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ENERGY POTENTIAL OF MITOCHONDRIA UNDER LED LIGHTING AND RISKS OF EYES DISEASES

V.A. Kaptsov[1], V.N. Deinego[2], V.N. Ulasyuk[3]

[1]All-Russian Research Institute of Railway Hygiene, 1 Pakgauznoe shosse Str., Bldg. 1, Moscow, 125438, Russian Federation
[2] «Biolumen» scientific and technical center, 8 Mira avenue, Fryazino, Moscow, 141195, Russian Federation
[3] «Platan Scientific Research Institute with In-House Plant» PLC, 2 Zavodskoy lane, Fryazino, 141190, Russian Federation

Disorders in refraction, myopia and other eye disorders lead to a decrease in efficiency of any activity and impose certain limitations on educational and working capabilities of economically active population. As light denaturation grows, fatigue caused by performing test visual efforts also increases. The lowest decrease in physiological and mental parameters occurs when a person works under natural luminance, and the greatest one, under completely artificial luminance. Artificial light sources, as opposed to an even sunlight spectrum, have peaks and notches in photon flow under specific wave lengths.

It is shown in the paper that a drastic decrease in spectral-energy characteristics occurs in red light area with wave length 670 nm as compared to sunlight spectrum. The authors consider how 670 nm red light deficiency influences visual analyzer cells and mitochondria in particular. A theory that focuses on mitochondria aging states that oxidative stress caused by DNA mutations in mitochondria is associated with a decrease in adenosine triphosphate (ATP) production leading to cell degeneration. A rate at which this degradation develops is related to metabolic demands of a body, progressing inflammation in the outer retina, macrophages penetration and cells loss; as a result, eye sight deteriorates. A mechanism of a decrease in efficiency of ATP-synthesizing structures is examined within "670 nm light – water structural properties – efficiency of mitochondria rotary engine operations" cause-and-effect chain. The authors substantiate the necessity to synthesize red 670 nm luminopfor and to optimize LED lighting in this spectrum area.

Key words: *red 670 nm light, water structure, ATP synthesis efficiency, energy potential of mitochondria, LED lighting.*

Influence exerted by light on human circadian rhythms and visual analyzer efficiency is a global issue arising when health risks are assessed. F.F. Erisman, who established hygiene as a branch of science, highlighted a correlation between lighting environment and myopia development in his research [1]; at present this disease is becoming an epidemic one as it is spreading fast all over the world [2–4].

At the same time, F.F. Erisman pointed out that «myopia is not to be considered an inevitable evil that is essentially caused by educational conditions at school; on the contrary, progressive myopia is an evil that is caused only by inadequate lay-outs at schools, and it could be easily eliminated should the society pay greater attention to arrangements provided for educational process» [5].

Leading Russian and foreign ophthalmologists had an opportunity to discuss international experience gained in efforts to control myopia at the XII All-Russian conference entitled «Public health as grounds for prosperity in Russia» [6]. The Conference was opened by its chairs, RF Public Healthcare Minister V.I. Skvortsova and RAS Academician and The President of the Public Health League L.A. Bokeria. There was a report delivered by T.V. Pavlova, Associate Professor at the Ophthalmology Department of N.I. Pirogov's Russian National Research Medical University; it was entitled «Issues and achieve-

Valerii A. Kaptsov – Doctor of Medical Sciences, The Corresponding Member of the RAS, Head of the Occupational Hygiene Department (e-mail: kapcovva39@mail.ru; tel.: +7 (499) 15-33-628; ORCID: http: //orcid.org/0000-0002-3130-2592).

Vitalii N. Deinego – Senior researcher (e-mail: vn-led@bk.ru; tel.: +7 (916) 530-68-82).

Vladimir N. Ulasyuk – Doctor of Physical and Mathematical Sciences, Chief scientific consultant (e-mail: v_n_uls@mail.ru; tel.: +7 (495) 70-29-658; ORCID: http: //orcid.org/0000-0002-1130-710X).

ments related to control over myopia. Role that belongs to a public organization in consolidating efforts aimed at fighting against myopia». She noted that refraction disorders, myopia, and other eyesight disorders led to a decrease in efficiency as regards any activity and imposed certain limits on educational and labor capacities of employable population. Shimidzu Tadashi, The President of Asia Networks JSC (Japan), noted that wide use of smartphones, pads, and other up-to-date technical devices was the primary cause for wide spread of myopia in Japan. As a result, according to experts' evaluation, the global economy suffers annual productivity losses that amount to approximately 269 billion dollars [7].

