Lecture notes on Rheology of Complex Fluids and Blood Flows

Rheology of Complex Fluids and Blood Flows

Vitaly A. Kalion, Ivan V. Kazachkov, and Yuri I. Shmakov

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Vitaly A. Kalion, Associate Professor,
Faculty of Mathematics and Mechanics, Kiev
T. Shevchenko National University

Ivan V. Kazachkov, Professor, Visiting
Professor at the Division of Heat and Power
Technology, EGI, Royal Institute of
Technology, Stockholm

Yuri I. Shmakov, Professor,
Faculty of Mathematics and Mechanics,
Kiev T. Shevchenko National University

Stockholm-2004

Preface to the book

In discussing the applicability of purely physical ideas to living organisms we have, of course, treated life just as any other phenomenon of the material world. I need hardly emphasize, however, that this attitude, which is characteristic of biological research, involves no disregard of the psychological aspect of life.


This course of lectures is intended for the 3rd – 4th year university students (“bachelor” degree) of mechanical-mathematical faculties, which specialize to “Aerohydromechanics” and “Mechanics of continua”. It will be also useful for the students of the 5th – 6th year of university study (“master” degree) and graduate students of technical universities, which are interested in the problems of applied biophysics and biomedicine. The authors thus come from the idea that in case of many important problems of biology and medicine discussion, successful implementation of the methodology accepted in the scientific disciplines, which are related neither to biology, nor to medicine is possible. Some materials were chosen under the great influence of the Lightfoot E.N monograph [12]. The fact that, mainly, the circulatory system of humans and higher animals is considered had a strong influence on the style of material representation. Thus, it’s expedient that the main attention in the lectures notes will be paid to some special questions of complex fluids rheology (blood, in particular) and to the problem of blood flows in different parts of human and higher animals blood circulation system.

The course of lectures includes introduction, six basic sections (“System of blood circulation from the mechanics point of view”, “Introduction into rheology of blood”, “Some mathematical models of blood flows in a heart and in large blood vessels”, “Mathematical models of blood flows in capillaries”, “Features of mathematical modeling of blood flows in a small blood vessels and microcirculatory cells”, “Some approaches to
the modeling of the blood circulation system in a whole”), conclusion and addition, list of quoted and recommended literature. In addition materials on blood pressure indirect measuring, blood type determination, rhesus factor and hematocrit together with the other blood parameters are set.

The authors are Ukrainian scientists. Professor Ivan V. Kazachkov received his Candidate’s degree (Ph.D.) in Physics and Mathematics from the National Taras Shevchenko Kiev University in 1981, and the Full Doctorship (Dr. habil.) in Mechanical Engineering from the Institute of Physics of Latvian Academy of Sciences, Riga 1991. Associate Professor Vitaly A. Kalion has a Candidate’s degree (Ph.D.) in Physics and Mathematics (from the National Taras Shevchenko Kiev University, 1984). I.V. Kazachkov and V.A. Kalion graduated from the National Taras Shevchenko Kiev University (Faculty of Mechanics and Mathematics, Specialization: Fluid Dynamics and Heat Transfer) in the 1970s: Kazachkov in 1976 and Kalion in 1977. Professor Yuriy I. Shmakov was university teacher and supervisor by Ph.D. theses for both Kazachkov I.V. and Kalion V.A. Professor Shmakov Yu.I. has been working at Kiev University since the beginning of 60-th, and he has created a new scientific school in rheology of complex fluids and blood flows. A few dozens of Ph.D. theses were defended under his supervision, and a few of his pupils became Full Professors.

The set of lectures has been taught during many years for the undergraduate and graduate students at the National Taras Shevchenko Kiev University. The textbook was first prepared in Russian and Ukrainian. In 1998, Ivan Kazachkov has got an opportunity to work as Visiting Professor at the Energy Technology Department of the Royal Institute of Technology (Stockholm), where in 2002 he began to prepare this textbook in English for the KTH students. The idea to prepare such a lecture course arose from Ivan Kazachkov’s work within the Computerised Education Project at the Division of Heat and Power Technology under the supervision of Professor Torsten H. Fransson, Prefect of the Energy Technology Department and Chair of Heat and Power Technology Division.
First of all, the authors wish to thank the Swedish Institute for financial support by the VISBY PROGRAMME for collaborative project “Books and chapters creation by Hydrodynamics of Blood to be included in CompEdu” under which the collaboration between Kiev National University and Royal Institute of Technology became available and has shown mutual interests. The authors wish to thank Prefect of Energy Technology Dept at KTH, Professor Torsten H. Fransson for his support and valuable assistance during the writing of this book. His careful reading of the manuscript, discussion of the material and comments helped the authors to improve the textbook. In addition, it should be noted that some of the book’s chapters were included in the Computerised Educational Program for the students in their interactive education and distance education.

Stockholm and Kyiv, 2003-2004
V.A. Kalion, I.V. Kazachkov, and Yu.I. Shmakov
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Introduction

Subject of bioengineering, biorheology and biomechanics of blood circulation

Blood flow in vessels, from the mechanics point of view, as physics section prone to the same laws as fluid flow in the pipes. Therefore for specialists in mechanics working on the modeling in physiology of blood circulation the most complex task is to divide the displays of universal laws of physics and effects, which are related to the physiological processes and can not be explained only with the use of physics laws. From the other side, in the last 30-40 years, both in the modern physiology, as well as in the practical medicine, biomechanics approaches are more and more implemented along with the traditional physiological approach. Both approaches are interconnected; nevertheless the biomechanics approaches are based on mechanics of continua. Thus, it is important to note that traditional physiology of blood circulation links all rich diversity of functional states to the fine regulatory interconnection of the processes in organism but describes them qualitatively only through the total parameters like flow rate and pressure. Meanwhile in the biomechanics of blood circulation there are used models, which describe precise mechanisms of blood flows taking into account the microstructure of blood. But the natural question arises up about the physiological sense of these mechanisms, e.g. their adaptability, rate of their importance for the slow (for example, morphogenetic) structural and functional changes in the system and for the rapid structural and functional changes, registered during one or a few cardiac cycles.

By development of biomechanics methods of researches, more and more precise physiological mechanisms will find more adequate reflection in the mathematical models. In the future it will allow to reject the practice of human and other living creatures use in physiological researches, in new methods development for medical treatment, in testing
of the new medical and cosmetic preparations, as well as in study of stress influence on the living organisms\(^1\).

Thus, biorheology (rheo - flow) explores the motion of biological liquids (blood, lymph, sinovial liquid) both in organism (in vivo), and outside of organism (in vitro), including apparatus for extra corporal blood circulation (AEBBC), hemodialisers (apparatus “artificial liver” and “kidney machine”) and viscometers. Then biomechanics of blood circulation system represents a motion of liquid having complex internal structure in the system of blood circulation of human and animals. Researches in biorheology and biomechanics of blood circulation, in turn, are parts of more general disciplines, such as Bioengineering and Biomedical Engineering.

Bioengineers, except scientific researches, are also involved in the applied developments, related to the commercialization of scientific results. Moreover, they are responsible for the development of new methods for medical treatment, for creation of new medical and cosmetic preparations, and also for researches of human extreme possibilities. In addition, it is possible to suppose that the results got in case of blood circulation system study will be found useful for traditional, technical fields as well. It is known that for many general tasks the biological evolution found the solutions different from those, which were offered by engineers. For example, there is echolocation of dolphins and bats. Presumably, results of the study of complex chemical and electrochemical processes, which take place in the system of blood circulation at the cellular level, are also of interest for bioengineers.

In the recent years, the educational programs by engineering specialties in the whole world have been sparing the extraordinary attention to the observation and explanation of diverse interesting phenomena taking place in the living organisms. However it is

\(^1\) The organism feels influence of stress under unusual environmental conditions, for instance, in the ocean and space investigations and under extreme conditions in sport.
necessary to have in mind that the observation and explanation of phenomena have not
direct attitude toward the engineering methods, they serve only as a base for the invention
activity. Therefore obviously we have still a lot of problems to solve in the future, and
planning for those future studies is as always very hard task. Nevertheless, bioengineering
has already got both long and glorious history, which is able to teach a correct way ahead
after failures, as well as to inspire researchers for further investigations. Motives,
successes and the failures of the pioneering researchers in this fascinating field still
provoke high interest by scientists and engineers nowadays.

**History of the problem**

If we define bioengineering as systematic application of science and technique modern
achievements to the tasks of biology and medicine, it will appears that this field of
science actually arose up in Renaissance age, and the roots of biomechanics of blood
circulation are appeared to be even earlier, in Ancient Greece. Descriptions of blood
vessels, which can be found at Aristotle (384-322 BC), Hippocrates and Democritus,

seem to be applicable both to physiology of blood circulation, as well as to mechanics of
blood circulation. Later on, Ibn Sina (Avicenna) (980-1037) wrote: “In vessels liquid is
running up, and its surplus extends the veins. When blood flow goes down, the veins look
like an empty sack”. But the strongest stimulus to development of bioengineering as a
whole and to development of mechanics of blood circulation, in particular, has been given
by the works of Renaissance titans. Leonardo da Vinci (1452-1519), Florentine artist, one
of the great masters of the High Renaissance, celebrated as a painter, sculptor, architect,
engineer, and scientist. His profound love of knowledge and research was the keynote of
both his artistic and scientific endeavours. His scientific studies, particularly in the fields
of anatomy, optics, and hydraulics, anticipated many of the developments of modern
science. The first his work was done on cardiac valves. Then he has also attended to the
study of motion of bones and muscles and created the first anatomic atlas of man. The
other great scientist Galileo Galilei (1564-1636) performed very important cycle of researches on the frequency of a heart pulse.

This short outlook in the ancient science is necessary in order to understand the great deal of W. Harvey (1578—1657), English physician, the discoverer of blood circulation. At the age of twenty-four Harvey became a doctor of medicine, in April 1602. Returning to England in the first year of James I he settled in London; the same year he became a candidate of the Royal College of Physicians, and was duly admitted a fellow. In 1616 he began his course of lectures, and first brought forward his views on the movements of a heart and blood. Meantime his practice increased, and he had the Lord Chancellor, Francis Bacon, and the earl of Arundel among his patients. In 1618 he was appointed physician extraordinary to James I, and on the next vacancy physician in ordinary to his successor. In 1628, the year of the publication of the “Exercitatio anatomica de motu cordis et sasi guinis” (“Anatomic researches about motion of heart and blood of animals”), is considered a year of birth of physiology of blood circulation. As well as every genius scientist, Harvey was far ahead of his time. Medical practice of that time was not ready to use this discovery, while the science was still expecting the appearance of I. Newton, whose “The Mathematical Principles of Natural Philosophy” appeared only in 1716. Therefore his colleagues did not understand Harvey’s study up to his death.

Soon after Harvey’s death in 1661, M. Malpighi (1628-1694) who is considered to be the father of embryology and early histology, was the first to prove a controversial theory of the time stated that blood circulates in a circular motion from the heart around the body and back to the heart. Although we take this idea for granted, it was not until 1660 when Malpigi actually saw capillaries, the microscopic connection between arteries and veins, that this theory was accepted. Unfortunately for the originator of the circulation theory, William Harvey, this discovery was made three years after his death. Instead of Harvey’s misty “pores”, Malpighi introduced real capillaries. But it is necessary to pay justice to the Harvey’s foresight. Having no possibility to see the capillaries, he guessed an
existence of this major part of the blood circulation system. All the above-mentioned prominent discoveries in physiology were simultaneously the prominent achievements of bioengineering, as well as of mechanics of blood circulation. Although the terms appeared only in the second half of XX century.

From the other side, discoveries in the area of exact sciences and technique have given not only new instruments of research to the biologists but also they brought new important ideas into biology. Mathematician R. Decart (1596-1650) was the first who made an effort to create a mechanical model of living organism, which would have taken into account the role of the nervous system; he has also wrote the first textbook on physiology. L. Eiler (1707-1783) executed the first mathematical research of wave motion of blood in artery. And J.L. Poiseuille (1799-1869), by name of which a basic law of liquid motion in pipes is adopted, was a doctor. Poiseuille’s interest in the forces that affected a blood flow in small blood vessels caused him to perform meticulous tests on the resistance of flow of liquids through capillary tubes. In 1846, he published a paper on his experimental research. Using compressed air, Poiseuille forced water (instead of blood due to the lack of anti-coagulants) through capillary tubes. Because he controlled the applied pressure and the diameter of the tubes, Poiseuille’s measurement of the amount of fluid flowing showed there was a relationship. He discovered that the rate of flow through a tube increases proportionately to the pressure applied and to the fourth power of the tube diameter. All above-mentioned scientists we can boldly call “bioengineers”.

A number of remarkable results in bioengineering and hydromechanics of the blood circulation system was also got in XIX century and in the first half of XX century. First of all, the following names must be mentioned:

- Researches of A. Fick (1829-1901) by diffusive mass transfer;
- Study of the pulse wave spreading by D. Korteveg (1848-1941), H. Lamb (1849-1934), I.S. Gromeko (1851-1889) and by O. Frank (1865-1944);
• Study of cardiac activity processes, gas exchange in lungs and urination by O. Ludvig (1816-1895);
• Nobel prize of A. Krogh (1874-1949) for the development of microcirculation mechanics.

The above-mentioned researches are related to biohydrodynamics of the blood circulation system, which is a branch of bioengineering. The main directions of such researches are the following. First of all, these are researches of hydrodynamic parameters of blood circulation. These researches began before other but serious results were got only for measuring of blood pressure in vessels. Blood flow was thus determined very imperfectly, by the either approximate and complex direct methods or indirect methods (doctor Korotkov, 1905). The absence of reliable actual data on correlation of pressure and flow in a vascular pipe and in a heart did not stimulate development of the proper theoretical models. Although a heart was explored in this aspect by Franc (1895) and Starling (1918) much better. This became available only due to the possibility to work with the defibrination blood on the cardiac-pulmonary preparation or on the isolated heart. The success in research of hydrodynamic parameters of blood circulation has been accompanied to the both physiologists and representatives of fundamental sciences.

Nevertheless despite the marked incompleteness of study related to the blood flow in vessels, the knowledge of adjusting a heart and vessel were developed very substantially, especially as concern to the nervous regulation. The successes here completely belong to physiology of the blood circulation system.

A present stage of study of the blood circulation system, which began in the 50-th of XX century, is conditioned by many important discoveries in chemistry, physics, cybernetics and mathematics. For example, the use of heparin gave a possibility to apply the apparatus even with a very thrombogen surfaces during many hours. That gave possibility to begin the detailed research of regional blood flow and quickly execute those
experiments and measuring, which were so needed. The same allowed developing a number of new measuring methods, e.g. plastic catheters, the inertia-free flow meters, devices of extra-corporal circulation, hemodialisers (apparatus “artificial liver” and “kidney machine”), etc. In this sense the history with development of the apparatus for extracorporal blood circulation (EBC) is quite interesting. It is known, that the first Jacobi’s apparatus “heart-lugn” (EBC) was built in 1895 having practically modern construction for saturation of blood by oxygen in case of operations on an open heart. However, in medical practice, as a mean of saving patient’s life it was proved unsuccessful since it damaged a lot of blood cells. Thus, the only use of modern synthetic materials in EBC revived an apparatus “heart-lugn” to a new life and then allowed to rescue hundreds thousands of people.

