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V INTERNATIONAL CONFERENCE OF

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BOOK of ABSTRACTS

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PREFACE

V International Conference of Biotechnology and Health 2020 (ICBH 2020) which will be held on October 29–31, 2020 Yerevan, Armenia, Russian Armenian University (RAU). The following topics will be covered at the conference:

- Special Track: COVID-19
- Applied Biotechnology
- Biochemical and Pharmaceutical Biotechnology
- Bioenergetics & Biomechanics
- Bioenergy, Biofuels and Biogas Technology
- Biophysics, Bioinformatics, and Biosensor
- Biotechnology in Medical and Health Care
- Cell and Molecular Biology
- Cell Culture and Tissue Engineering
- Computational Biology
- Microbial Biotechnology
- Nano-biotechnology and Biomaterials
- Information Science, Technology and Embedded Systems
- Machine Learning/Artificial Intelligence and Scientific Computing

The upcoming conference will be a continuation of the previous 4 International conferences “Biotechnology and health” & DAAD Alumni seminar were held at the Russian-Armenian University in 2005, 2008, 2009, 2010. Among the invited were leading scientists in the field of medical biotechnology, biochemistry, biophysics, molecular biology, bioinformatics, bioengineering from the USA, UK, Germany, Denmark, France, Greece, Czech Republic, Nigeria, Iran, the RF and the RA. Armenia was represented

by leading scientists, professors of universities and academic institutions. The initiator and organizer of all the conferences was doctor – professor Hrachik Rafael Vardapetyan. The ICBH 2020 conference is dedicated to the memory of Prof. Vardapetyan.

Chairmen Hovhannisyan A.

MEMORY OF

Prof. Hrachik Vardapetyan

He received M.S. from the Department of Biology at Yerevan State University at Yerevan, Armenia with honors. Prof. Vardapetyan received his Ph.D. (Candidate of Biol. Sci.) in 1977 and Doctor of Biological Sciences (Biochemistry, Molecular Biology) in 1991.

He was Assistant Professor (1982–1992) and Professor (1992–2005) at the Department of Biophysics, Yerevan State University. During 1980–2005 he was the Head of the Research Group of the Laboratory of "Cell Biotechnology", Department of Biophysics, Yerevan State University. Hrachik Vardapetyan was the Dean of Biomedical Faculty at Russian-Armenian University (2004–2012) and Head of the Department of "Medical Biochemistry and Bioengineering" (2007–2017). He was a professor at the University of Information Technologies, Mechanics and Optics (ITMO) in Saint Petersburg, Russia.

Prof. Hrachik Vardapetyan has been part of the special council for the award of scientific degree (Ph.D.) 051 on Biochemistry and Biophysics at the Yerevan State University (since 1985), and Special council for award of scientific degree (Ph.D.) 018 on Biotechnology and Bioorganic chemistry (2010–2017).

Prof. Hrachik Vardapetyan was a member of the Phytochemical Society of Europe (since 1999); European Federation of Biotechnology (since 2001). Since 2011 he was an Academic of the Russian Academy of Natural Sciences and since 2003 – a member of All-Armenian Biophysics Association. 1994–1998 – expert of the Ministry of Nature Protection of RA. 1999–2001 expert of several programs of the Ministry of Nature Protection of RA. 1999–2003 Environmental and social issues expert of the National Assembly of the Republic of Armenia. 2002–2017 Deputy Chairman of DAAD in RA, 2003–2005 – Advisor to the program.

Throughout his career he has been a Visiting Scholar at institutions in different countries:

- 1981–1982 – the Institute for Applied and Experimental Oncology, University of Vienna, Austria (c/o/ Prof. Karl Letnansky);
- 1988 – the Institut für Biologie II der Universität Tübingen, FRG, (c/o Prof. Vera Hemleben);
- 1998–2000, 2002 – the Institut für Entwicklungs- und Molekularbiologie der Pflanzen, Heinrich-Heine-Universität Düsseldorf, FRG (c/o Prof. Willi Alfermann) (Grant DFG ARM-1999-2001);

And scientific trips:

- 2006, 2013 – Division of Pharmaceutical Biology at the University of Erlangen-Nürnberg, Germany;
- 2014 – Patras (Greece), Varna (Bulgaria);
- 2016, 2017 – Athens (Greece), within the TEMPUS programme;
- 2016 – lecturer at the Stavropol State Medical University, Stavropol, Russia;
- 2017 – Moscow, Saint Petersburg, and others.

For his research efforts, he was funded by:

- Grant for the best Researcher project of junior scientific workers of the Yerevan State University (1979);
- Grant of International Scientific Foundation (1993);
- DLR Grants, ARM 1998-001, Germany, Manager (1999–2002);
- ANSEF Grant NS-82, USA Manager (2003);
- Grant 0166, Ministry of Education of RA, Manager (2005–2007);
- Thematic financing № 202, Ministry of Education of RA, Manager (2007–2008);
- Basic scientific financing № 242-N, Ministry of Education of RF for development 2016;
- Ministry of Education of RA, Manager (2007–2017), № 10-2/I-1; № 10-2/I-4 grants;
- Ministry of Education of RF, Manager 2016, 2017;
- TEMPUS IV BME ENA 2014–2017.

He has given numerous invited/plenary talks at international conferences (more than 100) including Wien, Austria – 1982, 1999; Tubingen, FRG – 1988; Berlin, Germany – 1991, Bad Herrenalb, Germany – 1998; Sant-Luis, USA – 1999; Campobasso, Italy – 2000; Lisbon, Portugal – 2000; Halle, Germany – 2000; Spain – 2002; Poland – 2004; Germany – 2013, 2014; Moldova – 2015, 2016; Greece – 2017; Moscow – 2017, etc.

Professor Hrachik Vardapetyan was initiator and organizer of 4 International conferences “Biotechnology and health” & DAAD Alumni seminar (2005, 2008–2010), funded by DAAD, SSC of the Ministry of Education and Science of the RA.

He is the author or coauthor of more than 202 papers in international refereed journals and more than 110 conference contributions. Coauthor and editor of 3 educational books on biology.

Scientific consultant for one doctoral thesis and the head of 19 PhD dissertations. They are all renowned scientists working in the USA, Canada, Australia, Germany, Belgium, France, Russia, and Armenia. In 2006 the government of the Russian Federation awarded a gold medal for scientific guidance of the best student work. H. Vardapetyan made a lot of efforts to raise the international prestige of Armenian science. He was one of the founders of the Department of Medical Biology at Russian-Armenian University.

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Computational Modeling of Potential Inhibitors of the QS System of Antibiotic-Resistant Bacteria P.aeruginosa

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Antibiotic resistance is a global public health problem. Deaths from resistant infections are projected to reach 10 million by 2050 [1], equal to the number of people currently dying from carcinogenesis each passing year. In 2017 the World Health Organization published the list of bacteria for which treatment are urgently needed, where Pseudomonas aeruginosa is of critical priority. Current therapies lack efficacy because this organism creates biofilms conferring increased resistance to antibiotics and host immune responses. The strategy is to "not kill, but disarm" the pathogen and resistance will be developed slowly. It has been shown that LasI/LasR system is the main component of the quorum sensing system in *P. aeruginosa* [2]. LasR is activated by the interaction with its native autoinducer. A lot of flavones and their derivatives are used as antibacterial drug compounds. The purpose is to search compounds that will inhibit LasR. This leads to the inhibition of the synthesis of virulence factors thus the bacteria will be vulnerable and not virulent. We performed virtual screening using multiple docking programs for obtaining consensus predictions. The results of virtual screening suggest benzamides which are synthetical derivatives of flavones as potential inhibitors of transcriptional regulator LasR. These are consistent with recently

published experimental data, which demonstrate the high antibacterial activity of benzamides [3]. The compounds interact with the ligand binding domain of LasR with higher binding affinity than with DNA binding domain. Among the selected compounds, by conformational analysis, it was found that there are compounds that bind to the same amino acids of ligand binding domain as the native autoinducer. This could indicate the possibility of competitive interaction of these compounds. A number of compounds that bind to other conservative amino acids ligand binding domain have also been discovered, which will be of interest for further study. Selected compounds meet the criteria necessary for their consideration as drugs and can serve as a basis for conducting further in *vitro/in vivo* experiments. It could be used for the development of modern anti-infective therapy based on the quorum sensing system of *P. aeruginosa.*

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Using Machine Learning for Prediction of F_s and γ_C Parameters from the Rb Vapour Fluorescence Spectra

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In this paper we would like to show how machine learning can be used in the study of physical research. The basis is our previous work [1], where we have studied modification of the fluorescence spectra of Rb atomic vapor D_2 line while changing the temporal rate of linear (triangular) scanning of laser radiation frequency. Increase of the ramping speed over certain value ($\approx 10^6$ MHz/s) results in essential modification of magnitudes of individual atomic transitions.

The aim of the study is to predict f_s and γ_0 parameters from the fluorescence spectra of Rb atomic vapor. The prediction is done using Machine Learning [2,3]. The problem we are modeling is Supervised Learning, regression task [2]. The labels are the parameters to be predicted, in this case f_s and γ_0. Both traditional Machine Learning algorithms and Deep Learning [3] approaches have been implemented and analyzed for our data, along with different ways of data preprocessing and feature extraction. The models have been tested not only on data with parameters coming from the

ranges similar to that of training data, but also on data with considerably different parameter ranges. The best model was chosen based on the highest performance on all test data.

This paper is in memory of Dr. Hrayr Azizbekyan.

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Study of the Influence of the Ionic Strength on Complex-Formation of Ethidium Bromide with DNA and RNA

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The influence of the ionic strength of the solution on ethidium bromide (EtBr) complex-formation with nucleic acids, especially, with DNA and the analogue of double-stranded-RNA – synthetic polynucleotide poly(rA)-poly(rU) has been studied using the UV melting, absorption and fluorescence spectroscopy methods. The obtained results indicate that in case of DNA within the change in interval of the ionic strength of the solution $0.002 \leq \mu \leq 0.02$ and in case of poly(rA)-poly(rU) in an interval of $0.02 \leq \mu \leq 0.1$ M, both DNA and poly(rA)-poly(rU) exist in double-stranded (ds-) state in the presence of single-valence Na^+ cations. On the other hand, the obtained experimental data indicate that DNA or the mentioned polynucleotide is not transformed into three-stranded state. Another important result is that ds-RNA can perform a high affinity to ligands binding specifically to ds-DNA, and the mentioned ligands interacting with ds-RNA display their intrinsic modes. It is indicated by the experimental data revealing that EtBr interacts with ds-RNA by those modes as with ds-DNA [1]. It was also shown that the increase of the ionic strength of the solution in the interval $0.02 \rightarrow 0.04$ results in both rising of the binding constant values of EtBr with poly(rA)-poly(rU) by the mentioned modes and decreasing of number of

base pairs (n) per binding site. At further increasing of Na^+ concentration, a decrease of the values of K and growth of the values of n are observed.

Generalizing the above presented data, we conclude that in the interval of the ionic strength of the solution $0.02 \leq \mu \leq 0.1$ M, the structure of poly(rA)-poly(rU) is exposed to the certain alterations, from unstable, partially denatured form transforming to more stable ds-state, which is absent in the case of DNA. Meanwhile, this polynucleotide is not transformed into three-stranded state in the conditions of relatively low ionic strengths of the solution, especially in the presence of only single-valence cations [2]. Another important result is that the intercalating molecules of EtBr with higher affinity to dsRNA make a substantial impact onto the stability of ds-RNA and the intercalation is believed to be the leading mechanism of the stabilization of ds-form of poly(rA)-poly(rU). Particularly, the binding mechanisms of EtBr actually depend neither on the solution ionic strength nor on the nucleic acid type in double-stranded state.

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The Functional Alteration of Rat Neonatal Cardiomyocytes and Cardiac Fibroblasts Caused by *Macrovipera Lebetina Obtusa* Venom

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The Caucasian viper *Macrovipera lebetina obtusa* (MLO) is one of the most prevalent and venomous snakes in the Caucasus and the surrounding regions, yet the effects of MLO venom on cardiac function remain largely unknown. We sought to determine the effects of the crude venom from MLO on the morphology and physiology of neonatal rat cardiomyocytes (CM) and cardiac fibroblasts (CF). Both CM and CF were treated with serially diluted MLO venom and the effects were observed 1 and 24 hours thereafter. At 100 μg/ml concentration, MLO venom was cytotoxic to both cell types detaching them from culture substrate immediately after addition of the venom. Lower, physiologically relevant concentrations of MLO venom affected adhesion of both cell types to culture surfaces in a dose-dependent manner. Importantly, inhibition of venom metalloproteinases resulted in improved attachment and normalization of metabolic activity of cardiac fibroblasts exposed to MLO for one hour. MLO venom also exhibited adverse effects on the amplitude of calcium transients and spontaneous

beating rate of rat neonatal cardiac myocytes. The results can serve as a useful platform to address the effects of MLO venom on cardiac function of a prey. They also call for further exploration of individual venom components for pharmaceutical purposes.

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Several Issues of Hepato-Pulmonary-Renal Pathogenic Relationships and the Possibility of their Prevention with Flamin/Silymarin Herbal Mixture

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Cirrhosis is the outcome of all chronic liver disease, which can accompany pulmonary and renal dysfunction [1–3]. Actual for preventing and treatment of liver cirrhosis use herbal medications [4]. Nowadays, effective strategies to treat liver cirrhosis are still lacking. Consequently, a better understanding of the pathogenesis of liver cirrhosis would facilitate the development of more effective treatment options.

The present study was aimed to investigate the effective hepatoprotective ratio of Flamin/Silymarin mixture, as well as aspects hepato-pulmonary-renal pathogenic relationships in toxic liver cirrhosis and during their treatment. The Flamin and Silymarin were obtained from Helichrysum Rubicundum and Silybum Marianum plants growing in Armenia. The varying ratios of Flamin /Sylimarin (1:1 or 1:2) mixture was administrated orally for 8 weeks in 300mg/kg dosage.

Histopathological examination showed that both mixtures had a hepatoprotective effect in CCl4-induced liver cirrhosis reducing destructive processes and necrosis in the liver parenchyma. In acute hepatic injury (2 weeks of CCl4 injection) there was pulmonary fibrosis, as well as processes

of renal glomerulonephritis. Chronic hepatic injury (CCl4 8-week recovery) accompany by the intensifying of fibrosis in the liver and lung, which are relatively absent in treated groups.

This study showed, that Flamin/Silymarin (1:2) mixture, display more prominent hepatoprotective activity, which can be implied as a novel medication both in the prevention and in treatment of liver cirrhosis.

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Growing the Consortium of Different Labs with Probiotic Properties for Obtaining Functional Food

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The objects of research are the endemic strains of lactic acid bacteria with probiotic propeties which isolated from dairy products and milk of different domestic animals from several regions of Artsakh. Culture media. MRS, MRS broth (Merk, Germany), milk of fat 1.5%, 30°C and 37°C temperature.

