

OUR “SHAGREEN LEATHER” IS OUR PROBLEM, AND WE ARE THE ONES TO SOLVE IT.

7. THE CHANGE OF PARADIGM. FIRST STEPS.

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"Dreams that come true are not dreams but plans."

A. Vampilov

The problem of Timeliness of scientific and technological achievements is brought up for discussion. Existence of more sophisticated mechanisms rather than the real implementation of a new idea, development, and even prototype is being postulated in order for this novelty to enter life and everyday routine. As for our “shagreen leather” problem under consideration, Timeliness is conditioned by Mankind passing into the new system of his existence called the Noosphere. And this fact predetermines the inevitability of its solving. The notion of biological time is analyzed on the grounds of its difference from physical one. The last, though, still not resolved fundamental restriction on the way to the biological time control, i.e. heterochronous incompatibility, is highlighted. The reality of the beginning of the individual’s parting in biological time with his subsequent heterochronous compatibility was also marked to have passed into practice, in the form of cord blood preserving and storing in liquid nitrogen (i.e. at the condition, when the biological time is stopped) with its subsequent usage as autologous material for tissue and organ reconstruction (“regenerative medicine”) for a young, adult and old organism to be. Possible ways of heterochronous material usage and expected establishment of the new “age regulating” trend in medicine are analyzed.

Keywords: biological time, heterochronous compatibility, cord blood

Newness and Its Time. The notion of *Newness* is very ambiguous in its very sense. It is most likely to be denied to start with (“what a nonsense”, “absurdity”, “you could have read some textbooks at least”, *etc.*). Later, in some time, after approbation, validation, and theoretical analysis, *etc.*, in the generalized form, the mentioned *Newness* comes to two probable variants depending on the person and his way of perception. The

first variant says that the *New* is the *Old*, though well-forgotten. The second one says that the *New* is clearly obvious (however, only on its being formulated, grounded, and conceived).

The matter of time parameter of conceiving the *New* stands in a considerably more complicated way. The point is that the notion of “in some time” may be measured in weeks, as well as in centuries. To appraise such a time parameter, there are definitions, marvelous in their obvious commonness, and at the same time incon-

ceivable in their essence of inner mechanisms, namely *Timely* and *Untimely*. The commonness and obviousness of these definitions is clear. So what is inconceivable, then? Let us consider the problem of our “shagreen leather” from these standpoints (obviousness and inconceivability), shall we?

The fact that the man does not accept his End is as old as the mankind itself. Throughout time there have been very many smart (very smart, talented, ingenious, *etc.*) people. Likewise, there have been countless attempts to analyze all the variants of solutions to End disclaimer, calculations and innovations (which will be evaluated only after people grow up to their comprehension). And there surely have been enough rulers, ready to give everything and everyone for their Precious Self (hence, there should not have been any problems with economic or any other support). There has been much more stuff to reach the desired. The whole History of Man was like that. Still, once we depart from hoary antiquity and limit ourselves with well-known historically and solemnly trustworthy facts, we will discover that the most notable ideas of modern times are of rather venerable age.

More than 100 years ago Weissmann introduced the notion of germ plasma, grounded and pointed its localization. A century ago Mechnikov [1] wrote “...it would be extremely important to define the reason of old age. We do not lack hypotheses concerning this matter”. He was also the one to formulate the general conceptual idea of toxic products, generated in human body, as factors of continuous destruction of the organism and to suggest the method of dealing with it. A hundred years ago, Maximov proposed, grounded, described, and made known to the whole world the idea of human stem cells *i.e.* the idea of continuous self-renewal. About a hundred years ago, Carrell developed and introduced into world practice the technology of obtaining and maintaining the cell cultures of vertebrates. Almost 80 years ago Griffith proved by experiments the separation of heredity from the Living (*i.e.* in fact, the existence of heredity substance and the first technology of dealing with it, namely the transfer of hereditary information, selection of transformants, *etc.*). Approximately 70 years ago, there was a literal “explosion” of world interest to the progress of biology and medicine, caused by equally tremendous progress

in the knowledge of the Living and the ways of its maintaining, which is of great importance as well. However, only in the recent decade, the problem of “shagreen leather” was adopted to the Agenda as a strategic task. It was finally adopted not on the level of conversations, wishes, dreams, or science fiction, *etc.*, but on the level of problem setting, force and means concentrations to solve them, mechanisms creation for their implementation and the like. Why? The answer manifests itself so obviously – because only nowadays it has become *timely*, as only nowadays the Science has reached the proper level. But still why is it only nowadays? The people who do not understand it and, thus, ask such questions are sure to be explained that the development of everything (society, science, culture, thinking, and so on and so forth) is gradual, therefore, it is only now that all the mentioned have come to be *timely*. At this point the mechanisms are imperceptibly substituted for phenomenology. Why has the time come only now and what kind of time is that? And what does “the time has come” mean? Why has it happened all of a sudden that everything has got centered around the “specific time”, around the individual lifetime, has actually grown into the major problem of developed countries, and which has become the longing point of physics, and chemistry, and nanotechnology, and the mind of society, science, politics, *etc.* (though there have been countless attempts to fulfill the mentioned wish, and the wish itself is as old as the Mankind)? What is the foundation of it, what are the mechanisms of the *Timely*?

The whole history of mankind reveals that all this is so extremely complicated (while seeming absolutely common and obvious). Let me give you the example from a completely different sphere. Once upon a time, which actually was in the previous millennium (though, at the very end of it), the Author happened to be at the Chivalry Hall of the Hermitage. Everything had its place. The mannequins of knights in medieval armour, knights’ horses in forged defense, swords, spears, and other necessities of that period. And at the walls there were displays of arquebuses, muskets, and other arising new technology of killing your own kin, which was awkward, heavy, slow, though rather up-to-date and very advanced for that time (comparing to spears and swords). All of these gradually entered the arsenal,

slowly joining traditional battle axes, spears, swords, and other customary, handy and convenient "for proper usage" arming. All this new arming was loaded through the muzzle, to make only one shot in the battlefield (killing range ability of a bullet was small and before one could reload such a "shooting stick" confronting sides had enough time to reach each other on foot and fought man-to-man, whereas muskets and arquebuses were of hindrance only).

And all of a sudden one of the displays of the 17th century arsenal had a gun whose loading mechanism was made as revolving feed system which was a very simple but absolutely real prototype of cartridge having enough gunpowder and bullets to make six shots. This was neither an idea, nor a picture, nor a draft, but a real weapon capable of changing the course of any battle. Having such weapons even a small group would have defeated the whole army – they would have shot all the attackers, that is it. The significance of such a novelty should have been understood by all the characters of that time: from regiment donkey to the King. The *Timely* of this device for the time period, worthily following the traditions of 20-year, 100-year and other wars, when weapons were the main means of solving the "question" of anybody's existence - from regiment donkeys to kings, should have gone without saying. Oh, nope. Nothing had happened. The novelty was not put on large scale. Only in 200 years analogous revolving feed system devices of universal solution to human conflicts in the whole range of their being – from prairie to stone jungles - appeared and spread widely. The reliability of such a system was almost absolute, was it not?

The Author heard from World War II soldiers that when they had to go to the rear of the enemy where split seconds separated life from death, they used to take revolvers(nagants), if they managed to get them, produced in the beginning of the century (the previous one) rather than guns of the latest models. Unlike the latter the revolvers(nagants) never failed. The whole history of Mankind is filled with the *Untimely* of the obvious *Timely*. The *Untimely* vanished even after being put on large scale and proved as absolutely perfect.

That was the case with the vanishing of "Greek fire" – thousand-year-old napalm. This burning "something", not extinguished with water, vanished together with the fire-throwing device, hurling all-consuming

mass destruction means aiming rather precisely to considerable distances in both sea and land performance. And all this occurred after its successful applications, solving the result of battles. Instead of seemingly absolutely obvious spreading, everything turned to be *vice versa* – towards its more scarce usage (and each time with the highest efficiency). It was such a radical disappearance, that even nowadays the mighty Science and Technology of the third millennium can not render its composition.

Archimedes' reliable battlefield devices, made and effectively used more than 2200 years ago for the defense of the city of Syracuse, however, did not receive a great effort of development, preserving him to us as a great scientist and inventor, who *timely* discovered the principle of buoying up force of a body immersed in a fluid, as well as left mathematical calculations, very sophisticated for that time and understood by a few for the next several centuries.

The gunpowder was known in China from immemorable times. The explosive potential demonstrated everyone its mighty power with absolute visualization. Yet it was used for entertainment only. For a millennium! And only several hundred years ago the time had come for it to be used by its "direct application". The same can be said about other, many other things.

So that's the way it turns out, when behind the *Untimely* and the *Timely*, except something obviously lying on the surface (which could not be accomplished technologically at that *untimely* time), there is also something very deep-laid. And it is this deep-laid something, that determines whether the New will develop (*i.e.* whether it is *timely*) or it will not (*i.e.* it is still *untimely* now). Let us look now from the standpoint of these deep-laid mechanisms (and not from the standpoint of phenomenology – the Time Has Come), what is behind the *Timely* here and now, at this point, in the problem of "shagreenity" accepted for practical realisation. It is not mere curiosity. It is the matter of principal importance. Will this commenced assault of the problem come to the conclusion, will nowadays boom in biology and medicine be not substituted by something else, will it not turn to something else (exploration of the Moon, colonisation of Mars, interstellar flights, realisation of endless opportunities of space vacuum,

exile to virtual world, ideas of travelling in time and many other things)?

The Beginning of the Beginning. Human perception of the surrounding inconceivable, adjoining to unreality, World as obviousness, banal commonness, that is taken for granted and understood by itself, was enhanced by its human nature to almost absolute. Thus, a small difference indicated by *almost*, distinguishes the Man as something special (the very *sapiens*) from purely biological, completely submerged and fully belonging object of Biosphere, only rationally perceiving the surrounding as well as only rationally reacting to it, in an adequate way.