Separate and descriptive qualitative works in biohydromechanics of the blood circulation system were replaced later on with systematic researches performed using modern physical methods and computers. The biohydromechanics “matured” for the study of the living organisms thanks to achievements of general theory of continua, construction of complex rheological models, implementation of numerical methods for the solution of complex boundary-value problems, and development of experimental methodology for micro-objects. Biology, in turn, has got out of traditional way and started using mathematical methods, first for the treatment of experimental results, and then for construction of biological processes models. In the last decade of XX century, the process of creation and development of mathematical models gained an avalanche-type character. The examples of impressive results got with bioengineering approaches were the creation of Trental-400 preparation based on results of mathematical modeling of the aggregation (adhesion) processes of red blood cells in the microcirculation system, and the development of express-diagnostics methods for different pathological changes in organism based on the methods of rheological researches of blood.
Modern discoveries in the problem

One of the greatest modern discoveries in physiology of blood circulation is that of Belorussian scientists under the direction of Professor N.I. Arinchin who reported that a skeletal muscle, in absence of action of external forces (heart), is able to reveal independent active the intra-organ micro-pump ability.

In the schematic W. Harvey’s blood circulation system, which already has been used by physiologists for more than 350 years, there are only two interactive parts: a heart and vessels. A heart acts as a pump, and vessels serve as elastic pipes, which a heart drives blood by. A heart is a surprising organ, which accomplishes 3-4 billions of cycles during the human life driving (by W. Harvey) about 150-175 tons of blood in all cells and tissues of organism for this period of time. Moreover, in contrast to the other organs and systems, the reliability of which is secured by duplication from Nature (God) (eyes, ears, lung, kidney, etc.), heart-vessel system, from this point of view, is shared unfairly because a heart has not an understudy.

At the beginning of XX century the Russian doctor M.V. Yanovskii introduced a hypothesis about existence in organism, except for central, also “peripheral” heart, which he counted an aorta. According to Yanovskii, blood circulation goes due to its peristaltic motion. However, as it will be shown further, the “travelling wave” in aorta does not result in the additional pushing through of blood. Effect of pushing a blood through veins due to their deformation by working muscles was known long time ago and carried the name of “vein pump”. But the vein pump works only at the working heart.

Thus, only one part, ordinary skeletal muscle, remained unverified for Prof. Arinchin in all this long history. “Engine with autonomous energy supply of linear type. It is very simple in use and reliable. Construction has been improved by experiments, which were conducted during long time. Models represent a variety of fuel elements with high
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performance working in a wide range of the moderately-priced popular fuels. Module construction supplies intensification of energy 106 times. Number of executable operations, without the major overhaul, is $2.6 \times 10^9$, moreover, it generates a heat, which is utilized. The conventionally accepted name is muscle…” W. Harvey (1628) has casually mentioned in its “Anatomic researches about motion of heart and blood of animals” about the possible participation of skeletal muscles in circulation of blood. The point was by the neatly put experiment on artificial blood circulation with participation of one and only one skeletal muscle. Such experiment was carried out in November 1972 in the laboratory of Prof. Arinchin [1] (see Fig.1). Thus, the fact well known to the doctors that the organism does not need the rest but motion for the heart’s support was scientifically confirmed. The aphorism of french doctor Gess (18-th century) “The motion can replace all medications but all medications of the world will not replace the motion” was confirmed.

However, our historical reference could be incomplete, if only along with achievements, we would not have mentioned vital errors of the first “bioengineers”. In its famous textbook on physiology “De homine” published in 1662 after his death, R. Decart deeply erred insisting on “rational”, as it seemed to him, explanation of all observed phenomena without taking into account the low-level status of science and technique at that time. Thus, he refused to adopt the scheme of the blood circulation system experimentally discovered by W. Harvey. He has offered its own scheme according to which blood is heated in a heart, and then pumped over vessels due to its thermal expansion. Therefore, in spite of the first indicated by Decart important role of the nervous system on co-ordination of physical activity of organism, his physiology was forgotten. Similar impediment is inherent to the applied bioengineering. The modern “kidney machine” serves only simple (although, fortunately, the most vitally important) functions of living kidney doing removal of all low-molecular dissolved matters. The situation achieved to the 50-ties of XX century was clear to many bioengineers as such one, when the
a) Integrated circuit of blood circulation taking into account action of intramuscular “peripheral hearts”, vein pumps thoracic and abdominal caves.
b) Explanation of Prof. Arinchin for mechanism of pumping-sucking action of “peripheral heart”: 1,7 - muscle fibres are in quiescent state; 2 - the muscle got the irritation, the deformation of muscle fibres began in this place; 3,4 - the deformation spreads in both sides from the irritation place and pushes through blood in capillary by the travelling wave; 5,6 - relaxation, the muscle fibres suck arterial blood in capillaries.

Fig.1. The scheme of experiment.
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engineers perfectly understand the simple physical laws of fluid flows and some mass transfer processes in practically useful limits, however their knowledge on rheology, biophysics, biochemistry and physiology is very poor. But there is no way to follow the case of R. Decart who was the great mathematician but poor physiologist.

Success in bioengineering projects most likely achieved, when mechanical engineer works in a close collaboration with doctors and medical scientists of the other proper specialities. Practicing medical doctor due to his professional status can better understand other practical tasks and necessities, and also conditions, in which new solutions will be realized. Scientist investigating fundamental medical problems can formulate medical problems, which require the answer and might be solved through development of the models and numerical simulation. The role of a mechanical engineer actually consists in simplification of the task stated, its physical and mathematical modeling, and execution of computations with further experimental provement of the results obtained and their implementation into construction. The scheme of the process of scientific cognition is given in Fig.2.

![Fig.2. The scheme of scientific cognition process.](image_url)
One must also remember that the highest priority for the living organism is homeostasis, which means maintenance of viable state near the steady-state regime. Homeostasis is, foremost, extraordinarily complex regulatory processes, however in the given course it will not be considered. In addition, the living organisms are so complex anatomically, physiologically and biochemically that proper description of biological mass transfer phenomena and regulatory processes with the use of mathematical models do not still provide sufficient preparation for conducting of independent biological researches. Therefore a scrupulous study of anatomy, physiology, biochemistry and disciplines of practical medicine are still highly appreciated.
1. System of blood circulation from mechanistic point of view

Since human organism is of our greatest interest, let us start with a short review of the most substantial descriptions of organism and blood circulation for their further use in the development of mathematical models. And this short discussion about the levels of human organism organization (or, in general, mammalian) starts with the note that an organism from the mechanical point of view is too complex mechanism for detail study. Therefore it is always necessary to choose a simplified point of view, suitable for the solution of the stated task. This choice, in turn, is available at the different levels of organization:

- Organism, as a single whole;
- Organism as a network of associate structures (organs);
- Separate organs;
- Separate cells, which organs are built of;
- Structural elements of separate cells, cellular membranes in particular.

It could be possible to continue this description up to the molecular level but the levels situated below the level of separate cells structural elements belong not to biomechanics but to biochemistry. Therefore they will not be discussed here.

1.1 Organism as a single whole

To keep attention on a definite object and establish the order of explored scales, basic description of a „standard man” is introduced in the Table 1.1. This data is very approximate. For example, women are of smaller sizes and other body proportions; they have considerably higher relative contain of fat. However, the presented data allow estimating the scales by order.
<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>30 years</td>
</tr>
<tr>
<td><strong>Height</strong></td>
<td>1.76 m</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>70 kg</td>
</tr>
<tr>
<td><strong>Body surface area</strong></td>
<td>1.8 m²</td>
</tr>
<tr>
<td><strong>Normal temperature of body</strong></td>
<td>37 °C</td>
</tr>
<tr>
<td><strong>Normal middle temperature of skin</strong></td>
<td>34 °C</td>
</tr>
<tr>
<td><strong>Specific heat capacity</strong></td>
<td>0.86 Cal/(g °C)</td>
</tr>
<tr>
<td><strong>Body description:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>General amount of fat</strong></td>
<td>10.2 kg (15%)</td>
</tr>
<tr>
<td><strong>Thickness of hypodermic fat layer</strong></td>
<td>5 mm</td>
</tr>
<tr>
<td><strong>Content of body liquids</strong></td>
<td>51 l (75%)</td>
</tr>
<tr>
<td><strong>Liquid inside the cells</strong></td>
<td>27.2 l (40%)</td>
</tr>
<tr>
<td><strong>Tissue liquid and lymph</strong></td>
<td>20.4 l (30%)</td>
</tr>
<tr>
<td><strong>Blood plasma</strong></td>
<td>3.5 l (5%)</td>
</tr>
<tr>
<td><strong>Blood volume (plasma + blood elements)</strong></td>
<td>5.5 l</td>
</tr>
<tr>
<td><strong>Hematocrit</strong></td>
<td>0.43</td>
</tr>
<tr>
<td><strong>Lung description:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>General capacity</strong></td>
<td>6 l</td>
</tr>
<tr>
<td><strong>Living capacity</strong></td>
<td>4.2 l</td>
</tr>
<tr>
<td><strong>Respiratory volume</strong></td>
<td>500 ml</td>
</tr>
<tr>
<td><strong>Unused volume</strong></td>
<td>150 ml</td>
</tr>
<tr>
<td><strong>Area of mass transfer</strong></td>
<td>90 m²</td>
</tr>
<tr>
<td><strong>Energy and mass transfer characteristics for breathing and quiescent state:</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Energy transformation rate</strong></td>
<td>72 kCal/ hour</td>
</tr>
<tr>
<td><strong>Consumption of O₂</strong></td>
<td>250 ml/ min</td>
</tr>
<tr>
<td><strong>Production of CO₂</strong></td>
<td>200 ml/ min</td>
</tr>
<tr>
<td><strong>Palpitation frequency</strong></td>
<td>65 min⁻¹</td>
</tr>
<tr>
<td><strong>Minute volume of heart</strong></td>
<td>5 l/min</td>
</tr>
<tr>
<td><strong>Arterial blood pressure</strong></td>
<td>120 / 80 mm Hg</td>
</tr>
</tbody>
</table>

*During the quiescent state. In general case 3.0+8M l/min, where M is consumption of O₂.
1.2 General overview of the blood circulation system

From the point of view of geometrical structure and distributing of liquid fluxes, an organism is considered as a complex of narrow-specialized and interconnected organs: heart, cerebrum, lungs, kidneys, gastrointestinal tract, skeletal muscles, skin etc. These organs are interconnected through the blood flow, which carries oxygen and other nutritive elements. Thus, the key role of blood circulation is in the help to overcome the high diffusive resistance conditioned by the body large sizes.

The number of organs in the considered system is great and blood moves in a complex way. Therefore it is often desirable to pay attention to more limited group of organs, for example, to the system of blood circulation (see scheme in Fig.1.1).

Numbers on the scheme at the organs names show the value of blood circulation (in % to the minute volume); numbers down show the volume of contained blood (in % to the general volume) in different regions of vascular system; the upper Roman numerals correspond to the names of these regions. The arrows show direction of blood flow.

On the functional diagram in Fig.1.1 to the right, the arterial part of the blood circulation system is represented (I). The numbers evidently show that this part of the system contains 15-20% of a general blood volume in the system, and it is characterized by a high pressure (see also Tables 1.2-1.4). A region of transcapillary exchange (II) or region of capillary (exchange) vessels is placed in the centre of the scheme; providing of their normal functioning is the main task of all activity of the blood circulation system (see also Tables 1.2-1.4). Nevertheless, the numbers below indicate the comparatively small volume of blood in capillaries in the quiescent state (5-10%). As it shown in the scheme,
Fig. 1.1. Functional diagram of the blood circulation system [24].
Numbers on the scheme at the organs names show the value of blood circulation (in % to the minute volume); numbers down show the volume of contained blood (in % to the general volume) in different regions of vascular system; the upper Roman numerals correspond to the names of these regions. The arrows show direction of blood flow.

On the functional diagram in Fig.1.1 to the right, the arterial part of the blood circulation system is represented (I). The numbers evidently show that this part of the system contains 15-20% of a general blood volume in the system, and it is characterized by a high pressure (see also Tables 1.2-1.4). A region of transcapillary exchange (II) or region of capillary (exchange) vessels is placed in the centre of the scheme; providing of their normal functioning is the main task of all activity of the blood circulation system (see also Tables 1.2-1.4). Nevertheless, the numbers below indicate the comparatively small volume of blood in capillaries in the quiescent state (5-10%). As it shown in the scheme, most of blood is contained in the vein region (III), which is the largest by volume (70-80%). The represented functional diagram of the blood circulation system is taken from the fundamental monograph on physiology [24] and gives the most precise picture of the blood circulation system basic sections, their basic parameters and functional descriptions.

The scheme evidently shows that saturated by oxygen arterial blood is thrown out from the left ventricle in aorta, and then through different arteries of large blood circulation circle, the arteriole, capillaries and postcapillary parts of venules, and it is delivered into tissues of different organs. Poor in oxygen venous blood goes back to the right auricle on venules and different veins. Then through the right ventricle venous blood enters a lung by pulmonary arteries, where it is saturated by oxygen and goes back by pulmonary veins through the right auricle into the right ventricle.

Distributing of blood flow by organs and tissues can be estimated either by direct measuring of blood flow or by indirect methods with the use of dyes or other indicators.
According to the functional diagram shown in Fig.1.1 blood flow computed in relation to 100 g of tissue weight has the highest intensity in kidneys, then in liver, heart and cerebrum. In percents from the general volume of blood, the best blood supply among the organs is in digestive tract (22%), then in muscles (18%), cerebrum (14%), heart (5%) and skin (4%). Quantity of the oxygen extracted from blood in separate organ is equal to the difference between its content in arterial and venous blood in vessels of this organ. This difference is the highest for heart tissue, then kidneys, cerebrum and liver [2,24].

Modern studies of the blood circulation system in the development of biomechanics and physiology require computing of all system characteristics quantitatively. Only such approach allow strict estimation of system functioning, comparison of its separate parts, determination of regulation efficiency and range of parameters’ deviations in case of pathologic processes development, and (what is the most important for mechanical engineers) building of mathematical models of phenomena, which take place in the system.

Table 1.2. Geometrical characteristics of human vascular flow pipes

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter, sm</th>
<th>General quantity in organism</th>
<th>Length, sm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>1.6 – 3.2</td>
<td>1</td>
<td>80</td>
</tr>
<tr>
<td>Large arteries</td>
<td>0.1 – 0.6</td>
<td>103</td>
<td>20 – 40</td>
</tr>
<tr>
<td>Small arteries, arterioles</td>
<td>0.02 – 0.1</td>
<td>108</td>
<td>0.2 – 5.0</td>
</tr>
<tr>
<td>Capillaries</td>
<td>0.0005 – 0.001</td>
<td>109</td>
<td>0.1</td>
</tr>
<tr>
<td>Venules, small veins</td>
<td>0.02 – 0.2</td>
<td>109</td>
<td>0.2 – 1.0</td>
</tr>
<tr>
<td>Large veins</td>
<td>0.5 – 1.0</td>
<td>103</td>
<td>10 – 30</td>
</tr>
<tr>
<td>Hollow veins</td>
<td>2.0</td>
<td>2</td>
<td>50</td>
</tr>
</tbody>
</table>

Taken from different sources [2,11,24], basic „average” geometrical and hydrodynamic parameters of human and dog blood vessels are presented in Tables1.2 - 1.4. A man and a dog differ by body size that reflects the registered lengths of vessels, however diameters of their proper vessels are close. Thus, the Reynolds numbers for the blood circulation
systems of a man and a dog have the same order. Therefore basic hydrodynamic characteristics of the dog’s blood circulation system given in Table 1.4 can be used in future developments of human blood circulation system mathematical models.

