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PHYSICS IN MEDICINE AND ECONOMY OF CONTEMPORARY SOCIETY

This paper describes the main methods of separating blood into components. The most common methods used in medicinal practice include centrifugation and filtration. Currently, there has been a lot of research on the application of ultrasound as the new, innovative method of separation of blood components. Ultrasound use is a theoretically elaborated method and experimental research is in process with the aim of its implementation in medical diagnostics. Contemporary societies are aware of the importance of findings of physics as well as of the fact that our everyday life is strongly connected to physics and to technical devices that have been created on the basis of its fundamental laws.

Keywords: laws of physics, human blood, centrifugation, filtration, acoustic standing wave, medical applications of ultrasound

INTRODUCTION

Physics is a cornerstone of contemporary economy, civilization and culture. It makes it possible to learn about environment and discover natural laws from the smallest particles to the entire universe. Technical sciences make use of findings of physicists and present application possibilities of physics in various sectors of commerce, economy and medicine. Laws and terms of physics are also used to explain biological processes. In the 21st century physics has become a driving force for the scientific, technological and economic development of the entire world.

Diagnostic medicine is based on physical sciences due to which it is possible, inter alia, to precisely specify the composition of human blood. Blood structure allows for a separation of red cells from plasma. Since blood cells perform a variety of biological functions and take part in many disease processes, they are widely researched and, therefore, it is essential from the point of view of diagnostics to define blood composition [1]. Recently, researchers from all over the coun-

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try have been involved in developing cooperation with economic environments which are equally interested in working with scientific entities. Physics' contribution is, furthermore, of great importance for solving economic, civilizational and medical problems.

This paper presents an analysis of physical processes underlying traditional methods of blood separation as well as it outlines an innovative method that makes use of ultrasound [2].

The conventional methods for separating blood components include centrifugation and filtration. These methods are a cornerstone of contemporary diagnostic medicine being subject to constant improvements. New, innovative and efficient methods are also sought. One of them is blood separation using ultrasound with parameters selected appropriately to the physical parameters of blood components [3, 4].

This topic is now subject of an extensive research both theoretical and experimental.

1. HUMAN BLOOD – COMPOSITION, PROPERTIES, CHARACTERISTICS

Since blood constantly flows through the human organs, it is an important source of information on the body condition and a fundamental diagnostic specimen which can be easily and safely taken from the patient. It is after losing 30% of the total blood volume that blood loss is dangerous and life-threatening [5].

Blood is a suspension of erythrocytes, platelets and leukocytes in blood plasma. Plasma is composed of water (approx. 90%), organic materials (mainly proteins), organic compounds (such as glucose) and inorganic materials (mainly chlorine and sodium ions). The ratio of the volume of erythrocytes to the total volume of blood is called hematocrit (HCT). Hematocrit value is expressed as a percentage. The normal hematocrit for adult women ranges from 37 to 47% whereas for adult men from 42 to 54% [5].

Marure erythrocytes have round, biconcave shape and an average diameter of 7 to 7.5 micrometers [5]. They have high elasticity due to which they become deformed while flowing through narrow capillaries.

Blood and its components play many important roles in the human body and all life processes.

Human blood is known as a liquid connective tissue and it performs many important functions such as coagulation, transportation and thermoregulation. Transportation is mostly related to oxygen transport to the cells and removal of carbon dioxide from organs. In addition, blood removes metabolic waste products such as uric acid. High water content in blood helps to ensure thermal regulation of the body.

The principal function of red cells is bonding of oxygen and its transport to tissues as well as transport of carbon dioxide from tissues to the respiratory organs. Erythrocytes are produced by bone marrow that generates about 200 billion of new red blood cells every day with maximal lifespan of 120 days [5].

An important parameter of every liquid is viscosity defined as a fluid's internal resistance to flow. Viscosity η is the ratio of shear stress τ and shear rate γ [6]:

$$\eta = \frac{\tau}{\gamma} \tag{1}$$

The SI unit for viscosity is the Pascal-second $1\ \mathrm{Pa \cdot s} = \frac{1\ \mathrm{kg}}{1\ \mathrm{m \cdot s}}$. Shear stress τ (applied parallel to the material) is defined as the ratio of the force causing displacement of layer to the material surface over which the force is applied:

$$\gamma = \frac{T_F}{S} \tag{2}$$

Shear rate is the ratio of layer displacement velocity and distance between layers: $\tau = \frac{v}{x}$.