A great astronomer Shklovsky wrote an excellent book “Universe, Life, Intelligence”. Everything in this book was simple, accessible and clear. Somehow the Universe appeared by itself, to be such a riot, though absolutely osseous, inanimate matter. The way of its appearing is not clear yet, however, it does not matter. The result is what really matters: it APPEARED. Out of it, just by itself, in some always gradually perfecting way (what difference does it make?), the Life appeared. How did it appear? – the Science does not know yet, we will know eventually, anyway. Well, and the Life, of course, produced the Intelligence in some time. As a matter of fact, at that time (just some 50 years ago), that was the way it was thought of (except for Creationism, of course). Anyway, the questions like “and why in the world?” - were not even discussed, were just limited by shrugging one’s shoulders and expressing a pity for those-who-asks’ immaturity and/or natural stupidity. Everything was absolutely obvious, as that’s how it is, hence, as it is, what is not clear then?

Something has changed in the course of several recent decades. They began thinking, very cautiously, though, but still they did, of really – why? As “that’s how it is”, then there are certain principles, mechanisms, conditioning why “it is so”, why it is this way and not the other, *i.e.* why out of something, which existed before, there appeared “as it is” (and only “As It Is”), and where this “as it is” is going to? Regardless of the outlooks of “why-explainers”, the admittance of objectivity of the principles of the Universe (*i.e.* the existence of certain rules, that all the Being is subdued to) is a real fact now. The dispute is going on about only the mechanisms, providing the observance of these rules by

the whole Being (in fact, the existence of the whole Being in accordance to strict rules and their realization in the form of the rules and implementations, *i.e.* the mechanisms, directing the Being). These (probably) are the principles of the Universe for inanimate matter formulated by physicists at least in some way. The development of the Universe, as a whole, as well as of its separate constituents of any scales, based on these formulations, has been described (as it is thought of today). It is not known yet, however, what is in store for this Universe – endless expanding (where to?) or “collapse” back into a certain point, in order to start all over again. Though, one should not expand our physics to such remote distances – the singularity is there, which has all the things in quite a different way (and in what way? – is practically inconceivable). Nevertheless, in local space and time, our modern physics works with rather significant resolution (that is, accuracy). Principal transformations in the status of Universe remain unknown. Why would the Life appear all of a sudden? The logics of thermodynamics, randomization of the information, accidental statistics, and all the rest of perfectly working Universe laws should have kept up absolutely to “the Laws of Nature”, as an indefinable barrier of such development, not permitting even the remote approaches of inanimate matter to Life. But the Life exists, certain information and the program of development lies in its fundamental principle. The fact that we call it “genetic” does not change the essence: there is a program in the basis of the living, by which it is developing. And anyone who is reading these lines can extrapolate it on his personality – what does he come from and by what program out of “what” he became what he became.

Then on the basis of Life the Intelligence was formed. Nobody knows what it really is, but the fact of its existence is known to everybody. Intelligence and Comprehension are two different things. The Comprehension lies in the basis of animate behavior. The rabbit runs away from the fox very comprehensibly, and the latter runs from the wolf, as well as all together they run away from the hunter. Regarding this context, everything is comprehensible with animals. In the context of existence and procreation (*i.e.* multiplication). Much more comprehensible than in regard to humans. But the Intelligence excels Comprehension. The Intelligence is

a sort of excessiveness of Comprehension. And so, from the standpoint of practicability of Comprehension of animate behavior, the Intelligence should not have appeared from animate. The excessiveness always demands additional expenses (in animate: construction materials, energy, space and so forth). The Intelligence is illogical, from animate practicability comprehension standpoint. The characteristic feature of Intelligence is the tendency to introversion in the borders of Intelligence. All sorts of abstractions like art, science, dreams, *i.e.* of the virtual world and the real one. Imagine a rabbit abstracting and dreaming some or a lion taking up some art. The former would be eaten immediately, and the latter would starve to death. And the foolishness of Intelligence is not dealt with in the rational world of Biosphere. It is the civilized society where individuals behave in a different way. Neither in the jungles nor in prairies there was anything like that before the Man. It was impossible to dream and to hang around with obscenities. Having appeared, the civilization (now the human one), constantly, throughout its history, has always been locking on itself, hindering its own development with full gear.

There is an excellent and very vivid example to it: Ancient Egypt. Egyptian civilization existed for many thousand years, and knew no equal; however, it left nothing but archeological remains, but it did not transform into anything. Though it had everything. Thus, other nations – barbarians, savages, having disappeared one by one, or “having been frozen up” for thousands years, like let’s say – Bushmen or Aborigines, giving new sprouts, however, managed to come to Intelligence. And about 250 years ago something inconceivable, impetuous (uncontrollable at present), taking place as sort of explosion, started the development. Of what? Civilization? With nuclear bombs and gas chambers? Destroying everything on the Earth by its technologies and aiming the same at Space? Of Humanism? With drug addictions and mafias? With all thinkable perversions under the banner of “Human Rights”? The Intelligence is standing behind it all and is leading it all. And no matter how you look at it, about 250 years ago the development of the Intelligence, in particular, started. Particularly of this kind. Where to? Why? What for? Certainly, there are answers to anything, if only we analyze what is going on. Let us try to do it. There is a

proverb about a shepherd-boy, ability of getting used to everything, and wolves. The proverb says that the boy decided to play a joke: he shouted “Wolves!” in the village and everybody, armed with all auxiliary means, rushed off their homes to beat them off. But there were no wolves. He would do the same several times and everybody got used to the fact that “Wolves!” was nothing but mere words. And when the real wolves showed up – nobody reacted to the “Wolves” cry. There was nothing left to wolves as to do their business, which they did successfully.

A similar thing happened to us. About a hundred years ago the development of the idea of Noosphere started. There was no Noosphere but there were conversations about it. Many conversations, nice and various. The topic was splendid to talk about, to write something on, to get together for discussion at the conference *etc.* Everybody got used to it. But when finally the Noosphere came into existence – nobody noticed that. Though everything was neat and clear. It is the Noosphere that does its own business. Its own.

Inanimate matter, the Universe, was realized as a result of a certain event, which obtained the name of “Great Explosion”, which nobody can imagine, and which was proclaimed practically inconceivable for peace of mind sake, as all the principles of our world do not work in the singularity point, therefore, what is that point, where it came from (and all the rest), is meaningless. Clear and simple. But once the Universe was realized, the principles of inanimate Universe started working in it. That is, it continues to develop in accordance to some mechanisms, which (in accessible understanding) are determined by some principles, the “Laws of Nature”, implemented by the Universe (and all their inanimate constituents).

We do not know how the Life appeared either. Having appeared, it, (the Life), formed a certain system of particular manifestations by particular manifestations – the Biosphere. All the animate exists and develops by the Laws of Biosphere, *i.e.* by certain mechanisms of animate living. In the system of the animate, the living behavior is determined by certain mechanisms and the external manifestations, determined by the operation of these mechanisms, are realized into something, which phenomenologically looks like certain behavior rules of particular representatives of the living in their system

– the Biosphere. But the duality is present here. Every particular manifestation – an individual being – exists and develops by the mechanisms (program, systems, which maintain it and have the realization of program information) of life as a phenomenon. Being joined together into the system and existing in it as individuals, they are subdued to the laws of the system, which is called the Biosphere in our terminology. And some unknown place in all this is occupied by the Man.

He is a typical living being by all of his parameters. By all (with no exceptions!) of these parameters, as a living being, he is not different from his “animal brothers” (and sisters too). Although, unlike all other living beings, he manifests the features of Intelligence and even, as it is commonly assumed, he is the material bearer of one, however, by a certain part of his brain. As a matter of fact, it is better not to think about that, for the sake of mental health preserving. Zalmanov was the one who wrote about it very impressively [2]: “If we get to remember that the cerebral cortex contains 14 billion of neurons, enclosed in depth of gelatinous mass, which does not exceed 2.5mm; if we get to remember that the brain contains 90% of mineralized water, we would be forced to assume that the anatomical substance of our thought, art, our technical and scientific achievements does not excel 300?m”. This being the case with our “animal brothers and sisters” that have the brain, arranged similarly to a human brain in many respects, moreover, the molecular composition is actually the same, then its mere quantitative increase does not solve the problem of mind: both whale and elephant have the total neuron amount which is much higher than the man’s, and all discussions regarding the proportion of brain weight to body weight are rather far-fetched (though it really is so). There is some other quality. And if this quality correlates with the quantity possessing this quality, than the figure will not be significant at all, however it still belongs to biology. That is why everything in a man is animate, practically Biospherical. And only something exceeding this “ALL” is what we called the Intelligence, and it comprises the Noosphere. And these Noospherical principles (*i.e.* the external manifestation of some mechanisms) have effect on everything, including the biological constituent of the bearer of Intelligence. But now they act for the sake of the other system – not Biosphere, but Noosphere. We fulfill these

principles (not thinking about it and even not suspecting about it), being already the operation material of Noosphere mechanisms.

The situation turns out to be very strange. Everything in the Man is the property of Biosphere, and the Man himself is the particular manifestation of Life as the phenomenon, and its small piece is nothing else, but the bearer and (or?) the “manifestator” of Intelligence. In fact, what is this Man? The answer to this very question contains the explanation of everything that is taking place in human civilization today. The main point of the answer is, that regardless of complete biological essence, the Man has formed his own, practically all-sufficient system since the middle of the previous century. But he formed it in a non-final shape for the time being, and only on its minimal sufficient level. What does “formed” mean and what does the “minimal sufficient level” mean? In order for some assembly to be called a system, this assembly has got to be self-sufficient. The notion of “self-sufficiency”, in the absolute shape, most likely has no meaning. Self-sufficiency has the meaning with the reference to its particular variants of “something”. Recently, two unequal, though self-sufficient, systems have been available for our observation in the field of the Universe.