Table 1.3. Geometrical characteristics of vascular flow pipes of a dog

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Diameter, sm</th>
<th>General quantity in organism</th>
<th>Length, sm</th>
<th>General transversal section of vessels, sm²</th>
<th>General volume of vessels, sm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascending aorta</td>
<td>1.5</td>
<td>1</td>
<td>5</td>
<td>2.0</td>
<td>30</td>
</tr>
<tr>
<td>Descending aorta</td>
<td>1.3</td>
<td>1</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large arteries</td>
<td>0.3</td>
<td>40</td>
<td>15</td>
<td>3.0</td>
<td>60</td>
</tr>
<tr>
<td>Main arterial branches</td>
<td>0.1</td>
<td>600</td>
<td>10</td>
<td>5.0</td>
<td>50</td>
</tr>
<tr>
<td>Terminal arteries</td>
<td>0.05</td>
<td>1800</td>
<td>15</td>
<td>5.0</td>
<td>25</td>
</tr>
<tr>
<td>The arteriole</td>
<td>0.005</td>
<td>4 108</td>
<td>0.2</td>
<td>125</td>
<td>25</td>
</tr>
<tr>
<td>Capillaries</td>
<td>0.0006</td>
<td>1.2 109</td>
<td>0.06</td>
<td>600</td>
<td>60</td>
</tr>
<tr>
<td>Venules</td>
<td>0.004</td>
<td>8 108</td>
<td>0.15</td>
<td>570</td>
<td>110</td>
</tr>
<tr>
<td>Terminal veins</td>
<td>0.15</td>
<td>2800</td>
<td>1.0</td>
<td>30</td>
<td>130</td>
</tr>
<tr>
<td>Main branches of the veins</td>
<td>0.24</td>
<td>800</td>
<td>10</td>
<td>27</td>
<td>270</td>
</tr>
<tr>
<td>Venous collectors</td>
<td>0.6</td>
<td>40</td>
<td>20</td>
<td>11</td>
<td>220</td>
</tr>
<tr>
<td>Back hollow vein</td>
<td>1.0</td>
<td>1</td>
<td>30</td>
<td>1.2</td>
<td>50</td>
</tr>
</tbody>
</table>

Comparison of some geometrical characteristics of vessels gives a possibility to make some conclusions. For example, modelling the capillaries and venules by cylindrical pipes, one can compute the surface area for mass transfer of all capillaries and postcapillary segments of venules in organism. It makes about 1000m²! Then, obviously, according to the flow rate conservation law, the average volumetric blood flow rate through the whole section of capillaries must be the same as blood flow rate through the aorta. Meantime, if compare a characteristic value of the cardiac blood flow rate at the quiescent state and average blood flow rate in capillary, it is easy to compute that counted in accordance with the flow rate, capillaries transversal section is about 700 times more than area of aorta transversal section at the quiescent state. Therefore, it is naturally to
suppose (and modern experimental data confirm it) that no more than 25-35% of all capillaries are functioning at the quiescent state. Thus, the general area of mass exchange surface for the opened capillaries makes no more than 250-350 m².

Table 1.4. Hydrodynamic characteristics of vascular flow pipes of a dog

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Pulse pressure, mm, Hg</th>
<th>Middle resistance¹</th>
<th>Velocity of blood flow, sm/s</th>
<th>Reynolds number</th>
<th>Mean shear rate, 1/s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>100 - 120</td>
<td>4.0</td>
<td>50</td>
<td>1670</td>
<td>270</td>
</tr>
<tr>
<td>Main arterial branches</td>
<td>100 - 120</td>
<td>5.0</td>
<td>15</td>
<td>27</td>
<td>400</td>
</tr>
<tr>
<td>Large arteries</td>
<td>80 - 90</td>
<td>9.0</td>
<td>8</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>Terminal arteries</td>
<td>80 - 90</td>
<td>6.0</td>
<td>6</td>
<td>0.2</td>
<td>-</td>
</tr>
<tr>
<td>The arteriole</td>
<td>40 - 60</td>
<td>41</td>
<td>0.3</td>
<td>2 10-2</td>
<td>-</td>
</tr>
<tr>
<td>Capillaries</td>
<td>15 - 25</td>
<td>26</td>
<td>0.07</td>
<td>2 10-3</td>
<td>450</td>
</tr>
<tr>
<td>Venules</td>
<td>12 - 18</td>
<td>4.0</td>
<td>0.07</td>
<td>7 10-3</td>
<td>-</td>
</tr>
<tr>
<td>Terminal veins</td>
<td>10 - 12</td>
<td>0.3</td>
<td>1.3</td>
<td>6.5</td>
<td>-</td>
</tr>
<tr>
<td>Branching veins</td>
<td>5 - 8</td>
<td>1.2</td>
<td>1.5</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>Venous collectors</td>
<td>3 - 5</td>
<td>1.5</td>
<td>3.6</td>
<td>72</td>
<td>35</td>
</tr>
<tr>
<td>Back hollow vein</td>
<td>1-3</td>
<td>2.0</td>
<td>30</td>
<td>1375</td>
<td>140</td>
</tr>
</tbody>
</table>

Particularities of wall structure of aorta, arteries, arteriole, capillaries, venule and veins rely on values of pressure differences, which are characteristic for these blood vessels (see Fig. 1.2 and Table 1.4). The walls of blood vessels possess considerable pliability, so that they can change size and form under influence of attached forces, without irreversible destruction. Vessel pliability is determined by its geometry and rheological properties of the wall material. Morphological basis of the wall of an uncapsillary vessel, which is 70% consists of water (density of the wall is ~ 1060 kg/m³) being complex interlaced fibrous framework. Cells between fibres are filled with fibrous tissue mainly consisting of glycoproteins. Mechanical properties of vascular wall are conditioned by fibres of three types. The collagen fibres consist of fibrous protein collagen being the

¹ In % to general peripheral resistance.
² Here and below through-lines in the tables indicate the absence of data.
hardest constituents. The Young’s modulus for them is approximately $10^8 \text{ N/m}^2$. The collagen fibres reveal viscoelastic properties such as stress relaxation, hysteresis of the stress-deformation curve etc. The **elastin** fibres (made of the fibrous protein elastin) are more pliable and practically purely elastic, with Young’s modulus approximately $3 \times 10^5 \text{ N/m}^2$. The **smooth-muscle fibres** (cells with a diameter of $\sim 5 \text{ mkm}$ and with a length of 25-60 mkm) have variable Young’s modulus varying depending on the stress in the range $10^5$-$10^6 \text{ N/m}^2$. It is believed that namely smooth-muscle fibres are responsible for visco-elastic properties of walls in whole. This corresponds to the circumstance (see Fig.1.2) that elasto-viscid effects are stronger in small arteries and arterioles than in other vessels. Depending on relative quantity of different fibres in a wall, vessels can be of elastic, mixed or muscle types. Aorta and large arteries (pulmonary, shoulder-head, general sleepy) are elastic vessels. Influence of elastin fibres prevails in the properties of elastic vessels. In mixed and muscle type arteries, relative mass of elastin goes down, in veins it makes no more than 1/3 of a collagen mass. Elastin fibres form the conglomerates of clamped elastic membranes and plates in a wall. Smooth-muscle cells are attached to elastic elements directly or by means of collagenic fibres, and in large vessels they are oriented inclined or longitudinally, while in small vessels they are oriented circular or spirally. Mechanical properties of vascular wall at low intravascular pressures are mainly determined by properties of elastin. At high pressures, the initially unstretched collagenic fibres develop the tensile strength. Activation of smooth muscles stretches the elastin elements, which they are attached to, and muscles themselves connect in parallel to the collagen-elastin framework.

Blood vessels change their size\(^1\) in two substantially different ways, which are designated as **active and passive vascular reactions**. The reactions of vascular wall to a change in the pressure of internal or external vascular bed, without a change in the primary rheological properties of vessel wall itself are implied here as passive reactions. Passive changes of

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\(^1\) There are supposed “fast” (minutes or hours) reversible physiological reactions; the changes with growth or differentiation of the vessels are not discussed.
blood vessels form actually do not qualitatively differ from the similar phenomena in elastic rubber pipes. Active vascular reactions are primarily caused by changes in the contracting tone of the smooth-muscle cells, which form part of the vascular wall. They can therefore take place by constant external forces operating on vessel. For example, the active narrowing of aorta in case of artificially stabilized pressure and maximal stimulating of smooth muscles results just in 5% narrowing of space. Similar reactions in small arteries and arteriole result in narrowing of space almost on 80%, thanks to this, small arterial vessels carries out the physiological function of blood flow distribution.

![Fig.1.2. Structure of blood vessels walls.](image-url)
The capillary wall has only a layer of endothelial cells. Capillaries are relatively passive and their behaviour is determined by the processes in arteriole and venule. In spite of small thickness, capillary wall has low capacity for tension determined even not so much by the Young’s modulus ($\sim 10^7 \text{ N/m}^2$, close to collagen) but mainly by the mechanical properties of surrounding capillaries connective tissue. The direct measuring shows that tissue surrounding capillaries causes about 99% of their total rigidity. From the mechanical point of view, capillary is suggested to consider not as a pipe but as a tunnel in gel [12,30]. Tensility of such capillary-tunnel, as computations show, makes only 30% of capillary-pipe tensility. Capillaries, arterioles and veins form the microcirculation system, which takes about 80% of the initial pressure difference according to Table 1.4, with resistance of more than 60% of general peripheral resistance of the blood circulation system.

The information about blood vessels will be also given below, in the proper sections.

### 1.3 Blood composition and properties

Normal blood is a suspension of comparatively large cells, blood elements in liquid plasma of blood. Basic blood elements are red blood cells (RBC) (erythrocytes), white blood cells (WBC) (leukocytes, among which the basic are neutrophils, eosinophils, basophils, lymphocytes and monocytes) and blood plates (BP) (thrombocytes) (see Table 1.5). Blood plasma is a salt solution, 1 ml of which contains approximately 8.5 mg of NaCl, substantially less quantity of KCl and other salts; 65 mg of protein including 35 mg of albumen, 25 mg of globulins and 5 mg of fibrinogen. Other characteristics of blood plasma proteins are given in Table 1.6. Blood contains also some other components in weighed and dissolved state, among which are cholesterol, emulsion and free oxides of fats, dissolved gases oxygen and carbon dioxide. The data provided is
average because the actual values of blood components concentrations rely on the individual features of organism and its state.

Table 1.5. Uniform elements of blood

<table>
<thead>
<tr>
<th>Blood elements</th>
<th>Quantity $10^9$ g/l</th>
<th>%</th>
<th>Density $10^3$ kg/m$^3$</th>
<th>Form</th>
<th>Size $10^6$ m</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Red Corpuscles</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3900-5000</td>
<td>93</td>
<td>1.085</td>
<td>Biconcave disk</td>
<td>2.5 – 8.5</td>
</tr>
<tr>
<td><strong>Leukocytes</strong>:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Neutrophils:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Myelocytes</td>
<td>4 - 9</td>
<td>93</td>
<td>2.5</td>
<td>1.07</td>
<td>Spheroid</td>
</tr>
<tr>
<td>• Metamyelocytes</td>
<td>2.04 – 5.8</td>
<td>0.46</td>
<td>47 – 78$^1$</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>• Sticknuclear</td>
<td>0.04 – 0.3</td>
<td>0</td>
<td>1 - 6</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>• Segmentonuclear</td>
<td>2.0 – 5.5</td>
<td>0</td>
<td>47 - 72</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1. Eosinophils</td>
<td>0.02 – 0.3</td>
<td>0.46</td>
<td>0.5 – 5.0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>2. Basophils</td>
<td>0 – 0.065</td>
<td>0</td>
<td>0 – 1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>3. Lymphocytes</td>
<td>1.2 -3.0</td>
<td>0</td>
<td>19 – 37</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>4. Monocytes</td>
<td>0.09 – 0.6</td>
<td>0</td>
<td>3 - 11</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Thrombocytes</strong></td>
<td>180 - 320</td>
<td>4.5</td>
<td>-</td>
<td>Ellipsoid</td>
<td>1 - 2</td>
</tr>
</tbody>
</table>

Table 1.6. Proteins of blood plasma

<table>
<thead>
<tr>
<th>Protein</th>
<th>Relative molecular mass</th>
<th>Form of the macromolecule</th>
<th>Size $10^9$m</th>
<th>Mass concentration in blood plasma %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumen</td>
<td>(0.65-0.8) $10^5$</td>
<td>Prism</td>
<td>15.0 x 5.0</td>
<td>3.5 – 5.3</td>
</tr>
<tr>
<td>$\alpha$ - globulin</td>
<td>(5.0-10) $10^7$</td>
<td>-</td>
<td>-</td>
<td>0.7 – 1.1</td>
</tr>
<tr>
<td>$\beta$ - globulin</td>
<td>15 – $10^4$</td>
<td>-</td>
<td>-</td>
<td>0.8 – 1.3</td>
</tr>
<tr>
<td>$\gamma$ - globulin</td>
<td>(1.4-8.8) $10^5$</td>
<td>Ellipsoid</td>
<td>23.5 x 4.5</td>
<td>0.6 – 0.9</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>(3.4-4.4) $10^3$</td>
<td>Elongated with the thickenings</td>
<td>47.4 x 4.0</td>
<td>0.2 – 0.4</td>
</tr>
</tbody>
</table>

Except special functions executable by blood elements, which will be discussed further, blood plays the leading role in the following processes:

- suction and transfer of nutritives from the digestive tract to the tissue;

---

$^1$ Haematocrit.

$^2$ Zero value of parameter means that these cells are absent in the norm.
1: SYSTEM OF BLOOD CIRCULATION FROM MECHANISTIC POINT OF VIEW

- transfer of gases from lungs to tissue and vice versa; the removal of the products of vital activity of cells;
- transport of hormones, which execute a control of vital functions of organism;
- the regulation of water balance of tissue, pH and body temperature;
- production of antibodies and other matters fighting with infection.

Since both blood plasma, as well as the solution of haemoglobin in the RBC, contain a large quantity of water, density of whole blood (~1075 kg/m\(^3\)), blood plasma (~1035 kg/m\(^3\)) and erythrocytic mass (~1085 kg/m\(^3\)) at 36.6°C is slightly differ from the water density (~10\(^3\) kg/m\(^3\)). However, such small difference in densities is quite enough for the separation of blood elements from blood plasma via centrifugation (haematocrit) and sedimentation (the settling rate of erythrocytes, SRE). More detailed procedure for determination of erythrocytes settling rate is presented in Addition 3D. Normally, the value of SRE varies from 2 mm/h to 10 mm/h. In case of some pathological changes in organism (rheumatism, tuberculosis, arthritis, toxemia) SRE rises sharply and can get up to 60 mm/h. Later on, by examination of blood rheology models, the mechanisms of SRE’s connection with different pathologies in the organism will be touched upon in more detail.