Determination of antimicrobial activity. Antagonistic activity of LAB against pathogenic bacteria studied with microbiological methods. The antimicrobial activity calculated according and expressed in arbitrary units (AU/ml) [2]. Lactic acid bacteria identified by the methods of genotyping including API test, 16S rRNA sequencing and RAPD PCR. It is known that during co-cultivation of LAB strains may occur synergism or antagonism. Studies have shown that strains of LABs isolated from the milk of different domestic animals (goat, sheep, buffalo, donkey) with probiotic properties [1] after co-cultivation have antimicrobial activity against conditionally pathogenic Gram-negative Salmonella typhimurium G-38 and Gram-positive Bacillus subtilis G17-89. For example: LAB of strain Ent. durans M42 show 600 AU/ml antimicrobial activity, Ent. durans M44` 400 AU/ml and Ent. durans P13` 550 AU/ml. Comparative investigation of co-cultivation LAB strains shown antimicrobial activity is increasing. Ent.

durans M42 +Ent. durans M44 has 1500 AU/ml antimicrobial activity, Ent. durans M42 + Ent. durans P13 has 1200 AU/ml antimicrobial activity and Ent. durans M44 + Ent. durans P13 has 1400 AU/ml.

Thus, may be conclude the phenomena of synergism or antagonism in the co-cultivation of LAB strains depend on genus affiliation, growing conditions (temperature), environment, and the relationship of the strains.

The obtained data prove the necessity of isolation and advanced research of the new endemic strains of LAB from different domestic animals milk for creation of products of functional nutrition with large spectrum of antimicrobial activity and probiotic properties.

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Comparative Analysis of Secondary Metabolites Contained in the Seeds of *Salvia Hispanica* L.

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Chia (*Salvia hispanica* L.) is an annual herb [1]. Chia seeds are common in many countries and are used as "novel food". The European Food Safety Authority approved chia seeds as food in 2009 [5].

The aim of this work is a comparative analysis of the bioactive components and antioxidantproperties of *S. hispanica* seeds grown in different geographic regions (Armenia, Russia, USA).

The aqueous-methanolic seed extracts were obtained [5]. The colorimetric method was used to determine the total flavonoids content (TFC) and the total phenols content (TPC) [2, 4]. The HPLC analysis of various extracts was performed [3]. The antiradical activity (ARA) was determined [6].

The study has shown that the TFC in Russian and American seed extracts has the same value, while in the Armenian seed extract the TFC is 9 times lower. The TPC in the Russian sample is 4.5 and 3 times higher than in the American and Armenian ones, respectively. The HPLC analysis showed that the rosmarinic acid (RA) and the artemisinin (ART) are present in all samples. The ART in seeds was detected at $\lambda = 226$ nm (Rt = 13.55 min). The concentration of the RA is prevailing in Armenian seed extract by 2 times. The concentration of ART in the Armenian seed extract is 3.3 and 1.3 times higher than in American and Russian seed extracts accordingly.

However, the lack of data on the content of ART in chia seed extracts gives rise to a deeper analysis. All studied samples showed high ARA, which was dose-dependent.

The high content of micronutrients, unsaturated fatty acids, secondary metabolites, and, especially, ART gives chia seeds relevance, opening up new research interests related to the study of the correlation between chia seed consumption and the cognitive properties of healthy people and/or patients with neurodegenerative diseases.

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Genetic Variants of Second Phase Metabolic Enzymes in Schizophrenia Patients

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Second phase metabolic enzymes play an important role in the metabolism of various drugs including those used for the treatment of schizophrenia (SCZ) patients. It is well known that treatment efficacy is strongly affected by genetic variants of antipsychotic drug metabolic enzymes and molecular targets. Here we aimed to assess gene expression levels and select the most informative variants within the genes of second stage metabolic enzymes, namely, glutathione S-transferase (GSM) Mu 1 (GSTM1), *GSTT1*, N-acetyltransferase (NAT)-1 *(NAT1), NAT2*, Catechol-O-methyltransferase *(COMT),* sulfotransferase family 1 members *SULT1* and *SULT2*. We also evaluated potential differences in gene expression levels of second phase metabolic enzymes between SCZ patients and controls to estimate interactions between the corresponding proteins. For this purpose, expression data available in the GEO (Gene Expression Omnibus) repository was used [1].Comparison of the genes expression levels in the postmortem brain revealed no significant differences between the groups. Further, we have analyzed protein-protein interactions using the STRING database [2]: almost all proteins are involved in the same network of brain metabolism proteins. More widened search showed that they also interact with networks, formed by cytochrome P450 isoenzymes and oxidases. Further, the frequency of 23

selected variants was assessed using whole-genome sequencing data and is available for 99 healthy Armenians. 9 out of 23 selected variants are present in the genome of healthy Armenians with frequency >38%. Also the potential association of the *COMT* gene rs4680 variant with SCZ was studied, but no association was detected. It is planned to measure gene expression levels and remaining selected SNPs in order to clarify their contribution to SCZ development. This work was supported by the RA MES Science Committee, in the frames of the research project №19YR1F053 (PI: Roksana Zakharyan).

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Relation Between Viral Load And Hematological Changes in the Blood of COVID-19 Positive Patients

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The pathogenesis of Covid-19 is largely uncharacterized and the effects of viral infection in human still requires extensive studies. Particularly, there are few studies on the effects of viral infection on host hematopoietic and immune systems. In this study we performed systematic assessment of infection associated quantitative and qualitative changes of blood cellular composition in response to viral infection.

We performed an observational cohort study of all consecutive patients admitted ≥ 48 hours to the National Center for Infectious Diseases for COVID-19 (August-September 30th, 2020). One hundred twenty COVID-19 positive patients admitted to the "National center for infectious diseases" were included in the study. All patients had a diagnosis of COVID-19 confirmed by qRT-PCR testing performed on nasopharyngeal throat swab specimens, and/or by fulfilling clinical diagnostic criteria provided during the pandemic peak for SARS-CoV-2. All patients provided their informed consent; the study was approved by the Ethics Committee of the Institute of Molecular Biology of NAS RA (IRB00004079). Blood smears were fixed in

pure methanol and stained with modified Giemsa solution (azure B/azure II, eosin and methylene blue) according to the manufacturer's protocol. Viral titers were calculated with qRT-PCR targeting the *N* gene and *ORF1ab* gene in the conserved region of the SARS-CoV-2 genome.

Our results show that patients can be subdivided into three groups based on the WBC counts. The first group is characterized by severe pancytopenia (leukopenia) with the number of cellular component less than 3000 cells/mm^3. In the second group of patients we observed a pronounced shift of myeloid cells to the left. Finally, the third group of patients was characterized by normal composition of blood cell populations. In addition, we have revealed that blood smears of COVID-positive patients contain 1–6% destroyed cells, as well as aberrant and reactive lymphocytes and lymphoblasts. Mean virus titers were surprisingly lower in patients of the first group compared with others, though it did not reach statistical significance.

Our results indicate that the observed hematological changes observed in the blood of the COVID-19 patients may not be directly related to the SARS-CoV-2 infection titers and other mechanisms, such as genetic background, should be considered and studied.

New Classes of Tartaric Acid Derivatives as Prospective Tools for Antimicrobial Resistance Combating

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Multi-drug resistance is very actual medical and ecological problem [1]. The majority of *Stenotrophomonas, Xanthomonas, Pseudomonas* are common, drug resistant and highly adaptive opportunistic pathogens, as well as human, animal and plant pathogens [2, 3]. They have a huge potential to xenobiotic biodegradation and bioactive substances synthesis [4]. Natural L-tartaric acid is well-known as antimicrobial safe agent, broadly used in food technology. In current paper the elaboration L-tartaric acid new cyclic, nitrogen derivatives were discussed [5, 6]. Using our technology of target derivatization to optically active products, benzyl-, cyclohexyl-, phenyl- and mono ethanolamine- substituted imides and complex salts were synthesized. As the row material it was used the wine industry main waste product: the cream of tartar, from which L-tartaric acid was purified. Antimicrobial activity was tested *in silico* and *in vitro* on native soil *Pseudomonas,*

Xanthomonas, Stenotrophomonas, etc. from The National Microbe Collection of SPC "Armbiotechnology" NAS RA.

As a result of cultivations, transformation and docking analyses series, it was found out new compounds high efficiency as non-selective growth inhibitors. Complex salts are biodegradable by some soil *P. chlororaphis*, *P. fluorescens*. According to the transformation data, the resistance these compounds is not transferring by plasmids. Thus, the elaborated compounds can be recommended for further study as effective, ecologically safe alternative antibiotics, elaborated as green technology products based on economically cheap and harmless source.

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Medicinal Hymenochaetales Mushrooms (Agaricomycetes) Distributed in Armenia

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White-rot xylotrophic Hymenochaetales mushrooms (HM) in Armenia are represented by 27 species [1]. They are producers of several enzymes (phenoloxidases, proteases, etc.) and bioactive compounds (polysaccharides, terpenoids, etc.) with biotechnological and therapeutic interest [2–4]. Several *Phellinus* and *Inonotus* species possess antioxidant, anti-inflammatory, neuroprotective, anti-diabetic, antitumor and other activities applicable in biomedicine [1,3]. HM have been used in traditional medicine as coagulant, anti-diabetic (*Ph. igniarius, Ph. linteus)*, laxative (*I. hispidus)*, wound-healing and cardioprotective *(I. obliquus,* chaga mushroom) agents, as well as for treatment of cancer and gastrointestinal diseases (*Ph. pini*). The polysaccharide-based chaga products are widely used during chemotherapy [3]. The immunomodulatory, antitumor and hypoglycemic effects of *Ph. linteus* was associated with the presence of polysaccharides and peptide-glucans. A new styrylpyrone baumin has been isolated from edible species *Ph. baumii*. Highly oxygenated and unsaturated compounds interfungins, hispidin derivatives, inoscavins and others were isolated from *I. xeranticus.* [1]

Further myco-pharmacological studies of biotechnologically important species of HM in Armenia will open new perspectives for their biomedical exploitation.

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Antibacterial and Cytotoxic Effects of Biological Liquids of Armenian Scorpions

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The occurrence of the multi-resistance phenomenon of pathogenic agents against contemporary conventional antibiotics and the emergence of new infectious agent's force to discover new targets in pathogenic bacteria, as well as new biological antibiotic sources, and develop the new direction in modern biomedicine. With the significant discoveries in the number of valuable biologically active components of scorpion venom can be perfect candidates of numerous drugs with the potential to encounter many of the emerging global health crises. The research on the investigation of Armenian scorpions' fauna biodiversity, biology and ecology was carried out fragmentarily and unsatisfactory. The Armenian scorpion fauna must be more diverse in species composition, and very interesting as a potential source of biological active components.

The aim of the study was to investigate the biomedical potential of Armenian scorpion venom and hemolymph. The antibacterial, toxin-like activities, as well as their minimal inhibitory activity were studied.

It was shown that both venoms and hemolymphs of scorpions collected from different regions of Armenia namely *Androctonus crassicauda*, *Mesobuthus* cf. *caucasica* and *Mesobuthus eupeus* species demonstrated the antibacterial activity against Gram-positive bacteria. The minimal inhibitory activity of *A. crassicauda* hemolymph was confirmed to be 0.5 μg, while for all other scorpions were 1.0 μg. *A. crassicauda*, *M.* cf. *caucasica* and *M. eupeus* scorpion hemolymphs exhibited a cytotoxic effect on *Artemia salina* larva at a concentration of 0.143μg/ml. The data obtained may play a promising role in the development of new drugs that will be used against various pathogens and will be useful in the treatment of cancer.

Oscillator Strength of Biexciton Excited States in Ellipsoidal Quantum Dot

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Investigation of the complexes of four charged particles is of fundamental importance, especially in semiconductors, where it is possible to vary parameters in a wide range. The experimental observation of biexcitons and trions in bulk semiconductors is rather difficult because of the low binding energy [1, 2]. However, the binding energy can increase due to the effect of dimensional quantization in semiconductor nanostructures (quantum wells, quantum wires, quantum dots) [3, 4]. In this connection, the theoretical and experimental investigation of biexciton states in quantum nanostructures is an actual problem. Semiconductor quantum dots (QDs) have a great potential for the further development of nanoelectronics due to their unique exciton–biexciton physics and the important contribution they make to quantum information processes.

The biexciton is a neutral compound quasiparticle, that is also effectively a boson and it has an integer spin when the spin-orbit coupling can be neglected. The conversion of excitons to biexciton complexes leads to various optical and other interesting effects such as change in the nonlinear susceptibility, photoluminescence emission peaks shift etc [5, 6]. The excitied states of biexcitons also have various applications and one of them is in

sharp increase in two-photon absorption. So the theoretical investigation of biexciton states in QDs is actual problem.

In this paper the excited states of biexciton states in ellipsoidal QD will be investigated theoretically. The ground state of the biexciton is a singlet state. It should be noted that the trial wave function is not symmetric with respect to electrons and holes.

The variational function for the biexciton will be constructed on the single-particle wave functions and will have the following form [7]:

$$\Psi_{trial}\left(\vec{\rho}_1,\vec{\rho}_2,\vec{\rho}_\alpha,\vec{\rho}_\beta\right)=C\psi_{100}\left(\vec{\rho}_1\right)\psi_{100}\left(\vec{\rho}_2\right)\psi_{100}\left(\vec{\rho}_\alpha\right)\psi_{100}\left(\vec{\rho}_\beta\right)\times \\ \times e^{-\gamma\rho_{\alpha\beta}}\left\{e^{-\lambda\left(\rho_{1\alpha}+\rho_{2\beta}\right)-\delta\left(\rho_{1\beta}+\rho_{2\alpha}\right)}+e^{-\lambda\left(\rho_{1\beta}+\rho_{2\alpha}\right)-\delta\left(\rho_{1\alpha}+\rho_{2\beta}\right)}\right\} \quad (1)$$

where C – normalization constant, $\rho_{ik}=\left|\vec{\rho}_i-\vec{\rho}_k\right|$, $j,k=\{1,2,\alpha,\beta\}$, λ, δ and γ are variational parameters, which are determined after minimizing the integral:

$$E_{XX}=\left\langle\Psi_{trial}(\vec{r}_1,\vec{r}_2,\vec{r}_\alpha,\vec{r}_\beta)\middle|\hat{H}\middle|\Psi_{trial}(\vec{r}_1,\vec{r}_2,\vec{r}_\alpha,\vec{r}_\beta)\right\rangle. \quad (2)$$

The variational function for the excited biexciton (excited by one hole or by one electron) will have the following form:

$$\Psi_{trial}\left(\vec{\rho}_1,\vec{\rho}_2,\vec{\rho}_\alpha,\vec{\rho}_\beta\right)=C\psi_{110}\left(\vec{\rho}_1\right)\psi_{100}\left(\vec{\rho}_2\right)\psi_{100}\left(\vec{\rho}_\alpha\right)\psi_{100}\left(\vec{\rho}_\beta\right)\times \\ \times e^{-\gamma\rho_{\alpha\beta}}\left\{e^{-\lambda\left(\rho_{1\alpha}+\rho_{2\beta}\right)-\delta\left(\rho_{1\beta}+\rho_{2\alpha}\right)}+e^{-\lambda\left(\rho_{1\beta}+\rho_{2\alpha}\right)-\delta\left(\rho_{1\alpha}+\rho_{2\beta}\right)}\right\} \quad (3)$$

By the help of the variational method one can calculate the energy of biexciton for the ground and excited levels.