The first one is the “inanimate” matter, organized in the shape of the Universe, existing by its inherent mechanisms, which provide such existence and revealing its properties in accordance with such mechanisms, which in the shape of phenomenological generalization of the manifestations of mechanisms operation was stated by physicists as “the Laws of Nature“. The self-sufficiency of the Universe is evident: it is in its composition (matter, energy). Something incomprehensible till now, though well described from the phenomenological standpoint by “the Laws of Nature” as the condition of existence, is the Time: “everything takes place in Time“. The Space (that “Something” that everything is located in). The Program is – not examined by the Science yet, but specific, - direction of changes of everything in every place, which really take place. The Time finds its realization (but does not create it!) of direction as of providing its succession (the same “irreversibility”). And the program carries the information about the direction (the same succession of events), however, it does not realize it. Finally, the mechanisms,

which drive everything into action and which reveal themselves as certain principles of behavior of everything, condition all this in coordination. So far we have not a slightest idea of what these actual mechanisms are (not the final phenomenology in the shape of the “Laws of Nature” described mathematically, but something that causes and realizes everything into something, which is accepted as its resultant – the “Laws of Nature”). Moreover, we do not even think that they exist.

The second self-sufficient system is the animate world. Being a system, it is organized as of self-sufficient Biosphere. Generally, its self-sufficiency is already understood. The foundation of Biosphere lies in Life as a phenomenon, providing potentially unlimited time of its existence as particular manifestations. The organization of the Biosphere is formed out of all unformed particular manifestations as a phenomenon throughout the internal biospherical streams, which condition the united interdependence of existence (one being eaten by the other, *i.e.* compatibility of those who are eaten with those who eat them up, biological turnover of matter and energy, pantobiospherical evolution, *etc.*). And all this is regulated, providing high-quality system stability, by control mechanisms: all particular manifestations of life as a phenomenon are nothing but consumables (nothing more to say!); excessiveness of multiplication in the form of absolutely necessary mechanism of “the second level” (for the selection “in adequacy”), laid as the mechanism of “the primary level” to fight information randomization, is, in its turn, the mechanism of evolution and diversity, which is required for system stability; interconvertibility and unification of molecular informational flows provide principal unification of “filling agents” of possible ecological niche which results in automatic regulation of the amount of all particular derivatives without any exception (either the niches are overcrowded which results in total deficiency of all the necessities for their inhabitants’ existence that causes rapid decrease of their quantity, or they are freed due to starvation, consummation, *etc.*, and become vacant for a new filling wave at the expense of the residents who have remained but become rarefied less than the critical density level, or for being filled from the outside by “more adapted ones”). For even to eat someone with the advantage to oneself, one must be interconvertible with one’s food (there should

be absorbency of the eaten, otherwise the eaten will not serve as “the constructing and energetic material”).

The Noosphere became (already) the third system. The Intelligence provided inner self-sufficiency due to the production of not existent, neither in inanimate matter nor in the Biosphere, artificial processes of production of all self-supporting systems [3] and broke almost all control mechanisms of the Biosphere in respect to itself as animate, as the constituent of the Biosphere. Regarding this meaning, this is the content of the conception of “had been formed”: the Noosphere really found its place, *i.e.* became a self-sufficient system. But self-sufficiency levels can be different. And the “minimal sufficient level” means something that always is at the beginning of creation (occurrence, appearance, and so forth) of a new system – its critical stability level. The level is critical for the Noosphere due to minimal sufficiency as, having destroyed almost all control mechanisms from the side of the Biosphere (the system from which the Man departed), he did not make any of his own, the Noospheric control mechanisms of his System, different from Biospherical ones. Inasmuch as the Man is the only (yet) constituent of the Noosphere (its filling agent), then the consequences of the control mechanisms absence come to him as the resultant of the absence of one of the critical conditions of self-existence – the Mankind does not control itself. The way of self-control implementation has not even been touched upon, everything is confined by general reasoning, wishes, and theoretically abstract calculations.

However, after breaking up *almost* all control mechanisms, something unbroken still remains (that something which has been abovementioned as “*almost*”). This “*almost*” is the “species term”. It is the last unbroken control mechanism of the Biosphere for its (biospherical) constituents. The delay in breaking this mechanism is connected with its complexity. In the essence of its nature this “species term” is not the control mechanism of Biosphere as the System, but of the foundation of the Biosphere (*i.e.* its occurrence and existence) – of the Life as a phenomenon. That is why the break up of the last control mechanism, in the strict sense, is not only and not so much of the Biosphere but of the system of individual consumable manifestations of life as the phenomenon, needed by the Biosphere in order to exist as a system. It is the break up of the con-

control mechanism of Life as the phenomenon standpoint for the creation of consumable materials, needed by Life as the phenomenon in the form of consumables, in order for Life to exist as the phenomenon of no limits and beyond the senescence. But this control mechanism for consumable materials is the most inadmissible for the Intelligence (the Intelligence as a phenomenon now), both the most defiant, and the most insurmountable one, and other *the most*, mechanism. It is the last thing that the Noosphere did not break up from the system it came from. Both the inevitability and the *Timeliness* issue (the Noosphere occurrence) of this break are in the mentioned fact. Therefore, in accordance with the mechanisms of existence and the program which gave birth to Noosphere, everything occurs “all of a sudden”. It occurs with all problems, uncertainties, and unpredictabilities. But there is no other way – the Noosphere found its place and its laws, that nobody has even an idea of, are already working: “*Leave the conversations aside! Straight up and forward. And then...*” (V.Vysotsky).

Biological Time Split. The Time is ultra-special among everything special in the Universe. And not only because nobody knows what it is, though everybody, with no exceptions, feels the march of time. In our perception the time does not exist as such, but rather some consequence of it, in the form of changing everything and everybody, including the percipient. In this respect, the time is more like the mechanism of being, and not its constituent. Contrary to all the rest (space, energy, matter) it can be neither stopped, nor accumulated, nor transformed into something, nor can it be controlled. By virtue of its absolute and in order to be restrained from all kinds of omissions, misunderstandings, terminological variations, it is called specifically distinctive – the Physical Time. Regardless of all the attempts to prove the opposite, the Physical Time is sole for any object. Even at near light velocities no physical time splitting takes place – for every object in the system it is of its own. The same thing is with the twin paradox mentioned in literature – it is imaginary. The time goes by with appropriate (to it!) velocity for the twin in the spaceship cabin, and it, the time, is as much absolute as it is for the other twin, the observing one. For the other twin (the observing one) the time goes by in the absolute way as well (in his system). All hypothetical para-

doxes of a hypothetic meeting of different age twins are nothing but psychological exercise: sublight velocity cosmonaut and the observer went along the same life, for themselves and on their own, with the same speed of all the processes, which are adequate to their “local time”, absolute to each of them. The fact that their age is different at the meeting is regarded to the other problem – the problem of biological age. And it is regarded to the problem of biological time.

The biological time behaves quite differently. It is almost completely stopped in deep anabiosis. And at similar conditions the physical time (in which the object stays practically always) does not influence the biological one. That is the point the earliest “technologies of eternity” came up to, when human cells and tissues (including the ones, rich in stem cells, *e.g.* bone marrow) were cryopreserved for different reasons. Something happened, something that nobody paid special attention to (however, having marked it out as the useful one), just one of those “common” things. As a matter of fact, even at that time, something really incredible took place – the biological time was stopped. It was stopped “by the desire”, technologically. The temperature of liquid nitrogen was sufficient for that. From the standpoint of 4 milliard years of continuous life as a phenomenon, the temperature of liquid nitrogen would not be sufficient for its complete stop – even at -200°C , at trifling speed and effectiveness, the simplest chemical reactions (tunneling effects) take place. No matter how small the randomizations at this temperature are, the information of the animate would get broken gradually. It would get broken, though may be in a thousand years, may be, in a million or a hundred million years. However, it would not be significant already. If it was necessary to slow down such processes for milliard of years, they would use liquid helium, other more effective cryopreservants, *etc.* But what for? If you bring these cells back to life, allow them to be divided several times and slow them down again, then their lifetime could be theoretically prolonged to the whole time of existence of the Universe – the previous one, as well as the next one. Was it necessary, then it would last the new Universe, after the next explosion or whatever it would be. No one needs it at least now. Although, the very fact of activating this technology of a biological time stop was very important. But its significance was realized com-

Fig. 1 The organism may be divided into its “constituents” – heart, liver, kidneys, arms, legs, *etc.*, not only by mere convention, but in an absolutely real way. And in an absolutely representational way the transplantation of organs and tissues testifies both to the fact that “it is so”, and to the way of its practical implementation. The organs of the Man can be preserved separately from him for a long time before the transplantation. But in transplantations there will be organs of different people, transplanted not to the ones, they were taken from. The transplantation “gathers” (“re-gathers”) an individual out of “constituents”, not belonging to him. The transplantation is casual (which became habitual at least psychologically) everyday parting of the individual in space and time (before his being “gathered”). But the organism has its “constituents” which may be parted in time and space for subsequent combination without hurting the individual. For example, at the birth of a child it is possible to collect cord blood, containing his stem (as well as non-stem) cells, and place it into liquid nitrogen. And their biological time will stop. The child will grow, aged, and old, while his “constituent”, taken at birth, will remain on the zero level of the biological time. The individual gets parted both in space and in biological time. If needed, it will be possible to grow tissues, organs, perform any substitutions (or directly change everything in the organism itself) out of his “newborn” stem cells (in still large and larger scale, depending on the technological progress), *i.e.* to combine the individual, parted in space and time, with himself, but in a heterochronous way. This is too complicated for fantasy, it can be implemented in everyday life only, and that is the way everything is headed towards.

pletely only after the appearance of the biological time split. This is the point that the regenerative medicine came up to.