S.I Vavilov, a truly great scientist, cited J.W. Goethe in his book entitled «The Eye and the Sun»: «The Eye owes its existence to the light. Out of indifferent animal auxiliary organs, the light picks up an organ that could be its equal; thus the eye is formed only in the light, to see the light, to make internal light meet external one». Sergey Vavilov also pointed out that from a biological point of view «optimal illumination» should result from the evolutionary adaptation of the eye to average illumination created on the Earth by the Sun. As regards energy, the eye is adapted not to the Sun itself, but to sunlight diffused from all surrounding objects.

Starting from 2017, «NTS Svetotekhnika», the Scientific-Technical Council, has been functioning to solve global issues related to lighting technologies and their practical application. The Council unites public and state figures, authorities, representative from the RF State Duma and Federation Council, scientists, (academicians, professors, and doctors of science), representatives of big business and who are socially responsible, and leading experts in the lighting technology sphere. Gennadiy Onishchenko, RF State Duma Deputy, the first Deputy to the Head of the State Duma Committee on Education and Science, took part in The Council regular meeting. He stated that «in spite of this meeting being overwhelmingly technical, there is an interesting report entitled «Peculiarities related to impacts exerted by LED lighting sources on visual organs of children, teenagers, and adults» by I.E. Aznauryan and it means that the Council is heading to the right direction». At present public organizations and associations are trying to take on responsibility for negative outcomes that may occur due to artificial light sources being sold by them on the lighting devices market.

Here we should note that, starting from 70-ties last century, biological effects produced by natural and artificial illumination have been assessed on the state level by experts employed at the Illumination Hygiene Laboratory (Radiant Energy Laboratory) at the A.N. Syisin' s Institute of Common and Communal Hygiene that is now called «The Center for Strategic Planning and Management of Medical and Biological Health Risks». Research performed by those experts [8] at the Laboratory focused on analyzing to what extent fatigue of observers determined by the fucntional F [f_i, E] depended on overall illumination [E] calculated as per dynamics of each examined function f_i [E]. It was shown that as light denaturation grew, that is, a share of natural light in the overall light flow dropped, fatigue caused by accomplishing test visual work also increased. The most insignificant drop in physiological and mental parameters of examined observers' state was detected under natural illumination, and the greatest one, under completely artificial illumination. Figure 1 shows a relationship between fatigue and a ratio of natural and artificial light under illumination created by luminous LB type lamps (light flow is equal to 2,800–3,000 lm and 3,450 K–4,200 K when illumination level on a work surface was controlled).

Experts employed at A.N. Syisin's Institute determined hygienic minimum of natural light in working areas inside public buildings and it gave grounds for hygienic requirements to combined illumination that fixed 250–300 meter-candela of natural light, η.

When luminous illumination was implemented, experts employed at the USSR Gosstroy's Scientific Research Institute for Construction Physics also noted that visual working capacity was higher under natural light

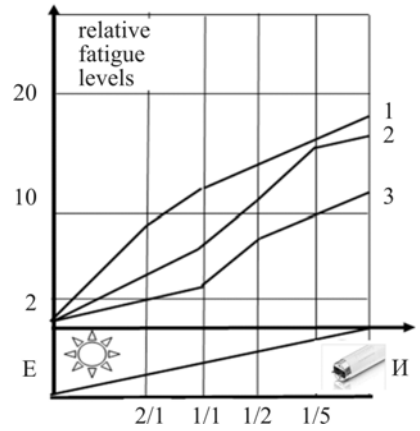

Figure 1. A relaitonship between fatigue and raito of natural and artificial light [8]
Note: under illumination being 300 meter-candela – line 1; 500 meter-candela, line 2; 1,000 meter-candela, line 3; E means natural light, И means artificial light.

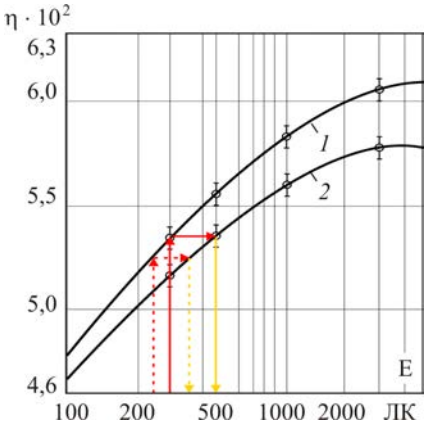

Figure 2. Relationship between visual working capacity and illuminaiton under natural light (curve 1) and artificial one (curve 2) [9]

than under artificial one. To make a comparison, they took luminous LB40 type lamps. Numerical values of visual working capacity parameters were determined as a product of discerning time and correct identification probability (Figure 2).