According to Newton's Law, the friction force between two layers of a fluid is directly proportional to the difference in velocity of the displacing layers Δu and inversely proportional to the distance between the layers Δx; and it also depends on the viscosity of a fluid η.

$$F_T = \eta S_P \frac{\Delta u}{\Delta x} \tag{3}$$

where: S_P – plate surface. Whole blood is a non-Newtonian fluid i.e. its viscosity is not constant (it depends on the shear rate γ), hence it does not follow the Newton's Law.

The Table 1 presents the viscosity of some physiological fluids [6].

Viscosity of water in the temperature of 20°C is $\eta_0 = 1.0 \cdot 10^{-3} \frac{\mathrm{Ns}}{\mathrm{m}^2}$. Some of the important factors affecting viscosity of blood include:

- shear rate – viscosity increases with the decrease of shear rate;
- temperature – with the rise of temperature viscosity decreases;
- HCT – the lower hematocrit, the lower viscosity.

Blood is a heterogeneous mixture.

Table 1. The viscosity of some physiological fluids [6]

Fluid	$\frac{\eta}{\eta_0}$ on average	η, $\frac{\mathrm{Ns}}{\mathrm{m}^2}$
Whole blood	4.75	$4.75 \cdot 10^{-3}$
Plasma	2.01	$2.01 \cdot 10^{-3}$
Serum	1.88	$1.88 \cdot 10^{-3}$

2. FALLING OF BLOOD CELLS IN THE GRAVITATIONAL FIELD

Spontaneous fall of the blood cells is known as sedimentation. The process of sedimentation is a result of gravitational force and begins just after taking blood sample from a patient. Because of their heaviness erythrocytes fall to the bottom of the tube creating dark purple suspension which is approximately 45% of the total volume [5]. Above the layer of red cells, a creamy buffy coat is created by leucocytes and platelets.

The next layer is made by plasma which is a straw coloured liquid component constituting not more than 55% of the tube volume. It is after more than ten hours that sedimentation ceases.

In order to accelerate this process, laboratory centrifuges are used for separation of blood into components by spinning a sample with an anti-coagulant (compound preventing from clotting and enabling centrifugation of serum). Measuring the erythrocyte sedimentation rate (ESR) is known as Biernacki's Reaction (OB) and it is one of the most common tests taken.

The value of ESR depends on many factors ranging from 7 to 15 mm/h for adult women and from 5 to 10 mm/h for men [5]. The test should be performed at a constant temperature (around 20°C) without exposure to any external stimuli. Sedimentation rate while spinning depends on the protein content as well as the shape, size and quantity of red blood cells.

3. CONVENTIONAL METHODS FOR SEPARATING BLOOD INTO COMPONENTS

3.1. Centrifugation

Centrifugation is one of the traditional methods for separation of blood into components and it is based on the application of the centrifugal force [1]. The process uses differences in density of cells subject to test. A centrifuge is equipped with a rotor that regulates the velocity of spinning. Since the temperature affects separation of blood components significantly, thermoregulation systems are applied to keep temperature constant.

An important part of a centrifuge is a vacuum chamber in which a rotor is installed. The vacuum eliminates friction that heats the rotor when in contact with

air. Centrifugation requires samples to be put in hermetically sealed containers. While spinning, centrifugal force that is hundreds of thousands times bigger than gravity is created in rotor.

Thanks to centrifugation it is possible to shorten the time of blood fractionation. Specific parameters must be set to carry out the whole process properly. During validation of the process parameters must be modified in a way that ensures compliance of blood components with quality control standards.

Some types of centrifuges are equipped with additional functions such as acceleration of rotating or stop function [1].