The Principle of “Biological Time Machine”. Everything started as usual – with peculiarities. In the search of necessary sources of stem cells (besides bone marrow), in order to obtain *ex vivo* “spare parts” and to “repair” the human directly within, all tissues and organs were examined one by one. Some of the things looked very attractive (*e.g.* adipose tissue stem cells). But the most interesting one was cord blood. It contained the stem cells of a newborn, though not in abundance, of course. The source is absolutely accessible, as well as absolutely harmless for a donor. After a while the situation turned to a new plane. Cord blood stem cells have zero biological age (moreover, in the strict sense, the “negative” one, *i.e.*, fetal, although, they are

isolated at the moment of birth, still they were formed earlier, let it be late, but still embryonal stage). At the same time they correspond completely to the newborn as they are his derivatives. That is why by storing them, “when needed” it will be possible to create any tissues and organs out of previously stored, perfectly matching the patients. At the moment when a child is born, the biological time stops for cord blood stem cells (as well as for any other ones, present in it) on their being placed into liquid nitrogen. As for the newborn, he is growing, as he is supposed to, getting older, and when the time comes, will grow old. The mentioned biological time split appears (Fig. 1). The time of stem cells in liquid nitrogen is stopped and remains this way, at “the zero level” *ad libitum*. And the time goes by for the individual, it is specific, gradually approaching the “individual term” (in the borders of “species term”, if he is lucky enough, of course). However, the split is something special. No matter how paradoxical it may sound, it is accompanied by the individual’s (physical!) split. Moreover, the split has got just fantastically special nature. On the one hand, only a part of the individual, which before birth comprised a whole with all other “parts”, resides in the stopped time. On the other hand, it is a peculiar individual’s part (cord blood) as it is designed by life as “particular of particular” - the particular of it, Life’s, manifestation as some individual *Homo sapiens*, necessary as a consumable only, liable to elimination. And only on fulfilling its function as the carrier, the owner, and the imparter of germ plasma (or as the one who did not pass the selection “correspondence-wise” and as a result is eliminating with the germ plasma inside). The cord blood has a completely different function and the time of its natural existence. It is listed into consumables at the moment of individual’s birth. At birth the cord blood is “self-detached” from the newborn like it is not needed anymore, though prior it was fulfilling an absolutely necessary function and the stem cells in it are as much full-fledged as any other ones. And cord blood preserving in liquid nitrogen is, in fact, the first case of disruption of a life control mechanism as a notion with something which is determined by itself as a consumable. Actually, everybody’s attitude towards somatic cells is imperatively original. They (somatic cells) are not treated “seriously” as they are generated constantly and in huge amounts, re-

placed, substituted, and nobody even notices them. Yet, every cell is a principally potential individual and cloning is an absolutely “materialized” example of it. It is not worth thinking constantly (“seriously”) about. The potential reality of the fact that the one who is reading these lines (as well as the one who is not) can be parted into separate cells and each of them can produce oneself an identical individual (at least, biologically), the quantity of which would amount to the billiards of “pieces” at this procedure, again, if we begin thinking “seriously” about it, is capable of dismantling the most concrete mental health. Though, the potential of cells is not changed by that. And cord blood stem cells are full-fledged, the most; potentially and actually multi-potent, the most; the youngest and other the most, found in any individual since the moment of birth and till the end of the journey path. They are a part of a human and, once stored, will remain forever. Even after the human’s death. And it is not a supposition anymore. The famous Dolly sheep was cloned of frozen cells of the adult sheep, which had passed away long before. But the individual in his “remained constituent” is also a part of that ALL, which was before birth, when the cord blood was still replenished by preborn individual’s stem cells. Thus, this is the way the material parting of the individual in his own biological time is realized by. That is the way it is, that the biological time is neither absolute nor independent.

This biological time matches only *its* biological object. And something conceptually new appears: the possibility to control the biological time, as now it can be parted technologically. In the current example – at the zero biological time level, and at the same time at any other biological age of any (growing, aged, old) individual. The control of Physical time is science-fiction writers’ lot. The Time Machine of Herbert G. Wells, which time-transfers the observer in physical time, is a lovely fantasy. Yet, partial substitution of cells destroyed or partially damaged by stem cells or their derivatives is “yesterday’s reality” in regenerative medicine. And there are no limits to the quantity of substituted cells. Including the substitution of all cells in the whole organism. The substitution with cells of zero age of those old ones, which comprise the grown old individual. The substitution of oneself for oneself, yet parted in time (and with appropriate cell differentiation,

of course). Let us leave aside the way of doing it for a moment. The principal issue is that there are no fundamental prohibitions for such a substitution. Meanwhile, some (abstract, yet but having no fundamental prohibitions) “Biological Time Machine” appears.

We may also analyse the situation when stem cells (most often from bone marrow or blood) are taken from young people, who run risks, *e.g.* go to war, or it is done providently, just in case, to be stored in liquid nitrogen. The mentioned cases are numerous in the world today and their number will grow. From this moment on, such individuals acknowledge the split of both them as “biological objects” and their biological time. Not from zero on, but from liveable young age. And if now these cells (to be more precise, the derivatives of these cells) substitute all (and, who knows, we may not need all) cells (at the identical differentiation stage) of an old “autologous” individual, then something, which was mentioned above as “biological time machine”, appears again, though in some “modification”.

Is everything so simple? Stocked up enough of your cells, became aged, replaced the old ones for new ones and became young and healthy? And that is merely it? Of course, not. Life would not be Life if everything was so simple in it. Moreover, for its consumables. But the man has come to be the “filling agent” of the Noosphere. The Intelligence has already overcome many of its (the-Life-as-notion’s) limits, protections, and traps, and what is left can be stated clearly. The absence of corresponding technologies is utterly obvious. Let’s talk more about that downwards. However, regardless of technological problems, there is some principally unsolved fundamental problem which, by the force of habit, is elevated to next “The Law of Nature” class. This problem is the problem of *heterochronic parabiosis effect* and it needs solving.

The Last Barricade. The idea of “borrowing” “life energy” from a young organism is as old as *Homo sapiens* itself. Though all attempts (from naive to the wild ones, even by all barbarism criteria) led invariably to nothing (I mean nothing good). It seemed like everything was quite logical, by that time understanding, and yet it remained unknown why nothing led to the desirable effect. Finally, recently (by History’s measures), just several decades ago, the technologies of fairly correct scientific investigation of these WHYs appeared.

Much turned out to be simply naive. Yet when they came up to the most sensitive check-ups, the situation deadlocked. Everything started with *heterochronous parabiosis* problem, which seemed to be ideal for clearing out the essence of the problem. Small laboratory animals (mice, rats, rabbits) of the same line but of different age were united into some *pseudogeneral “unity”*. It was called the “unity” because as a result of surgical procedures they provided cross blood flow for these two partners. “Pseudo-“ as all the rest (except interchangeable blood flow) of parabionts remained individual. In such unified individuals, blood circulated together with cells, capable of circulating inside one’s organism with blood, and, of course, all extracellular components [4], as there were no barriers (placental, blood-brain, *etc.*) on the way of cross blood flows (though all barriers in organisms were preserved).

The first results of such investigations were rather lamentable. In general, the authors expressed the results of their investigation in such a way – at the combination of blood flows of old and young organisms, the old one is not getting younger, but the young one is getting older rapidly [5]. Nevertheless, if we turn from the “general view” towards particular manifestations, *i.e.* try to get as close as possible, to the mechanisms which lie in the basis of such effect, we can reveal some very interesting peculiarities. The first of such principal peculiarities occurred to be the fact that not good effects of *heterochronous parabiosis* are conditioned basically (not exclusively, but basically) by pure tissue incompatibility. Such tissue incompatibility had a specific feature: its basic troubles were endured by the young organism [6]. If the immunological system of the old partner was turned off (something similar was achieved by irradiation, which destroys immunological system cells), then all negative effects disappeared. The young organism stopped getting old rapidly and as for the old one, though evidently it was not getting younger (which is rather hard to imagine after being irradiated at 1000Gy), still it was restoring quite well [7].

Hence, the first peculiarity of “different age incompatibility” was localised. It (let’s repeat it one more time – not exclusively, but basically) is connected with some immunological “discrepancies”. In the strict sense, such “discrepancies” could have been foreseen – advancing age leads to synthesising new proteins and as

some earlier present ones disappear; mutations lead to the appearance of modified antigens; all correlations of the most extensive spectre of lymphoquins are changed immensely and so forth. Finally, which is of extreme significance, although, the animals in such parabiotic couples were of the same line, still, they represented different individuals. At any examinations and variants of breeding, mutational differences are unavoidable by the “untestable” locuses. And they will make their own contribution (not a huge one though). The second factor (the nature of which has remained unidentified still) turned out to be represented by some extracellular components, contained in the old organism blood and inhibiting the functions of the young partner (proliferation served a common test) [8]. Nevertheless, even at such unfavourable consequences of parabiosis, some functions of the old organism were getting better. Even at the most “dangerous zone” – the immunity. However, the later works stated the favourable consequences for the old animal in the parabiotic system with the young one [9, 10]. The authors do not discuss the reasons for diversity of such results.

So, the works on *heterochronous parabiosis* localised the problem. But, in order to reverse the biological time, the technologies must be based not on combining of the individuals but on some variants of cell convergence. The convergence of young organs, tissues, obtained out of young stem cells, with organs and tissues of the old organism. Following modern terminology it will be heterochronous transplantation [5]. The most interesting matter regarding this issue is the part concerning heterochronous translocation of stem cells. The similar picture to parabiosis was observed at bone marrow transplantation. But even in this case, the autologous heterochronous systems (such systems would be stem cells, frozen at birth) have not been investigated. At the same time the “combining of the individual”, parted in biological time (for example, his stem cells isolated at birth and stored in liquid nitrogen, and “all the rest”, *i.e.* the “basic part” of the individual, that lived its postnatal life up to 80 years, let’s say) would be performed by isologous, though heterochronous, material. In fact, one has to find those specific molecular processes which may lead to heterochronous conflict at individual’s heterochronous combining. As a matter of fact, the terms like “parted biological time”,

“heterochronous combining of the individual”, *etc.*, are absolutely uncommon (speaking dainty softly). But all this uncommonness is already listed in the practical experience agenda and the task is formulated in the absolutely specific way. All the experiments on animals with heterochronous intralinear combining point out that the basis for heterochronous conflict lays in two phenomenologically identified processes. The first one is purely immune. The second one is not addressed to any system yet, even phenomenologically. It is the inhibition of young cells functions by some extracellular agents of the old organism. The lymphokines might as well be such components. Hence everything will come to the immune system only. Or there may be some other factors not connected (at least, directly) with immunity. Anyway, all this, *i.e.* both processes are conditioned by molecular interactions and judging by the specific features of these processes, such undesirable molecular interactions are few. And heterochronous combinings, well worked out methodologically and studied phenomenologically, allow their usage as model systems for identification of the mentioned molecular interactions, their molecular identification and blocking conditions (by cytokines, factors; agents calculated by molecular design methods; protein engineering products; antibodies, *etc.*). It is not even blocking “forever”, but just for the time of reverse, the substitution of old cells by the new ones. Having performed such substitution, the basis of “heterochronous interferences” is put aside, as the principal basis, the task of creating “reverse-technologies” is not in providing heterochronous compatibility “generally”, but in providing heterochronous substitution. Heterochronous compatibility is nothing but the stage of such substitution necessary for a period of substitution. It is being performed even at transplantations. However, it is performed too unphysiologically, rigidly, medicamentously. The situation needs displacing the accents, search directions, defining agents’ molecular nature, prohibiting heterochronous autologous combining. Not *allo-* but *auto-*! And to heterochronous only! It will be sufficiently enough to block such interferences, even temporarily!!! The mentioned task is vividly real for the modern level of Science development.