Of all liquid spaces of organism, blood, after lymph, is smallest, however, as already mentioned above, it carries out the most important functions on the regulation of other spaces composition, blood pressure, venous recovery and heart pumping. According to our general characteristics of a standard man, blood contains about 7% of body weight (~5.5 l) including the share of erythrocytes, which is just a little more than 2 l. Determination of blood quantity of human organism is carried out either by introduction of colloidal paint into the vascular channel (usually soot) harmless for the organism, which slowly leaves bloodstream, or by implementation of radioactive phosphorus as the

\(^1\) Data by different types of leukocytes are given in % to the general quantity of the leukocytes.
tracer. In a few minutes after introduction into a vein, the paint (or radioactive tracer) is equally distributed throughout the entire system of blood circulation. After this, a portion of blood is taken, and the total quantity of blood is determined by simple conversion according to the colour of its plasma (or to the level of the radioactivity of model). Although it is known that substantial part of blood is located in so-called “blood depot”, being excluded from the circulation, the measurements prove to be sufficiently precise. It was tested by experiments with animals, when there is a possibility to compare the result obtained by the method of indicator, with the results of determining the total quantity of blood via the complete exsanguinations of the animal organism. Therefore, obviously, the indicator rapidly enough gets mixed also with blood, which is located in the “blood depot”.

The volume blood as other aqueous spaces of human is sufficiently constant. Blood loss, which is accompanied by sharp reduction in the volume of blood, is initially compensated by the yield of liquid from the tissue space into blood. Then the other mechanisms are turning on, which work toward the retention of liquid, for example, the decrease of urine evaporation and secretion. The loss of blood liquid components can be filled in by the abundant drink; however, a normal quantity of erythrocytes is restored only through several days. Thus, in the extra-heavy cases the blood substitutes are used.

The selection of blood substitutes is directly connected with the concepts of osmotic and oncotic pressure in blood (see Addition 4D for more details). The osmotic pressure of blood, lymph and tissue liquid play the most important role in the metabolism regulation of water and solutions between blood and tissue. Any cell wall is semipermeable membrane; therefore a change of the osmotic pressure in the fluid surrounding cells leads to the breakdown of water balance in the cell itself. So, if place normal erythrocytes in NaCl solution, which possesses large osmotic pressure, they sharply lose water and shrivel. But if erythrocytes are placed into the solution, which osmotic pressure is less than inside the cell, erythrocytes will swell, grow in the volume, and finally, they can
collapse. The osmotic pressure of blood of human and other mammals is held at the relatively fixed level. **Kidneys and sweat glands** are the regulators of osmotic pressure in blood. Because of their activity, products of metabolism, which are formed in the organism, have not substantial influence on the level of osmotic pressure in blood. Nevertheless, the fluctuations of osmotic pressure in sweat reach 350%, and in urine it is up to 1100%.

Artificial solutions, which possess osmotic pressure identical to blood pressure are called **isotonic**, those having higher osmotic pressure are called **hypertonic**, and those having smaller osmotic pressure are called **hypotonic**, e.g. 0.9% NaCl solution is isotonic, therefore it can be used as the simplest plasma and a blood substitute. The solutions of Ringer and Tirode are good plasma and blood substitutes as they are closer to plasma also by the ionic composition. But the best plasma substitute is blood serum.

It is well known that osmotic pressure is created by not only the crystalloids (salts) but also by colloids, by the proteins of plasma. The osmotic pressure caused by the proteins of plasma is called **oncotic pressure**. In spite of its low value (~ 0.03-0.04 atm), the oncotic pressure plays exceptionally important role in liquid filtration through the walls of capillaries. The large molecules of proteins cannot get through the gaps between the cells of endothelium, through which the salt solutions are easily passing. Remaining inside the capillaries, the molecules of proteins retain water and contribute, thus, to the maintenance of the water balance of the tissue.

\(^1\) 0.9% solution of NaCl is also called the physiological solution.
1.4 Blood elements

Blood elements are formed in a marrow, where they pass several stages of the cellular division (see Fig. 1.3a). On the contemporary point of view all regular elements originate from one undifferentiated cell. This cell does give birth to three types of cells, which, in turn, give origine to blast cells, the predecessors of mature regular elements (see Fig. 1.3b).

![Fig. 1.3](image)

Fig. 1.3. The schemes of blood elements formation.
  a) the blast cells aging; b) the stages of blood elements formation.

The erythrocytes

The normal erythrocyte (normocyte, discocyte) is the cell with a very thin wall (thickness ~7.5-10 nm) of biconcave form filled with a complex liquid (see Fig. 1.4). Maximal diameter of "normocyte" is ~8.5 mkm, thickness ~2.5 mkm, surface area ~120-170 mkm², volume ~70-100 mkm³. Surface area of discocyte exceeds 20% the surface area of sphere of the same volume². During experiments and in pathology, the discocyte can

---

¹ Appearance of swelling in the tissue by replacement of blood plasma with physiological solution and, on the contrary, the resolution of swelling by replacement of physiological solution with blood serum

² Surface area of the sphere is minimal by given volume.
transform into burr (echinocyte; the surface is covered with shafts), berry (crenated), target (codocyte), stomatocyte (one-sided concave disk), spherocytes, oat, sickled, helmet, pinched, pointed, indented, poikilocyte, etc. The mean life of erythrocytes is about 120 days. When they come to the end of their life, they are retained by the spleen where they are phagocyted by macrophages. The electronic photographs of different types of erythrocytes are widely represented in the monograph [22]. The matured RBC do not have a nucleus and do not possess mobility; however, their predecessors normoblasts, as well as erythrocytes of low-organized animals (bird, reptile) are nucleated cells. An erythrocyte consists of about 70% water, 25% haemoglobin, 5% compose lipids, sugar, salt and lipid proteins. The form of haemoglobin molecule can be approximated by cylinder with sizes $11.0 \times 11.0 \times 7.0$ nm. The haemoglobin molecules have no preferable orientation. Except haemoglobin, RBC contains some other proteins, which compose stroma (that is cytoplasm “armature”), lipids and proteins that form part of the membrane. Viscosity of liquid content of RBC is $-7 \times 10^{-3}$ Pa*s (or about 7 sP).

![Fig.1.4. Geometry of “normal” RBC.](image)

The content of RBC has been proven by experiments as liquid, e.g. by passing RBC on capillaries, diameter of which is substantially less than maximal diameter of RBC (see Fig.1.5). Form, which they get (blunted in front and sharpened behind) indicates that their

---

1 The disturbance of erythrocytes development can lead to the incurable disease of blood, during which erythroblasts predominate in a fetus and a newly born child (nuclear erythrocytes).
contents in this case overflows into the forward section of the cell. The observations made with electronic-microscopic study show that uncrippled RBC have not a definite internal structure. Observations of RBC shades \(^1\) suggest an idea that the form of red blood cells is also caused by properties of their membrane. This conclusion is confirmed by the results of study of the glued erythrocytes stuck on the microscope stage in the shear flow.

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\(^1\) Corpuscles, which have lost the entire contents as a result of hemolysis and break of the membrane.
according to which the resistance of the membrane to bending is negligibly small in comparison with its tensile strength.

Nevertheless, it is still unknown, why RBC having liquid content, transform from the biconcave state to the spherical one and reversibly without any change of the cell surface area, that is without tension of membrane. Obviously, that the cell, which membrane is mechanically homogeneous, can not behave like this. A simple computation shows that the transition from discocyte to sphere requires reduction of length of cell circuit on equator. Therefore in case of moving apart poles the equatorial region of spherocytes must shrivel. This phenomenon was observed by many researchers in case of deformations of RBC models with the homogeneous membrane but nobody has ever

Fig.1.6. The RBC schemes:
a) a “tank-treading” motion of RBC in a stream (the numbers are ones of photo);
b) structure of RBC membrane.
observed this on the real RBC [11,28,30]. Therefore, it was naturally to suppose, that Young’s module or thickness of RBC cell wall (or both simultaneously) is higher in equatorial area than at its poles. However, presently no confirmative or denying experimental data for this hypothesis were reported.

If return to the isotonic solution after hypo-osmotic hemolysis, the “shades”, or “ghosts” of RBC, which do not contain haemoglobin, but their form repeats the form of the original erythrocyte, come to the light. Thus, no content of RBC but its wall determines its form. The role of stroma in the determination of the form of erythrocyte also causes doubt, if one takes into account experiments with the erythrocytes flowing in the transparent chamber (vertical gap with a width 10-20 mkm and a height 2-3 mm) [11]. In these experiments, a chamber was filled by suspension of RBCs, which were freely weighed in the isotonic solution containing albumen. By settling down, RBCs were spontaneously fastened on the non-silicon glass and were deformed by the appearing stream of liquid. Note that the hydrodynamic force deforming the RBC is easily estimated. By microscopic study of the deformed RBC, either natural thorns on its membrane, or artificially inflicted laser marks were used. The property of the RBC shell to roll “around content” like the “tank-treading” first was exposed in these experiments. The concave area of RBC could have been on the arbitrary area of the rolled membrane (see Fig.1.6a).

Experiments on the definition of mechanical properties of RBC membranes were initiated in 1930-th. The first researches have shown that typical cellular membrane has complex composition and contains two layers of lipid molecules with additional inclusions of albumens. It was primary suggested [9] to consider a membrane as liquid-mosaic structure, the molecules of which possess mobility only in the membrane plane. However, further experiments showed that the membrane possessed the resiliency property as well. Since lipids of the membranes are in a liquid state, the membrane properties as a solid are conditioned by proteins and other molecules included in its composition. The technique
of reflecting raster electronic microscopy allows exposing the basic features of membrane structure. According to Fig.1.6b [9,11], the membrane of RBC tissue consists mainly of bimolecular phospholipid layers clamped by numerous transversal albuminous bridges, with inclusions of the larger molecules of glycoprotein. Outside of membrane, the antenna of antigenic oligosaccharides is directed, and below the membrane, a cytoskeleton formed by proteins of spectrin (membrane-associated dimeric protein, 240 and 220 kD) of erythrocytes is located. Spectrin forms a complex with ankyrin, actin, and probably other components of the ‘membrane cytoskeleton’, so that there is a meshwork of proteins underlying the plasma membrane potentially restricting the lateral mobility of integral proteins. Presently biochemists study the interaction of the spectrin meshwork with different non-membrane lipids and proteins.

The mechanical parameters of RBC membrane characterize its structure as a continua. In other words, the temporal and spatial scales for measuring the properties must be chosen so that the scales include a generous amount of molecules, while fluctuations related to the behaviour of separate molecules are negligible. In case of RBC membrane, the medium can be modelled as continua only in two dimensions determined by the membrane surface. In the third dimension (by thickness), a molecular structure of membrane is substantially discrete. But since a general thickness of RBC membrane is three orders less than any linear size along its surfaces, the mechanical properties averaged by membrane volume can be successfully replaced with those averaged by its surface. Thus, the basic mechanical parameters quantitatively describing properties and behaviour of membrane have 2-D nature. In particular, a kinematics is described in terms similar to geometry of surfaces; dilatational strains and shift along the membrane, and bending deformations measured by changes of the main radiuses of curvature, are introduced. Dynamic variables are presented by tensions or (the same) by two-dimensional stresses along the surface of membrane (two normal components and one tangent), and by two bending moments. Two-dimensional analogues for the
thermodynamic values (pressure, temperature, etc.), and 2-D (surface) concentrations for the chemical constituents are introduced.

The direct methods for calculation of mechanical parameters of RBC wall normally include measuring of membrane deformations at the different ways of RBC fixing wholly in the microscope’s sight and at the different ways of its loading. For example, the above-mentioned experiments in the transparent running chamber belong to the direct methods. These experiments revealed that in case of RBC deformation by shear stress of about 6 N/m², the RBC body lengthened 80 % more than in case of shear stress about 0.6 N/m². Simple computation allows to estimate a value of the Young module for RBC wall in the transversal direction at $\sim 7 \times 10^3$ N/m² [11], and in the longitudinal direction at an order of $\sim 10^7$-10⁸ N/m² [11,28]. The indirect methods usually include different “tests on filtration properties”[10,16,21]. In more details these and other methods will be considered in Chapter 4.

Normal erythrocytes are sufficiently durable. The study of erythrocyte suspension in the conditions of laminar flow shows that a medium shear stress in flow of the order of 200 N/m² is necessary for their haemolysis. At the same time, already at 40 N/m², detachment or destruction of endothelial cells occurs in the wall of aorta. Using the theory of thin walls and numerical experiment for the analysis of RBC walls properties, Zarda and Skalak [30] showed that the concave-concave form of erythrocyte was natural (at the quiescent state, RBC is in unstressed state), and it is formed via exfort of mother cell with organelles from nucleus.

RBC form provides its maximal pliability and maximal contact area by passing through the smallest capillaries with diameter 2-8 mkm. Nevertheless, after completion of their life (~120 days), RBC membrane loses its elasticity, becomes fragile and mechanically collapses in very narrow kidney channels. Iron freed in this case is used repeatedly, while
the heme, a component of haemoglobin, transforms into bilirubin and is removed from organism.

It is known that RBC has a negative electric charge creating $\zeta$-potential - a difference of potentials between RBC and plasma. Practically $\zeta$-potential is estimated according to the electrophoresis mobility of erythrocytes, i.e., by the speed of the steady motion of RBC in the permanent electric field, in reference to the field strength. The measuring is realized in RBC suspension, which is strongly diluted by plasma (hematocrit $H \approx 0.05-0.1\%$). Under normal conditions, $\zeta$ - potential of RBC is estimated at 15 mV. However, non-spherical form of RBC is not taken into account. The negative charge of RBC ($\approx 120445 e$) results in increase of concentration of positive cations. Therefore RBC turns out surrounded by at least two layers of ionic atmosphere, counter-ionic and co-ionic. By known $\zeta$-potential of RBC, the mean density of charges on surface is computed. Although the data on RBC deformation in case of varying directions of the electric field indirectly testify the non-homogeneous distribution of charges on RBC surface. There are extended reviews on the electrokinetics characteristics of RBC in norm and in pathology [14].

**Leucocytes and thrombosites.**

White blood cells (leucocytes) in norm make only $\approx1.2\%$ of blood volume, and the volume of blood plates (thrombosites) is even less, just $\approx0.3\%$. The total volume of the leucocytes and thrombosites is 20 times less than the total volume of RBC, therefore rheological properties of blood, *in vitro*, are determined by RBC.

Unlike red cells, the leucocytes of mammals and human have a nucleus. It is easily visible under the microscope but only after having stained the smear. The nucleus of these cells can show multiple lobes, or be indented or kidney-shaped (reniform). Usually, the shape of the nucleus of various kinds of leukocytes is different. Together with different colours of granules, the shape of nucleus helps to recognize these cells. Leukocytes are divided
Fig. 1.7. Images of leucocyte from screen of scanning (a) translucent; (b) electronic microscopes [19,25]. The scale down corresponds (a) 10 mkm; (b) 1 mkm.
into granulocytes and lymphoid cells. Leucocytes are substantially worse deformable than RBC. Therefore with the passage of leucocytes on the micro-vessels, both the separate thromboses of vessels and the curtailment of the passage of blood through the entire microcirculatory cells are observed. The role of leukocytes in the phenomena of immunity, to large extent, is based on their ability to move independently with a speed of ~0.6-7×10⁻⁷ m/s.

According to the Table 1.5, neutrophils are the most common leukocytes, that is why their role in the phagocytosis is the most significant. The eosinophils are quite rare elements of blood. They have the same size as neutrophils. Generally, their nucleus is bi-lobed but even nuclei with three or four lobes have been observed. Basophils are the rarest leukocytes (less than 1%). They are quite small: 9-10 mkm in diameter. Cytoplasm is very rich in granules, which take a dark purple colour. The role of eosinophils and basophils is not clear. Lymphocytes (~20% of leukocytes) do not participate in phagocytosis but they play important role in other immune mechanisms, e.g. they synthesize the antibodies. If the number of leukocytes sharply grows (leukocytosis) or falls (leucosis or leukemia), there is a pathology in blood.