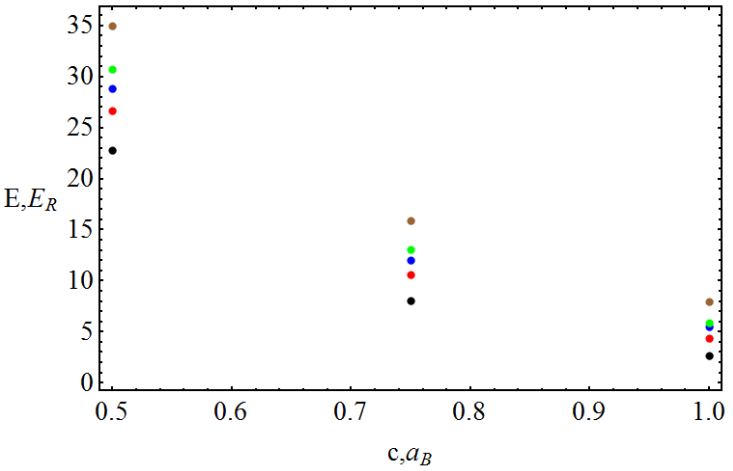

Figure 1. Dependencies of the energies of biexciton for the ground and excited levels () on the small semiaxis.

Let us proceed to the calculation of the oscillator strength. The oscillator strength for the ground and excited biexcitons can be calculated using the following formula [8]:

$$f_{\left(XX^0,XX^1\right)} = A\frac{E_P}{2E_{\left(XX^0,XX^1\right)}}\left|\int_V \Psi^{0(1)}{}_{exc}\left(\vec{r}_e,\vec{r}_h\right)d\vec{r}\right|^2, \qquad (4)$$

where E_P is the Keyn energy, A – recombination probability factor.

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Study of N-Substituted Amino Acids Dialkyl-Amino Alkylamides in Possible Treatment of Alzheimer Disease

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According to WHO, annually millions of people are susceptible to neurodegenerative diseases, such as Parkinson's disease and Alzheimer's disease (AD). Hence, testing of new drugs to slow down the process of their development is an actual problem in medicine. It is known that the main cause of AD is misfolding of Aβ-peptides, which leads to the formation of extracellular aggregates of Aβ [1, 2]. Thus, we sought to develop new agents that can effectively inhibit the formation of β-amyloid aggregates. From this viewpoint compounds such as N-substituted amino acids dialkylamino alkylamides has a special interest as they act as acetylcholinesterase inhibitors. Therefore, we synthesized novel compounds 1-diethylaminoethyl-2-phenyl-4-benzylidene-5-imidazolone (TVS) and N-benzoyl-DL-valine dimethylamino-ethylamine iodmetilate (TVA) and studied their neuroprotective effects in AD models.

Histopathological examination showed that destructive and dystrophic processes in the hippocampus were significantly reduced under the influence of TVS and TVA, compared with the control group. Neurons have normal structures and their qualitative and quantitative indicators have resembled the intact. Between these compounds, TVS possess more prominent neuroprotective activity.

This study confirms that N-substituted amino acid amino amides like TVS and TVA possess a neuroprotective activity and can reduce neurodegeneration induced by Aβ and potentially can be used for slow down AD development.

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Interaction of Small Molecules with Telomeric G-Quadruplex DNA

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Telomere region of human genome have always been in the spotlight of scientists working in the field of drug design and discovery of anticancer drugs. Recently G-quadruplex structures that form at the distal 3' end telomere region of the human DNA were considered as a potential target in modern anticancer therapy [1]. Unfortunately, common structural biophysical and molecular biology methods are very limited in the study of non-canonical DNA secondary structures, because of the exceptional specificites of this structures. Therefore, human telomeric G-quadruplex DNA lead drug compound still has not been discovered. The main problem that hinders investigations in this field is structural polymorphism associated with G-quadruplex molecules and limitations of traditional structural biophysical methods in studying these phenomena [2]. The limitations of mentioned traditional experimental methods created strong need for new alternative approaches for solving occurred problems. We applied the advances of modern bioinformatics methods and tools such as molecular modeling, in silico screening, docking and molecular dynamics simulations to overcome difficulties associated with structural polymorphism. As a result of our research we identified compounds that have high binding affinity to several structural topologies of telomeric G-quadruplex DNA.

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Prediction the Risk of Development for Schizophrenia and Bipolar Disorders in Different Populations, Using Machine Learning Approaches

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New high-throughput genomics technologies have opened the new era in "big biological data" analysis. That information contributes to disease prognosis and monitoring, which is a crucial part of personalized medicine [1]. Meanwhile, big data analysis contributes to the development of personalized medicine. Hence, there is a need for new approaches for analysing accumulated data. In this regard, machine learning, neural networks algorithms have proven their ability to efficiently analyse big biological data.

Nowadays, the most common causes of death in the world complex diseases, such as metabolic and heart disease, neurodegeneration etc. (https://www.who.int/healthinfo/mortality_data/en/). Complex diseases are caused by a combination of genetic and environment [2]. The most common approaches for identifying genetic markers e.g Single Nucleotide Polymorphism (SNPs), which are associated with complex diseases is genome-wide association studies (GWAS). However, GWAS studies have a major limitation. SNPs, which are associated with diseases in one population, can have different effects for others [3]. Hence, there is a need for a new approach for

evaluating the genetic risk of disease development, which will be adjusted by population belongingness of the individuals.

In our study, we aimed at identifying population-specific disease-related genetic markers, create population-level disease genetic risk portraits, and based on these portraits predict disease development risk for schizophrenia and bipolar disorder. In order to identify those genetic markers, we have used the Self-organizing map (SOM) [4] approach. We have determined the background distribution of disease-associated SNPs in 51 worldwide populations, from the Human Genome Diversity Project (HGDP) [5]. Additionally, we have used supervised machine learning methods (support vector machines) [6] to predict the disease development risk, which is adjusted for population belongingness of the studied individuals.

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Implementation of Expansion Microscopy Method to Neuronal Morphology Visualization In Vivo

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Ultra-high-resolution fluorescence microscopy methods allows studying the morphology of cell ultrastructures and organelles, the visualization of which was previously limited by the diffraction limit of a confocal microscope. However, the implementation of these methods remains technically complex and expensive. The recently developed method of expansion microscopy (ProExM) improves the resolution of a confocal microscope by increasing the size of the sample up to 4 times [1, 2]. In ProExM fluorescently labeled antibodies and fluorescent proteins expressed in the cell are fixed on the gel, after which its physical anisotropic expansion is performed. The advantage of the method is that prepared samples are optically transparent, which allows high-resolution images to be acquired deep in tissues with conventional fluorescence microscopes.

The disadvantage of this method is a decrease in the luminescence intensity in expanded samples. In this work ProExM technique is adapted for visualizing the morphology of neurons in the brain slices from Thy1-GFP line M transgenic mice. Fixed brain sections were stained with primary anti-GFP antibodies and secondary Alexa Fluor 488 conjugated antibodies to

enhance the luminescence intensity. For cross-linking of protein molecules of the sample with the gel, the sections were treated with methacrylic acid N-hydroxysuccinimide ester (MA-NHS), embedded in the gel and then treated with Proteinase K. After this, the sample was successively expanded 3 times. Optimization of incubation time with MA-NHS and Proteinase K is needed to find the balance between the sample expansion rate and fluorophore intensity. The size of studied samples increased up to 3.5 times. Using ProExM we obtained high-resolution images of not only neuronal soma, but also the smallest details of neuron morphology, including dendritic spines. Expansion microscopy is a promising method for studying the ultrastructure of neurons. This work was supported by the Russian Science Foundation Grant 20-45-01004 (IB).

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Positive Modulation of Calcium-Activated Potassium Channels Exerts Beneficial Effects in Mice with Ataxic Phenotype

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Cerebellar Purkinje cells (PCs) are affected in many movement disorders with ataxic phenotype. The severe degeneration of PCs is observed during the late stages of ataxia. Previous studies have shown that the abnormal PC firing is happening before the actual cell degeneration [1]. Thus, the disturbed PC pacemaking was observed previously in mice models of neurodegenerative diseases (NDDs) with ataxic phenotype [2, 3]. PC pacemaker activity is controlled by SK channels. The pharmacological activation of calcium-activated potassium channels (including SK channels) has demonstrated some beneficial effects in ataxic mice [2, 3]. The aim of the present study was to analyze the effect of SK channels' activation by Chlorzoxazone (CHZ) on the abnormal PC firing in transgenic mice models of spinocerebellar ataxia type 2 (SCA2) and Huntington's disease (HD). For this purposes, SCA2-58Q and YAC128 HD transgenic mice were used. Via the method of extracellular *in vivo* recording, we have shown that simple spikes' (SS) frequency was much lower and firing variability was much higher in case of SCA2 and HD PCs compared to WT PCs of the same age [4]. CHZ recovered SS frequency in HD mice, while it has no effect on SS

frequency in SCA2 mice. Meanwhile, the firing precision was recovered in both SCA2 and HD mice [4, 5]. Our results suggest that CHZ can be used as a general way to treat NDDs with ataxic phenotype.

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Influence of Melatonin on the Processes of Tissue Energy Supply in Diabetes Mellitus

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Diabetes mellitus (DM) – a group of metabolic diseases characterized by chronic hyperglycemia, which is the result of impaired insulin secretion, the action of insulin, or both of these effects [1]. Pathomorphological changes in the insular part of the pancreas and disruption of the beam structure of the lobules of hepatocytes are associated with the transformation of the main pathways of cellular metabolism. One of the ways to correct impaired homeostasis is rational pharmacotherapy of DM. In this regard, the pineal hormone melatonin (MT), which is considered a powerful antioxidant and a universal therapeutic agent [2], with a high degree of safety, may be promising. The results of our studies showed that the activity of succinate dehydrogenase (SDH) in the liver in animals with LUS increased to 0.48 nmol/mg protein, and in rats with HUS 0.75 nmol/mg protein in comparison with the data of the control group of rats – 0.4 nmol/mg squirrel. We investigated the effect of MT on SDH in DM.

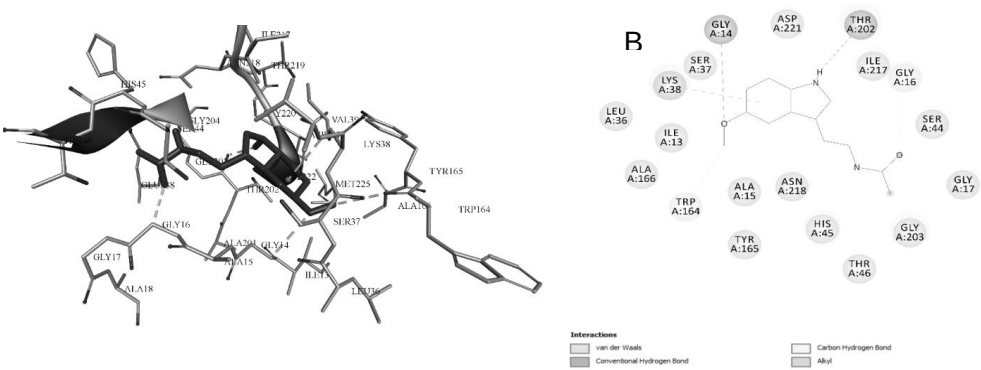

Fig.1. A. visualization of the interaction of melatonin in catalytic center of SDH.; B. conformational map of complexation.

The results of the study of the activity of SDH showed that the severity of changes is observed in the liver only in animals with HUS. We were able to show that the introduction of MT promotes the normalization of SDH activity. Interaction between MT and SDH was studied *in silico*. The obtained stereochemical parameters indicate the spatial orientation of MT on the A domain of SDH (Fig.1).

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Plugin Development for High-Level Analysis of Miniscope Data

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A miniature fluorescence microscope (miniscope) is a promising tool for visualizing neuronal activity [1]. The obtained miniscope data will provide new, previously inaccessible information about neuronal activity. The processing of miniscope data obtained with a number of difficulties: the extraction of neural activity and its subsequent analysis, including high-level analysis.

Due to the absence in open sources a tool that allows a high-level analysis of neural activity [2], the authors present a new software module that combines the capabilities of primary processing of video recording using the CNMF_E [3] algorithms, a procedure for registering neurons for several experiments using the CellReg algorithm [4], as well as a high-level analysis of changes in neuronal activity from experiment to experiment. The MATLAB (MathWorks) environment was chosen as a development platform which allows to easily combine algorithms and their implementations

of other researchers. The current version of the software module allows you to import the processing data of the video sequence of one experiment, carry out correlation analysis and present the result in graphical form. The graphical interface of the software module that was used to process this data is available by the link – https://is.gd/W1bctp. In subsequent versions of the presented software module, it is planned to add the option of comparing neural activity recorded in one experimental animal between several experiments. This work was supported by the Russian Scientific Fund (grant 19-15-00184 to IB) and by the Academic Excellence Project 5–100 from Peter the Great St Petersburg Polytechnic University (to IB).

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Cytotoxicity Assessment of Different Extracts and Stabilized Iron (III) Oxide Nanoparticles on E. Coli Growth

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Iron oxide nanoparticles (NPs) are widely investigated due to their behavior and unique properties [1]. Nowadays, "green" synthesis of NPs is getting larger attention, since NPs, derived from plant extracts, are less toxic, than ones, derived from physical and chemical methods, which allows better biocompatibility [2].

The aim of this study was the investigation of the cytotoxicity of NPs, derived from various plant extracts, as well as of those extracts themselves on E. coli's growth.

Iron (III) oxide NPs were synthesized using aqueous, 50% and 96% ethanolic extracts of dried *H. perforatum*, fresh and dried leaves of O. basilicum. The cytotoxicity was assessed by measuring the growth of *E. coli* DSM 1116 under the exposure to test samples in the liquid media during 24 hours of incubation.

Our results reviled, that all of the NPs, derived from investigated extracts, as well as 96% ethanolic extract of dried leaves of O. basilicum and 50% ethanolic extract of dried *H. perforatum* themselves, had growth stimulating activity during the exponential growth phase of *E. coli*. Meanwhile, aqueous and 96% ethanolic extracts of dried *H. perforatum*, as well as aqueous and 50% ethanolic extracts of *O. basilicum* fresh leaves shown

growth inhibiting activity during the exponential growth phase. All of the remaining extracts did not affect the exponential growth phase. Almost all of the studied samples were decreasing the growth of *E. coli* in the stationary phase.

Thus, from the obtained results can be concluded, that the mentioned extracts and NPs do not have cytotoxic properties on the *E. coli*, and they can be used as growth controlling agents for different phases of growth.