Approaches to the technologies of biological time control. From the start-point of biological time revers-

ibility technologies as well as from practical realizability of this start-point, all people can be divided into those “who managed in time” and those “who did not manage in time”. The one “who managed in time” is the one who being of young age (from the moment of birth till very relative and uncertain border on the level of some 40 years of calendar age) has providently put his personal stem cells for storing, or the one who did not reach this relative uncertain border and who, at least potentially, may still succeed in doing it. And the one “who did not manage” is the one who stepped over the border and even if he puts his fairly mutationally-overloaded stem cells for storing, taking into account necessary (before radical cell substitution in organism) fundamental multiplication of such stem cells, their residual “vital potential” will simply be not enough for performing biological time reverse. So, is it coming out to that “the one who did not manage is late”? For storing – yes, most likely. But as for reverse, if we analyze the principal possibilities at the deepest bottom of the problem, at least conceptually, - no. The conclusion is based on the paradigm of the technology of universal biological time reversibility. At Noospheric solution, the technology is organized in such a way that the continuity of life as the phenomenon gets into the consumable for individual’s reverse.

The continuity of life as a phenomenon goes through the germ plasma with constant tremendous selection “for correspondence”. We know the stage which in germ plasma is ready for dividing the paths, yet, the division into subsequent two paths has not taken place: the germinal path and the future individual, defined for consumable, *i.e.* soma. This is the stage, at which the germinal path still preserves the immortality of life as a phenomenon, yet it can already be used as consumable for reverse technologies. Early blastocyst is such a stage, and its inner cellular mass is such cells [11]. At this very stage the lines of embryonic stem cells are obtained. Their potential is so high that it can provide any reverse technological procedures required. Let us make a “technical enquiry” for such requirements. The first is the capability of obtained embryonic stem cells to transform “adjusting to the individual”, *i.e.* complete histocompatibility, determined by its own gene pattern, personified for each individual. The general number of these genes is rather significant – several hundreds [12].

But not all of them are different individual-wise. One part of genes is identical, the other part is different. And two people, "finely selected", turn out to have not too many different genes. As a matter of fact, this is the basis of donor-recipient couple selection at bone marrow transplantation, the source of stem cells. Several genes - that is all that lies in the principal possibility of substitutions using the methods of gene technologies. And what is more, the genes of the main histocompatibility complex are compactly located, the locus occupies approximately 4 mln b.p. on the 6th chromosome [13].

The second requirement of the "technical enquiry" concerns the real potential value of embryonic stem cells, as possible material for the creation of what is needed for the reverse, "adjusting to the individual". The general number of cells of an adult individual amounts to the estimating value of approximate $5 \cdot 10^{13}$, and their mass amounts to several dozens of kilograms [14]. And the necessary amount of derivatives must be obtained out of several embryonic stem cells which are in early blastocyst, matching the transformation into master line. The amount, sufficient for committing into these 50 trillion, which are necessary for the substitution of old resident cells by the same differentiated but the young cells. In fact, this amount has got to be even really significantly larger than such a huge number, as it will be necessary to substitute genes of the main histocompatibility complex in their predecessors, different in initial embryonic cells and in the cells of a specific individual. And the further work has to be supplied by their posterity only. Even leaving aside the technological problems for the time being, it still seems incredible that the stem cells may be multiplied in such a way, while preserving their totipotency, and then (after multiplication) differentiated into all types of human cells. But Life as a phenomenon does that. Continuously, in the course of 4 billion years. That is why the estimation should not be "general", but technologically specific. After rather long years of searching, finally, the perfect technology of embryonal stem cells support was developed. The mentioned support might have been performed both by storing and discontinuous series of duplications. Thus, it became possible to estimate the real, *i.e.* allowing its practical application, potential of embryonic stem cells in the technological line of their multiplication outside the organism. It was re-

vealed that at "proper" conducting the process it is possible to obtain 300 duplications, after which the stem cells still preserve the capability to differentiate into different types of human cells [15].

Even the craziest fantasy is not enough to imagine absolute incredibility of three hundred of subsequent duplications. The calculation of the mass which would be obtained out of a single cell after far less than 300 duplications is presented below:

Quantity of Duplication	Quantity of Cells
10	10^3
20	10^6
30	10^9
...	...
100	10^{30}
...	...
200	10^{60}
220	10^{66}
...	...
300	10^{90}

simultlThe mass of one cell is $\sim 10^{-9}$ g ($\sim 10^{-12}$ kg or $\sim 10^{-15}$ t). 10^{60} of cells have got the mass of $\sim 10^{45}$ t; 10^{66} of cells - $\sim 10^{51}$ t; $\sim 10^{90}$ - $\sim 10^{75}$ t. There are about $\sim 7 \cdot 10^{22}$ of stars in the whole visible Universe; the weight of the Sun (the "average size" star) equals $\sim 2 \cdot 10^{27}$ t; the weight of $7 \cdot 10^{22}$ of stars - $\sim 14 \cdot 10^{49}$ t. Let us suppose that "non-stellar" weight of the Universe is 10 times bigger than the "stellar" one. We will get the value of $\sim 14 \cdot 10^{50}$ t ($1.4 \cdot 10^{51}$ t).

On 220 duplications, the further calculation is impractical, as there is nothing to be compared with. The whole Universe is such a trifle, which is not the object for comparison at any scale, in the relation to the potential of a single embryonic stem cell. But this exact potential is necessary to Life as a phenomenon to provide the way of selection "for correspondence", quantitatively endless and absolutely alternativeless by rigidity, which allows Life as a phenomenon to exist regardless of senescence. No Universe would be enough

for that. That is why it is growing old. While Life as a phenomenon is not. Therefore, the potential of the germ line is not to be compared with the Universe. It has complete implementation – though even this potential is not enough for many germ plasma lines in the course of its natural development, and, there is nothing that would pass the selection “for correspondence”. They, the mentioned germ plasmas, are eliminated. Together with their carriers. However, having acquired the technology of this potential, it may be used in practice. It will be sufficient for both the obtaining lines completely “adjusted to the individual” and multiplication for all subsequent technological procedures. We only need to be completely aware of the fact that in reality similar technologies are exceptionally sophisticated. Both the most accurate introduction conditions as well as superfine control methods are required at the multiplication of embryonic stem cells. A part of cells is changed at multiplication [16, 17]. They ought to be identified and only the unchanged ones are to be used for further researches. “In the Nature” it takes place in accordance to the mechanisms of selection “for correspondence” in the natural way. Thus, in order to be used for its “not intended purpose”, *i.e.* for the Noospherical, and not the Biospherical one, it has got to be performed technologically. This is the way of practical solving the matter for those “who did not manage”. For them the reverse will comprise one more variant of “biological time machine”.

And only in technological solutions, where the subject of the action is the eternity of Life as a phenomenon and its consumables are individuals, nothing takes place just so “plainly”. It seemed like a purely technological procedure (the substitution of old cells for the new ones) leads to the appearance of the fundamental problem – the problem of a personality. Basically it is stated in the following way. The man has got a special tissue – the brain. Muscles may be replaced, bones may be replaced and the man, changed biologically, will not change as a personality. The personality is defined by brain, by the means of brain, and through the brain. So, if we replace the brain – at once as a whole or in some time “cell by cell”, then what kind of personality will the one who went through such procedure be? Till recently, all the talks on the topic of “What is Personality?” were of speculative character only. What happens

if the brain is injured was known long time ago. There was no doubt, as there has been more than enough of the “material for experiments” in all the centuries. And in the aspect of “replacement” – nothing could get any further than “discussions”. The “material for experiments” for the analyses has appeared relatively recently, when they started using fetal brain tissue transplantation for the treatment of various brain injuries and damages. And only in the most recent time, they started conducting the estimation – the influence of fetal material transplantation (*i.e.* containing stem, committed, or already differentiated embryonic cells) on the recipient’s personal assessments - in the well-developed test system at strictly controlled conditions. And then the apprehensions, expressed out of “general considerations”, were validated experimentally.