The thrombocytes of mammals and human have no nucleus being cytoplasmic formations with a diameter of ~2-4 mkm¹. On the contemporary point of view, the dominant role of thrombocytes is the stoppage of haemorrhage (coagulation of blood). Being accumulated in the region of vessel break (due to the mechanism of thrombocytes aggregation), they contribute to the process of the blood clot formation together with plates. This process starts with destruction of thrombocytes, gets through a few stages and relies on the numerous factors. At the last stage of blood coagulation, the insoluble fibrinous threads are formed from the molecules of fibrinogen, which catch regular blood elements like trapping networks. Thus, blood clot is formed from the fibrinous threads and regular

¹ The thrombocytes of birds and reptiles have a nucleus.
elements of blood. After removal of the clot from blood, the transparent serum is formed, which, like blood plasma, is deprived of regular elements and moreover it does not contain fibrinogen. The rate of blood clot formation is evaluated by the time of blood coagulation\(^1\), which normally takes 3-8 minutes.

**Anticoagulants** prevent coagulation of the blood. Anticoagulants are some substances (mainly oxalates and citrates), which constrain calcium in blood, thus tearing up the chain of the transformation of fibrinogen into fibrin. Heparin, a natural anticoagulant constantly being present in blood, does prevent coagulation of blood in the organism.

\(^1\) Time of blood coagulation is the time interval, during which blood placed into the test tube at a temperature of 37°C forms the clot.
2. Introduction to the rheology of blood

2.1 Classification of liquids

The rheological equations for the wide spectrum of incompressible\(^1\) liquids can be represented in the following general form

\[ \tau_{ij} = -p \delta_{ij} + 2\eta e_{ij}, \quad (2.1) \]

where \( \tau_{ij}, e_{ij} \) are components of the fluid stress tensor and components of the strain rate tensor, accordingly; \( p \) is pressure; \( \eta \) is coefficient of dynamic viscosity\(^2\).

An incompressible fluid is called Newtonian, if it follows the law of the Newton’s viscous friction expressed by (2.1), where \( \eta \) depends only on temperature. Liquid mixtures (suspensions, emulsions, melts, etc.) are called Newtonian if the rheological equation (2.1) is correct for them, where \( \eta \) depends only on temperature and concentration of components. The other liquids are called non-Newtonian.

The main mechanisms of the non-Newtonian properties of liquids are related to the presence in a liquid of the weighed particles (or large molecules and molecular aggregates), which change the properties of the flow of liquid phase. The rheological properties of mixtures depend also on the properties of their structural elements, e.g. deformability, strength, capability for the formation of aggregates. The special features of the motion of the structural elements, for example, their rotation and orientation in the

---

\(^1\) All real liquids possess at least weak but finite compressibility, i.e., their density is the growing function of pressure. However, these changes in the density are negligible for many processes; therefore all liquids (and sometimes also gases) are considered here as incompressible.

\(^2\) In contrast to the kinematic viscosity coefficient \( \nu = \eta / \rho \), where \( \rho \) is density.
flow field, fluctuation, capture of the liquid phase, are important for the rheological behaviors of liquid. These factors influence rheology, as well as another properties of the mixtures (heat- and electrical conductivity, optical and diffusive properties, and so on). Thus, let us consider the classes of the non-Newtonian liquids paying a special attention to the mechanisms, which cause the non-Newtonian behavior of the liquids [11,27].

**Nonlinear-viscid liquids**

One class of the nonlinear-viscid liquids is presented by power-law liquids, which can be described by the rheological equations similar to (2.1), when in these equations, the apparent viscosity\(^1\) (or coefficient of effective dynamic viscosity) is presented as the second invariant of the rate-of-strain tensor

\[
\eta_a = \eta(I_{2e}), \quad I_{2e} = \sqrt{2\left(e_{11}^2 + e_{22}^2 + e_{33}^2 + 2\left[e_{12}^2 + e_{23}^2 + e_{31}^2\right]\right)},
\]  

(2.2)

The name of Power-law liquids appeared due to type of their rheological equation for the simple shear flow\(^2\)

\[
\tau = m\dot{\gamma}^n, \quad \tau = |\tau_{xy}|, \quad \dot{\gamma} = 2|e_{xy}|.
\]  

(2.3)

The Power-law liquids are divided into the Pseudo-plastic and Dilatant liquids. Pseudo-plastic liquids have apparent viscosity \(\eta\) as decreasing function of \(I_{2e}\) (0 < \(n < 1\)). For the Dilatant liquids, \(\eta\) is increasing function \(I_{2e}\) (\(n > 1\)). Basically, all above-mentioned mechanisms of the non-Newtonian nature of liquids yield the nonlinear-viscid behaviors.

---

\(^1\) The ratio of stress to rate of strain, calculated from measurements of forces and velocities as though the liquid were Newtonian. If the liquid is actually non-Newtonian, the apparent viscosity depends on the type and dimensions of the apparatus used.

\(^2\) \(v_y = k y, v_i = v_i = 0\).

\(^3\) Here and below, the dot over the variable indicates temporal derivative of the variable.
The most important source of pseudo-plastic properties is the disintegration of particles in fluid, while the dilatant features take place both due disorientation of particles by stream, as well as due to the “dry friction” between the colliding particles. Behaviors of different classes of the nonlinear-viscid liquids in a simple shear flow are presented in Fig. 2.1. The straightforward line $\tau = \tau(\dot{\gamma})$ in the Fig. 2.1 corresponds to the Newtonian behaviors.

In some cases of the nonlinear-viscid behaviors of liquids, there is observed an abrupt transition from the almost elastic deformations, by small stresses, to the viscid flow, when the stress exceeds some threshold (curves 4 in Fig. 2.1). Two most common models of such viscid-plastic liquids in case of simple shear flow are the Bingham-Shvedov model

$$\tau = \tau_0 + k \dot{\gamma}, \quad \tau > \tau_0; \quad \dot{\gamma} = 0, \quad \tau < \tau_0,$$

and the Casson model

$$\tau = \tau_0 + k \dot{\gamma}, \quad \tau > \tau_0; \quad \dot{\gamma} = 0, \quad \tau < \tau_0.$$
\[ \tau^{1/2} = \tau_0^{1/2} + k \dot{\gamma}^{1/2}, \quad \tau > \tau_0; \quad \dot{\gamma} = 0, \quad \tau < \tau_0. \]  

(2.5)

Generalization of the rheological equations (2.4)-(2.5) is as follows:

\[ \tau_{ij} = -p \delta_{ij} + 2 \left( \frac{\tau_0}{I_{2e}} + k \right) \epsilon_{ij}, \quad I_{2e} > 2 \tau_0; \]

\[ \epsilon_{ij} = 0, \quad I_{2e} < 2 \tau_0 \]  

(2.6)

for the Bingham-Shvedov model, and

\[ \tau_{ij} = -p \delta_{ij} + 2 \left( \frac{\tau_0^{1/2}}{I_{2e}^{1/2}} + k^{1/2} \right)^2 \epsilon_{ij}, \quad I_{2e} > 2 \tau_0; \]

\[ \epsilon_{ij} = 0, \quad I_{2e} < 2 \tau_0 \]  

(2.7)

for the Casson model. Here \( I_{2e} = \sqrt{2 \left( \tau_{11}^2 + \tau_{22}^2 + \tau_{33}^2 + 2 \left[ \tau_{12}^2 + \tau_{23}^2 + \tau_{31}^2 \right] \right)} \) is the second invariant of the stress tensor. Comparing the equations (2.6) and (2.7) with (2.1), by analogy with (2.2), yields the apparent (effective) viscosity for the Bingham-Shvedov model and for the Casson model, respectively:

\[ \eta_a = \frac{\tau_0}{I_{2e}} + k, \]  

(2.8)

\[ \eta_a = \left( \frac{\tau_0^{1/2}}{I_{2e}^{1/2}} + k^{1/2} \right)^2. \]  

(2.9)

Infinite growth of apparent viscosity with deformation rate going to zero is a common feature for both models shown in Fig.2.1b.
Another important class of nonlinear-viscid liquids is represented by the models of liquids with transversal viscosity

\[
\tau_{ij} = -p\delta_{ij} + 2\eta(I_{ij})e_{ij} + \eta_c(e^2)_{ij}.
\]  

(2.10)

Since in a shear flow, the tangential component of the tensor \((e^2)_{xy}\) is going to zero, the rheological equations for the Power-law liquid, as well as for the liquid with transversal viscosity, the components \(\tau_{xy}\) coincide completely. Difference of normal stresses \((\tau_{xx} - \tau_{yy})\) is zero for Power-law liquid but it is non-zero for the liquid with transversal viscosity:

\[
\tau_{xx} - \tau_{yy} = \eta_c(e^2)_{xx} - (e^2)_{yy}.
\]  

(2.11)

Thus, the so-called “effect of normal stresses” is generated by the shear flow.

**Liquids with the temporal properties**

The internal processes in suspensions (disintegration of aggregates, capture of a liquid phase, change of orientation of particles, etc.) are going not always so quickly to account only the final state ignoring an initial and intermediate states. For example, thixotropic liquids satisfy to common rheological law (2.1) but their apparent viscosity is computed through the time-dependent parameters, which satisfy some additional equations

\[
\tau_{ij} = -p\delta_{ij} + 2\eta(N)e_{ij};
\]

\[
\dot{N} = \Gamma^+ (N, I_{2e}) - \Gamma^- (N, I_{2e}).
\]  

(2.12)

Here \(N\) is the size of aggregates; \(\Gamma^+ > 0\) and \(\Gamma^- > 0\) are the rates of disintegration and formation of aggregates, respectively. Both these processes are controlled by flow, therefore they also depend on \(I_{2e}\). If \(\dot{N} = 0\), the equation (2.12) links the instantaneous
values \( N \) and \( I_\sigma \), consequently, the behaviors of Thixotropic liquids in a stationary flow yield in the nonlinear viscosity. If time required for the change of size of \( N \) aggregates is small, the apparent viscosity is instantly tuned under the stream and influence of temporal effects is negligible. In more general case, the apparent viscosity of Thixotropic liquid depends both on size of aggregates and their volumetric concentration \( C \). Therefore \( \eta = \eta(C, N) \), and thus the diffusion equation must be added to the model (2.12).

The viscoelastic liquids represent the other class with temporal properties, which answer to a very rapid shear stress as an elastic solid, and on slow shear stress as a viscid liquid. Viscoelastic properties are inherent to the liquids, which contain elastic weighed particles or large molecules. For the viscoelastic liquids, the effect of normal stresses reveals in the shear flow. One of the most popular models for the Viscoelastic liquids is as follows

\[
\lambda_1 \epsilon_{ij} + \tau = -p \delta_{ij} + 2\eta \left( e_{ij} + \lambda_2 \dot{e}_{ij} \right), \tag{2.13}
\]

where \( \lambda_1 = \frac{\eta_2}{E} \), \( \lambda_2 = \frac{\eta_2}{\eta_1 + \eta_2} \), \( \eta = \eta_1 + \eta_2 \). Here \( \eta_1 \), \( \eta_2 \) are different coefficients of dynamic viscosity; \( E \) is the Young’s module. The parameters \( \lambda_1 \), \( \lambda_2 \) are called relaxation times for the stress tensor and deformation rate tensor, accordingly. When flow stops \( (e_{ij} = 0) \), the stresses, which took place prior to the stop, are decreasing (relaxation) proportionally to \( e^{-t/\lambda_1} \). And in case of stress removal \( (\tau_{ij} = 0) \), the flow is decreasing as \( e^{-t/\lambda_2} \). For all liquids with the temporal effects, the stress at the moment \( t \) relies on stresses and deformation rates at the all preceding moments of time, that gives another name to this class of liquids, as liquids with memory.

**Liquids with internal degrees of freedom**

Sometimes there are used more exotic models of liquids, for which the components of stresses depend, except the deformation rates, also on other kinematics parameters.
representing the influence of degrees of freedom. The Oriented liquid model is one of such models of liquids

\[
\tau_{ij} = -p\delta_{ij} + 2\eta e_{ij} + T_{ij}(\vec{n}),
\]

(2.14)

where \(T_{ij}\) is some function; \(\vec{n}\) is orientation vector; the model of micro-polar liquid takes into account the rotation of particles

\[
\tau_{ij} = -p\delta_{ij} + 2\eta e_{ij} + T_{ij}(\vec{\omega}_p - \vec{\Omega}),
\]

(2.15)

where \(\vec{\omega}_p, \vec{\Omega}\) – accordingly, own rotation of particle and vortex. Then for the model of the micro-morphic liquids, there are essential even the speeds of the microdeformation of the particle \(w_i\):

\[
\tau_{ij} = -p\delta_{ij} + 2\eta e_{ij} + T_{ij}(\vec{\omega}_p - \vec{\Omega}, w_{i1}, \ldots, w_{i1}).
\]

(2.16)

Some additional relationships must be included into (2.14)-(2.16) because, except the usual hydrodynamic stresses, such media are also characterized by other dynamic parameters [11]. However all these models have a common feature, which narrows their use. The point is that measuring \(\tau_{xy}\) and \(e_{xy}\) in the shear flow does not allow defining the apparent viscosity in the ordinary way (dividing \(\tau_{xy}\) on \(2e_{xy}\)) because \(\tau_{xy} = 2\eta e_{xy} + T_{xy}\).

Thus, it is impossible to measure the coefficients for these models using the known viscometers. Moreover, implementation of the models of liquids with internal degrees of freedom to study the suspensions, emulsions, melts and other liquids with complex properties was dictated by the desire to account more mechanisms of non-Newtonian behaviors. But, in fact, all these continua cannot be considered as the non-Newtonian liquids in the commonly accepted sense. Nevertheless, all effects mentioned for the
liquids with internal degrees of freedom could be taken into account using more traditional models, for example, those offered by Ericksen [7,8]. The structural-continuous approach by Prof. Yu.I. Shmakov [26] allows computing the numerous coefficients in the Ericksen's models and thus removes the majority of objections.

2.2 About rheological testing

In rheological experiments, some parameters are set up by device (investigator can vary these parameters), the other are measured (material answer on the applied influence), and third are calculated. The methods for processing of the data are two types. One of them serve for the direct obtaining of functional relations for the parameters both stated and measured. The other ones are intended for finding the constant coefficients, which are supposed in the sought rheological equations. The above-mentioned conception of the apparent (effective) viscosity is also linked to such methods of the data processing.

Thus, let the flow of viscid Newtonian liquid to be determined by two values \((a,b)\). It can be, for example, shear stress – shear rate, pressure drop – flow rate, or any other pair of parameters available for the direct measuring in the experiment. Then assume that dynamic viscosity of this liquid, \(\eta\) is uniquely determined as \(F(a,b,\eta) = 0\), so that the type of the function \(F\) uniquely reflects the flow geometry. Now, if \((a,b)\) is defined for arbitrary non-Newtonian liquid, then parameter \(\eta_a\) computed from equation \(F(a,b,\eta_a)=0\) is apparent viscosity of the non-Newtonian liquid studied\(^1\).