It is obvious that minimal level of luminous illumination that is 400–500 meter-candela at the given working capacity corresponds to hygienic minimum level of natural light being equal to 250–300 meter-candela. If we make a light spectrum of an artificial lighting source closer to the sunlight spectrum, we can not only save energy but also secure compatibility of these two light sources functioning; it will create safe lighting environment with a biologically adequate radiation spectrum.

Z.A. Skobareva and L.M. Teksheva, scientists working for A.N. Syisin's Institute, came to the following conclusions:

1. Examining biological effects produced by light on a human body is still a vital issue in illumination hygiene;

2. It was proven at cellular, biological, and psychophysiological levels, that natural and artificial light with the same intensity were still biologically inadequate; the difference remained when illumination by artificial light sources grew;

3. Natural light has great hygienic significance and it should be taken into account when developing illumination standards and new technical means for light environment optimization in places where people have to spend a considerable amount of time [8].

It is important to point out that experts at the Institute didn't perform a spectral evaluation of inadequacy between natural and artificial light.

Figure 3 shows spectra of luminous lamps, LEDs, and sunlight.

Artificial light sources, in comparison with the even sunlight spectrum, have spikes and dips in the photon flow at certain wave lengths, namely, spikes in the blue light area, dips at 480 nm wave length, and also dips in the red light area at 670 nm wave length.

Wide implementation of LED lighting with the blue light dose in its spectrum being considerably higher than in luminous lamps resulted in a great number of research on assessing health risks related to possible damage to the visual analyzer caused by «the blue danger».

But still, ophthalmologists and experts in light technologies didn't pay attention to the fact that 670 nm red light in modern white LEDs was lower than in the sunlight spectrum. A role played by the red light was underestimated due to this radiation range being beyond the spectral sensitivity curve of the human eye (luminosity curve). Experts in photobiological safety employed maximum values of light flows at specific wave lengths and considered that their minimum values couldn't do any significant damage to the eye. This concept was