So, it was stated by five different NEO-test scales that in the group of 30 Parkinson’s disease patients (with complete equality in rights of men and women, as they were in equal amounts) with fetal brain tissue transplanted, that by one of them (“the honesty scale”) the index decrease took place in 24 months. The group which had stereotactic surgery with no transplantation was used as a control. This group had no changes stated [18]. Regarding such changes proper, there is no possibility to provide the explanation (also the proper one). However, according to neurophysiologists’ views (and the established phenomenology), at least one of the critical constituents, determining personality, is the neuronal links architecture. On the introduction of new stem or committed cells, which may be differentiated into neurons, some new interneuronal links will occur and some changes in personality may take place. Still, the man apprehends himself as a personality not immediately since the moment of birth and inflexibly permanently in the course of his life. Everyone can easily recollect that he apprehended the world and his own personality in quite a different way being of 20 years old, not in the same way as 10 of years of age, 40 was different from 20, as well as 50 was not the same as 40, *etc.* Nevertheless, all this time everyone apprehended himself as “himself”. There is a sort of “creeping continuity” of personality apprehension succession. Every single moment the individual apprehends the fact that he is him, and, in the norm, (*i.e.* at the absence of any kind of mental disorder) there are no doubts attached. And

throughout this continuity everyone considers and apprehends himself as an individual, the only one in the whole time (though, in the strict sense, at different times by all manifestations they were different personalities). The same continuity will arise at gradual substitution of cells. Though the continuity will take place, and due to this continuity, the individual will preserve the concept of his individuality, however, the way it turns out to be at the end of cellular substitution is absolutely unpredictable. So far, at least. Of course, this problem is critical for the "biological time machine". The architecture disorders of tissues in general, and of brain, in particular, as well as the following unpredictability of personal qualities changes will be found very powerful restrictive factors. Though, facing the alternative of either disappearing or successive personality changing (accepting such continuity in the same way as a regular course of life) many, nevertheless, will choose changing. Indeed, the works in overcoming this obstacle will develop very intensively. And in future, when psychics, intellect, personality will become the technology property, such replacement may turn out to be a sort of original "psychocosmetics". In the same way as nowadays people change their hair colour, nose shape, gender, and everything that allows to be changed technologically, one day they will change their personalities. The "smallest" thing is left: the technology of complete substitution itself, *i.e.* real practical reverse. It is not out yet and the first workups in this trend have just been started. Started cautiously, indirectly, in the close succession with regenerative medicine proper. And this is justified completely. These methods of organs and tissues reconstruction do not cause emotional turndowns, as they are firmly directed towards already perceptible things. They are tried out on both animals (as it is presupposed to begin with) and on people (at clinical conditions for the time being). But the main thing is – they are tried out.

And it is not limited by just them. The biological time is parted "in the face" of everybody. The clinical trials in using cord blood stem cells (both exogenous and allogenic) in the course of regenerative medicine are starting. Both the donor and the recipient are really parted in time. Combining the parted in biological time "material" will cause new explosion of delights, protests, emotions, solutions and likewise things even just

psychologically which will supply a new turn of fundamental science and of technology too. And so far (and absolutely independently) the New is being developed.

The Other Way. It is astonishing, but in all, with no exception, modern works only the possibilities within traditional borders (let them be most unbelievable) are viewed. Even the concepts of separation, detachment of heredity from its carrier – the individual, of human genetic technologies, genome sequencing, functional genomics, stem cells and their practical realization, regenerative medicine, storing and using cord blood stem cells, *i.e.* in fact, about the biological time split of the individual (remaining "at zero level" cryopreserved stem cells and continuing his course of life "remaining" individual) and his successive combining, as well as about all the rest of great discoveries, revolutionizing all the conceivable, which had led it, the conceivable, into absolutely unconceivable, did not change basic traditional concepts, formulated more than one and a half centuries ago by Virhov: "a cell from the cell" [19]. It was a brilliant definition. Conceptually nothing has been changed since that time. In general conceptual view only though. In the rest – "everything" has changed. "Everything" got elevated, with no violation regarding the concept itself in its specific understanding "a cell (as such, as an absolute, complete living unit) from the cell (also as an absolute, complete in its cellular perfection, living unit)", to absolutely different levels. One of these levels is the informational streams in the Biosphere, which, at the same time, are its evolutionary mechanism (not the only, but very significant one) [20, 21]. If we transform it to the comparative analogy of the next and even higher level, then an organism originates from an organism only (which is evident, as otherwise, some sort of return to the medieval concept of aseity is unavoidable), however, not abstractly by itself, but only at the conditions of general informational space of the Biosphere. "Just as it is", isolated in any possible way, the reproduction of the "organism of organism" "by itself" is also possible, of course (and realizable technologically). But it is going to be a whole different system. But for all that the degree of significance of general informational space increases from vanishingly small in the scale of a single act of reproduction to unifying all living in general, not allowing the species (on the species level, *i.e.* popula-

tion of comprising individuals) to deviate into something new or to come out of the Biosphere content [21]. In other words, the genetic information of every individual is included into the general pool of all genomes of the Biosphere in some way (what way is that? It is the subject for a separate review). Though this inclusion does not prevent preserving the individual's individuality. The general informational space of the Biosphere keeps its fundamental unity (commonality), *i.e.* every organism in the Biosphere simultaneously receives the genetic material from both the organism in the course of reproduction (in a single act, generally) and via informational streams of the Biosphere as a whole (continuously, but in small portions). But the organism as such remained unaware of all these new notions. Still, the new notions appeared in countless multitudes. And the notions development went far beyond from what was "obvious" and was professed as the most prominent level in Virhov's times. In everything, except for the remaining inviolable "a cell from the cell" postulate. The organism integrity is based on practically the same concepts. On the same notions, as, according to present views, the organism consists of cells, which, being independent units, provide their self-preservation. And if they fail to provide, then they die and are replaced by the other cells. The organism self-preservation is based on the self-preservation of the cell. And if we take the most general look at today's ideas of integrity maintaining, as well as organism safety, all of them come to "the school of whales" (contrary to the Earth, integrity maintaining and safety of which were once satisfied with three of such swimming "atlantes").

In order to specify, let us limit the notions of "integrity and safety" by the complex of all structural and functional superfamilies ("whales") of structures and processes which provide the living in the whole complex of "self-...". The biological notions of "integrity and safety" are often used together, inseparably and obligatorily, as the structural and functional ones, which is true, as a matter of fact. However, in order to supply the convenience of specific investigation of notions and processes in them, they are preferable to be viewed "in turn": sometimes structurally, sometimes functionally, and sometimes both structurally and functionally. Certainly, every single thing in a living being is interrelated, interdependent, intercorrelated, as well

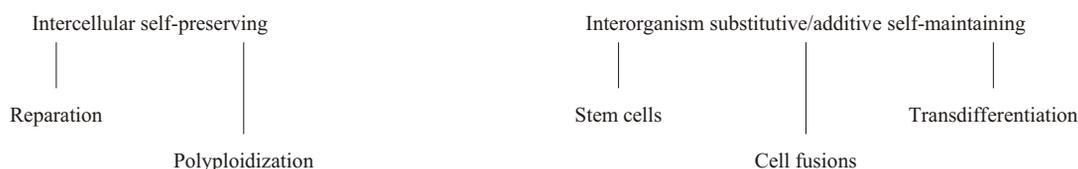
as all other "inter-..."-notions. Nevertheless, having all the mentioned "inter-..." (let it be rather conditional, taking into account the "inter-..."-notions) 5 following superfamilies can be distinguished.

1. Informationally basic. It is represented by genome, *i.e.* the information for all "self-...", recorded on its special carrier (DNA).

2. Structurally self-organizing all "inter-..." complex. In fact, it is almost the whole cell. Thus, it is specifically distinguished as a superfamily in order to highlight the structurally self-organizing "self-...". Such structural self-organizability is inherent to all macro- (and not macro- only) molecules of the cell. It is also a program, which determines macromolecules capabilities and their behavior at different conditions, although it is different from the one in genome. As a matter of fact, a self-organizing program (*i.e.* the location of sites of interacting domains, the change of spacious structure in macromolecules and their separate areas, interaction order, determined by opening and/or closing sites for new interactions, in the course of the whole self-organizing cycle, macrostructures changes in the process of function fulfilling, *etc*) is not considered as such. They talk about "features". There must have been the time when they used the term "a feature" for genome (a feature of granting "inheritance") as well, and when finally it became absolutely impossible to deny the obvious, they turned to the term "a program".

The same happened to other macromolecules (and not macro- only), their interactions, self-organization and its lability and alternativity, functioning. The acknowledgement of programs, responsible for their behavior (and the peculiarities of their recording on such media), is yet to come. Whether they acknowledge the programs responsible for their behavior or not, does not change the essence – the program works, even though it is not called in such a way. But for the cell to be fulfilled, the self structure formation "laying in" (self-organizing) has got to pre-exist. And the function fulfilling starts only, when the structure (fulfilling such functions) is organized. Self structure formation forms everything in the cell, while in the organism (in the borders of tissue); it takes place via rift contacts [14], combining the tissues into a common continuous system (limited by films, *i.e.* "fascias", spatially parted in the borders of organism, *etc.*).

Supersystem of self-preserving and self-maintaining (according to modern views)



Scheme 1

3. Trophic metabolism supersystem. It includes all metabolic cycles and systems (practically “metabolizing” too), protecting all “self-...” from damage. That is true protection, not allowing damage (antioxidative system, for example).

4. Ligand-affinity supersystem and its signaling chains. In other words, “the coordinating one”, providing the coordination of functions in the organism, in general, and between organs and tissues parted in its borders, in particular.

5. Self-preservation supersystem (Scheme 1). As a matter of fact it is the very “object” which is laid in the basis of the organism reconstruction technology, being developed and fulfilled (as much as they are ready) by the regenerative medicine, very cautiously, it starts being worked out “from the depth” to be used for reverse. That is why this particular “fifth whale” will be examined in detail.

The cells are self-preserved due to reparation, and self-preserving cells provide the organism integrity self-maintaining via the replacement of dead cells (via self-maintaining and self-preservation of cells).

Of course, that is the way it is. Almost exhaustively studied reparation takes place inside the cells. And those cells which, in spite of everything, (or *vice versa* as a result of some commands to self-destruction) are eliminated, are substituted by stem cells derivatives (where the reparation keeps the genomes “on the level”). There are also two more processes which are mentioned rather “by the way”, as of about some sort of peculiarities, though existent (and even of some biological sense), still rather insufficient. In the context of intracellular self-preservation and self-maintaining, this process is polyploidization (it is generally reduced to “functional capacity increase of tissue (organ)”). In the context of inner organism and on the cell level,

self-maintaining, this cell conjugation is recently discovered, rigorously proven and causing no doubts. It does not have its own specific place, on the consideration, that such conjugation (in the course of which the partners’ nuclei are either conjugated or either seem like preserved as independent structures in the dikaryon status) may amplify or at the outermost preserve the function of tissue (organ) [22-24].

