} = L_{pb}\Delta P,$$

where $J_{va} = J_{vwa}$ is the volume flow of water which permeates across the semi-permeable pores of the membrane, whose filtration coefficient amounts to L_{pa}. The flow J_{vb}, in turn, is the volume (hydromechanical) flow of the solution pumped across the permeable pores of the membrane (permeable to water and a given solute). The parameter L_{pb} here is the filtration coefficient of these permeable pores. Within the mechanistic transport formalism, the following relations are satisfied:

(6) $$L_p = L_{pa} + L_{pb},$$

(7) $$L_{pa} = \sigma Lp,$$

(8) $$L_{pb} = (1-\sigma)\, L_p$$

and (9) $$\omega_d = (1-\sigma)\bar{c}_s L_p$$

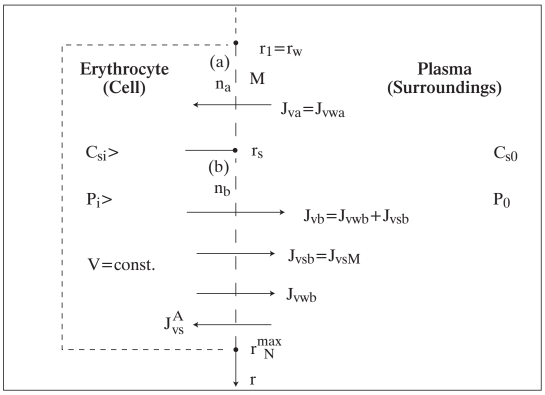
By applying the equations for mechanistic transport formalism, we shall demonstrate in the present paper that human red blood cells can, under stationary conditions, exchange considerable amounts of water with the plasma. This adds a new dimension to the investigations into stationary water exchange by living cells. This aspect of the research appears to be very significant from the medical viewpoint, especially in the diagnosis of blood disease as well as blood circulation failure.

Cell membrane as heterogeneous porous structure

The cell membrane performs several functions which are fundamental to the cell's life. One of these pertains to controlled water permeability. The fundamental character of this function results from the fact that each living cell – in order to live – must (as has been stated in the Introduction) continue to exchange water with its surroundings. This exchange occurs across the cell membrane, and with its active participation. In this context, attention must be drawn to the fact that in the light of the progressing biophysical and biomechanical research, the cell membrane is increasingly perceived as a porous structure. Namely, it has certain channels (pores) which are permeable to water. By these pores, we mean the channels created by transport proteins (aquaporins) [5-7,18-21], the pores created by some antibiotics [5,6,27], as well as the pores which occur in the lipid bilayer (Korohoda [22]). The porous structure of the cell membrane is also provided by ion channels across which (when open) ions may permeate. Suffice it to say at this point that these channels have hydrophilic inner walls and are filled with water [5-7,20,23,25,26]. In view of this, they should be permeable to water (when open), as well as to certain fine-molecule solutes.

From the above-quoted works, it follows that the pores of the cell membrane which are permeable to water vary in their linear dimensions. Consequently, this membrane may be treated as a heterogeneous porous structure. That pertains also to the cell membrane of human erythrocytes.

Figure 1. **Model of an erythrocyte cell and its surroundings (M – replacement cell membrane; C_{si}, C_{s0} – concentrations; P_i, P_0 – mechanical pressures; r_w and r_s – molecule radiuses of water and the solute; r_n^{max} – maximum pore radius; V – cell volume; $J_{va} = J_{vwa}$, J_{vb}; J_{vwb}, $J_{vsb} = J_{vsM}$ – flows)**



Research system. Equation describing water absorption

In order to consider the issue of stationary water exchange by human red blood cells, let us consider a model research system as presented schematically in *Fig. 1*. In this system, the investigated erythrocyte is found in the plasma which constitutes its surroundings. In order to facilitate the solutions, let us assume that the entire cell membrane of the erythrocyte (which has the number N of pores with varying linear dimensions) is represented by the replacement membrane M, which is located to the right of the cell. In this membrane, all the pores (N) have been, for the sake of the model, arranged in such a way that the smallest of them ($r_1 \geq r_w$) are found at the top, while the largest ones r_N^{max}– at the bottom. Let us also assume that the inside of the erythrocyte is actively penetrated by the volume flow J_{vs}^{A} of a certain given solute (s). Let the radius r_s of this solute's molecules be contained in the value interval $r_1<r_s<r_N^{max}$.

In the situation at issue, the membrane M may, in accordance with the idea of the mechanistic membrane transport formalism [11-15], be ascribed with the filtration coefficient L_p, the reflection coefficient σ (contained in the interval $0<\sigma<1$) as well as the diffusion permeability coefficient ω_d for the substance (s). It can also be divided into part (a) which contains n_a semi-permeable pores impermeable to the substance (s), and part (b) which contains $n_b=N-n_a$ of pores permeable to the molecules of the said substance. We can also ascribe to these parts the filtration coefficient L_{pa} and L_{pb}, as well as the reflection coefficient $\sigma_a=1$ and $\sigma_b=0$ respectively [11-15]. In connection with the existence of the flow J_{vs}^{A}, it is legitimate to assume that the concentration C_{si} of the substance (s) inside the cell is greater than the concentration C_{s0} of this substance in the surroundings ($C_{si}>C_{s0}$). Consequently, on the membrane M, the concentration difference $\Delta C_s=C_{si}-C_{s0}$ will appear, and so will the osmotic pressure difference $\Delta\Pi=RT(C_{si}-C_{s0})$. Driven by the pressure difference ΔΠ, water shall permeate into the cell, causing an increase in the mechanical pressure P_i inside the cell. Under stationary conditions, P_i shall be constant and greater than the pressure P_0, which occurs in the cell's surroundings ($P_i>P_0$). Suffice it to say that under stationary conditions, on the membrane, a constant osmotic pressure difference shall appear (ΔΠ=const.), together with the constant mechanical pressure difference ($\Delta P=P_i-P_0=$const.).