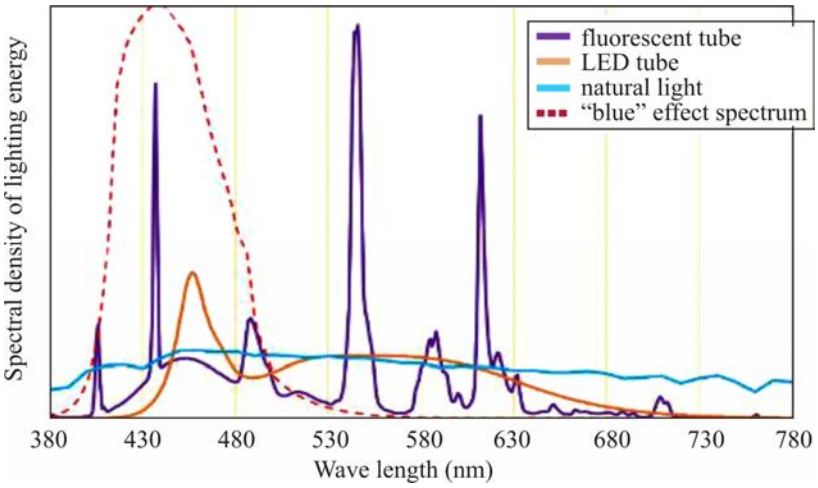

Figure 3. Spectra of luminous and LED lamps compared with the sunlight spectrum

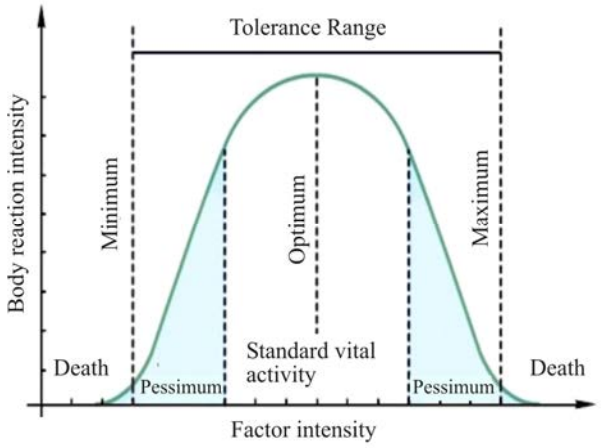

Figure 4. Optimum law (Shelford's Law) curve

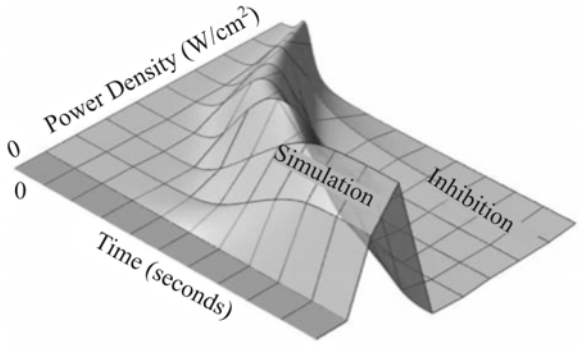

Figure 5. Three-dimensional model of Arndt-Schulz curve showing a possible two-phase dose reaction of radiation or illumination time when low-level laser therapy is applied [10]

determined by assessing how safe the visual analyzer was from impacts exerted by laser light sources. But hygienists and light therapists know that both excessive and insufficient light flow produce adverse effects on vital capacity of cells in a live biological object.

Hygienists assess risks caused by such impacts as per Shelford's Law of Tolerance (Figure 4).

The Law states that there are optimal values of an influencing factor and they secure normal vital activity of a cell as well as there are pessimum and death zones. This hygienic approach was further developed when laser therapy was implemented. Low-level laser therapy (LLLT) was first introduced in 1967; the technique involved applying visible light, as a rule, red or almost infrared one generated by a laser or a LED and was used to treat various pathologies in people and animals. That light usually had narrow spectral width between 600 and 1,000 nm. To select influence intensity, a three-dimensional model creased as per Arndt-Schulz rule was applied (Figure 5).

According to the quantum theory of light, each wave length in electromagnetic fluctuations has its corresponding energetic photon flow that creates its own chain of photochemical reactions. F.H. Grotthuss in Russia (1817) and Draper in the USA (1839) independently formulated a law stating that only that light which was absorbed by a reactive mixture could be chemically active. The basic photobiology law states that a biological effect can be produced only by spectrum waves with such a length at which they can be absorbed by molecules in cells. If a photobiological effect occurs, it unambiguously means that there are mole-

cules in cells that absorb quanta of light in the given spectrum area [11]. A relationship between absorbing capacity of a substance and a light wave length is determined by an absorption spectrum.

Light absorption by a substance is an intramolecular physical process. Light is absorbed by molecules (their complexes, atoms, radicals, or ions) and not by complex biological structures such as nucleus, mitochondria, cells, or eye retina. The only exemption is semiconductors that absorb light with combined energy levels created due to interaction between many centers (atoms, ions, or molecules). When a substance interacts with light absorbing it, both quantum (corpuscular) and wave properties of the latter become apparent [12].

Spectra of modern LEDs (a blue crystal covered with yellow phosphor) are based on the above mentioned regularities (Figure 6).

Previously we examined negative influence exerted by blue light spikes on the human retina and hormonal system as well as effects produced by a dip within light-blue 480 nm light range on the eye pupil response [14–17].

The present paper focuses on an influence exerted by a decrease in 670 nm red light dose on vital capacity of cell mitochondria. Mitochondria are basic free radicals producers in eukaryotic cells. Such free radicals as superoxide radical or hydroxide radical normally occur in mitochondria due to the respiratory chain functioning that provides synthesis of adenosine triphosphate (ATP synthesis) which is the primary energy «currency» of any cell. Mitochondria are also to a greater extent prone to damage by free radicals due to mitochondrial DNA, as opposed to nuclear one, not being protected by histons or any other DNA-binding proteins. And since mitochondria are important cellular organelles, any disorders in their proper functioning can lead to adverse outcomes, for example, apoptosis or programmed cell death.