Though the current picture does not reflect real genetic stream flows inside the organism, which are already known for several decades [25], “re-discovered” again [26, 27], proven absolutely correctly, and, nevertheless, left “over the board” of modern ideas as, in the frames of modern ideas, they can not be attached in any way – there is no room for them among these modern ideas. In one of the previous messages it was analyzed in the general form and the concept of single integrated informational space of the organism was proposed [14]. In several of our experimental works a series of elements of such space was described [28-30]. If we combine now what was known long ago, and what has been turned back to only recently (but on a new methodical level) with what we managed to define experimentally, then a sufficiently complete picture of self-maintaining and self-preserving of the organism, which combines both new and earlier known organically as its constituents (Scheme 2).

The foundation of life is “self-...” information. “A cell from the cell” concept is reasonable on cell reproduction level. However, on cell populations level of any complexity before cell reproduction, outside of it, the cell is located in general informational space, moreover, is included into it, and serves as its constituent throughout the whole time of cell existence.

United informational space starts with the cell, with its self-maintaining. And amplification processes dif-

Scheme 1

ferent in scales and intensity (the ultimate variant of which is polyploidization) are the material for recombinational substitution, at which the chromosomes (containing different mutations of a current gene) are restored not merely and not due to “reshifting” of mutations between two homologous chromosomes, but due to their “transference” to the amplificate, subsequent degradation of which carries mutations to nonentity. The full gene (or its fragment) is recombined into the chromosome from amplificate, substituting the defect. The same recombination (though well perceived) may remove mutations out of one chromosome during allele recombination. However, only in the presence of identical mutations (or closely located ones) on different chromosomes (or as a consequence of such type of common restoration slowing), the cell is not capable of correcting the mutation by itself, with its “power” only. It may be performed at the expense of inner organism informational space. The

latter has got two qualitatively-different constituents which may be divided (purely conditionally only) into “*addressless*” and “*addressed*” ones. The mentioned division is based on the mechanisms of organisation and execution of genetic substitution inside the organism.

The “*addressless*” information transfer takes place due to cell genetic material efflux, its transfer, and absorption by other cells. We may think that this process is tightly combined with the organisation and functioning of intracellular informational space. The amplification (of all levels and scales) provides DNA, for both “inner”, intracellular consumption, and for efflux. And intracellular recombinational substitutions between extrachromosomal and chromosomal material (taking place in the frames of inner intracellular informational space) involve DNA obtained from outside as well. This process may be observed at combined cultivation of cells marked in a different way. One should keep in

Fig.2. One of the variants of the experiment scheme concerning genetic features transfer and its results (the evaluation of markers was performed using different selective agents) [29].

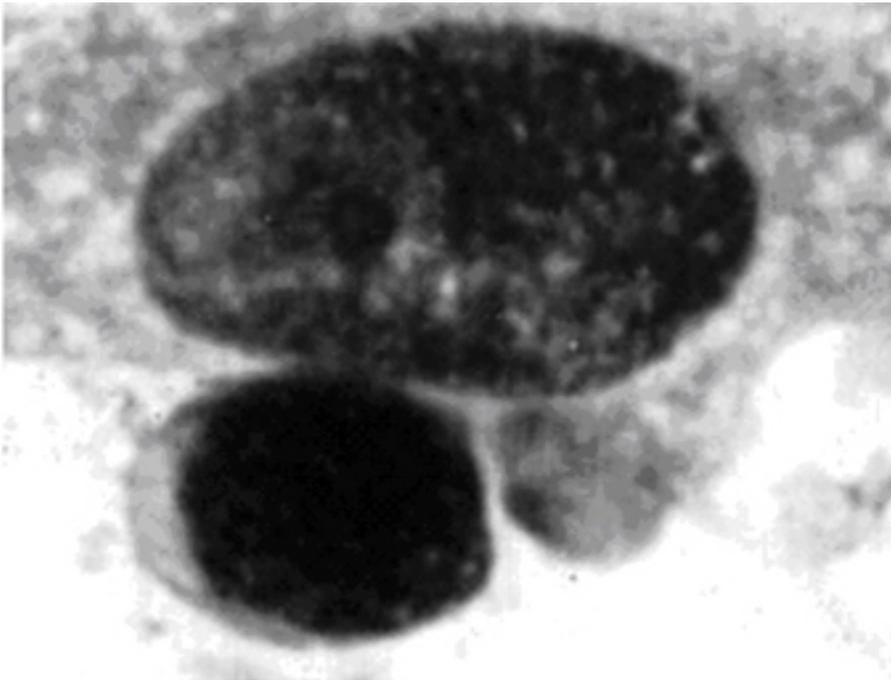


Fig.3. Keeping the mixture of mouse embryonic liver cells and cells of continuous line for some time, it is evident that after the contact the nuclei come closer, and there is efflux of nuclear material from the cell – blood predecessor into the cell nucleus of the continuous line. Staining after Romanovsky.

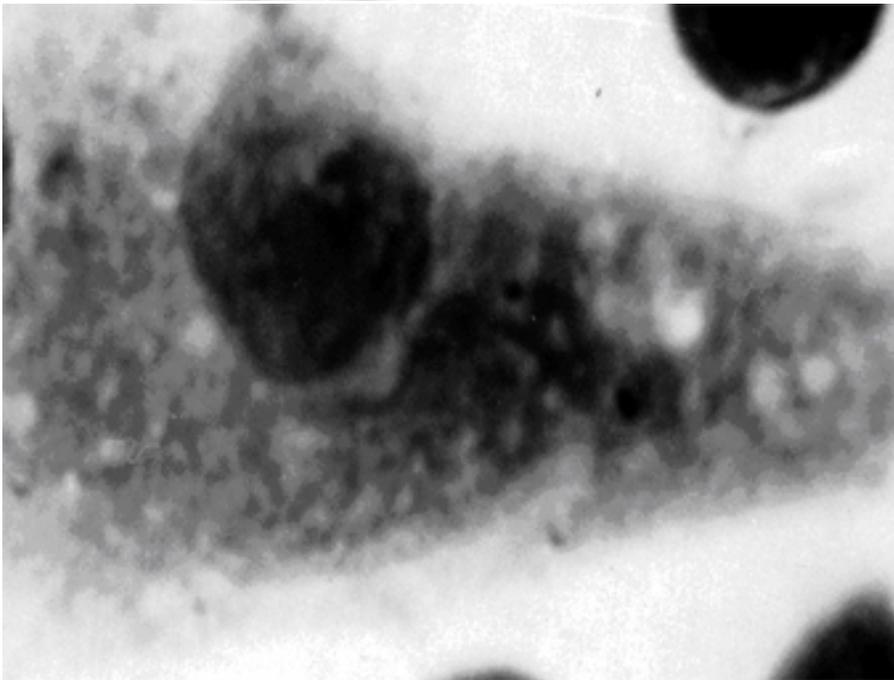


Fig.4. The substitution of cell nucleus CHO-K1 by the nucleus of the restorer cell, which entered it. Staining after Romanovsky [29].

mind also that the partners are to have compatible genomes. Otherwise, different variants of instability, excluding substitutions, will appear. One of such schemes is represented in Fig. 2. In a number of cases when the marker is not visualized, its spreading may be observed among the cells, which do not have such a marker,.

Some interesting results are obtained by the comparison of anatomic details of the organism and expected local “*addressless*” transfer of genetic information. In the organism, different groups of tissues are compartmentalized. They are gathered into fascias, parts, *etc.* isolated by thin films. This isolation does not disrupt the organism unity by any means, as all compartments are united by the general network of vessels.

But thin films between compartments, free spaces between organs, dense mucus, make them informationally and contactly isolated among themselves, but distantly generalized (via the network of vessels). The exchange of genetic information via “*addressless*” local system is compartmentalized. This exchange allows unifying genomes of the cells. Without such unification (and at the same time effective confronting mutational pressure) the general assemble of tissue would soon turn into chaos. The compartment itself provides genetic material transfer in functionally local, tissue-specific performance (with special methylation, for example) [29].

However, complete isolating does not take place. Having got into liquids of the organism (lymph, blood), such “local addressless” DNA is generalized into some averaged circulating (as well as constantly extracting out of the organism) intercompartmental pool. And that is what one finds in blood sample analysis.

Different organisation occurs at “distantly addressed” genetic information transfer inside the organism [31]. It is performed by various cells and one of particular cases (in its extreme manifestation) is cell fusion, already known to us. This type of transfers may be observed in both fixed preparations (and stained later) and the vital ones. According to the degree of genetic material transfer, by the form of interaction and other parameters, the whole possible range of effects can be found. At the same time the cells may and may not fuse. Regarding the first case, genetic material is transferred via assignable cell contacts (Fig.3) or due to penetration of the whole nucleus into the recipient’s cell.

In the essence of the notion, such genetic information transfers are the restoration (in contrast to reparation, which takes place on the cell genome level proper). Cell preserving restoration. In its extreme manifestations such restoration leads to complete nuclear substitution (Fig.4).

Some sort of deviation from the topic is necessary here. As everything is substitutable in the cell (naturally, continuously, and intensively), except for genetic material, then the substitution of a DNA part by a specialized system from outside is a scaled cell restoration. DNA is identical (not mentioning mutations) in its initial sequence in all cells of the organism. Common informational space unifies it, purifying from mutations

in genetic conditioning process, which is common for the whole organism (as much as it is possible in closed informational space of the organism). That is why damaged genome substitution from the outside by the undamaged one will preserve the cell safe, not disrupting its functions, connections to other cells, general tissue architecture, organ, and the individual himself. And complete nuclear substitution is capable of not disrupting the functioning of the most sophisticated architecture systems, human brain, for example. At the same time the whole system of interneuronic connections, as well as the cells themselves, all of their spatial configuration, contacts, interactions, will remain unchanged. With the complete preservation of individuality.

Only such a principal feature of restoration, provided by special cell populations (restorers), will result not in the substitution of the cell, but in its preservation on the level of tissue or organ – capabilities for safe architecture integrity.