Measuring rheological properties of liquids is called viscometry, although it got a long ago out of the viscosity measurement scopes. Therefore flows, the theoretical models of

\(^1\) Each hypothetical model and each procedure of experiment have their apparent coefficients. Therefore, in order to avoid misunderstandings, it is necessary to indicate correspondence between particular geometry and apparent coefficients specifically to the formula used.
which allow computing the rheological equations by experimental data, are called viscometric flows. The most important of them are the above-considered simple shear flow (plane or rotatory) and axisymmetric shear flow under longitudinal pressure gradient. Certainly, not one of those flows can be realized exactly. For example, it is impossible to create the flow between two infinite planes or in pipe of infinite length. However, it is possible to build the facility, in which the deviations from the ideal geometry either do not make a significant contribution to the result of measurements, or they can be estimated in calculation with the required accuracy.

The rotary viscometers, in which a shear flow is carried out, are the systems with rigid co-axially located cylinders, disks or cones (see Fig.2.2). In the last case, one of cones often has a corner angle $180^\circ$ that is a plane. In order to approach around the ideal geometry, a gap width between cylinders is done far less than height, the corner between cones is done small, etc. A gap between cylinders better to do small comparing to the radius of the internal cylinder (bob) too, laboring for the as less as possible curvature of liquid layer and approaching the plane shear Cuette flow. One of the working elements (as a rule, it is an external element (cap)) is set up for rotation with the angular velocity $\Omega(t)$ using the precision engine. Simultaneously, the rotational moment $M(t)$ is measured, transferred through the liquid to the second working element, which is normally weighed on elastic string with the known characteristics. Then $M(t)$ is found by the angle of the pendant’s torsion (with the correction for its rotatory inertia). The data on $\Omega(t)$, $M(t)$ and geometries of the facility are substituted into the processing formulas, which yield the necessary rheological equations:

a) utilizing equation of force balance, the shear stress at the bob ($r=R_b$) can be defined as

$$\tau = \frac{M}{2\pi(h+h_b)R_b^2}, \quad \dot{\gamma} = \frac{2\Omega \alpha^2}{\alpha^2 - 1} \quad \text{at } \alpha = \frac{R_c}{R_b} \ll 2, \quad \eta_a = \frac{\tau}{\dot{\gamma}}. \quad (2.17a)$$

Similarly, shear stress at the cap ($R_c$) can be defined as
\[
\tau = \frac{M}{2\pi (h + h_0) R_c^2}, \quad \dot{\gamma} = \frac{2\Omega}{\alpha^2 - 1} \cdot \eta = \frac{\tau}{\dot{\gamma}}; \quad (2.17b)
\]

b) in rotatory shear flow between the cone and plate at the corner angle \( \theta < 5^\circ \):

\[
\tau = \tau_w = \frac{3M \cos \theta}{2\pi R^3}, \quad \dot{\gamma} = \dot{\gamma}_w = \frac{\Omega}{\sin \theta} \quad \eta = \frac{\tau}{\dot{\gamma}}; \quad (2.18)
\]

c) in rotatory shear flow between parallel plate:

\[
\dot{\gamma}_k = \frac{\Omega R}{h}, \quad \tau_k = \frac{M}{2\pi R^3} \left[ 3 + \frac{d \ln(M)}{d \ln(\dot{\gamma}_k)} \right]. \quad (2.19)
\]

![Fig.2.2. Geometry of rotatory viscometer.](image)

Capillary viscometers have working part as a rigid cylindrical pipe (capillary), a diameter of which is very small on the comparison to its length, that allows to evade influencing its

\[1\] Designations in this formula and formulas below are explained in the figures. The values of the parameter on the wall are designated by index.
ends and get around the ideal geometry infinitely long pipe. In such viscometers, flow is
going due to the pressure drop $\Delta p(t) = p_1 - p_2$ at the ends of working area of pipe. This
pressure drop is set by the peripheral devices (for example, due to difference of water
levels in reservoirs). A flow rate $Q(t)$ is simultaneously measured through the output
section of the capillary. The data on $\Delta p(t)$, $Q(t)$ and geometry of the facility are used in
the data processing:

$$\eta = \frac{\pi R^4 \Delta p}{8 Q L}, \quad \tau_w = R_c \Delta p / 2L, \quad \dot{\gamma}_w = \left( \frac{3n' + 1}{n'} \right) \Phi.$$  \hspace{1cm} (2.20)

where $\Phi = 4Q/\pi R^3_w$ is apparent shear rate ($\dot{\gamma}_w \equiv 4 \cdot \Phi$ for Newtonian fluid);
$n' = d (\ln \tau_w) / d (\ln \Phi)$. The formulas (2.20) allow finding the dependence between the
shear rate and shear stress on the wall, or apparent viscosity by the flow rate
characteristics $\Phi(\tau_w)$ or $\Phi(\eta_w)$.

In research of liquids, which show temporal properties, most often procedure of selection
of coefficients is used in some hypothetical models. Among the dynamic experiments,
most widespread are:

- Measuring by periodic (usually sinusoidal) temporal variation of given parameters;
- Measuring of stress relaxation ($\lambda_1$) or flow relaxation ($\lambda_2$) in the transient regimes.

### 2.3. Features of the viscometric blood testing

The viscometers for blood must measure the shear stress in the wide range of shear rates
from the small (no more than $10^{-3} \text{ c}^{-1}$) supported values up to about $1-1.5 \times 10^{3} \text{ c}^{-1}$. Due to

---

1. If the tested liquid is Newtonian, then for the instruments of any construction all formulas (2.17)-(2.20) give the same result. But if liquid is non-Newtonian, then, for the different flow conditions, the results can differ depending on the initial state of liquid and the scaling effects.

2. Example of such flow is considered below in subchapter 5.
this, the error of shear stress measuring must be $\sim 5 \times 10^{-4} \text{ N/m}^2$. In addition, it is desirable to conduct measuring with the as less as possible quantity of blood. In the process of measuring it is also necessary to support a normal temperature of blood, and the researches must take as less as possible time in order to get minimal changes of blood. The rotary viscometers fit the best to the above requirements. Capillary viscometers are closer to the system of blood circulation by flow geometry, however all above-mentioned requirements are considerably more difficult to execute for them.

The precise industrial viscometers\(^1\) are the most frequently used in rheological measurements of the blood. They have cone-plane working part, e.g. the GDM-viscometer ($\dot{\gamma} \sim 10^{-2} - 100 \text{ s}^{-1}$), LVT viscometer of Brookfield firm ($\dot{\gamma} \sim 5 - 212 \text{ s}^{-1}$), and Weissenberg rheogoniometer ($\dot{\gamma} \sim 10^{-3} - 1500 \text{ s}^{-1}$). Both devices are expensive research complexes with the large set of removable elements, thus not only different cones and plates but also coaxial cylinders. Weissenberg rheogoniometer (see Fig.2.3) allows exploring the stationary flows, as well as oscillating modes.

In the former Soviet Union for the rheological blood measuring, more cheap industrial automatic viscometers of foreign firms were used (for example, see Fig.2.4) and piece-made viscometers, an example of which is the well-known Trapeznikov EV viscometer having very good range of shear rates $\dot{\gamma} \sim 10^{-3} - 150 \text{ s}^{-1}$ and simple registration methods.

The authors [11] registered non-Newtonian behaviors of plasma using the “LVT” Brookfield viscometer in rheological measuring of blood plasma. But then it was revealed that phenomenon was caused just by formation of lipid film, which is due to contact of plasma with air. Later on, this artifact was removed with use of the preserving ring made

\(^1\) The requirements to the blood viscometers, are reduced with the design of purely diagnostic and monitoring instruments. Instruments of such type are usually portable and simple in the operation.
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Fig. 2.3. The working part of the Weissenberg rheogoniometer.

Fig. 2.4. Holland viscometer “Rheodeer”; working range of shear rates is \( \gamma \sim 10^{-2} \text{--} 50 \text{ s}^{-1} \).
by the layer of paraffin oil with viscosity \((3-4) \times 10^{-3}\) Pa*s. For the Weissenberg rheogoniometer, the rigid preserving ring showed out effective use for these purposes.

When the task arose up in viscosimetry, to explore the RBC aggregation depending on a shear rate, the cones, planes, cylinders and thermostatic jacket of device were made of transparent plexiglass and put together with microscope. Such system allowed observing the area of viscometric gap close to its center, together with its photomicrographs [11]. For the processing of the experimental data, it is necessary to take into account influencing of the edges of cone and cylinders, nature of flow in the corner areas of the gap and possible loss of flow stability, especially in case of rotatory internal cylinder.

Fundamental simplicity of device and likeness of flow in capillary viscometer with the real blood flow in vivo meets, nevertheless, the impediments in touch with difficult requirements for operation of some parts of the device, e.g. flow control and measuring a pressure difference at the pipe ends. For instance, by internal diameter of pipe \(\sim 1\) mm, for obtaining the flow curve in the range \(\gamma \sim 10^{-3} - 10^{3}\) s\(^{-1}\), one needs to vary a blood flow rate in the range from \(10^{-5}\) to \(1\) sm\(^3\)/s and reliably measure pressure differences \(\leq 1\) Pa. The other facility has been described, in which very long capillary (\(\sim 4-8\) m) was connected directly to the blood vessel and worked “on expiration” [11]. The application of automation allowed to decrease duration of measuring and work without anticoagulants at the complete cycle of measuring \(\sim 15\) s and blood flow rate no more than \(5\) sm\(^3\). In simplified capillary viscometers, the relative viscosity of blood is measured instead of absolute viscosity. For this purpose, under the same conditions, the times of complete expiration of blood and water from the graduated glass capillaries are measured. Then the ratio of expiration rates is supposed to be equal to the ratio of viscosities. The measured thus relative viscosity of blood, in norm, makes for men and for women, respectively, \(4.3-5.3\) and \(3.9-4.9\). Relative viscosity of blood serum was computed as \(1.4-1.7\), while relative viscosity of plasma was around \(1.5-1.8\).
2.4. Results of the viscometric blood testing

In the literature there is presented an extensive experimental data on blood rheology obtained from the studies of the blood in the capillary viscometers and Couette type viscometers [5,6,11,29]. The first published rheological measurements of the blood performed with the rotational viscometers are dated 1961 [11].

The blood reveals a number of non-Newtonian properties, first of all, abnormal viscosity. The apparent viscosity of blood depends on the shear rate (see Fig.2.5).

![Fig.2.5. Dependence of apparent viscosity of blood (ηₐ) from the shear rate (γ).](image)

On the modern presentations, at the relatively small shear rates (see Fig.2.5, area I), the governing mechanism for variation of viscosity ηₐ is production and destruction of the RBC aggregates, while in the area II a change of viscosity is mainly determined by features of orientation–deformation behavior of single RBC in the shear flow, and in the area III ηₐ=const. Along with the viscosity anomaly, the blood possesses also visco–plasticity property (initial shear stress of blood is in norm τ₀=0.005–0.05 N/m²); features of the formation of RBC aggregates (“mooring”, formation of bridges from molecules of fibrinogen, gathering of RBC) are conditioning a temporal dependence of rheological properties of blood.
In the same time, the blood plasma and serum have constant viscosity under stationary conditions. It has been confirmed by data got with the use of capillary voscometers. Further researches showed a number of important dependences for rheological properties of blood from its composition, temperature and other factors.

2.4.1 Dependence of apparent viscosity on the shear rate

The above-mentioned is confirmed by presented in Fig.2.6 a typical curve of flow for the entire stabilized blood of practically healthy donor got in coaxial-cylinder viscometer GDM [5]. Note, that the graph begins not at the beginning of co-ordinates starting from some thresholding shear rate $\tau_0 \approx 0.005$ N/m$^2$. The dynamic viscosity $\eta = \tau/\dot{\gamma}$ computed according to this graph shows that the smallest investigated shear rate $\dot{\gamma} \approx 10^{-2}$ makes viscosity of blood $\sim 0.8$ Pa*s, which is approximately 130 times higher than at the shear rate $\dot{\gamma} \approx 100$ s$^{-1}$. At $\dot{\gamma} > 100$ s$^{-1}$, the viscosity variation is much lower, and at $\dot{\gamma} \geq 200$ s$^{-1}$.

![Fig.2.6. Dependence of shear stress from shear rate (flow curve) for the whole blood.](image)
viscosity becomes constant asymptotically approaching a value, which is under normal conditions approximately \( -(4-5) \times 10^{-3} \text{ Pa}\cdot\text{s} \).  

In the range of shear rates \(0.01 < \dot{\gamma} < 1 \text{ s}^{-1}\), the flow curve for the whole blood in co-ordinates \(\tau^{1/2}, \dot{\gamma}^{1/2}\) is almost a straightforward line and thus is satisfactorily described by the Casson equations (2.5), (2.7). Similar behavior of flow curve for the entire blood is characteristic for range of shear rates \(1 < \dot{\gamma} < 20 \text{ s}^{-1}\) as well, however here the hematocrit is already \(H \leq 30\%\). In case of the hematocrit values \(H > 35\%\), the flow curve for the entire blood in co-ordinates \(\tau^{1/2}, \dot{\gamma}^{1/2}\) considerably deviates from the straightforward line that testifies to the fact that here the Casson equation does not work anymore. The coincidence of data on blood with the Casson model prompts that the reason for the non-Newtonian behavior of blood at the small shear rates is the process of convertible structuring of aggregates in blood (“coin columns”). The aggregating mechanism of convertible structuring of blood was proved by comparison of the viscometry data with the blood photomicrographs in transparent cone-plane viscometer of the LVT type Brookfield.

### 2.4.2 Dependence of apparent viscosity on the hematocrit

Volumetric RBC concentration (hematocrit index) is the major factor, which determines a blood viscosity. Typical dependences of apparent viscosity of blood on hematocrit, by different values of shear rates, are led in Fig.2.6. However, theoretical models taking into account influence of hematocrit on the blood viscosity are suitable just for the small volumetric concentrations of RBC, when hydrodynamic interactions among particles in suspension are practically absent. For example, if RBC suspension in some buffer solvent

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1 Practically constant viscosity of blood by high shear rates is called asymptotic viscosity of blood.
has concentration no more than 5% (H=0.05), then its rheological behaviors are described by equation of kind (2.1), where effective viscosity is a function of hematocrit

\[ \eta_a = \eta_0 (1 + \alpha H), \quad (2.21) \]

where \( \eta_0 \) is viscosity of solvent, \( \alpha \) is form-parameter (for suspension of spheres, \( \alpha=2.5 \))\(^1\). With increase of concentration, the RBCs begin to interact and the correlation (2.21) becomes unfair. A great number of generalizations for the Einstein’s formula, which allow accounting the RBC form more precisely, were proposed [3,4,6]. For example,

\[ \frac{\eta_a}{\eta_0} = \left(1 - H^{1/3}\right)^{-1}, \quad \frac{\eta_a}{\eta_0} = \left(1 - H\right)^{-2.5} \quad (2.22) \]

By higher hematocrit (H>0.1), dependence of apparent viscosity of blood on hematocrit is satisfactorily approximated by the empiric exponential formula

\[ \eta_a = \eta_0 e^{\alpha H}, \quad (2.23) \]

where \( \alpha=2.5 \). Equation (2.23) gives an example of approximation for a set of dependences presented in Fig.2.7 with just one relation, for which \( \alpha=(3–0.761)g \gamma \). Here \( g \) is acceleration due to gravity.

