LABORATORY OF RADIATION BIOLOGY

In 2012, the Laboratory of Radiation Biology (LRB) continued research in the framework of Topic 04-9-1077-2009/2014 «Research on the Biological Effect of Heavy Charged Particles with Different Energies» in the following fields: fundamental radiobiological and radiation genetics research with heavy charged particles; research on the effect of accelerated charged particles on eye structures; molecular dynamics research; mathematical modeling of radiation-induced effects; radiation research and radiation protection of JINR's basic facilities and the environment.

RADIATION GENETICS AND RADIOBIOLOGY

The effect was studied of DNA repair and replicative synthesis inhibitors cytosine arabinoside (AraC) and hydroxyurea (HU) on the induction of the apoptotic death of human peripheral blood lymphocytes by accelerated ^{18}O ions with a linear energy transfer (LET) of 130 keV/μm. It is known that the action of DNA repair and replicative synthesis inhibitors is related to disorder in the functioning of the DNA single-strand break (SSB) repair systems, which ultimately leads to the formation of enzymatic DNA double-strand breaks (DNA DSBs). It was shown that under exposure to accelerated ^{18}O ions under normal conditions, the apoptosis induction level reaches the maximum 48 hours after irradiation. Unlike the case with gamma rays (Fig. 1, *a*), no increase in apoptotic cell yield is observed for irradiation with accelerated ^{18}O ions in the presence of radiomodifying agents (Fig. 1, *b*).

The absence of the modifying effect of AraC and HU on apoptotic cell yield under irradiation with accelerated ^{18}O ions can be explained as follows. The high-LET charged particles induce mainly direct DNA DSBs; SSB yield decreases, which results in a sharp decrease in the enzymatic DNA DSB component [1].

In cooperation with institutes of the Czech Republic, research was started on DNA DSB induction and repair

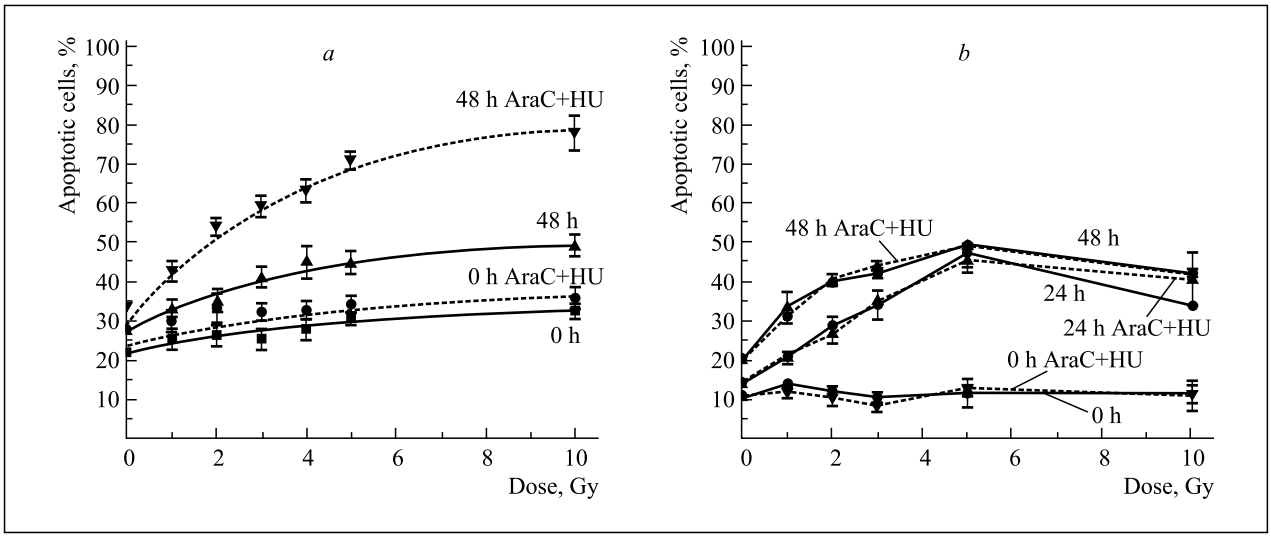

Fig. 1. Apoptotic death induction by ^{60}Co gamma rays (*a*) and accelerated ^{18}O ions (*b*) in the presence of AraC and HU