However, the death of cells is an objective, continuous, and massive process. Therefore, all organism self-maintaining systems function in coordination. Locally intercellular conditioning provides genetic coordination of contacting cells; distant restoration system allows the cells to exist in the complicated complex for the time required; cell substitution (addition) performs the programmed architecture change and dead cells restoration. Such a combination provides both safety of organs architecture (and of the whole organism) and succession of individuality in time, as well as the existence of the individual at all the unbelievable conditions, destroying anything (starting with atom and up to the Universe) by the Laws-of-Nature power (and in human case with the “help” of other humans as well). And thus, it is a new reverse possibility. The possibility, which, being new one, is looked at from the technological standpoint fundamentally, at first glance even.

Now, using well-developed gene technologies, realizing the stem cells “adjusted to the individual”, transformed via genes of the main histocompatibility complex, using them for the replacement of all systems of self-preservation, it will become possible to plan the reverse with maximal preservation of both architecture and individuality. Neural network will be preserved, and their nuclei will be replaced for new ones – some sort of “Aladdin’s Lamp effect”. A new variant of

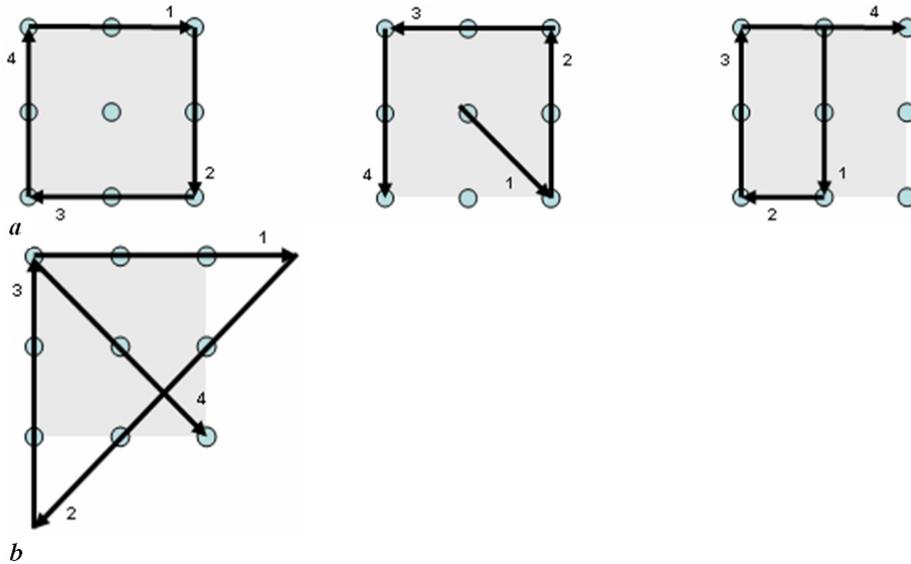


Fig.5. Try to cross all 9 dots of the “system” – the square in the figure by 4 straight lines not allowing your writing tool to leave the paper (*i.e.* not leaving the plane of the figure). At usual approach to the solution the set up task is impossible to achieve (a): the solutions is possible only at non-traditional approach – going out of this “system” (though in its plane) (b).

“Biological Time Machine” appears. And the restless discuss *bion on the reasons of getting old does not matter anymore – this strict compulsory self-destruction program, in order (God forbid!) not to cross “the species term”, or the Laws of Nature fulfilling, obligatorily and alternativelessly destroying everything. Substitution of old cells for the new ones, substitution of old nuclei (or their damaged fragments) for the new ones in the borders of architecture (the substitution of malformed parts, grown using ex vivo technologies of regenerative medicine, if needed) evade all theoretical dudgeons. Now the ball goes to practical application.*

On the Horizon. Purely theoretically (so far only theoretically abstractly) we may imagine the seemingly absolutely ideal variant of reverse in future. The line of embryonic stem cells of a specific individual is obtained by the method of therapeutic cloning. In-depth sequencing analysis is conducted, determining what kind of mutations (in comparison to reference “full-fledged” human DNA, in the form of “commonly accepted” computer version) are there and where they are gathered, full-fledged matching fragments are synthesized, the mutated ones are substituted for them, and the reverse procedure is conducted with such full-value stem cells proper. Then the variant of “Perfect Biological Time Machine” will appear. It is pure fantasy so far, as neither from technological standpoint nor from fun-

damental science point of view the performance of this procedure may be started even experimentally. However, genomics is developing rapidly, acquiring all kinds of prefixes like “functional”, “metabolic”, “structural”, and so forth, which demonstrates the appearance of new branches and strategies.

The real possibility of starting experimental “Perfect Biological Time Machine” work-over will appear in 7-10 years. But nobody will wait for this triumphant moment. Nobody is waiting in the Noosphere. It seems like they finally cast out the “All or Nothing At All” principle. Nowadays “All” starts with something, let it be small, not centrally strategic, but something which became possible for technological application of one step forward on the way to “At All”. Step by step. Insensibly for ourselves, we stepped over (have already stepped over) “from Biosphere’s solving us out” in a “natural way” to a principally new status: to Noospherical technological “solving us out”. And likewise in everything. And likewise in direction of biological time reverse. Before our very eyes, the essence of the notion of Medicine is changing. Until the recent times it was set up in rather limited contents: maintaining “organism life-powers” by means of some procedures, called in general as “treatment”: restrictions from harmful and dangerous, stimulation or compensation of any function, “healing”, surgery – rapid interfer-

ence into organism integrity, *etc.*, however, all this was in the borders of natural compensatory possibilities. There are no "organism reserves" – the Medicine is helpless. Today, the question of Medicine as the sum of all human biotechnologies, going out beyond the scope of compensatory possibilities, which add to "organism reserves", is already put forward both *de facto* and on the level of conceptual analysis. And the direction of such ideas evolution (as well as their practical application development) has already been distinguished absolutely clearly – complete scientifically fundamental and technological resolving of the Man. In the forums the reconstruction of the Man is already discussed by the regenerative medicine as practical accomplishment in clinics. The local reconstruction, for now. For the perspective – the large-scaled one (which is already being developed experimentally). The final goal is the complete one. In accordance with today's ideas – in the borders of the biological age of the individual. But the Intelligence does not see itself as a consumable. Has never seen itself as such. As long as it, being the brood of the Biosphere and remaining its constituent, could oppose nothing to it. And everything was *Untimely*. Because the Man was completely subdued to the Laws (and mechanisms providing them) of the Biosphere. Having acquired the Noosphere status, the Intelligence as a phenomenon became incompatible with Life as a phenomenon, for which it, the Intelligence, is nothing but one kind of consumable in its biological carrier. The Intelligence is incompatible with Life as its particular manifestation in its carrier's existence, but with Life as a phenomenon for which it is a consumable. At the same time, the human, as a living being, the biological carrier of Intelligence (Intelligence as a phenomenon), can change his biological essence as a life consumable personally for himself, absolutely *vice versa*, *i.e.* transform the natural technology of continuous existence of Life as a phenomenon, into Noospheric technology of biological Intelligence carrier – individual, beyond the senescence. Because the human already lives (not realizing it so far even) by the Laws of the Noosphere (and by the mechanisms providing these Laws). Now the Man is determined by the Laws of the Noosphere. And inevitability, imminence, and direction of the future are all in it. The mechanisms of *Timeliness* are present here.

There is a good psychological brainteaser. 9 dots are marked out in 3 rows on a sheet of paper in such a way that 8 of them, being placed around the contour, comprise a square, and the 9th one is marked in the center (Fig. 5, *a*). The task is to cross all 9 dots in 4 straight lines not allowing your pencil (pen, goose-quill, or any other writing tool) to leave the paper. Being in the borders of "traditionally" functioning mind, when all moves of the pencil are performed in the area of the square, the set up task is impossible to achieve. And only non-traditionally – going out of square area, the achievement of the mentioned becomes possible (Fig. 5, *b*).

This concept is general: what can not be achieved in borders of the system, may be achieved on leaving it. In borders of the individual, in borders of his closed informational space, randomizing closed etalon, nothing radical is possible to achieve. And throughout the History of Man the problem of biological time could not be solved. We should leave the borders of this space and change the unrandomized for what was parted in biological time, working from the outside. Such trend may as well be called an "Age-regulating medicine". The trend which will be one of the controlling (this time it is of self-controlling ones) mechanisms of the Noosphere. It will be – but when? There are no simple and direct answers to the simplest questions, as usual. This is the truth known since ancient times. One more thing that remained for us since ancient times is the parable of two travelers.

Two travelers met on a road to a big city. The first traveler, who was going to the city, asked the second traveler who was eventually going from the city, "How much time would it take me to achieve my goal?" The second traveler stopped for a second and spoke out the only word, "Go". The one-who-asked was indignant; he sounded off every single thing he thought of the boorish answer, and went along. In a short time, the "Boor" shouted out in the first traveler's back, "It will take you 3 more hours". The first one expressed his thought in a more radical way, and having run out of his eloquence, he asked wickedly, "Couldn't you tell me that to begin with?" There was a general answer to such a simple and direct question – "No, I couldn't", said the second one, "In order for me to estimate the time of

your trip, I had to find out what speed you are going to walk with”.

If we translate this story into modern language of definitions, in the generalized universal form it will sound like this: “The time of achieving the goal depends on efforts applied on the way to it”. It will happen with age-regulating medicine in the same way. But on its way (this time not ‘*on the way to it*’, but on ‘*its way*’, as the foundation has already been laid) the most principal obstacle has been overcome – the paralysis of thought, caused by steadfast persuasion of “principal indefinability” of biological time reverse as the absolute delirium, based on “primeval ignorance”, and lack of understanding of the Laws of Nature. Only after overcoming this obstacle, not from the depth of gerontology, but other trends, still cautiously in many things, very often looking back, however, the moving towards the goal has been started. It has been started as the Noosphere came into existence, its Laws came into power, and the *Timely*-time has come. Thus, the achievement of first practical results depends on us only, on the efforts that we will apply. Nobody but us will do this. Moreover, there is nobody but humans in the Noosphere. So far. Our “shagreen leather” is our problem, and we are the ones to solve it.

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