3.2. Filtering

Membrane is a continuous phase which forms an obstacle for the components of a solution [7]. Particles which flow through the membrane at different velocity are retained by permeate. The process takes place in membrane module to ensure the flow of separated fluid in parallel or perpendicular direction to the membrane surface. For the purposes of dialysis crossflow filtration is used in which the feed solution flows parallel to the membrane surface while the direction of solution flow and permeate is perpendicular. Apart from permeate, retentate is obtained (feed solution without components that went to the permeate).

In dialyses porous membranes are used (Fig. 1) in which the separation is based on sieve effect and the factor determining effective separation is the size of pores. Transportation through membrane is due to the application of a proper driving force which for membrane processes is usually the difference in concentration, pressure, electric potential or temperature.

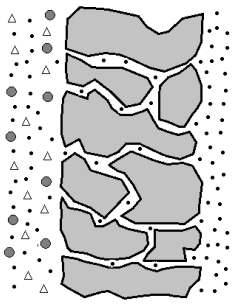

Fig. 1. Structure of porous membrane.
Own elaboration based on [7]

Membrane performance is characterized by two parameters:

- permeate stream describing membrane efficiency;
- efficiency characterizing membrane filtration capacity.

Permeate stream J_i is one of the following parameters: weight, volume or number of moles of a substance P_i, which passes through unit surface area of a membrane S_m per unit time [7]:

$$J_i = \frac{P_i}{S_m t_p} \tag{4}$$

expressed in the following unit, $\frac{\text{kg}}{\text{m}^2 \cdot \text{s}}$.

Membrane effeciency is defined by the following parameters: selectivity β or rejection coefficient R_r. Selectivity β is defined as the ratio of permeability of components of a fluid through the membrane and it is expressed by the following equation [7]:

$$\beta_{\frac{A}{B}} = \frac{y_A}{y_B} \cdot \frac{x_B}{x_A} \tag{5}$$

where: y_A, y_B – concentration of component A, B in permeate; x_A, x_B – concentration of component A, B in feed solution.

Rejection coefficient R_r is defined by the following equation [7]:

$$R_r = \frac{C_n - C_p}{C_n} = 1 - \frac{C_p}{C_n} \tag{6}$$

where: C_n – concentration of a given component in feed solution; C_p – concentration of a given component in permeate.

Membranes are used for adhesive and adsorbent filters to separate leucocytes and erythrocytes from the whole blood. Membrane with a proper diameter of pores is an important component of dialyzers which clean blood from contaminations in case of renal insufficiency.

4. INNOVATIVE METHOD OF SEPARATING BLOOD INTO COMPONENTS WITH THE USE OF ULTRASOUNDS

Ultrasounds are mechanical waves (elastic waves) of frequency higher than 20 kHz with the upper limit of 10 GHz. The range of frequency of different elastic waves is presented in Fig. 2.

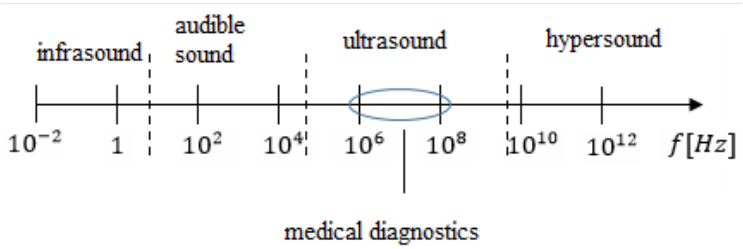

Fig. 2. Frequency range of ultrasound used in medical diagnostics.
Own elaboration based on [8]

The effects of ultrasound are divided into passive and active. Passive use of ultrasound consists in the use of ultrasound wave of low intensity that does not destroy the wave bearing medium. Passive effects of ultrasound waves are used in medical and technical diagnostics.

Active ultrasound involves the use of waves of medium and high intensity. Such waves cause chemical, biological and physical changes of a medium in which they are spread out. Active effects of ultrasound cause irreversible changes of the medium and are used, for instance, in medical therapy. Media in which waves are spread out may be divided into two groups: ideal and real ones.

In ideal (lossless) media there is no attenuation of waves whereas in the real ones the waves are absorbed. Due to heterogeneity of real media the waves are dispersed. Such heterogeneity may result from contaminations, defects in structure or internal stress. If attenuation is low, it might be ignored and the medium may be treated as an ideal one.