The volume flow J_{vwa} of water (w), which permeates across part (a) of the membrane, is given by the formula:

$$J_{va}=J_{vwa}=L_{pa}\Delta P-L_{pa}\Delta\Pi.$$

Considering the formula (7) as well as the formula below, quoted from the work [16], i.e.:

$$\Delta P=\bar{\sigma}\Delta\Pi,\quad \text{where } \bar{\sigma}=\frac{\sigma+(1-\sigma)c_sV_s}{1-(1-\sigma)c_sV_s} \tag{10}$$

we obtain

$$J_{vwa}=L_p\sigma(\bar{\sigma}-1)\Delta\Pi=L_p\sigma(\bar{\sigma}-1)RT(C_{si}-C_{s0}) \tag{11}$$

This is the sought formula for the flow J_{vwa} of water absorbed from the surroundings by the erythrocyte.

Equation describing water removal

In order to consider the problem of water removal by the investigated model erythrocyte (which functions under stationary conditions, i.e. at constant volume), let us consider the volume flow J_{vb} which permeates across Part (b) of the membrane M (*Fig. 1*). The reflection coefficient of this part of the membrane amounts to $\sigma_b=0$, and the volume flow which permeates across it is given by the formula:

$$J_{vb}=L_{pb}\Delta P. \tag{12}$$

Table 1. **Figures and calculation results for cell membranes of human erythrocytes**

No	Solute (s)	L_p x 10^{12} [m^3/N·s]	σ	$\bar{V}_s$ x 10^3 [m^3/mol]	Source	J_{vwa} x 10^8 [m/s]	J_{vwb} x 10^8 [m/s]
I	II	III	IV	V	VI	VII	VIII
1	Ethylene glycol	0.92	0.63	0.0566	Katchalsky and Curran [9]	-5.29	5.29
2	Urea	1.27	0.55	0.042	Sha'afi and Gary-Bobo [24]	-7.77	7.77

Other data: $C_{si}=150$ [mol/m^3]; $C_{so}=50$ [mol/m^3]; $\bar{c}_s=100$ [mol/m^3]; $R=8.3$ [N·m/mol·K]; $T=300$ [K]

Hence, having made allowances for the expression (7), we have:

$$J_{vb}=(1-\sigma)L_p\Delta P. \tag{13}$$

In the mechanistic formalism for membrane transport, the flow J_{vb} is given by the formula:

$$J_{vb}=J_{vwb}+J_{vsb}, \tag{14}$$

where J_{vwb} is the volume flow of water (w), and J_{vsb} – the volume flow of the solute (s). Therefore, due to introducing the notation $J_{vsb}=J_{vsM}$, the formula (14), having taken into account the expression (13), assumes the following form:

$$(1-\sigma)L_p\Delta P=J_{vwb}+J_{vsM}=J_{vwb}+J_{vsM}\bar{V}_s \tag{15}$$

since $J_{vsM}=j_{sM}\bar{V}_s$.

Hence, having made allowances for Eqs. (2), (10) and (15), we finally find the sought expression for the flow J_{vwb} of the water removed by the cell. Its form is as follows:

$$J_{vwb}=(1-\sigma)[(1-\bar{c}_s\bar{V}_s)\bar{\sigma}-\bar{c}_s\bar{V}_s]L_pRT(C_{si}-C_{s0}). \tag{16}$$

Results of quantitative research into water exchange by red blood cells

For the purposes of the present paper, the most reliable experimental figures pertaining to transport properties of the human erythrocytes have been selected from literature. The results of this papers have been presented in *Tab. 1*, and they comprise the numerical values of filtration coefficients L_p and reflection coefficients σ of these cells' membranes for two solutes (ethylene glycol and urea). These figures have been quoted after Katchalsky and Curran [9], as well as Sha'afi and Gary-Bobo [24]. They concern cell membranes of statistical human erythrocytes and may be considered encyclopaedic data. By applying these data, as well as the formulas (11) and (16), the numerical values of the flows J_{vwa} of the absorbed water and the flows J_{vwb} of the removed water for the investigated membranes have been calculated. These values have been entered into columns VII and VIII of *Tab. 1* respectively.

The obtained values for these flows are relatively large. This testifies to the fact that – in order to perform their life functions – red blood cells must, and can, continue to absorb and remove relatively large amounts of water. Water absorption occurs according to the osmosis principle, and removal is driven by the turgor pressure of the erythrocytes.

Conclusions

If the red blood cells of the human body are to be able to perform their life functions, they must (just like any other living cells of the body) continue to absorb water from their surroundings, and simultaneously remove it into these very surroundings. Within the present paper, we have shown – by applying the mechanistic equations for membrane transport of substances – that human red blood cells are capable of exchanging considerable amounts of water with the plasma under stationary conditions (at its constant volume). Water absorption occurs according to the osmosis principle. Its removal, in turn (realized simultaneously with its absorption), is driven by turgor pressure of the erythrocytes. This interpretation of mechanisms of this exchange is a complete novelty. The following work opens some new research possibilities.

The Authors of the present paper believe that the herein discussed research results may be of interest and significance not only in the medical and cognitive fields, but also in terms of their clinical aspect. The comprehension of the biophysical mechanisms of physiological absorption and removal of water (as well as a variety of solutes) by red blood cells may prove extremely useful for the diagnosis of blood diseases and circulation disorders. A more detailed consideration of these subjects will be presented in the next paper concerning regulation of physiological water exchange between human red blood cells and plasma.

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