G. Ling explains in his monograph entitled «Life at the cell and below-cell level, the hidden history of fundamental revolution in biology» that a cell is not a water solution in a lipid membrane but a protein-water-electrolyte structure that is held together due to many-layers of polarized water around full-scaled protein structures. Ling's theory is confirmed by practice and the lipid membranes theory contradicts these observations as a cell tends to absorb more water than can be explained with the membranes theory. Association-induction theory is an effort by the author to shift «gravity center» in getting an insight into vital functions of a cell from the cellular membrane to the cytoplasm via considering changes in electronic density in macromolecules caused by external signals as a basic mechanism for cellular functions regulation. These concepts are built on a close correlation between three basic «players» in the cellular cytoplasm, namely, proteins, structured water, and non-organic ions [18] such as hydrogen, sodium, iron, copper, and zinc ions.

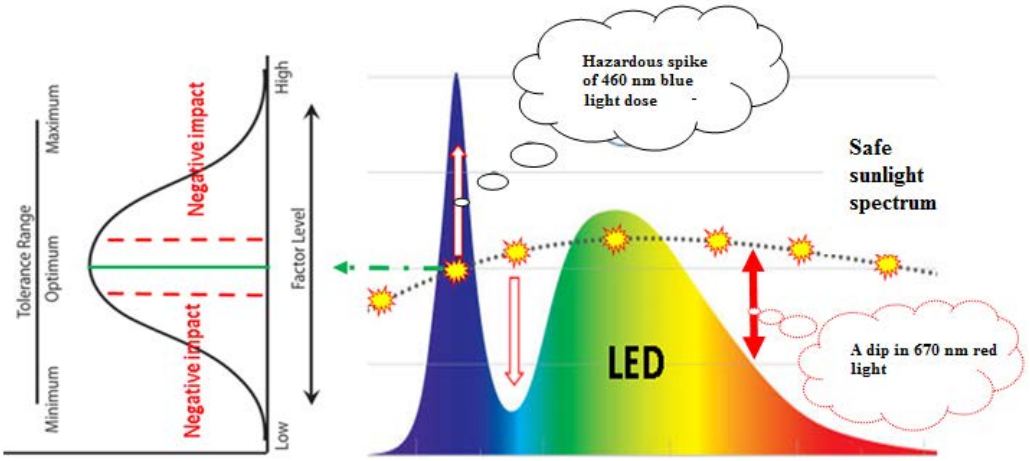

Figure 6. Spectral properties of sunlight and a traditional LED (a blue crystal covered with yellow phosphor) [13]

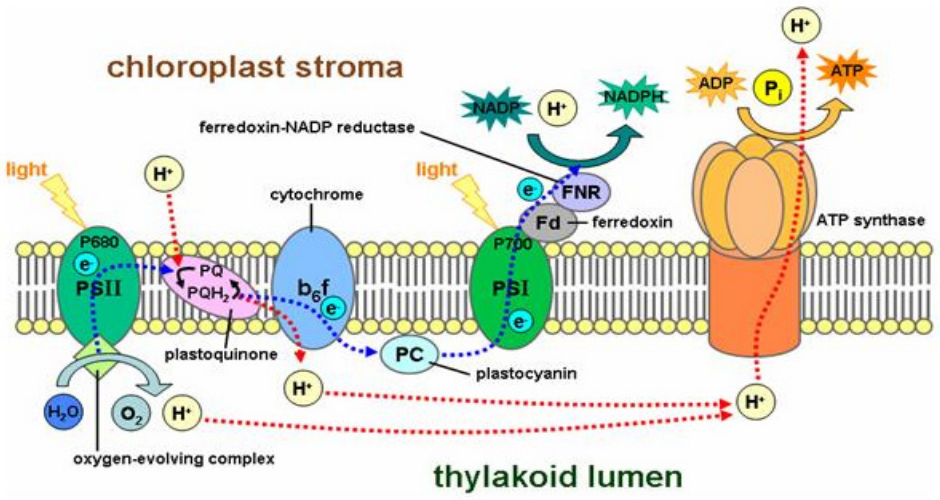

Figure 7. Photosynthetic transportation chain for thylakoid membrane electrons [19]

At present there are a lot of works on mitochondria functioning and mechanic-chemical models describing how mitochondrial structures produce ATP. The chemiosmotic theory developed by P. Mitchell, a British biochemist (1961) is the most recognized among them. He assumed that the electrons flow through a system of molecules-carriers was combined with carrying H+ ions through internal mitochondria membranes. As a result, electrochemical potential of H+ ions was created on membranes and it included both chemical (osmotic) and electric gradients (membrane potential). According to the chemiosmotic theory, it is electrochemical trans-membrane potential of H+ ions that provides energy for ATP synthesis due to H+ ion transportation through a proton channel in membrane H+ – adenosine triphosphate synthase (ATP). Mitchell's theory states that molecules-carriers lace up the membrane following one another in such an order that electrons and protons together can be transferred to one direction, but only electrons can be transferred to an opposite one. As a result, H+ ions accumulate on only one side of the membrane.