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Assessment of Sensitivity of AgNPs-Resistant E. Coli to Antibiotics and Antibiotic-Nanoparticle Complexes

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Silver nanoparticles (AgNPs) are widely used due to their great antibacterial activity, synergetic effect in conjugation with antibiotics and high biocompatibility [1]. Preparation of AgNPs by "green" synthesis methods is environmentally friendly and cost-effective [2]. Yet, there has been an increase of resistance to AgNPs in bacteria recently, which may alter the sensitivity to existing antibiotics [3]. Thus, the aim of this study was to investigate the influence of the "green" silver nanoparticle resistance of *E. coli DSM 1116* on it's sensitivity to benzylpenicillin (BP), kanamycin (KM) and their complexes with AgNPs.

"Green" AgNPs were synthetized using the extract of *Ocimum araratum*, the size and shape were identified via Scanning Electron Microscopy. The formation of antibiotic-AgNPs complexes was verified via spectral analysis. The antibacterial activity of test components was assessed via disk-diffusion and colony-forming activity methods [4]. Potential synergetic antibacterial activity of investigated antibiotic-AgNPs complexes was estimated using fractional inhibitory concentration index [5]. The results have shown that repetitive exposure to high concentrations of "green" AgNPs leads to development of resistance in short terms. According to the data obtained by the disk-diffusion method, neither BP-AgNPs, nor KM-AgNPs complex have a synergistic or additive effect comparing to BP and KM, re-

spectively. The minimal inhibitory concentration of BP in AgNPs-resistant *E. coli* is twice smaller than in AgNPs-sensitive *E. coli* [4]. The results of a study of the antibacterial effect on colony-forming activity, however, showed that both KM and BP in complexes with AgNPs act synergistically on AgNPs-resistant *E. coli*.

The study confirmed the possibility of a change in the sensitivity to BP and BP-AgNPs complex on the AgNPs-resistant *E. coli*. Nevertheless, further research is required.

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The Role of Astrocytes in Regulation of Cognitive Functions in Alzheimer's Disease

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At the present stage of development of neuroscience, it is common to consider neural activity with the obligatory participation of neuroglial interactions. Astrocytes can affect neuronal function in various ways, in particular by regulating the concentration of ions and neurotransmitters [1], releasing gliotransmitters that can act directly on neuronal receptors [2], modulating neuronal excitability, synaptic transmission, and plasticity [3]. Astrocytes are closely related to the pathogenesis and pathological processes of neurodegenerative diseases. However, the role of astroglia in restoring cognitive functions is still not fully understood. Our main goal is to determine the role of astrocytes in regulating changes in cognitive functions, in particular, memory in the development of Alzheimer's disease. For this purpose, one of the possible ways to regulate astrocytes can be optogenetics, as one of the most specific and physiological methods for spatio-temporal resolution. During optogenetic stimulation, it is important to understand how as-

trocytes will be activated, by changing the membrane potential by using ChR2 or by activating metabotropic G-protein receptors (OptoGq). To determine the most effective activation method, we plan to collect the following virus constructs: rAAV-GFAP-ChR2(H134R) -EYFP, AAV1-GFAP: OptoGq-eYFP and transduce them in mice hippocampal neurons. Optimal protocols of light stimulation would be found by patch-clamp technique on acute slices of hippocampus.

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Study of Co-Fermentation of Glucose and Glycerol in the Presence of External Formate in Escherichia Coli Bacteria at pH 6.5. The Role of Fhla Regulatory Protein

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Escherichia coli is widely applied in biotechnology due to the ability to utilize mixture of carbon sources and produce valuable end-products, such as molecular hydrogen (H_2) [1]. H_2 production in E. coli is implemented by FHL complexes, which formation is activated by HycA and FhlA proteins [2]. In this study co-utilization of carbon sources combination (11 mM glucose, 137 mM glycerol, 10 mM formate) by E. coli wild type and fhlA mutant strain (lacking FhlA protein) at pH 6.5 was investigated.

Specific growth rate decreased in fhlA ~ 25 % indicating the role of FhlA regulatory protein in the growth of bacteria. The utilization of glucose started from 2 h and 1 h in wt and fhlA strain, accordingly, and lasted until 24 h with 0.45 mM/h and 0.43 mM/h utilization rates. The utilization of glycerol started from 3 h and 1 h of growth with 0.027 mM/h and 0.014 mM/h utilization rates in wt and mutant strain, respectively. Early utilization of glycerol in fhlA strain is explained by the absence of H_2 generation, which has negative effect on glycerol utilization [3]. External formate is imported by wt during the lag phase of growth by ~ 1.43 mM, but H_2 genera-

tion was not determined. Formate can have an impact on appropriate enzymes operons transcription and consequently H_2 generation. The essential part of synthesized formate is oxidized to H_2 and CO_2 in wild type [1, 3], another part of it is transported via FocA/B channels and maintain relatively constant external concentration (8-10 mM). Otherwise, in fhlA mutant strain, this amount increased till ~ 28 mM, as there was no possibility of an enzymatic reaction.

It can be concluded that E. coli is able to perform co-fermentation and utilize glucose and glycerol simultaneously in the presence of external formate at pH 6.5. Moreover, FhlA regulatory protein has a considerable role in bacterial growth and on glycerol, but not glucose, utilization parameters during fermentation of mixed carbon sources.

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Interaction of Dihydroartemisinin and SCH772984 Inhibitor with ERK2

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Sesquiterpene trioxane lactones are secondary metabolites of plants Artemisia annua have multiple biological and pharmacological effects, including antimalarial, anti-inflammatory, antitumor, antiviral, antibacterial, vasodilative, and other properties. Nowadays, more attention is being paid to the neuroprotective properties of artemisinin, its derivatives, such as dihydroartemisinin (DHA) and many semi-synthetic analogs [1]. Artemisinins can have a neuroprotective effect by inhibiting oxidative stress via modulating various signaling pathways, including ERK [2]. The aim of the work was to study the peculiarities of direct interaction of DHA with ERK2 and comparison with SCH772984 inhibitor by molecular modeling methods.

We have performed molecular dynamics simulations of ERK2 with SCH772984 and DHA for three times of 500 ns (1.5 μs for each ligand). In all runs, the SCH772984 occupies the ATP binding pocket and the allosteric pocket of ERK2 (binding energy –108.33 kJ/mol), thus changing and maintaining a similar conformation to the crystal structure. The interaction involves amino acids of P-loop, DFG motif, and those that interact with inhibitors, which correlates with the literature data [3]. The salt bridge between K54 and E71 does not form frequently. DHA, on the other hand, is located

in the ATP binding pocket throughout the simulation (binding energy – 64.96 kJ/mol). The interaction is mainly contributed by some amino acids that coincide with SCH772984. The salt bridge is formed frequently. For both ligands, the DFG motif keeps the conformation "in" during all runs. Comparison shows that DHA does not behave as an inhibitor and its binding energy is significantly weaker. At the same time, ERK2 changes to an "active" conformation, i.e., DFG-in motif, αC-in and in most cases the formation of a salt bridge. Thus, DHA binding to ERK2 most likely supports active binding and probably makes it available for ATP, which binds with higher binding energy [4].

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Effect of Flavonoids on Quorum-Sensing Systems of *P. Aeruginosa* and *E. Coli*

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The antibiotic resistance problem is worsened by biofilms and quorum-sensing system. There are many strategies to combat biofilms. One promising strategy is targeting the individual components of the quorum-sensing system: Targeting signal generation, QS signal receptor, AHL signal dissemination [1]. In this context, we studied the interaction of flavonoids with transcriptional regulators LasR of *P. aeruginosa* [2] and Suppressor of division inhibitor (SdiA) of enteropathogenic *E. coli* [3], which regulate virulence and biofilm formation. The full structure of transcriptional regulator LasR was reconstructed using molecular modeling techniques. The results indicate that 3OC12-HSL, quercetin, and taxifolin can bind to both the LBD and the "bridge" of the transcriptional regulator LasR. This suggests that there are multiple binding modes. Conserved amino acids such as Leu236, Leu177, Lys182 play an important role during the interaction with "bridge". Quercetin and taxifolin interact through the hydroxyl group at position 7 from ring A which is important for inhibitory activity. This could explain how quercetin and taxifolin inhibit DNA binding by preventing the hinge rotation of DBD. The binding affinity of the 3OC12-HSL, quercetin, and taxifolin to the LBD-DBD "bridge" of LasR is close and not competitive which matches experimental studies. The removal of the OH group at posi-

tion 7 in taxifolin reduces the binding affinity, which speaks about its critical role in inhibition. An extensive number of MD simulations were performed for SdiA. From which we obtained the potential inactive form and the active form from crystallography data. These structures were used for molecular docking of flavonoids, antibiotics, and the Octanoyl-rac glycerol (Native autoinducer) with SdiA. We have shown that quercetin has the highest binding affinity, which can be arranged in the following descending order: Quercetin > Taxifolin > Benzylpenicillin > Octanoyl-rac glycerol > Kanamycin A.

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The Study of New Phytostimulator Activity Based on Tartaric Acid

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The antimicrobial effect and the positive influence of natural aldaric acids plant growth and the agricultural crops productivity is well-known [1]. Tartaric acid is the most abundant acid of plants, from trees to algae. It has a wide range of applications in food (as additive E334) and chemical industry [2].

In current paper, the effect of a new tartaric acid based phytostimulator preparation on plants of different taxonomic groups representative's growth was discussed. This preparation was elaborated at NPUA, and tested on the range of higher flowering plants: *Stapelia grandiflora Masson*, *Aloe vera*, *Kalanchoe Blossfeldiana*, *Agave tequilana*, *Agave americana L.*, *Sansevieriatrifasciata*, as well as on the range of significant agricultural crops: *Solanumtuberosum*, *Allium sativum*, *Phaseolus vulgaris*, *Fragaria×ananassa*, *Cucumissativus*, and *Lens culinaris* [3, 4]. Laboratory and field tests were carried out on various agricultural crops, houseplants

seedlings, potted crops and callus crops showed the high efficiency of the tested preparations.

As a result of experiments, the stimulating effect was indicated by the increase of both green biomass and roots growth speed, the decrease of periods between flowerings, seeds earlier germination, as well as the acceleration of emergence of seedlings.

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Biological Hydrogen Generation by Purple Bacteria as a Promising Way of Industrial Waste Treatment

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The advantages of hydrogen (H_2) as a future energy vector are versatile, but perhaps the most important one is addressing the environmental challenges [1]. The sources for H_2 production affect bacterial metabolism so their selection is critical for the process. Even though pure organic substrates give efficient H_2 generation, they increase the production cost. A promising approach is the application of industrial wastes in H_2 production [2]. Using industrial wastes as a source not only provides inexpensive energy production, but also utilizes wastes from local industries. Food industry wastes, such as brewery and distillers grains, provide practically unlimited source of natural nutrients. The growth properties and H_2 production by photofermentation of purple bacteria *Rhodobacter sphaeroides* were monitored during cultivation on different waste containing media. The nature and the quantity of substrates used affected bacterial growth. The strains used were unable to grow or produce H_2 on undiluted waste. Maximum specific growth rate was observed for 5-10 % waste containing media. H_2 production by control cells, grown on waste containing media, was detected at 48 h growth and continued up to 96 h. The H_2 yield from wastes was comparable or even higher to that of control medium with expensive carbon and nitro-

gen sources. *N,N'*-dicyclohexylcarbodiimide-sensitive ATPase activity of *R. sphaeroides* membrane vesicles from growth on waste containing media has increased 1.6-1.7-fold, in comparison with that of succinate containing medium correlating with enhanced H_2 production. Though it is in early stages of development, a technology that employs growth media containing optimal amount of wastes may be a promising alternative to expensive media for high H_2 yield in *R. sphaeroides* during the anaerobic growth upon illumination.

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Comparative Analysis of the Interaction of Artemisinins, Curcumin, and Ibuprofen with β-Amyloid Fibrils and BACE-1

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Experimental data accumulated over the past years suggest that Alzheimer's disease (AD) is caused by the formation of plaques in the brain due to Aβ aggregation in the amyloid cascade as a result of the expression of aspartyl protease β-secretase (BACE–1). Aβ can fold into amyloid β-sheet deposits, which leads to brain function damage [1]. In this regard, the prevention of formation of Aβ fibrils can be achieved either by suppressing the activity of BACE-1 or by preventing Aβ aggregation [2].

This work is dedicated to in silico studies of the interaction of artemisinin (ART), dihydroartemisinin (DHA) and its dimer (DDHA) with amyloid peptides $18Aβ_{9–40}$ (PDB ID: 2LMP) and $12Aβ_{9–40}$ (PDB ID: 2LMN), BACE-1 (PDB ID: 2WJO) and its further comparison with curcumin (CUR), which is in phase II of clinical trials and nonsteroidal anti-inflammatory drug ibuprofen (IBU).

It has been shown that all ligands bind to the amino acids that are responsible for the formation, growth and stabilization of $12Aβ_{9–40}$ as well as $18Aβ_{9–40}$ with the highest binding affinity for DDHA.

Of all the studied compounds, only CUR, and DHA bind to critical amino acids of catalytic center of BACE-1. All ligands interact with Tyr71 of

continuous chain of hydrogen-bound Trp76-Tyr71-W2-Ser35-Asp32 residues. The binding affinities for the favorite binding poses of ligands to Aβ fibrils as well as for BACE-1 can be arranged in the following decreasing order: DDHA>CUR>ART (DHA)>DHA (ART)>IBU.

Based on our studies it may be assumed that artemisinins can directly prevent the formation, growth and stabilization of amyloid fibrils, can modulate BACE-1 activity and, thus, can be considered as possible candidates for the treatment of AD.

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The Influence of WiFi Rays on Human Cell Cultures: The Difference Between Cancer and Non-Cancer Cells

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Sharing information is a necessary part of human life today. A very popular way to do this is WiFi, rays are dominant in the environment we live; they are an indivisible part of modern life; we are always surrounded by WiFi rays. Knowing this leads to worries.

Several experiments gave certain evidence about the influence of WiFi rays [1]. Many experiments were set on rats and rat and human spermatogenesis [2-5], they confirm the negative influence of WiFi rays. Some experiments reject its harmful effect [6]. Some experiments were done on WiFi rays' ability to index attention and working memory operation of the brain [7]. In many cases though, a certain spectrum of rays was used [8-10], which does not reflect the influence WiFi rays would have in normal conditions. Experiments were set on breast cancer cells even using the exact frequency spectrum of WiFi rays, 2.4 GHz, but this, too, may not show the real pattern.

There are some major differences between cancer cells and normal cells, including important metabolism differences. Most importantly many DNA changes (mutations) occur in cancer cells that are not present in healthy cells [11].

The differences in the ways normal and cancer cells respond to WiFi rays, remain unknown. This research will help better understand the minor differences between these cells and maybe will help in cancer treatment research.

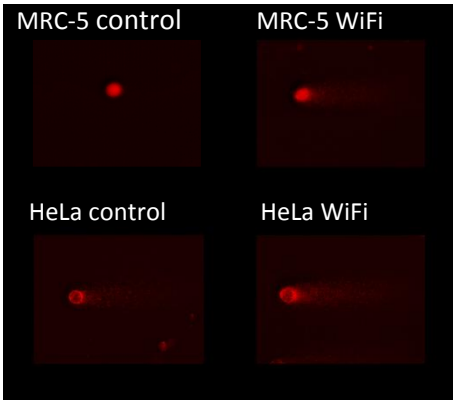

Figure. Images from comet assay (nucleus: the "head", damaged DNA: the "tail").