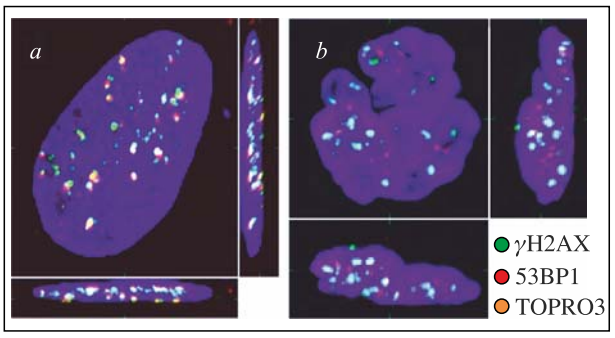

Fig. 2. DNA DSB induction (formation of γH2AX foci) in cells irradiated with 1.5 Gy of ^{60}Co gamma rays: human skin fibroblasts; immature granulocytes/monocytes. The images are made up of 40 confocal optical sections with a step of 0.3 μm along the z axis and are shown in all three planes ($x-y$, $x-z$, and $y-z$). The co-localization of the γH2AX foci with the 53BPI protein is observed in fibroblasts (*a*) and is absent in immature granulocytes/monocytes (*b*)

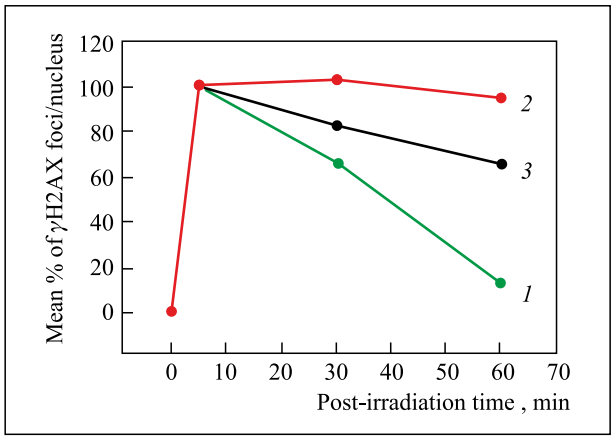

Fig. 3. DNA DSB (γH2AX foci) repair kinetics in human skin fibroblasts and in immature granulocytes/monocytes irradiated with 1.5 Gy of ^{60}Co gamma rays and exposed to 1.5% H_2O_2 (curves *1*, *2*, and *3*, respectively)

in human cells under ionizing radiations of different quality. To analyze DNA DSBs induced in skin fibroblasts, lymphocytes, and granulocytes of human peripheral blood, the DNA foci method was used, which is based on detecting specific proteins participating in the initial stages of DNA repair. Immunocytochemical staining with antibodies conjugated with fluorescent dyes and specific for individual proteins allows detection of these structures as bright fluorescent microregions: repair foci. DNA focus identification allows obtaining information on the localization of the DSBs in the nucleus, their number and repair efficiency and kinetics, participation of specific proteins in repair, as well as figuring out the main repair pathway (nonhomologous end joining or homologous recombination). With the use of high-resolution fluorescent microscopy techniques, a quantitative evaluation was performed of the activation of the co-localized proteins γH2AX and 53BP1 (Fig. 2), and their distribution was studied in cell nuclei for irradiation with 1.5 Gy of ^{60}Co gamma rays.

It was shown that DNA DSBs are efficiently repaired in lymphocytes, but both repair pathways (nonhomologous end joining and homologous recombination) are inactive in immature granulocytes (Fig. 3) [2].

The yield of primary radiation-induced DNA breaks in cal51 cells of human breast carcinoma was studied using the premature chromatin condensation (PCC) technique. To study the repair rate, calyculin was introduced at different times after irradiation. Cells were irradiated at the U400M cyclotron with ^{18}O ions with a LET of ~130 keV/μm and at the Rocus facility with ^{60}Co gamma rays. As is seen from Fig. 4, the number of the primary chromatin breaks per cell induced by accelerated ^{18}O ions is twice higher than in the case of gamma rays, which fully reflects the specifics of the action of heavy charged particles. Not only does the high density of ionization events in heavy ion tracks increase the quantitative yield of primary DNA damage, but it also results in damage clustering. It is known that the repair of such lesions is extremely hindered; for this

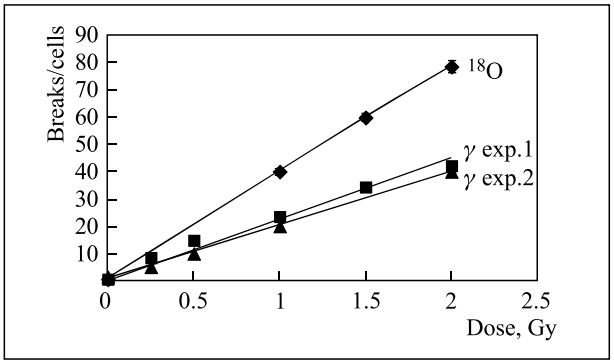

Fig. 4. Dose dependence of primary chromatin break yield in cal51 cells irradiated with ^{60}Co gamma rays (two independent experiments) and ^{18}O ions