Electrochemical potential occurs between two sides of the internal mitochondrial membrane due to a directed motion of protons against a concentration gradient. Energy that is accumulated in this way is used to synthesize ATP as a result of membrane discharge at reverse (as per a concentration gradient) transportation of protons through ATP that functions as ATP-synthase in this case (Figure 7).

P. Dimroth et al. [20] described a mechanic-chemical model for induction of transmembrane sodium-driving force into torque (Figure 8).

The same mechanism will probably function in other F-ATP synthases including proton H^2-F-ATP synthase [21]. All the above mentioned mechanic-chemical models for obtaining ATP are based on nano-electric motor functioning due to H^+ or Na^+ ion flows; the motor has both a rotor and stator, that is, it's a mitochondrial rotary drive called ATP-synthase.

P. Dimroth et al. [20] also pointed out that electrostatic interaction between rotor sections and stator charge made transfers from state to

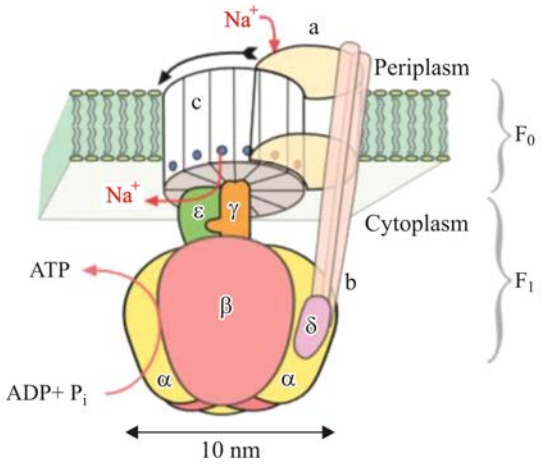

Figure 8. Basic diagram showing ATF synthase Na^+ FoF1 (An arrow shows rotating direction during ATF synthesis)

state depend on an angular position of a rotor denominated as θ. Chemical state of a rotor undergoes evolution that can be described symbolically with the following equation:

$$\frac{ds}{dt} = K(\theta)s, \qquad (1)$$

where K [θ] is a matrix of transition rates between chemical states. Movement of a rotor can be described via equating viscous resistance of a rotor to torques that influence it, to Brownian force that models thermal fluctuations of a rotor (that is, Langevin equation [22, 23]):

$$\underbrace{\zeta \frac{d\theta}{dt}}_{\text{Friction resistance}} = \underbrace{\tau_Q(\theta, s)}_{\text{Rotor-stator of interaction charge}} + \underbrace{\tau_{\Delta\psi}(\theta, s)}_{\text{Membranes with potential}} + \underbrace{\tau_{\Delta\varepsilon}(\theta, s)}_{\text{Dielectric barrier}} + \qquad (2)$$

$$\underbrace{\tau_{RS}(\theta)}_{\text{Rotor - stator passive interaction}} - \underbrace{\tau_L(\theta)}_{\text{F1 load torque}} + \underbrace{\tau_B(t)}_{\text{Brownian torque}},$$

There are the following addenda in the second part of the equation:

♦ **[*i*] τ_Q[θ,** s**]** is determined by electrostatic interaction between a stator charge (R227) and rotor components that are inside a hydrophilic line of rotor-stator. According to Coulomb's law, a charged (free) section will depend on a stator charge (R227) that corresponds to a dielectric and screening medium of a stator. Hydrophilia is a characteristic that describes how intensely a substance interacts with water, its ability to absorb water well, as well as high wettability of a surface. Together with water repellence, it can be applied both to solid objects in which it is a property of a surface and to separate molecules, their groups, atoms, or ions;

♦ **[*ii*] $\tau_{\Delta\psi}$[θ,** s**]** is determined by a drop in membranes potential via a horizontal segment between a periplasm channel and a boundary of a stator;

♦ **[*iii*] $\tau_{\Delta\varepsilon}$[θ,** s**]** is an electrostatic barrier that prevents a charged section from penetrating into a hydrophobic interface of a rotor-stator;

♦ **[*iv*] τ_{RS}[θ]** is passive interaction between a rotor and a stator;

♦ **[*v*] τ_L[θ]** is a load produced by F1 on a rotor via γ-shaft;

♦ **[*vi*] τ_B[*t*]** is a random Brownian torque caused by thermal fluctuations of a rotor.