HeLa and MRC-5 cell lines were the objects of the experiments. Studies were done using comet assay for measuring DNA damage.

Results show significant damage of DNA in case of MRC-5 cells ($p=0.03$) and no significant change in case of HeLa cells ($p=0.4$). Tails are clearly visible in the figure. Tail moment values were tested with student t test. After 4 days of WiFi ray's exposure, MRC-5 cells show the similar level of DNA damage as it was shown by HeLa cells control group. DNA breaks is a mechanism by which cancer cells can be created so there is a chance WiFi rays can make MRC-5 cells cancerous [12].

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Brain Circuits of Energy Homeostasis as a Key to Figure Out Obesity

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Nowadays the obesity is one of the most serious challenges for civilized world. The accessibility of food turned overeating into a routine, causing obesity level to grow up. Palatable food has its own place in obesity pathogenesis. It is consumed even if energy requirements of organism are already met. In physiologically healthy organism, feeling of hunger is formed when blood glucose level drops. In response, hypothalamus activates ghrelin synthesis in the stomach. In higher brain centers, ghrelin activates food seeking behavior and motivation to eat. If food contains much sugar and fat, soon a large amount of insulin is secreted to the blood flow. Consequently, glucose drop will follow. The same circle with participation of ghrelin may repeat many times. Simultaneously, under the effect of insulin adipose tissue synthesizes leptin, which has an essential role informing hypothalamus about energy stores of organism. On the other hand, until leptin reaches to hypothalamus quite more sugar and fat will be consumed, than organism actually needs. This kind of energy homeostasis is displayed on the belly and affects body mass index badly [1].

The key to use more sugar and fat than organism requires is palatability, which can be defined as complex of smell, appearance and content of calories in the food. The food that we have never tried cannot be considered as palatable. Dopamine, the main mediator of brain reward system, induces

pleasure and simultaneously consolidates the image of palatability in memory. Along with listed mechanisms, there is a strong interconnection between hypothalamus and brain reward system. Sometimes the effect of brain reward system on hypothalamus is stronger, and at that point, we start using more palatable food than organism requires [2].

This work aims to highlight brain circuits underlying obesity to understand features of this pathological condition as neural disorder.

Behavioral studies performed by us show that animals that continually consume palatable food cannot stop eating even if it is associated with aversive stimuli. Interestingly, markers normally elevated when animal is exposed to aversive stimulus are significantly lower in animals, which consume palatable food. It seems that brain gives central role to palatable food, causing unpleasant stimuli to be considered as less aversive.

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Age-Related Pathomorphological Changes of Neurons in 5xFAD-M Mouse Model of Alzheimer's Disease

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A decrease in the number of synaptic contacts of hippocampal neurons correlates with cognitive impairments in Alzheimer's disease (AD) [2]. Dendritic spines are dynamic postsynaptic structures that reflect functional changes in synapses during AD progression [3]. We have developed 5xFAD-M-line by cross-breeding 5xFAD-line mice and M-line mice which express green fluorescent protein in neurons of various brain areas, including the hippocampus, which allows visualizing spine morphology without using of additional techniques [1].

The aim of this work is to assess age-related pathomorphological changes in dendritic spines of 5xFAD-M-line mice.

The dendritic spines density was 15% higher ($p = 0.0412$) in control M-line mice at the age of 4 and 5 months compare to 5xFAD-M-line mice. There were no statistically significant changes in the number of mushroom spines in 5xFAD-M-line mice compared to M-line mice ($p = 0.62247$) at 4

months. A significant decrease in the number of mushroom spines – by 21% compared to the control group ($p = 0.00767$) – was registered in 5xFAD-M-line mice by their 5^{th} month of age. Thus, 5xFAD-M-line mice demonstrate a rapidly developing synapse loss in hippocampal neurons starting 5 months of age.

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Influence of Probiotic Labs on the Biochemical Composition of Silage

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The increase in the pace of production and output of livestock products is inextricably linked with the improvement and development of new resource-saving technologies, including through the involvement of innovative solutions in the field of biochemistry and microbiology. A special place among them is the use of probiotic preparations in animal husbandry [1].

Scientific experimental experiments have been carried out to find out how endemic probiotic bacteria of the Artsakh Republic appear in the process of silosing, taking into account their characteristics.

It has been shown that in laborator conditions in process of enrichment of green grasses of various origins (silage) by endemic probiotic strains isolated from the milk of different domestic animals Enterococcus durans P13, Enterococcus durans KE5, Lactobacillus acidophilus 1991, Streptococus lactis, Streptococcus termophilus (synthesizing bacteriocins) and yeast strain of Kluveromyces marxsianus 83 (synthesizing mycocin) are increasing origin essential amino acids (in particular lysine and methionine), protein and a decrease in the content of spore microflora, mold, bacteria contaminating silage with respect to control. The quantitative yield of protein and amino acids depends on the source and nature of the raw materials used. After enriching with probiotic bacteria, the protein content increased in corn

silos 68,75%, mixed grass silos 62,9%, in esparcette silos 54% and essential amino acids by 30% relative to silos sample of grasses without the use of biological additives.

Based on the experience gained from the use of probiotics, we can confidently say that they have great potential for enhancing livestock productivity, which is primarily reflected in increased productivity of animals. Therefore, probiotics should be introduced as widely as possible, as they have a positive effect on the health of both animals and humans.

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Using of Lactic Acid Bacteria for Biopreservation of Dairy Products

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Raw milk is usually colonized by a variety of zoonotic pathogens such as Campylobacter jejuni, Escherichia coli, Listeria monocytogenes, Staphylococcus aureus and Yersinia enterocolitica and can lead to foodborne diseases though consumption of contaminated milk and dairy products (yogurt, cheese and curd) [1]. The broad antimicrobial spectrum of lactic acid bacteria (LAB) and their bacteriocins has stimulated their application in the food industry as natural preservatives [2].

The aim of presented study was screening of LAB with antimicrobial activity against food contaminating microflora and their application as a bioprotective cultures for biopreservation.

It was shown, that the use of antimicrobial preparations (AMP) at a concentration of 100 AU/ml inhibited the growth of food–spoilage microorganisms with different efficiency and it depends on the LAB strain, from which the AMP was obtained. Preliminary results, obtained after in vitro growth inhibition of various E. coli serotypes by LAB cultures, shown, that for biopreservation of milk products and prevention of E. coli contamination, preferable the using of L. helveticus KG5' and L. acidophilus 1991 LAB strains.

Thus it is obvious efficiency of using the LAB and their bacteriocins with a broad spectrum of bactericidal activity as an alternative to chemical agents in the dairy food industry.

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Effects of Fe_3O_4 Nanoparticles on Outbred Wistar Rats Liver Function

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Due to physical and biological properties, magnetic Fe_3O_4 NPs are widely studied for possible use in medicine for the diagnosis of a number of diseases. It is known that Fe_3O_4 NPs exhibit a dose-dependent effect and are able to accumulate in liver. Because of systemic nature effect it is unknown what outcome will be the long-term effect of Fe_3O_4 NPs on the body [1].

The aim of this work was the study of Fe_3O_4 NPs effect on the morphological and functional characteristics of outbred Wistar rats' liver. The synthesis of Fe_3O_4 NPs was carried out by the co-precipitation method, the size and shape were determined by TEM (TEM, LEO 912 AB omega, Carl Zeiss, Germany). Fe_3O_4NPs were injected i/p for 2 months. To screen the Fe_3O_4 NPs exposure, biochemical parameters of liver functioning in blood of experimental animals and histological analysis of the liver tissue were carried out. As were reported earlier [2], the synthesized spherical Fe_3O_4 NPs 12–18 nm in diameter, have hypolipemic properties, lead to an increase in albumin and total protein content, and a slight increase in AST and ALP activity. At the same time, ALT activity was within the normal range, which indicates the absence of strong hepatotoxic properties. Histological analysis revealed normal structure of hepatic tissue with mild dystrophic changes in individual hepatocytes (cytoplasm turbidity, optically distinguishable empty vacuoles). Studies of PO activity in rat liver homogenates under Fe_3O_4 NPs

influence revealed a twofold increase in the enzyme activity (15052 ± 364 πcat /mg protein) compared to the control.

According to the literature, Fe_3O_4 NPs of various shapes and dimensions exhibit peroxidase-like activity, which manifests itself in the ability to oxidize many specific substrates of this enzyme in H_2O_2 low concentrations presence. However, most of these works were carried out *in vitro* with a short duration of exposure. So, from the above, we can assert that paramagnetic Fe_3O_4 NPs don't exhibit a strong hepatotoxicity, have hypolipemic properties, and contribute to an increase in PO activity in the liver.

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SARS-Cov-2 Detection by Extraction-Free Qrt-PCR for Massive and Rapid COVID-19 Diagnosis During a Pandemic

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COVID-19 pandemic severely impacted the healthcare and economy on a global scale. It is widely recognized that mass testing is an efficient way to contain the infection spread as well as the development of informed policies for disease management. However, the current COVID-19 worldwide infection rates increased demand in the rapid and reliable screening of SARS-CoV-2 infection.

We compared the performance of qRT–PCR in direct heat-inactivated, heat-inactivated/pelleted samples against RNA in a group of 74 subjects (44 positive and 30 negative). In addition, we compared the sensitivity of heat-inactivated/pelleted in another group of 196 COVID-19 positive samples.

Our study suggests that swab sample heat-inactivation and pelleting show higher accuracy for SARS-CoV-2 detection PCR assay compared to heat-inactivation only (89% vs 83% of the detection in RNA). The accuracy of detection using direct samples varied depending on the sample transport and storage media as well as the concentration of viral particles.

Our study suggests that purified RNA provides more accurate results, however, direct qRT-PCR may help to significantly increase testing capacity. Switching to the direct sample testing is justified if the number of tests is doubled at least.

The Legacy: Notable Footprints in My Natural Products Research

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Relatively little is yet known about the molecular mechanisms that are responsible for the production of value-added secondary metabolites, mainly due to the complexity of plant metabolism. Insights into answers to these questions were partly provided by looking at several model systems. The model systems chosen, chemotypes, elite germplasms, and cell cultures go a long way to help solve such problems, especially since we intended to bring an understanding to the regulation of metabolic pathways at the gene, protein, and metabolite levels. These studies might shed light on regulation of metabolite biosynthesis and eventually lead to the derivation of transgenic plants with an improved productivity of the desired compounds.

Another important direction is unraveling bioactive properties of several natural products due to emerging interests in plant-derived drugs and nutraceuticals. Our long-term goal is to understand how phytochemicals may be directly involving in health protection by altering target genes transcription and translation, thereby improving resistance to oxidative and inflammatory stressors. It surely is linked to the activity of single and interacting compounds from plants, as related to their action at target sites. More in-depth studies are ongoing to understand the genetic, molecular and cellular mechanisms by which plant bioactive compounds can exert their protective capacity, focusing especially on the signal pathways of several transcription factors, antioxidant and anti-inflammatory enzymes.

The Development and Evaluation of Efficacy of Animal Derived Monovalent Antivenom Against *Macrovipera Lebetina Obtusa* (MLO) Venom

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The current work describes in detail the processing and development of animal-derived monovalent antivenom against *Macrovipera lebetina obtusa* venom according to several protocols. We demonstrated that this new antivenom is preclinically effective in neutralizing lethal toxicity and hemorrhagicity of venom of the Armenian Levantine viper – a significant problem for public health in Armenia and a wide region from south-east parts of Europe till south-west Asia. The developed product shows a high capacity to inhibit metalloproteinases and phospholipase activity of venom included in the study, and after some more experimental approvals, it will be possible to derive the antivenom satisfying international standards which will be much cheaper and accessible compared with Market rivals.

Aldo we'll discuss the benefits and drawbacks of ability to neutralize toxins of some species and subspecies of snakes of the genus Vipera, Montivipera and Macrovipera, by few available monovalent antisera, which has been raised against the venoms of *Vipera berus berus*, *Vipera ammodytes ammodytes*, *Macrovipera lebetina turanica* and *Macrovipera lebetina obtusa*. Taking into consideration different molecular formats each of these products has their own therapeutic characteristics as toxin-targeting antibodies, pharmacokinetic features, a propensity to cause adverse reactions, etc.

Artificial Intelligence for Pain Study

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Assessment of pain is necessary for the correct medical diagnosis of pathologies and their dynamics. Correct assessment can facilitate, cure, and sometimes even prevent the development of the disease. At the moment, there is no convenient and economical method for the objective registration of a pain syndrome capable of verifying, localizing and objectively measuring the magnitude of pain [1]. At the Peter the Great St. Petersburg Polytechnic University, a method for analyzing the attenuation of electrical oscillations caused by an exciting electric pulse in a pathological zone is proposed [2].

The proposed method is based on the hypothesis about the relationship of pain with a local change in physical characteristics of biological tissues. The purpose of this study was to select and justify a suitable method of processing the data obtained in the process of diagnosis and study of pain and implement a correct analysis of data obtained.

As a result of the study, it was concluded that the use of convolutional neural network and its training by “without teacher” method is preferable [3, 4]. A laboratory sample of a diagnostic apparatus for the objective pain registration with first iteration interface was assembled. Two types of data processing were implemented: image processing and pre-processed in EXCEL values of capacity attenuation coefficient. Primary measurements show that

processing of values is more accurate in this case, but needs more labor expenditures.

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Effect of Electromagnetic Radiation on Growth Properties of Green Microalga Parachlorella Kessleri

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Green microalgae are promising candidates for biotechnology due to their diversity, availability and ability to grow rapidly [1]. The effect of electromagnetic radiation (EMR) on microorganisms is at the spotlight of researchers nowadays, since organisms living in different ecological conditions are affected by different levels of EMR [2]. The effects of EMR depend on various conditions, such as radiation intensity and frequency, duration of irradiation, growth conditions, etc. [2, 3].

In the current work the effect of extremely high frequency (51.8 and 53.0 GHz) EMR on growth properties of green microalga *Parachlorella kessleri* RA-002 during anaerobic growth has been investigated. After irradiation of algae by EMR for 60 min, an increase in the growth rate of *P. kessleri* was observed in comparison with non-irradiated control cells. The effect of EMR depended on the irradiation frequency: 51.8 GHz led to a more pronounced increase in the growth rate in comparison with 53.0 GHz. To test the EMR action on the photosynthetic apparatus, the absorption spectra of *P. kessleri* cell extracts in ethanol were obtained, as well as the concentration of photosynthetic pigments (chlorophyll (Chl) *a* and *b*, and carotenoids) in extracts was determined. The data obtained show that the photosynthetic pigments content of *P. kessleri* is sensitive to EMR. After irradiation the total carotenoids content enhanced 2 and 1.76 fold for 51.8

and 53.0 GHz frequencies, respectively. Irradiation with a frequency of 51.8 GHz caused a considerable increase (1.5-1.7 fold) in the content of Chl *a* and Chl *b*, while at 53.0 GHz the concentration of chlorophylls was not significantly increased.