Comparison of viscosimetry data for normal RBC and their “shades” with the identical hematocrit index (0.35≤H≤0.75) in the blood plasma shows that, at the shear rates \( \dot{\gamma}<100 \text{ s}^{-1} \), the viscosities of both suspensions do not differ. Only at the higher shear rates...
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Fig. 2.7. Apparent viscosity depending on hematocrit by different shear rates
(1 – $\gamma_1$$=52$ s$^{-1}$, 2 – 5.2 s$^{-1}$, 3 – 0.52 s$^{-1}$, 4 – 0.052 s$^{-1}$, 5 – rigid cells).

rates, the viscosity of plasma with RBC shades is something less than viscosity of plasma with the normal RBC.

2.4.3 Apparent viscosity depending on the deformable properties of RBC

Dependences of apparent viscosity of blood on hematocrit and shear rate for hardened $^1$ RBC conducted on rotary viscometer are shown in Fig. 2.7 (curve 5). Obviously, hardening of the cells does substantially multiply viscosity of their suspension by the high
RBC concentration, does not change viscosity by small RBC concentration and nearly completely eliminates viscosity dependence on the shear rate, so that the graphs at different shear rates practically coincide. That is, the suspension of hardening RBC is a Newtonian liquid. The above-mentioned experimental results led also to conclusion that decrease of viscosity in the areas II and III in Fig.2.6 is conditioned not only by destruction of RBC aggregates but by changes of deformability of RBC\(^2\) as well. Also there is data about disappearance of viscosity dependence from the shear rate in the cases when deformability of the cells has been changed through the osmotic phenomena, e.g. for the RBC placed in a low blood pressure (hypotonic) medium, that is by transformation of normal RBC in spherocytes.

Regarding the dependence of blood viscosity on form and sizes of RBC, reference data is present only for the normal cells of different sizes and forms by number of animals. The comparison of viscometric data for the blood of elephant, human, dog and goat thus showed dependence of results on RBC sizes only at presence of fibrinogen. In the defibrinated blood, in which the aggregation is excluded, clear differences were not observed. The latter corresponds to the theoretical knowledges, according to which the viscosity of suspension of the non-aggregating particles (at identical hematocrit) poorly relies on their form and shear rate.

2.4.4 Dependence of apparent viscosity on the temperature

Increase of liquid viscosity with the drop in temperature is conditioned by the molecular-kinetic processes and, naturally, exists for a blood. Thus, cooling a blood from 37°C to 10°C yields the increase of asymptotic viscosity of blood approximately twice. Moreover, this dependence is non-linear and can be expressed by Arrenius type equation

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1 Hardening of the cells has been performed through their by incubation in the glutaraldehyde.
2 Namely this supports the RBC mass flow even by 100% hematocrit.
\[ \eta_a = ae^{E/RT}, \] 

where \( a \) is a multiplier, energy of activating \( (E=5.15*10^3 \text{ J/kg at H=0.44}); R \) is the universal gas constant, \( T \) is a temperature. But the relative apparent viscosity of blood does not rely on temperature at the shear rates \( 1<\gamma<120 \text{ s}^{-1} \). Therefore, it is naturally to suppose that, since energy of activating for blood and water is practically identical, temperature dependence of blood is conditioned rather by the blood plasma properties than by interaction among the RBCs. Only for very low shear rates \( (0.1<\gamma<0.5 \text{ s}^{-1}) \), the relative apparent viscosity of blood slightly grows with a drop in temperature.

### 2.4.5 The scaling effects

The above-presented data on the apparent viscosity, which were got with the use of rotary voscometers, has been mainly confirmed by measuring the apparent viscosity, while the radius of working area of capillary kept more than 1 mm. With reduction of capillary radius (especially in range 5–200 mkm), the apparent viscosity calculated according to the formulas (2.20) turns out on 10-30% less than the apparent viscosity got with (2.17)-(2.19). This effect concerning the blood flow is called the Fahraeus-Lidqvist effect. In capillaries with diameters less than 50 mkm, the Fahraeus-Lidqvist effect can show up so strong that all the other effects of viscosity dependence on shear rate, on hematocrit index and on RBC deformability become negligible. The Fahraeus-Lidqvist effect shows up for the suspension of RBC “shades” as well. The effect has been observed even for the RBC suspension in the hypotonic salt solution, where RBCs were transformed into spherocytes and suspension must show no non-Newtonian properties. Moreover, with growth of concentration of such suspension of spherocytes, the effect intensifies.

\[ \text{1 Mechanism of the Fahraeus-Lidqvist effect is considered below in the Chapter 5.} \]
Later on, the Fahraeus-Lidqvist effect revealed in the capillary viscometers was observed also in the rotary viscometers with the coaxial cones (or cylinders) having the gap less than 200 mkm. For the rotary viscometers with the gap bigger than 200 mkm and for the cone-plane viscometers, the Fahraeus-Lidqvist effect has had no remarkable influence on the results of experiments. There also is data that for capillaries and gaps, which are less than 10 mkm, the reverse effect was revealed, namely, the apparent viscosity of blood is growing by further reduction of the capillary or gap.

2.4.6 Methods for calculation of limiting shear stresses

Classic measuring method for $\tau_0$ supposes drawing the graph $\tau^{1/2} = f(\dot{\gamma}^{1/2})$ in case of researches of blood viscosity at the smallest shear rates ($\dot{\gamma} < 0.1 \text{ s}^{-1}$). Then, using the Caisson model, linearly extrapolate this graph to crossing with y-axis. Intersection coordinate is taken as a sought value. However, features of measuring of shear stress at the small shear rates, compel to build a basic graph $\tau^{1/2} = f(\dot{\gamma}^{1/2})$ taking into account the value of minimal shear rate available for registration. Therefore the extrapolated value of the initial shear stress strongly relies on size of this minimum registered shear rates. For example, values of $\tau_0$ got with extrapolation of graphs, which are built at the minimum registered shear rate $\dot{\gamma}_\text{min} \sim 0.1 \text{ s}^{-1}$ and $\dot{\gamma}_\text{min} \sim 1 \text{ s}^{-1}$, differ about 50%. With the further reduction of minimum registered shear rate ($\dot{\gamma}_\text{min} < 0.1 \text{ s}^{-1}$) an indicated phenomenon reveals much less but such shear rates are available for measuring only at some viscometers.

Direct measuring of the value $\tau_0$ in viscometer turned out difficult, since the results by $\tau_0$ registered after the stop of flow on the remaining twist of the weighed string, as well as

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1 This effect is also considered below more in detail in the Chapter 4.
the results got with the use of similar method in capillary viscometry, are prone to the substantial influencing of RBC sedimentation. Therefore the direct methods give strong errors in measuring of $\tau_0$.

Relatively simple method of $\tau_0$ registration is based on measuring parameters of RBC sedimentation in the buffer solution in capillary with the expanded lower end. The column of RBC settled in such pipe is torn itself at some level of expansion, diameter of which $d_0$ is measured to calculate after the value of $\tau_0$ by formula:

$$\tau_0 = g \varphi (\rho_p - \rho_f) d_0 / 4 \cos \varphi .$$

(2.25)

Here $\varphi$ is the angle of the pipe extent ($\cos \varphi \approx 1$); $\rho_p \rho_f$ are the densities of RBC and buffer solution, accordingly; $g$ is acceleration due to gravity. The values of $\tau_0$ got with equation (2.25) turned out close to the values of $\tau_0$ obtained with the use of extrapolation, so that $\tau_0=0.01–0.03 \text{ N/m}^2$.

Suspension of RBC in the physiological solution, as well as the blood plasma and serum do not have threshhold in the shear rates. Therefore, it is possible to suppose, that dominant factor of the presence in blood $\tau_0$ is a presence of fibrinogen. In a blood of practically healthy donors, in the range of fibrinogen concentrations $0.21<\beta_f<0.46 \, \%$ and at hematocrit $H = H_0 \div 45 \, \%$, the following equation is satisfied

$$\tau_0^{1/2} = (H - H_0)^{3/2} (0.49 \beta_f + 0.24) .$$

(2.26)

Here $\tau_0$ is measured in N/m$^2$. The physical sense of the threshold in shear rates consists in that the RBCs form some continuous structure in all mass of the blood in the rest giving no possibility to develop the flow. Depending on the orientation and location,
some RBC aggregates are involved in this structure to a different extent, but obviously, that at higher hematocrit a quantity of such implicated elements must be larger, what is confirmed by the first cofactor in equation (2.26).

There is a certain critical level of hematocrit $H_0=0.013-0.07$, below which the threshold of shear stress in the blood is not recorded. Comparison in GDM- viscometer of the heparinized blood of elephant, dog, goat and human revealed some weak non-linear dependence of $\tau_0$ on the size of erythrocytes. However, according to the existing estimate of the magnitudes, the threshold of shear stress does not exceed on all $\tau_0 = 0.05 \text{N/m}^2$. Level of influence of the threshold on a blood flow depends on the ratio $\tau_0/\tau_w$, namely the influence remains with $\tau_0/\tau_w > 0.001$, where $\tau_w = \frac{R \Delta p}{2L}$ is the shear stress on the wall.

### 2.4.7 Temporal variation of the apparent viscosity

A necessity of conducting unstationary viscometric experiments is related to incompleteness of data, which are got for unchanging in time stresses and shear rates. In case of practically instantaneous start of rotation of outward cylinder in viscometer with the coaxial cylinders, the temporal dependence of twisting moment, which is registered on the weighed string, relies very much on the shear rate (see Fig.2.7). The curve has practically rectangular form at the shear rates $\dot{\gamma}>20 \text{ s}^{-1}$ (3), while at the small shear rates $10^{-2} < \dot{\gamma} < 5 \times 10^{-2} \text{ s}^{-1}$ the gradual relaxation leads to the stationary value (1), and in the intermediate range of shear rates $10^{-1} < \dot{\gamma} < 10 \text{ s}^{-1}$, first the peak value of torque is observed, which considerably exceeds its stationary value (2).

The above-mentioned facts\(^1\) can be logically treated as non-linear viscoelasticity of the blood due to elastic properties of RBC and their aggregates [11]. But viscoelasticity

\(^1\) Also the results by blood viscosity measurements in periodical regime considered in Chapter 5.
The above-mentioned facts\(^1\) can be logically treated as non-linear viscoelasticity of the blood due to elastic properties of RBC and their aggregates [11]. But viscoelasticity assumes the presence in the blood of the effect of the normal stresses (see (2.13)). The torsion head of the Weissenberg rheogoniometer can be supplied with a set for registering its displacement caused by a difference in the normal stresses. In this case, the instrument allows measuring the presence of a difference in the normal stresses \(\sim 0.09 \text{ N/m}^2\). However, none difference in the normal stresses was registered in any experiment. Thus, if in the blood there is a difference in the normal stresses, then they must be very small. The peak of torque in Fig.2.8 is caused by destruction of the structure of RBC aggregates due to which the blood reveals properties of Thixotropic liquid (see (2.12)). Actually, processing of RBCs with the preparations, which strength the RBC aggregation, increases

\(^1\) Also the results by blood viscosity measurements in periodical regime considered in Chapter 5.
a peak, and after addition of the low-molecular dextran or sodium salicylate, which destroy the aggregates, the peak disappears entirely. The presence of hysteresis loop for the blood was simultaneously discovered by several authors [11]. However, the form of hysteresis loop shown in Fig.2.9 is not canonical and does not coincide with the graphs for the purely thixotropic or purely viscoelastic liquids.

![Hysteresis loops for the blood](image)

**Fig.2.9. Hysteresis loops for the blood.**

### 2.4.8 Results in blood rheology got by KNU jointly with medical researchers

At the Kiev National Taras Shevchenko University together with the physicians (Ukrainian N.D.Strazhesko scientific research institute of cardiology, Kiev scientific research institute of hematology and blood transfusion) were carried out the experimental studies of the rheological behaviors of blood with the use of rotational viscometers Reotest-2 and EV-3 [18]. Mainly the experimental studies were conducted on the Elastoviscosimeter of Acad. Trapeznikov, EV-3, which allows measuring at the very low
shear rates, up to $\dot{\gamma} = 10^{-5} \text{s}^{-1}$, while Reotest-2 allows such measuring only with $\dot{\gamma} \geq 200 \text{s}^{-1}$. Studies were directed toward the solution of medical problems.

For example, in the Ukrainian N.D.Strazhesko scientific research institute of cardiology, the rheological characteristics of the stabilized blood, together with other clinical characteristics, were used for evaluating the severity of the diseases of cardiovascular system (ischemic disease of heart, myocardial infarction, etc..) and the control of the effectiveness of the utilized methods of the treatment. The nature of changes in the rheological characteristics of blood measured periodically in the process of treating the patients, was one of the important indices. Getting worse in the state of patient, as a rule, was accompanied by an increase in the apparent viscosity of blood, an improvement in the state - by its decrease.

As an example, the results of the experimental studies of effectiveness of intravenous injection to patient, who suffers the ischemic disease of heart, a heparin, which prevents the coagulation of a blood (experiments were carried out with intact non-stabilized blood on rotational viscometer Reotest-2 in the range of shearing rates from 200 to 1300 s$^{-1}$ [18]) are given in Fig.2.10. In the experiment, the intact non-stabilized blood shows up the obvious dependence of the flow curve on the time and on the tendency of a change in the shear rate. During the sequential loading and unloading, the flow curve, as a rule, acquires hysteresis nature (1,2,4,5), which is caused, as mentioned above, by the aggregative properties of the blood, to which is assigned the influence of the effect of blood coagulation due to destruction of blood plates by the walls of the instrument cylinders under the experimental conditions earlier than at rest. The injection of heparin into the organism leads to the decrease of shear stress in the blood but in this case hysteresis also disappears (3) - the health of patient is improved. After 4 hours, in spite of the continuous decrease of shear stress, the health of patient deteriorated, which is accompanied by the appearance of hysteresis (4,5).
Fig. 2.10. Flow curves (dependence of shear stress $\tau$ on shearing rate $\dot{\gamma}$) for non-stabilized intact blood with the intravenous injection of heparin: (1,2) - before the injection, (3) - 1 hour after injection, (4,5) - 4 hours after injection [18].

Together with colleagues from the Kiev scientific research institute for hematology and blood transfusion, a study of the rheological characteristics of the preserved blood and obtained from it erythrocytic mass in the process of their storage for a period of 21 days, were carried out [18]. Except rheological characteristics of these media, the characteristics of biophysical state of erythrocytes (presence of spinous and spheroidal cells, the electrophoresis mobility of erythrocytes, etc.) and a number of other biophysical characteristics of the media in question were investigated. Studies showed that substantial changes in the rheological properties of the preserved blood and erythrocytic mass, independent of the blood preservative used, occur during the first 14 days of storage.
(viscosity increases by 60-80%), while further changes up to 21 days, are unessential. The correlations of viscosity change with changes in the above-indicated biophysical characteristics of the media investigated, have been established. The conducted comprehensive investigations confirmed the possibility of an increase in period of storage of erythrocytic mass.