Previously experts assumed that ATP-synthase (the smallest rotor drive ever known) functioned with 100%-efficiency; such a concept was based on somewhat idealistic assumptions, including those stating that viscosity of the medium that surrounded a drive was to be considered only in the bulk [24], while any viscosity gradients close to surface were not taken into account [10]. When this viewpoint is neglected, it has critical importance due to mechanical behavior of molecular machines being different from mechanical behavior of their microscopic analogues that can't be applied at the molecular level. It is true in particular when a concept of viscous friction and lubrication is applied. There was recent experimental research that revealed it was important to distinguish between physical properties of water in bulk and levels of nanoscopic interphase water layers that were screening surfaces. Nanoscopic water layers that are linked to hydrophilic surfaces have viscosity properties that are significantly greater than those of water in bulk. Besides, it was experimentally shown that as confinement between hydrophilic surfaces grew, a drastic increase occurred in viscosity of nanoscopic water layers [24].

The suggested model for ATP-synthase motor load [20] shows that its rotation speed, and ATP-production efficiency as well, depends on the state of water. Calculations included into ATP-synthase motor modeling assumed that water viscosity inside mitochondria was constant and corresponded to viscosity of water itself. According to A.P. Sommer et al. [25], the assumption was not true due to two basic reasons:

1) There were data on water inside mitochondria, and interphase water prevailed there, its share being 100%;

2) Laboratory experiments that focused on interphase water properties assumed that its viscosity was higher than viscosity of water in bulk, especially at hydrophilic boundaries.

A.P. Sommer et al. [25] considered a physical-chemical mechanism that gave some insights into viscosity gradients inside mitochondrial waters and sequentially explained two cellular responses: an increase or a decrease in ATP syn-

thase as a response to reactive oxygen forms and non-destructive levels of NIR laser radiation respectively. The mechanism is based on results obtained via a new experimental procedure that included nano-identification and modulation of interphase water layers with laser radiation. Its results that may include determination of light-induced ATP-production are expected to have significant outcomes for all branches of medicine and ophthalmology in particular, especially when it comes to analyzing degradation processes related to eye retina ageing.

Ageing is associated with cellular decrease and weaker functions that are partly mediated with the mitochondrial compromise. However, the age function of mitochondria is adjusted under infra-red light (670 nm) that improves their membrane potential and adenosine phosphate production as well and decreases age-related inflammation. Some data indicate that 670 nm light can significantly improve aged functions of the retina and it can possibly provide additional adenosine triphosphate production for ion pumps in photoreceptors or for decreasing age-related inflammation. It can have some positive outcomes for treating ageing of the retina and such age-related diseases as macular degeneration [26].

A resolution approved by 3th Global Pediatric Congress listed recent significant achievements in ophthalmology for children but stressed there still was a lot of issues to be solved [27, 28].

Thus, there is an overall trend for creating safe illumination with semiconductor light sources and safe radiation from visual units or monitors. It states it is necessary for any light source or visual unit to have a biologically adequate spectrum that will provide harmonic functioning of the visual analyzer and hormonal system. The Congress participants appealed to heads of states and governments to understand it was necessary to provide funding for state programs aimed at developing national standards for visual work; such activities should involve participation of ophthalmologists and experts in occupational hygiene and labor protection.

Experts who participated in a working group on safe use of buildings approved on the Report No. 02/TP dated July 19, 2017[1]; they also recommended «… to take into account domestic and foreign experience in creating semiconductor white light sources with a biologically adequate radiation spectrum when technical and regulatory documents are being developed» [29].

Conclusions

1. All energy-saving artificial light sources have spectra with a dip within 670 nm section and it exerts negative influence on ATP synthesis in cellular mitochondria in the eye.

2. If a spectrum has a hygienically optimal dose of 670 nm red light, it produces positive effects on viscosity of water nano-layers and ATP synthesis.

3. It is necessary to conduct further research on determining influence exerted by a hygienically optimal dose of 670 nm red light on changes in viscosity of water nano-layers and ATP synthesis related to them.

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