Thus, the extremely high frequency EMR stimulates the growth process of green algae. The results obtained can find an application in algae biotechnology to regulate the biomass production and photosynthetic pigments accumulation in green algae.

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The Quercetin and Quercetin Semisynthetic Derivatives as Potential Inhibitors aor Aminopeptidase-N and ABCG2

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Cancer is a global problem nowadays and natural compounds, their semisynthetic derivatives are actual for cancer treatment. In order to design an effective cancer treatment strategy, a lot of flavones and their derivatives are used as anticancer drug compounds. One of the most promising flavonols is quercetin which can inhibit the activity of the expression of metastatic proteins including matrix metalloproteases. One of these metalloproteinases is Aminopeptidase N which expression has been reported on fibroblasts, brain cells, as well as on epithelial liver, kidney, intestinal and breast cells. Quercetin can be correlated with its inhibitory effects on Multidrug resistance. Multidrug resistance is an acquired drug resistance by cancer cells that consists of simultaneous emergence of cellular resistance to the toxic action of chemotherapeutic drugs originally used and to other chemicals having different chemical structures and mechanisms of action. As a result of Multidrug resistance, chemotherapeutic agents fail to target the cancer cells and cancer becomes untreatable by chemotherapy. One of the responsible proteins is Breast Cancer Resistance Protein or ABCG2 is a member of the superfamily of ATP binding cassette proteins that have been found to confer Multidrug resistance in cancer cells by transporting mole-

cules with an amphiphilic character out of the cells using energy from ATP hydrolysis. Inhibiting can be a solution to overcome multidrug resistance. Nowadays in anticancer therapy semisynthetic compounds which based on natural active compounds are considered as potential inhibitors for APN and ABCG2.

Serum MBL-MASP Complexes in Acute Schizophrenia

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Schizophrenia is a severe and chronic mental disorder with ~1% prevalence worldwide. Growing evidence indicates that prenatal exposure to infection contributes to the schizophrenia. Adversity *in utero*, evolving on the background of immunegenetic aberrations, underlies the neurodevelopment disturbances preceding schizophrenia [1]. The lectin pathway (LP) of complement is the first line immune defense against infection. In complement activation via LP, mannan-binding lectin (MBL), collectin 11, or H-, L-, M-ficolins recognize microorganisms and activate their bound MBL-associated serine proteases (MASP) triggering the complement activation cascade [2]. LP initiating key enzymes, MASP-1 and MASP-2, are suggestively expressed in developing brain cortex and mediate neuronal migration [3]. At ICBH-2010, we have reported an overview of our previous study, which revealed MBL-MASP-1 and MBL-MASP-2 complexes over- activity in serum of schizophrenia patients (SP) in remission [4]. Thus, the aim of present study was the exploration of functional state of MBL-MASP complexes in serum of SP at acute manifestation stage of psychosis.

We investigated MBL levels (ELISA), the activities of MBL bound MASP-1 (enzymic assay) and MASP-2 (C4 fixation assay) in 103 chronic schizophrenic patients (SP) in the acute phase of the disease and 127 healthy

volunteers (HV). Schizophrenic inpatients were recruited from the Republican and the Nubarashen Mental Health Centres (the Health Ministry of Armenia, Yerevan, Armenia). Structured diagnostic interviews were conducted by psychiatrists of the Centre according to the Schedules for Clinical Assessment in Neuropsychiatry (Who, 1992), and the Composite International Diagnostic Interview (CIDI; Core version 2.1) (Who, 1997), to establish ICD-10 diagnoses. Clinical, demographic, family history and lifestyle information came from medical records and interviews with family members, caregivers and/or physicians. Blood samples and socio-demographic information of the HV were obtained from the Blood Service Unit of the "Erebouni" Medical Center, the Health Ministry of Armenia. The Shapiro-Wilk W test was applied to determine data distribution normality. Depending on data distribution, an appropriate parametric or nonparametric test was used for data comparative analyses.

A non-significant difference in MBL serum concentration was found in schizophrenic inpatients (median: 1.90 μg/ml; 95% CI 1.20-2.30) in comparison with HV of second set (median: 1.05 μg/ml; 95% CI 0.70-1.50; Mann-Whitney $P<0.129$). However, MBL-bound MASP-1 and MBL-bound MASP-2 activities showed a significant increase in patients. Particularly, the median of MBL-bound MASP-1 activity in SP (5.4 RFU; 95% CI 3.20-8.22) was ~37% higher than in HV group (4.09 RFU; 95% CI 2.47-4.86) (Mann-Whitney $P<0.019$). Similarly, SP group (0.63 RU/ml; 95% CI 0.44-0.83) had high median activity of MBL-bound MASP-2 in comparison with HV (0.30 RU/ml; 95% CI 0.23-0.41), but with more than 107% difference between groups (Mann-Whitney $P<0.034$). Notably, serum over-activity of MBL-MASPs complexes in patients retained the significance even after

normalization to MBL quantity (nMASP). Unlike schizophrenic out-patients in remission, schizophrenic inpatients at manifestation stage of the disease had higher median nMASP-1 activity than healthy volunteers (Mann-Whitney $P<0.021$). Besides, a relative increase in nMASP-2 activity was again confirmed in SP (Mann-Whitney $P<0.047$).

Depending on the stage of schizophrenia and the state of neuro-immune crosstalk, the serum MBL-MASP complexes undergo fluctuations in [MBL] and MBL bound MASP-1 activity, perhaps, also in stoichiometry of the complex. In comparison with norm, the MBL bound MASP-2 activity is the only parameter, holding its direction in schizophrenia-related alterations. The explanation for the aforementioned finding may be the fact that, unlike MBL and MASP-1 components, MASP-2 is not an acute phase protein. KRM acknowledge the Royal Society-NATO fellowship #16312/03B/LD.

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Influence of Royal Jelly on the Growth of Yeasts Candida guilliermondii Exposed to Electromagnetic Radiation

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Day by day, due to the use of radiation energy in many areas of our life, the risk of exposure to ionizing radiation and electromagnetic waves of extremely high frequency for living organism's increases. Living organisms have effective mechanisms to adapt to extreme situations, so they can survive and multiply successfully after exposure to radiation of different frequencies. Certain natural substances can affect the process of cell survival, and among these substances, royal jelly (RJ), which has been used since ancient times for human care and health, may be important [1]. RJ is rich in various biologically active compounds and has antioxidant and anti-inflammatory effects [2], so it might also have a radioprotective effect.

The aim of our work was to study the effects of X-rays, electromagnetic waves with a frequency of 51.8 GHz and 1 MHz on the kinetic parameters of growth and colony-forming ability of the yeast *Candida guilliermondii* NP-4 and their changes in the presence of RJ. *C. guilliermondii* is of interest for biotechnology and medicine and is a convenient model for studying higher eukaryotic organisms due to the similarity of the structure and functions of their genetic apparatus [3]. The data obtained showed that the lag-phase growth of irradiated yeasts was 2 h longer than that of non-

irradiated ones, for all frequencies of electromagnetic waves, and lasted 8 h. In irradiated yeasts, a decrease in the specific growth rate was observed in comparison with non-irradiated ones, and the ability to colony formation also decreased from 50 to 70%, depending on different types of radiation. Due to these changes in the growth parameters of irradiated yeasts, the amount of accumulated biomass in the stationary growth phase decreased by about 10% in the case of waves with a frequency of 51.8 GHz and 1 MHz and by about 25% – for X-ray irradiation. When yeast cells were incubated in a medium, contained 5% RJ, an increase in the biomass accumulation of both non-irradiated and irradiated yeasts was observed from 13% in the case of X-ray radiation to 40% – for waves with a frequency of 51.8 GHz and 1 MHz. The ability to form colonies also increased from 17% to 40% depending on the different types of radiation. It can be concluded that different types of irradiation have negative effects on yeasts, and the presence of RJ in the yeast growth medium stimulates the growth and colony formation of yeasts, so it possibly has a radioprotective effect.

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Comparative Analysis of Cholinesterase Activity of Brain in Fish of the Lake Sevan Bays in the Condition of Water Level Fluctuations

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The bays during the "blooming" event can serve as a model for as accurate as possible assessing of the effect of "blooming" on the food web of the lake ecosystem or its selected components. Moreover, this effect is manifested not only at the level of populations or species, but also at the level of changes in the biochemical and physiological characteristics of organisms. In this regard, measurements of the activity of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) were carried out, which are a widely used method for monitoring pollution, mainly due to their high sensitivity to anticholinergic chemicals such as organophosphate pesticides and carbamates [1]. BChE has the ability to stoichiometrically bind organophosphorus (OP) and carbamate compounds (Cs), which leads to irreversible inhibition of ChE activity, thereby causing disruption of the normal functioning of the organism, ultimately leading to its death. Moreover, there are data ChE activity inhibition with cyanotoxins. In this connection, decrease of cholinesterase activity in animal tissues is a specific and long-time biomarker of

their poisoning with these compounds and presence the last in environment [2]. The aim of this work was to study the BChE activity in the brain of fish from different bays of Lake Sevan before and after water "blooming". The study was carried out on whitefish (*Coregonus lavaretus L.*) mature of both sexes caught from the Lchashen and Lichk bays of Lake Sevan. The results show that the brain BChE activity and protein content in fish are correlated to each other and have similar circannual rhythms. Weak but significant negative correlation was found between BChE activity and fish size. In August, after the complete blooming, the enzyme activity decreased in both Lchashen and Lichk bays by 1.5 and 1.4 times, respectively, which may be due to both an increase in the level of OP or cyanotoxins and as a result of circannual rhythms. However, for a complete understanding of the reasons for the inhibition of the enzyme activity, further comprehensive study of the bays of Lake Sevan is necessary.

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Clinical and Diagnostic Aspects of COVID-19 Patients in Armenia

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In the era of COVID-19, the liberal use of antimicrobials adds an unnecessary risk for possible unfavorable outcomes due to their potential toxicity [1, 3, 4]. WHO discourages the use of antibiotics for mild cases, while recommends it for severe cases at increased risk of secondary bacterial infections and death [1, 5]. Procalcitonin (PCT) measurements can be important for reducing the use of antimicrobials [2].

We conducted an observational cohort study of comparable patients with moderate and severe COVID-19 disease admitted within ≥48 hours to Nork hospital (March-August, 2020). Three anti SARS-CoV-2 treatment regimens were assessed: 1) hydroxychloroquine or lopinavir+ritonavir in combination with azithromycin; 2) combination of 2 different antimicrobials and 3) minimal or no antibiotics with steroidal adjustments (dexamethasone or methylprednisolone).

All patients had a diagnosis of COVID-19 confirmed by (RT-PCR) of nasopharyngeal throat swab specimens, and uni or bilateral interstitial infiltrates in the chest X-ray. 67% (188) of cases were desaturated. 69% of patients had chronic diseases (hypertension, diabetes, hypothyreosis). Of 280 patients, antimicrobial therapy (AMT) was administered in 58% (162) of cases, 13% of them did not have pneumonia on admission, but it was devel-

oped in dynamics (4th-6th day). Side effects of antibiotics (dizziness, nausea, vomiting, and diarrhea) were reported in 15% (42). Laboratory examination results showed a high level of ferritin (>2000, N13-350), LDH (>1000, N 225-400), CRP (>100, N <5), PCT (>2, N0.05) and lymphopenia (< 0.5, N1-3*109/l) in worse cases. The level of PCT <0.3 was recorded in 83%. The mean duration of hospitalization in the 1st and 2nd cohorts was 29 days, meanwhile in the 3rd one it was reduced to 13 days.

AMT in the early stages of the disease distorts normal microbiota and makes the organism more susceptible to secondary infection, which results in poor outcomes and prolonged hospitalization.

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Antinociceptive Potential of Cobra Venom

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Pain is a very important signal when tissue is damaged, but the long experience of pain or its chronic manifestation acts counterproductively on the behavior and psychology of the patients [1]. For people experiencing severe pain, it is undesirable to medicate with narcotic analgesics as opioids and cannabinoids, known as substances which lead to addiction and undesirable side effects. Therefore, the revealing of strong analgesics that do not lead to addiction is a very relevant issue. Venoms are one of the resources for such substances [2].

The study aimed to compare the analgesic effect of different species of cobras on the nociceptive behavior of mice under the same experimental conditions to identify the venom with the highest analgesic potential. The analgesic effects of the same venoms after venom's phospholipase A_2 inactivation were also out under the examination. In this study, the Naja n. oxiana (NNO), Naja n. pallida (NNP), Naja n. nigricincta (NNN), Naja n. kaouthia (NNK), and Ophiophagus Hannah (OH) venoms were used. The result of the research should be a derivative of one of the tested venoms that has the maximum antinociceptive activity.

The antinociceptive effect of five different cobra genera was investigated using formalin-induced nociceptive action [3]. All tested venoms had a slight sensitizing effect in the first phase response following the formalin test. Venoms of NNP, OH, NNN, and NNO demonstrated significant

antinociceptive action ($p<0.01$) during the second phase to a different degree.

The best candidates for pain relief are the NNP and OH venoms, the weakening effect which was expressed more than 3 times. Venoms with inhibited enzyme activity PLA_2 during the development of the second phase of the formalin test, exhibit greater antinociceptive activity. Further research of these venoms and their components will provide an opportunity to find out the mechanism of their antinociceptive action and propose a candidate for the analgesic drug for the relief of chronic and neuropathic pain.

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Thermodynamic Analysis of Hoechst 33258 Interaction with Poly(Ra)-Poly(Ru)

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Thermodynamic analysis of Hoechst 33258 interaction with poly(rA)-poly(rU) at the ionic strengths of the solution 0.04, 0.02 and 0.1 M has been carried out. Values of both binding constant (K) and number of nucleotides (n) per binding site were determined from Scatchard's curves that were obtained based on spectroscopic and electrochemical measurements. Values of changes of enthalpy (ΔH), entropy (ΔS) and free energy (ΔG) were also determined at the complex-formation. It should be mentioned that the binding of Hoechst 33258 to nucleic acids is accompanied by positive change of enthalpy, meanwhile depending on the ionic strength of the solution, for DNA the values of ΔH change insignificantly, while for poly(rA)-poly(rU) this parameter is exposed to relevant alterations.

On the other hand, along with the ionic strength growth, the binding of H33258 to poly(rA)-poly(rU) becomes more and more beneficial from the entropic point of view as compared to DNA, while during DNA-ligand interactions the entropic losses increase. Possible mechanism is the flexibility increase, due to the screening of electrostatic repulsion, which in turn leads to strengthening of geometrical coincidence between ligand and binding center. At the same time, the growth of the entropic losses can be

connected to the originally higher flexibility of poly(rA)-poly(rU) that increases with the growth of the solution ionic strength.

Thus, the obtained data show that DNA B-form specific ligand H33258 can also bind to ds-polynucleotides, being in A-form. Moreover, both in the case of DNA and poly(rA)-poly(rU) the interaction occurs according to enthalpy-entropy complexation mechanism, when the enthalpy change is positive. This fact indicates that one of factors of H33258 specificity to ds-NA is a geometrical coincidence between ligand molecule and minor groove of nucleic acid, which changes depending both on the temperature and on the solution ionic strength.