2.5 The mechanisms responsible for the non-Newtonian properties of blood

2.5.1 Motion and deformation of the RBC in a shear flow

According to the existing observations, blood cells are carried by flow along the axis of the pipe but simultaneously they accomplish the disorderly transverse oscillations\textsuperscript{1}. Permanent RBC collisions are the reason for the random nature of their trajectories. Moreover, the divergence of erythrocytes after their convergence is rather caused by flow hydrodynamics than by elastic properties of their shells. In the motion of single erythrocyte or several erythrocytes, inside the elementary volumetric element of the blood, it is possible, thus, to isolate regular (average) and disorderly (fluctuation) component. Evidently, Fig.2.11 shows that the profile of the average velocity of erythrocytes in the pipe is blunt (steeper than in parabola), which confirms the Pseudo-plastic properties in the blood. In a shear flow, BRCs do begin rotating (more precisely, turning somersaults) in the vicinity of the pipe wall. The angular rate of RBC rotation $\omega_p$ can be approximately considered equal to the vorticity $\Omega$ of the elementary volume of the blood containing the RBC. Therefore, in undiluted suspension of erythrocytes, the presence of the sealed velocity profile evidences the smallness of vorticity (but it means

\textsuperscript{1} With the standard conditions, the blood in the layers thicker than 100 mkm is practically opaque; therefore all microscopic observations were conducted either in the thinner layers or the suspension of the transparent shadows of the erythrocytes (in the rheological properties it was analogous to the intact blood), with the insignificant addition of normal RBC, was used.
shearing rates, since here $\dot{\gamma} = 2\Omega$ in the flow core. In the vicinity of the pipe wall, where the rotation of RBC slows down, $\omega_\rho < \dot{\gamma}$.

Microscopic observations of the behavior of erythrocytes in the gap between cylinders of viscometer showed that the somersaulting of RBC ceases already with shearing rates $\dot{\gamma} > 50 \text{s}^{-1}$. However, the RBC continues to revolve relatively to its contents (“tracked motion”). If in this case, the rigidity of the RBC membrane is somehow increased, for example, via the hyper-osmotic wrinkling of its membrane, then with $\dot{\gamma} > 100 \text{s}^{-1}$, the RBC continue somersaulting, however, already as a single whole (without “tank-
"treading" motion). Note that at the shearing rates $\dot{\gamma} > 24 \text{ s}^{-1}$, the erythrocytes acquire oval form, and at $\dot{\gamma} > 1200 \text{ s}^{-1}$ they become sharply elongated\(^1\).

According to the existing observations, it is also possible to draw the conclusion that the effects of orientation for the suspension of erythrocytes are essential only for the strongly diluted blood.

### 2.5.2 Aggregation of the RBC

Images of the RBC assembled into the “rouleau” of different forms\(^2\) are given in all manuals on hematology (for example, Fig. 2.12b). The aggregates are destroyed during the mixing of the blood ($\dot{\gamma} \uparrow$). And after the stop of mixing ($\dot{\gamma} \downarrow$), they are restored\(^3\).

Sizes of aggregates for a flow in vivo essentially depend on the conditions of blood flow. For a flow in vitro, they depend additionally on the geometry of a set, on time and initial state of the blood samples. The control of all these factors very complicates the microscopic examinations of aggregates; therefore first the indirect method of evaluating the size of aggregates was proposed based on the settling rate of erythrocytes (SRE). The spherical drop falling down in a liquid is described by the generalized Stokes formula

$$v_p - v_f = \left( \rho_p - \rho_f \right) g \frac{K_w^{3/2}}{\eta_0}, \quad (2.27)$$

\(^1\) Deformation of erythrocytes in a flow is going in a passive way.

\(^2\) Besides the reversible aggregation into the “rouleau”, the irreversible gluing of erythrocytes (agglutination) is observed in the pathology (e.g., under the group incompatibility of the donor blood).

\(^3\) For the designation of the pathologic aggregates of the red blood cells with the less regulated structure than the “rouleau”, the term “blood sludge” is introduced.
Fig. 2.12. Macrofilming of the blood in viscometer by high shear rates corresponding to the flow near the arterial wall (a – to the left), near the venial wall (a – to the right), and by small shear rates in the flow core (b).

where \( v_p, v_f \) are velocities of RBC and plasma, respectively, prone to the mass conservation equation for the mixture \( v_p H - v_f (1-H) = 0 \); \( \rho_p, \rho_f \) are the densities of RBC and plasma, correspondingly; \( \eta_0 \) is viscosity of plasma; \( K \) is coefficient dependent on the average size and form of aggregates and on hematocrit \( H \), which coincides with the coefficient \( 1/6\pi \) in the Stokes formula for a spherical particle falling down in infinite medium \( (v_f = 0) \); \( w \) is an average volume of a single aggregate; \( g \) is the acceleration due to gravity or centrifugal acceleration with the centrifugation. Calculation with the simple model of the kinetics of aggregates, according to Smoluchowski, allows estimating the coefficient \( K \) in equation (2.27) and the rate of change of the number of aggregates per unit of volume as well [11]. In this case, an existence of large-scale motions is evaluated only on the average, through the coefficient \( K \) and equation of the kinetics of aggregation. The small-scale effects (rotation and the fluctuating motion of the settling particles) are also evaluated at the average. Nevertheless, measuring the SRE index and evaluating the
viscosity of plasma, even according to the approximate Stokes formula, gives an average size of the aggregates. For instance, for SRE of 100 mm/h and $\eta_0=1.8 \times 10^{-3}$ Pa*s (1.8 sP), the mean diameter of aggregate is 38 mkm. As a result, although a physical sense of SRE index is not entirely clear [11], SRE increase corresponds to increase in average size of aggregates. Therefore measurements of the settling velocities of erythrocytes are also used for the quantitative assessment of the aggregative properties of red blood cells.

As a quantitative criterion in the microscopy of a strongly diluted blood (H<4 %), the average length of the “coin columns” is used. In this case, a length of aggregate is a linear function of the hematocrit H. With higher hematocrit, the aggregates do not always have more complex structure, and not only linear; moreover microscopy is strongly hindered in this case. Basic factor affecting an aggregation is undoubtedly contained in the plasma since the washed clean erythrocytes do not aggregate in the buffer solution. An addition of plasma immediately provokes an aggregation.

For estimation of aggregation in undilute blood, the special method was developed in the Laboratory of research cinematography of the Pavlov Institute for Physiology by Russian Academy of Sciences. For the researches, a flowing demountable cuvette of rectangular section (0.05x10 mm) was used, with a varying width of gap. By running through the cuvette of every test of blood, the photomicrography was conducted from the distance of 30 mm, for the stationary flow and after the stop of flow. The number of cells in aggregate was computed planimetrically. The number of aggregates was observed diminished with increase of flow velocity. After stop of flow, the growth of sizes of aggregates and their number have been immediately registered. Thus, on results of these experiments, the assumption was made on the hydrodynamic mechanism of primary convergence of RBC in a flow up to their sticking together in the “coin columns”. The aggregation photomicrography in the viscometric measuring showed that at $\dot{\gamma} \approx 46$ s^{-1}.
almost all aggregates are linear chainlets \( \sim 15 \, \text{mkm} \), and at \( \dot{\gamma} > 100 \, \text{s}^{-1} \) the aggregates in blood were not discovered. Thus, the assumption on hydrodynamic mechanism of RBC convergence and their sticking in “coin columns”, was confirmed in these experiments. Electronic-microscopic researches of thin cuts of “coin columns” exposed a constant intercellular distance with the aggregation of that caused by fibrinogen (\( \sim 25 \, \text{nm} \)) and by different high-molecular dextrans (\( \sim 16-22 \, \text{nm} \)), where from the conclusion was done that intercellular distance during RBC aggregation is blocked by one layer of adsorbed by their ends molecules of fibrinogen (or dextran).

On the basis of that outlined above concerning the mechanism of the aggregation of erythrocytes, the following conclusions can be made:

- Fibrinogen is necessary for the aggregation of erythrocytes on the surface of colliding in the flow cells\(^1\);
- Divergence of erythrocytes occurs due to their hydrodynamic interaction;
- The final cohesion of RBC is going through the system of the intermembrane bridges.

The “aggregation force” \( F_a \) is defined as

\[
F_a = F_b - F_e - F_s ,
\]

(2.28)

where \( F_b \) is the force in bridges; \( F_e \) is the electrostatic repulsive force; \( F_s \) is hydrodynamic shear force causing disaggregation in a flow. Electrostatic repulsive force between the parallel charged surfaces is proportional to the area and superficial charge. It exponentially decreases with growth of the ratio of distance between RBC surfaces to the thickness of double ionic layer [14]. The estimation show that in case of distance between RBC about 20 nm, the repulsive force of normally charged RBC is of order \( \sim 0.01 \, \text{N/m}^2 \)

\(^1\) During the injection into the blood of the additives, which cause echinospherocytosis of cells, the aggregation immediately ceased.

\(^2\) Aggregation is observed also in the presence of the high-molecular dextran.
that corresponds to the shear stress at the shear rate $\dot{\gamma} \sim 1 \text{ s}^{-1}$. And the force $F_a$ must have the same order ($\sim 0.01 \text{ N/m}^2$) calculated on the unit area of contacting surfaces.
Additions:

1D. Blood pressure and methods of its measuring

The maximal pressure achieved at the moment of blood rejection from heart into aorta is named systole pressure (SP). After rejection of blood from a heart, the pressure falls to the minimal level, diastole pressure (DP). The difference between systole and diastole pressure is named pulse pressure (Fig. 1D-1). The middle pressure $S_m$ is determined by the formula:

$$S_m = \frac{S_c}{L_c} \tag{1D.1}$$

Where $S_c$ – area under the pressure curve, $L_c$ – pressure curve length.

Fig. 1D-1. Typical pressure curve for one cardiac cycle.

The pulsating nature of blood flow and high elasticity and extensibility of blood vessels determine rippling of blood pressure. In human circulatory system the amplitude of pressure waves grows, and the volume speed of blood falls towards periphery. The speed of pulse wave distribution relies on the vessel size and resiliency. It is 3-5 m/sec in aorta,
7-9 m/sec in arteries (subclavian and femoral), and 15-40 m/sec in the shallow arteries of extremities.

When measuring blood pressure by direct methods, a needle or a catheter connected with a manometer is inserted into the explored vessel, and according to the manometer displays one can judge about the change of blood pressure in vessel.

In case of indirect blood pressure measuring by Korotkov method a rubber cuff blown up through the pump is put on the examinee forearm. When the pressure in the cuff begins to exceed the pressure in the humeral artery, it falls and blood flow in it is halted. Cuff pressure on hand is registered by manometer (by the electronic or mechanical device, which registers pressure). A doctor puts a stethoscope (or a probe of automatic analyzer) on hand below the cuff and registers tones, emitted by a current blood. At the artery collapse tones are not auscultated. Then the pressure in the cuff is slowly diminished. When the pressure outside the vessel becomes lower than inside, blood current in the artery below the cuff decreases. Thus Korotkov tones appear, which are registered by a doctor or submachine gun. The manometer reading thus correspond to SP. As pressure in the cuff continues to fall, bloodflow in the artery grows and tones are changed. Right before the complete disappearance or sharp weakening of Korotkov tones in artery, a normal bloodflow is restored. The pressure in the cuff thus equally DP.

Russian doctor Korotkov invented the method of indirect pressure measuring in distant 1905 year, but this method is basic for any practicing doctor until now.

**2D. Blood types and rhesus-factor.**

In case of blood transfusion from human to human heavy reactions of an organism tearing away are possible, which can sometimes result in death. It takes place because human red corpuscles (erythrocytes) contain the antigens, which enter in the reaction with the blood
plasma antibodies. As a result the irreversible agglutination of red corpuscles takes place. The difficulty of the reaction relies on the blood type of a donor and a recipient. There are four blood types in accepted nowadays system AB0: 0, A, B, AB.

When determine a blood type, examined blood is added to the whey of indicated group in accordance to the table:

<table>
<thead>
<tr>
<th>Whey</th>
<th>Agglutination</th>
<th>Blood type</th>
</tr>
</thead>
<tbody>
<tr>
<td>A and B</td>
<td>present</td>
<td>AB</td>
</tr>
<tr>
<td>A</td>
<td>present</td>
<td>B</td>
</tr>
<tr>
<td>B</td>
<td>present</td>
<td>A</td>
</tr>
<tr>
<td>A and B</td>
<td>absent</td>
<td>0</td>
</tr>
</tbody>
</table>

People with blood type AB are universal recipients, because they have no antibodies in blood at all. It is possible to give them a blood transfusion with blood of any type, not be afraid of red corpuscles agglutination. People blood type 0 – universal donors, because they have no antigens in blood. And their blood transfusion to other persons is not accompanied with the reactions of blood type incompatibility.

Another group of antigens is found in blood of most people (Rh). These antigens carriers are rhesus-positive (Rh+). In case of giving (Rh+) blood to (Rh-) man, the visible reaction will not happen. However, the rhesus-antibodies will appear in his blood, which in case of repeated blood transfusion (Rh+) will result in complications. Genes determining (Rh+) blood are dominant in relation to genes, determining (Rh-) blood. That is why offspring of (Rh+) and (Rh-) parents will be (Rh+). Thus if father (Rh+), and mother (Rh-), their child will be (Rh+). In case of fetus antigens penetration through the mother placenta in blood, the antibodies to (Rh+) red corpuscles will begin to be produced in her organism. Now, if these antibodies back through placenta to a fetus blood, it can cause the agglutination of red corpuscles and fetus death.

It is possible to reduce the rhesus-incompatibility to the minimum by prescription of anti-rhesus γ-globulin neutralizing (Rh-) fetus antigens to pregnant (Rh-) women.
3D. Haematocrite and SRE determination.

Haematocrite is a volume of red corpuscles, separated by blood centrifugation at 1500g for 30 minutes. For the determination of vein blood haematocrite, a stabilizator-anticoagulant (heparine, citrate or sodium oxolate) is added into blood, preventing its coagulation. Then blood is centrifuged in a special measuring tube until red corpuscles are precipitated and plasma is in the form of supernatant (see Fig. 3D-1). The numbers on the test tube thus indicate the volume correlation of plasma and blood elements.

The correlation of specific density of plasma and red corpuscles is one of the factors, determining settling rate of erythrocytes (SRE). For the determination of SRE a special graduated test tube with stabilized blood is placed vertically and a thickness of precipitated red corpuscles for the equal intervals of time is measured (the results usually presented in mm / hour).

![Fig. 3D-1. Test tube for haematocrite and SRE determination.](image)

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1 Or under the high speed but shorter period of time.
2 Obtained haematocrite is called apparent, because ~4% of plasma is left in red corpuscles mass. For getting of real haematocrite, apparent haematocrite should be multiplied by 0.96.
4D. Osmotic and oncotic pressure in blood.

If we divide two solutions, one of which is more concentrated (i.e. contains more dissolved particles), by the semipermeable membrane, which skips a solvent (for example water), but does not skip the dissolved matter, the water current exists from less concentrated solution in more concentrated (see Fig. 4D-1).

Fig. 4D-1. Nature of osmotic pressure (pointers show the direction of solvent motion ($P_1 > P_2$), darker color corresponds to the greater concentration of solution: $C_1 > C_2$).

Thus we can call osmotic pressure the force, which causes the motion of solvent through the semipermeable membrane. Human being has osmotic pressure of about 7.5 – 8.1 atmospheres, about 60% this pressure is caused by NaCl.

Osmotic pressure is created not only by crystalloids (by salts) but also by colloids – plasmatic proteins. Osmotic pressure, caused by plasmatic proteins is called oncotic pressure. Thus, although the absolute value of plasmatic proteins in blood is 7-8%, which is almost 10 times more than all salts dissolved in plasma, oncotic pressure created by them makes only 0.5% of osmotic pressure, which is about 0.03 – 0.04 atmosphere.
Literature.