Dispersion of ultrasound in blood is (in some approximation) proportional to the hematocrit[3] and to frequency. The main source of dispersion of ultrasound energy in the frequencies ranging from 4 to 16 MHz are erythrocytes [9]. Energy of a wave of frequency of 5 MHz dispersed in platelets is about 1000 times lower as compared to the energy dispersed in erythrocytes [9].

Table 2 includes different velocity values of ultrasound waves spread out in plasma and blood. The ratio of density of medium and velocity of waves spread out in this medium is known as acoustic impedance [9]:

$$Z = \rho_0 c = \sqrt{\rho_0 B_{ad}} \tag{7}$$

In the above equation it is considered that $c = \sqrt{\frac{B_{ad}}{\rho_0}}$, where B_{ad} – adiabatic elasticity coefficient.

[3] For HCT lower than 40%. For HCT = 45% and frequency of 5 MHz absorption equals 0.8 dB/cm [9].

Wave incident on media with different acoustic impedance undergoes a partial reflection. Table 2 presents acoustic properties of blood [9].

Table 2. Acoustic properties of blood. Source [9]

Medium	**Density ρ [kg·m^{-3}]·10^3**	**Impedance Z [kg·m^{-2}·s^{-1}]·10^6**	**Velocity c [m s^{-1}]**
Blood	1.06	1.66	1570
Erythrocytes	1.091	1.55	1590
Plasma	1.021	1.73	1520
Water	0.998	1.49	1500

5. CHANGES IN CONCENTRATION OF BLOOD COMPONENTS IN PLASMA IN AN ULTRASONIC STANDING WAVE FIELD

Red blood cells suspended in plasma are characterized by significant mobility. Ultrasound wave that is spread out in a fluid medium not only causes vibration but also progressive movement of particles [10]. As a result, movement of particles that are suspended in such medium is a sum of rapid vibrating movement and slow progressive movement towards the medium [11].

While exposing blood to standing ultrasound wave, changes in concentration of solid particles i.e. erythrocytes suspended in plasma are observed in the area between node and antinode of a wave [12, 13].

While $N = N(x,t)$ denotes number of particles per volume unit in a surface described by coordinate x at a time t, continuity equation is expressed as follows [14]:

$$N(x,t) = \frac{N_0}{\sin^2 kx \exp(-\partial t) + \cos^2 kx \exp(\partial t)} \tag{8}$$

where: $\delta = 2kv_D$; v_D – velocity of progressive movement of erythrocyte; k – wave number; N_0 – initial concentration of erythrocytes; δ^{-1} – time constant of concentration of erythrocytes.

Equation (8) indicates that there are changes in concentration of erythrocytes in the standing wave field. Concentration of erythrocytes in antinodes and nodes of standing wave changes exponentially. Erythrocytes are filtered out from the areas where concentration increases in accordance with the relationship $N_0 e^{\delta t}$. As shown by calculations [11] an increase in concentration of several hundreds of thousands times is achieved as compared to the initial concentration within fractions of a second.

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FIZYKA W MEDYCYNIE I GOSPODARCE WSPÓŁCZESNEGO SPOŁECZEŃSTWA

Współczesne społeczeństwa są świadome znaczenia odkryć fizycznych dla gospodarki i medycyny. Nasze codzienne życie jest silnie związane z urządzeniami technicznymi, które zostały wytworzone na podstawie fundamentalnych praw fizyki. W pracy analizowano fizyczne metody rozdzielania krwi ludzkiej na składniki. Obecnie w praktyce medycznej najczęściej stosowanymi metodami są wirowanie i filtracja. Dokonując analizy podstaw fizycznych metod tradycyjnych separacji krwi na składniki, zaprezentowano także innowacyjną metodę, która wykorzystuje fale ultradźwiękowe o parametrach dobranych do parametrów składników krwi. Metoda ta jest teoretycznie opracowana, wymaga natomiast weryfikacji eksperymentalnej w celu wdrożenia jej w diagnostyce medycznej.

Słowa kluczowe: prawa fizyki, ludzka krew, separacja krwi ludzkiej, wirowanie, filtracja, akustyczna fala stojąca, medyczne zastosowania ultradźwięków

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