Neuroprotective Effect of Microtubule Plus-End Tracking Protein EB3 in Alzheimer's Disease Models In Vitro

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Alzheimer`s disease (AD) is the most common incurable neurodegenerative disorder, which affects memory formation and storage processes. Tubulin cytoskeleton abnormalities in AD is one of the factors that initiate degenerative changes in neuronal dendritic spines and their subsequent loss. Recent advances in live cell imaging uncovered transient entry of dynamic microtubules (MTs) into dendritic spine, which triggers its enlargement and modulates synaptic plasticity [1]. Distal ends of growing microtubules are decorated by a specific group of microtubule plus-end-tracking proteins (+TIPs), which regulate their dynamics and interactions with other cellular components. +TIPs protein group contains End-binding protein 3 (EB3), which is a neuronal-specific member of EB protein family. Overexpression of the EB3 protein significantly increases and knockdown respectively decreases the number of stable synaptic contact formed by mushroom dendritic spines in primary wild-type hippocampal neurons. In addition, overexpression of the EB3 prevents the robust decrease in mushroom dendritic spines percent in primary neurons obtained from PS1-M146V-KI line AD

mice model [2] and in conditions of low amyloid toxicity. The interaction of the EB3 and PSD95, the most common protein that forms the postsynaptic density, affects the dynamics of microtubules and dendrite branching in neurons [3]. Overexpression of the EB3 protein causes an increase in the density of PSD-95 protein clusters without change in their size and prevents decrease in the density of PSD-95 clusters after addition of beta-amyloid in oligomeric form. EB3 protein is extremely important for the stabilization of postsynaptic contacts in normal conditions and its enhanced expression rescues degenerative changes in neurons in cellular AD models.

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Radioprotective Properties of Creatine

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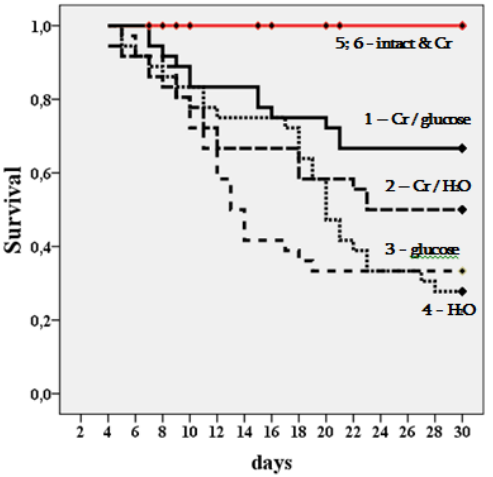
The study of the radioprotective properties of natural compounds becomes relevant due to some disadvantages of synthetic radioprotectors, such as high toxicity and limited duration of effect [1]. The aim of this work was to evaluate the radioprotective effect of creatine (Cr) as a dietary supplement using the Kaplan-Meier survival model after irradiation of rats at a dose of 6.5Gy=$LD_{70/30}$, as well as the effect of Cr on creatine-creatine kinase (Cr-CK) system, which is an indicator of the cell energy status.



Survival of irradiated rats receiving Cr.

The comparative analysis of the data obtained shows a 67% increase for the rats survival in the experimental group 1, compared to only 50% in group 2, which confirms the data on better Cr utilization by cells in the presence of carbohydrates [2]. The mortality of animals in the control group 3 is 72%, which exceeds that in the experimental group 1 (33%). The mean survival time for rats in experimental group 1 equals 24.4 and thus is higher than in group 2, which has received an aqueous solution of Cr-21.2 days. In the control groups receiving 0.9% glucose and water, mean survival time for rats was significantly less, 17.6 and 20.2 days respectively. The lifespan increases by 38.6% against the control group 3, as the diet becomes enriched with Cr/glucose. In addition, the dietary supplement Cr/glucose significantly stimulate the adaptive capabilities of the rats brain and liver Cr-CK system and increase the resistance and adaptability of the body to X-ray radiation.

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Investigation of the Linear And Nonlinear Optical Properties of Inas Cylindrical Quantum Dot With Different Confinement Potentials

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The theoretical investigation of linear and nonlinear optical properties, such as absorption coefficient (AC) and refractive index changes (RIC), of InAs cylindrical quantum dot with two models of confinement potentials in axial direction, namely, modified Pöschl-Teller [1] (MPTP) and Morse [2] (MP) potentials, and parabolic potential in radial direction, have been considered in the presence of external electric and magnetic fields [3, 4]. Selection of the first two potentials is based on the interest in the physical characteristics of the system in the axial direction, namely, selection of finite potentials like MPTP and MP gives one possibility to consider electron emission in the axial direction, while electron emission is impossible in the radial direction due to infinite nature of parabolic potential. An asymmetric potential like MP precisely models situations when the cylindrical QD is grown on a substrate. It is obvious that symmetric potential like MPTP can precisely model the situation when the cylindrical QD is placed in a semiconductor matrix and there is a possibility for electron quantum emission in both axial directions. The behavior of linear, nonlinear and total ACs have been observed for different values of temperatures for both potentials taking into account electron population on energy levels. The same dependencies have been obtained for RIC for both potentials.

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Optical Computing with Light Scattering

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Machine Learning and especially Deep Learning are gaining more and more popularity and importance nowadays. Deep Neural Networks are being used in many fields to solve various problems: object detection and recognition, image captioning, weather forecast, stock market prediction, natural language understanding, playing strategic games and many others [1]. However, the development and training of deep neural networks usually require lots of resources and time. Due to the limited computational resources, many restrictions rise regarding how huge data can be stored and how complicated mathematical operations are going to be performed. Therefore, many alternative approaches are being developed to optimize the complicated and time-consuming processes [2]. One of these approaches is the optical computing that uses the intrinsic parallelism of light diffraction through optical materials in order to mitigate the difficulties concerning the computation and memory [2, 3]. To this end, we modeled an optical architecture that can provide large, scalable and fast optical neural networks. The key elements in the optical scheme are the spatial light modulator that provides the input information encoding, the scattering medium that ensures the interconnection of input neurons and the camera that provides the nonlinear readout of the output.

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Biochemical Composition and Antioxidant Property of Some Bryophytes Common in Armenia

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Bryophytes, considered the first land plants, are a group of more than 24,000 species worldwide. They have been used since ancient times to treat diseases such as tuberculosis, pneumonia, burns, seizures, snake bites and others [1]. Interest in bryophytes is growing with the discovery of a large number of biologically active compounds, which, in addition to antibacterial action, have a positive effect in the treatment of tumors of various etiologies [2]. Some of these compounds are secondary metabolites and can be used in various fields of medicine, food and pharmaceutical industries [3–4]. The study of biologically active compounds (polysaccharides, amino acids), as well as antioxidant potential will expand the range of use of these plants as an affordable alternative to existing drugs.

The purpose of this study was to study the biochemical composition of the bryophytes Anomodontaceae spp., Anomodon viticulosus (Hedw), Mniaceae spp., Mnium spinosum (Voit) Schwaegr, Plagiomnium cuspidatum (Hedw) T. Kop, Dicranacese spp., Dicranum scoparium (Hedw), which are common in Armenia. The data obtained indicate the presence of glucose, fructose and sucrose in the studied mosses (glucose – 1.77 mg/g, fructose – 0.97 mg/g, sucrose – 9.50 mg/g). The study of the amino acid composition showed that the studied bryophytes have a rich amino acid composition,

among which essential amino acids predominate. The results of the study of the antioxidant activity of bryophytes showed that the ability of D. scoparium to trap 2,2-diphenyl-1-picrylhydrazilyl radical (inhibition 53%) was significantly higher than in other samples.

Based on these results and in addition to the data [1-4], it can be concluded that the studied bryophytes have valuable sugars and amino acids and it is assumed that the studied bryophytes especially D. scoparium are alternative available antioxidant agents.

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A Physical and Mathematical Method for the Study of Human Electroencephalograms

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Various methods of quantitative analysis have been developed for the study of electroencephalograms (EEG) using cross-correlation coefficients, coherence coefficients, the method of evoked potentials, and others. Different ways of studying the amplitude-frequency characteristics (AFC) are also used. Indeed, the amplitude and frequency are one of the most important physical indicators of the bioelectric signal of the brain. Moreover, energy spectral analysis [1] is one of the most successfully used methods for identifying biomarkers. And biomarkers are significant for the timely detection of various neuropsychiatric diseases and disorders.

We have developed a physical and mathematical model that adequately describes the amplitude-frequency characteristics of human electroencephalograms [2]. Three groups of people were selected: healthy people, patients with schizophrenia and people suffering from age-related vascular dementia. Quantitative parameters were obtained for each patients for each channel recording of the electroencephalogram, when approximating the proposed mathematical formula of the amplitude-frequency characteristics subject electroencephalograms. Comparing these coefficients, it was found that they differ among people from different groups. Therefore, the obtained quantita-

tive parameters can be used as biomarkers of various neuropsychiatric disorders. In other words, using the proposed mathematical model, it is possible to successfully differentiate the patients on diseases of various profiles.

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Genetic Liability of FOS rs7101 Variation for the Risk of Ischemic Stroke and Related Comorbidities stroke

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Ischemic stroke (IS) accounts >85% of stroke cases worldwide. It is a heterogeneous, multifactorial disorder with a complex etiology involving interactions between genetic and environmental factors [1]. One of genes, linking environmental stress to the risk for IS, is proto-oncogene *FOS. FOS* encodes a member of AP-1 transcription factor – c-Fos, which is involved in regulation of cell proliferation and apoptosis. Reportedly, *FOS* is unregulated in the peripheral blood mononuclear cells (PBMCs) of IS patients [2], and those cells mRNA expression correlates with the severity of atherosclerosis [3]. According to our preliminary findings, *FOS* rs7101 and rs1063169 variations might be associated with IS susceptibility [4]. Thus, the aim of the present study was confirmation of our preliminary findings and elucidation of a plausible molecular mechanism for IS-risk related genetic liability.

160 IS-cases and 225 unrelated controls of Armenian ancestry were enrolled in the study. Patients with acute IS admitted to hospital within a few hours of symptom onset were recruited from the Medical Clinic № 2 of the Yerevan State Medical University, «Surb Grigor Lusavorich» Medical Center and “Armenia” Republican Medical Center of the Ministry of Health of

the Republic of Armenia between September 2012 – November 2015. Diagnosis was made according to the ICD-10. The conscious state of patients was scored using the Glasgow Coma Scale. Arterial hypertension was defined based on high blood pressure (systolic/diastolic: >140/90mm Hg) lasting more than a week after stroke. Serum cholesterol level above 5.2 mmol/l was considered as a hypercholesterolemia. Concomitant heart diseases were either diagnosed after admission (e.g. coronary artery disease and atrial fibrillation) or based on self-reported history of myocardial infarction, coronary bypass surgery, or percutaneous coronary intervention. Atherosclerosis was defined based on the clinical history and laboratory tests. Infarct volume was determined by the brain computed tomography scanning and was expressed in ml. Outcome data were collected from clinical records and the hospital registries or from family members. SNP genotyping was performed in 160 IS-cases and 225 unrelated controls of Armenian ancestry using SSP-PCR. Genotypes Hardy-Weinberg equilibrium was checked using Fisher exact tested. For general statistics, logistic and linear regressions or ANOVA tests were used for comparison of frequencies and continues variables respectively. Kolmogorov-Smirnov test with Lilliefors correction was applied for inspection of normality of the data distribution. In case of non-normality, the specific distribution of the continuous variable of interest was determined via the distribution fitting procedures, using a Chi-square goodness of fit test. Statistics were performed using SPSS 17.0 (SPSS Inc, Chicago, IL, USA) and Statistica v.10 (Stat Soft Inc., Tulsa, OK USA) software programs.

We were not able to confirm association between *FOS* rs1063169 SNP and IS. However, the rs7101*T-allele ($P<0.0071$) retained its significant

association with IS susceptibility in additive mode, despite conditioning for sex of individuals (P<0.043). Hence, in a dose-dependent manner, the genotypes carrying T-allele significantly increased IS-risk compare to rs7101*C/C genotype (P<0.02), and the odds ratio reached to a significance at homozygote state (for C/T: OR(95% CI) = 1.48(0.91-2.42), P<0.11; and for T/T: OR(95% CI) = 2.24 (1.27-3.95), P<0.005). Remarkably, for rs7101*T bearing genotypes this dose-dependency was also observed in association with a number of IS comorbidities: i.e. arterial hypertension (general P<0.008: C/T, P<0.77; T/T, P<0.010), coronary arterial disease (CAD, general P<0.018: C/T, P<0.43; T/T, P<0.011), atherosclerosis (general P<0.051: C/T, OR= 4.16, P<0.036; T/T, OR= 4.42, P<0.050). Remarkably, we also observe a significant association of patient's rs7101 genotypes with atrial fibrillation (P<0.027), but this association tended rather be in a codominant model (C/C vs. T/T: OR=0.54, P<0.23; C/T vs. T/T: OR=0.31, P<0.008). There was no association between the genotypes and either hyperlipidemia, or smoking and alcohol use. In a general linear model controlling for sex, patients hetero- and homozygote for rs7101*T allele, on average, had early onset of IS stroke (P<0.015). Mimicking IS genetic association, per T-allele, stroke onset occurred ~5 years early. On the other hand, according to the Kaplan-Meier analysis, there was a drastic decline in survival after the IS for cases with T/T genotype (Cox F-test P<0.05).

Based on our findings, we hypothesized that the biological mechanism for the contribution of *FOS* rs7101*T carrying genotypes to IS-risk and age at stroke onset, largely, underlies via their association with atherosclerosis. This hypothesis is in accordance with recent report that rs7101*T allele, in additive mode, is also responsible for an increasing production of c-Fos in

serum [5]. Lastly, rs7101*T/T genotype liability for a poor outcome after stroke is rather relate to its association to atrial fibrillation comorbidity.

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Comparative Investigation of Silver Nanoparticles Action on Growth Peculiarities and Survival of Various Bacteria

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Staphylococcus, Salmonella and *Enterococcus* species are the common human pathogens causing to various types of diseases [1, 2]. The development of antibacterial resistance of pathogens is the significant problem of the 21th century medicine, which requires a finding of new approaches. Nanoparticles (NPs), in particular silver NPs, are the great alternative to antibiotics, since they have a potential to solve the problem of antibiotic resistance [2,3]. In this work the effects of colloidal silver NPs ("Silverton", "Tonus-Less", Armenia) on the growth properties and survival of Gram-positive bacteria Staphylococcus aureus MDC 5233 and Enterococcus hirae ATCC 9790, and Gram-negative bacteria Salmonella typhimurium MDC 1759 strains have been investigated. The data obtained show antibacterial effect of silver NPs, which depends on the concentration of NPs and species of bacteria. Silver NPs demonstrate more pronounced action on Gram-positive bacteria S. aureus and E. hirae, in comparison with Gram-negative S. typhimurium. The 30 μg/mL silver NPs led to ~7–7.6 fold suppression of growth of S. aureus MDC 5233 and E. hirae ATCC 9790, whereas growth rate of S. typhimurium MDC 1759 was decreased 4 fold. Moreover, silver NPs inhibited ~60, 71, and 76% of colony forming units of S. typhimurium

MDC 1759, S. aureus MDC 5233 and E. hirae ATCC 9790, respectively, indicating the bactericidal effect of these NPs. In order to reveal the mechanism of NPs' action, the protons flux through the bacterial membrane has been determined. The addition of NPs led to change of the energy-dependent proton flux through F_OF_1-ATPase, indicated the significant effect of silver NPs on the permeability of bacterial membrane. Thus, silver NPs demonstrate a pronounced antimicrobial effect against the investigated bacteria and can be applied in medicine for treatment of various diseases.

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Prospective Trends in Biotechnology for Biohydrogen

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The development of clean biofuel, including biohydrogen by microbes, is of significance. This is prospective goal to establish a low-carbon economy and flexible and adaptive power systems [1]. There is an argument in favor of biohydrogen from carbon-containing by-products and organic wastes. There are several methods for production of biohydrogen [1]. One method is the production of H_2 by bacteria performing dark – mixed acids (Escherichia coli, Clostridium bejerinckii) and light- fermentations (Rhodobacter sphaeroides). These bacteria use hydrogenases and other enzymes for H_2 metabolism; their mechanisms of action are allowing repeated use of fermentation revisited [2]. H_2 can also be produced through biophotolysis of water by microalgae (Parachlorella kessleri) as biocatalysts [3]. These pathways are intensively studied, and biotechnology for biohydrogen from by-products and organic wastes is developed. It can be further developed in the several trends: construction or selection of appropriate effective bacterial strains (mutants) and pure cultures; creation of mixed cultures of dark- and light fermentation for one step and multi-step technology; application of different carbon sources (sugars as hexoses and pentoses, alcohols as ethanol and glycerol, and organic acids as formic, succinic and lactic acids) and their mixtures for co-fermentation; control of external technology factors (dark and light, pH, redox potential, substrate con-

centration, protonophores), application of electromagnetic irradiation, addition of different compounds and their mixtures, especially some heavy metals (Ni, Fe, Mo, Mg, Cu, etc). The most effective trend is utilization of organic lignocellulose wastes (distillers' grains, brewery, office paper and roasted coffee wastes) [4–5] with their pretreatment to improve of biohydrogen in low-cost manner.

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Escherichia coli Hydrogenases Contribution to Proton Motive Force Generation; Can Hydrogenases Be Considered as Proton Sensors?

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During fermentation proton ATPase hydrolyzes ATP, coupling proton transport to proton motive force (Δp) generation. Δp generated by ATP hydrolysis does not satisfy the energy budget of a fermenting cell. However, Δp can also be generated by transport of weak organic acids such as lactate or succinate and by hydrogen-cycling catalyzed by hydrogenases.

E. coli encodes four membrane bound reversible hydrogenases (Hyd) [1]. Hyd-1 and Hyd-2 are working towards H_2 oxidation when glucose is fermented while they are responsible for H_2 production during fermentation of glycerol. Besides, it depends on external pH.

It was shown that during glucose fermentation at pH 7.5 E. coli generate Δp of -120 mV which is ~ 40 mV lower compared to respiratory conditions. During glycerol fermentation Δp of -99 mV is generated which is lower compared to glucose fermentation. The deletion of all four Hyd enzymes increases the Δp to ~ 120 mV during glycerol fermentation. Interestingly, absence of four Hyd enzymes affect both components of Δp: increase of membrane potential ~ 25 mV and ΔpH equals to 0.5. While during glucose

fermentation ΔpH equals to 0. Moreover, deletion of Hyd enzymes affects proton ATPase activity and proton flux during glucose or glycerol fermentation.

Taken together it is suggested that E. coli Hyd enzymes form big "Hydrogenase complex" which act as proton sensors "protonometers" for regulating and maintaining Δp. Furthermore, several questions are raised for future studies:

1. What are the molecular mechanisms that force FoF_1 in fermenting cells to interact with other membrane bound secondary transporters? Is there direct physical interaction or this interaction is based solely on energy conservation?

2. What is the physiological role of hydrogenase enzymes? Can hydrogenases mimic the respiratory complexes?

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Anaerobic Utilization of Spent Coffee Grounds (SCG) by E. Coli: the Importance of Pretreatment to Optimize Hydrogen and Biomass Generation

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Currently ecologically clean and renewable energy sources come forward to replace fossil fuels and extensive studies are implemented to find the most effective one. Hydrogen (H_2) is a promising, non-toxic fuel with high energy content and conversion efficiency, besides generation of H_2 by biological ways from organic wastes provide many advantages and can lead to cost-effectivity [1].

Coffee is one of the most consumed beverage and traded commodity worldwide, about 3.5 billion cups of coffee consumed daily [2]. Present study aimed to clarify possible usage of SCG, huge amount of which generated after coffee brewing every day. SCG as organic waste rich in carbohydrates have been applied to acidic hydrolysis. 1-10% SCG were treated with 0.4-1.5% sulfuric acid (H_2SO_4), for 20- and 45-minutes hydrolysis under 1 atmosphere pressure conditions. After hydrolysate pH was adjusted to pH 7.0 by alkali (KOH) and potassium salt (K_2HPO_4). Lastly, mediums were diluted twice and autoclaved.

It is shown that in the assays when pH was adjusted with KOH conditions were not favorable and H_2 production lasted maximum 24 hours, because during bacterial growth medium pH values dropped by 1.1–1.5 units, thus inhibiting hydrogenase activity, meanwhile K_2HPO_4 kept pH in a relatively stable ranges and thus prolonged H_2 production from 24 hours to 48 hours.

During bacterial growth *E. coli* wild type specific growth rate was 0.72 ± 0.01 h^{-1} when 4% SCG were treated with 0.4% sulfuric acid for 45min, and 2.25-fold lower when the same amount was treated with 0.75% sulfuric acid for 20min. Interestingly, high concentrations of SCG inhibit bacterial growth as specific growth rate was approximately absent when 6% SCG were treated.

To conclude we can state that *E. coli* can utilize SCG as a cheap and perspective substrate, furthermore selection of appropriate pretreatment technologies may lead to optimal bacterial growth and have a significant role in optimization of H_2 production.

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Interaction of Double Stranded Nucleic Acids with Different Ligands

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The interaction of intercalators such as the phenothiazinium dye methylene blue (MB), the phenantridinium dye ethidium bromide (EtBr) and the acridinium dye acridine orange (AO) with double stranded (ds-) DNA and RNA has been studied using the methods of absorption and fluorescence spectroscopies. This indicates that the binding modes of these ligands to ds-DNA and ds-RNA are similar. The results show that these ligands bind to double-stranded polynucleotide by both strong and weak modes. It was shown that the strong binding mode or MB occurs via semi-intercalation, AO – via intercalation and EtBr via both intercalation and semi-intercalation [1]. In addition to the strong binding mode, these ligands bind to DNA by weaker – electrostatic modes. It is also concluded from the obtained data that EtBr binds to ds-RNA by several modes as with ds-DNA. Moreover, in the intercalation binding mode a certain selectivity of EtBr to B and A forms of nucleic acids is observed, since for ds-poly(dA)-poly(dT) (B form) the interaction is cooperative, while in the case of ds-RNA (A form) the cooperativity is absent. These data indicate that the basic modes of binding of the intercalators depend mainly on whether the NA is single- or double-stranded. The values of the binding constant K and number of bases n per

binding site were calculated for these ligands binding to ds-RNA by the mentioned modes.

The interaction data between ds-RNA and the intercalators MB, AO and EtBr, differing from each other chemically and having various binding properties, are analogous to those obtained for the interaction of these ligands with ds-DNA. It indicates that the binding modes of these ligands to ds-DNA and ds-RNA are similar.

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Study of the Human Serum Albumin Interaction with Some Ligands

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It is known that proteins are the first targets in organisms for numerous high- and low-molecular compounds that enter inside a cell. Among such a huge number of binding compounds, drug preparations are of special interest, taking the fact into account that each drug gains to the destination cell being transported by proteins, including serum albumins. Besides, the binding of drugs to proteins relevantly affects the properties of the drug, beginning from adsorption up to metabolic and excretion properties. That is why the studies devoted to the interaction peculiarities of various low-molecular compounds – potential drugs to serum albumins are of great interest [1, 2].

The binding peculiarities of methylene blue (MB), methyl violet (MV), and Hoechst 33258 (H33258) with human serum albumin (HSA) has been studied, using the fluorescence spectroscopy and thermal denaturation methods. Based on the fluorescence spectra analysis it was shown that HSA binds to the all mentioned ligands and forms complexes, meanwhile a quenching of the ligand fluorescence occurs, which was found out to be a static quenching type. On the other hand, the denaturation data reveal that H33258 and MB stabilize the structure of HSA.

It was shown that human serum albumin binds to MB, MV, and H33258 and forms complexes, which is revealed by the static quenching of the fluo-

rescence intensities of MB, MV, and H33258 by HSA. It should be also mentioned that in the case of MB binding to HSA, at relatively high concentrations of HSA, the quenching occurs via both static and dynamic modes.

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Optogenetic Studies of Nervous System Function

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Molecular mechanisms of neurodegenerative diseases Alzheimer's disease (AD), Huntington's disease (HD), spinocerebellar ataxia type 2 (SCA2) associated with impaired calcium metabolism in neurons are studied in the laboratory of Molecular Neurodegeneration using cellular, molecular and biophysical methods and transgenic mice models. Studies using confocal microscopy showed changes in the morphology of neurons with impaired calcium signaling [1,2]. However, neurodegenerative abnormalities can be accompanied not only by changes in the morphology of neurons, but also by changes in their electrical activity and weakening of synaptic contacts. Optogenetics is a recently developed techniques that allows precise manipulation of neuronal function [3]. Optogenetics approach is based on the genetic expression of light-sensitive ion channels or light-sensitive signaling receptors in the plasma membrane that enables control of cellular activity with light stimulation.

The laboratory evaluated the possibilities of using optogenetics to compare the electrophysiological activity of hippocampal neurons in normal and AD mouse models [4], as well as to compare the strength of synaptic connections between cortical and striatum neurons in normal and HD mouse models [5]. The parameters of the light current caused by light excitation of

opsin (ChR2) expressed in hippocampal neurons from irradiation modes were quantified [6]. Current studies are focused on using optogenetic approaches to control activity of hippocampal astroglia and analysis of resulting effects on neuronal function.

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Bacterial Synthesis of Nanoparticles: Theory and Practice

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Following topics will be addressed in the present report: analysis of studies on the production and properties of metal nanoparticles and their sulfides by the "green synthesis" method in aqueous media with biological components – microorganisms, algae, fungi, yeast, plant extracts [1]. Biosynthesis of nanoparticles as an alternative and addition to physicochemical methods for obtaining nanomaterials; environmental safety, low cost, the possibility of obtaining nanostructures of various shapes with a narrow size distribution. Mechanisms of nanoparticle formation by the example of two main schemes: biosynthesis of metal nanoparticles due to the reduction of metal ions by reductases of biological substances and the formation of metal sulfides as a result of chemical reactions, followed by adsorption on the surface of all types of particles of protein molecules and other biopolymers, which stabilize nanoparticles in an aqueous medium and prevent agglomeration. The influence of various types of bacteria on the composition of proteins that coat nanoparticles; analysis of the protein coating with the identification of individual protein molecules [2]. Characterization of biogenic metal sulfide nanoparticles as semiconductor materials with quantum dot

properties; stability, level of fluorescence, ζ-potential, hydrodynamic diameter of nanoparticles [3]. The use of biogenic nanoparticles to create nanocomposite materials, photocatalysts, fluorophores, as antibacterial agents of a new generation, for biomedical applications.

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Biomedical Sensor with Analog Amplifier and Investigation Programs

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Nowadays, diagnostic devices propose to use advance methods for investigative and diagnosis purposes. The temperature which is going through the bio tissue is a fundamental informatory for the state of internal pathological process. So this temperature gives many information about patients.

Besides of temperature, we use different types of bio currents (i.e. sinusoidal, rectangular, and triangular). A developed device is in the prototyping stage and used only bio currents in audio range. This make the device very simple as we connect it to the Personnel Computer's or Notebook's audio port for generating audio signals and storing the investigation data and don't worry about storage (**Ошибка! Источник ссылки не найден.** A). Then we can compare it using graphical language tool (we use LabVIEW) (**Ошибка! Источник ссылки не найден.** B) [**Ошибка! Источник ссылки не найден.**, **Ошибка! Источник ссылки не найден.**]. We also developed special sensor which is combining electrical and thermal influences (**Ошибка! Источник ссылки не найден.** C) [**Ошибка! Источник ссылки не найден.**, **Ошибка! Источник ссылки не найден.**].

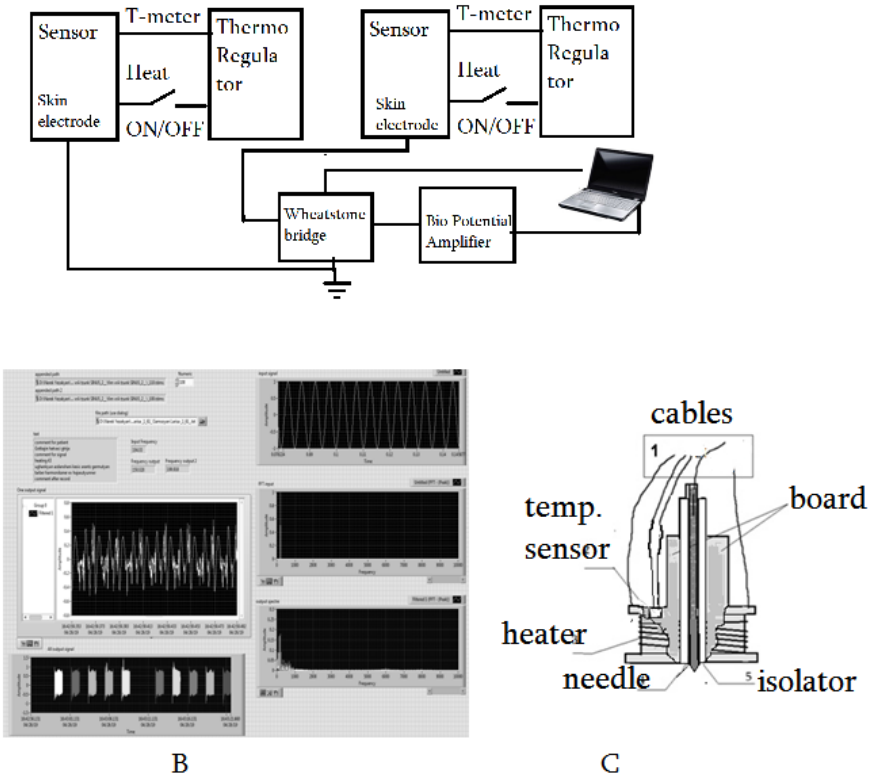

Figure 1. The developed device, sensor and program.

After development we have done some clinical and laboratory experiments. Thermal influence also makes the generated signal nonlinear, the specialist or doctor see the biological facts that change the signal and make diagnosis how to cure the patient and takes further experiments while the patient gets treatment.

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