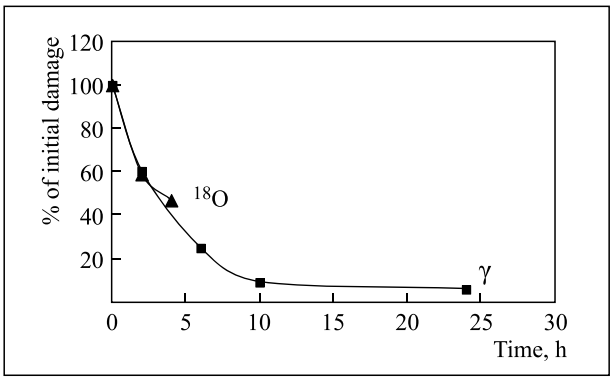

Fig. 5. Primary chromatin break elimination kinetics in cal51 cells irradiated with 2 Gy of ^{60}Co gamma rays

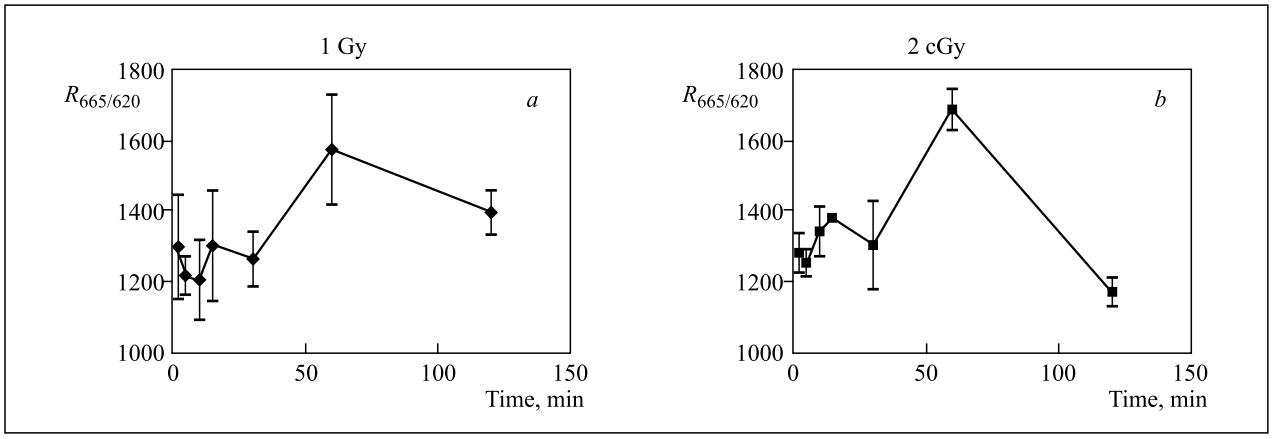

Fig. 6. Time dependence of ERK protein kinase activation in cal51 cells irradiated with 1 Gy (*a*) and 2 cGy (*b*) of gamma rays. The 665/620 ratio on the ordinate axis is the ratio of emission intensities at 665 and 620 nm

reason, the kinetics of primary chromatin break repair was studied in cells irradiated with gamma rays and accelerated ^{18}O ions. It was found that under gamma rays about 90% of the primary lesions are successfully repaired in 10 hours (Fig. 5). No difference was found in the rate of quick repair (up to two hours), which, as is known, removes easily repaired damage. However, four hours later, a decrease is observed in the rate of the elimination of the breaks induced by accelerated ^{18}O ions. It can be suggested that for densely ionizing radiations, the unrepaired damage level will be much higher than for sparsely ionizing gamma rays. To clarify it, experiments are planned in which the time interval will be significantly extended.

With the homogeneous time-resolved fluorescence technology, which allows fluorescent antibody-based measurement of the activation of different proteins, the level of the activated protein kinase ERK was measured with a BioTek microplate reader in cal51 cells at different times after their gamma irradiation at 2 cGy and 1 Gy. Under different types of stress, the protein kinase ERK can perform both the proapoptotic and cytoprotective functions in cells. It has not yet been established how is determined the way ERK would function. In particular, it is known that when central nervous system structures are damaged, the activation of this protein results in the apoptotic death of neurons. However, in the survived nervous cells, it plays the key role in the brain's neuroplasticity and the long-time memory consolidation processes. The experimental results show that gamma irradiation leads to the activation of the ERK protein kinase. The activation maximum was observed one hour after irradiation (Fig. 6). It is interesting that low and high doses caused effects of comparable magnitudes, but the kinetics character greatly differed: for the dose of 2 cGy, short-term early activation took place besides long-time activation at later times. This two-phase character of ERK activation under different stress factors was observed earlier by other authors. Based on these results, it was supposed that quick short-term ERK protein kinase activation performs a protective function in the cell, while long-term activation of this protein, which takes place later, leads to cell death. To study ERK's role in neurophysiological processes, it is planned to conduct research on neural-like PC12 cells of pheochromocytoma and primary cultures of nervous cells.

Nonstandard types of the growth of mutant subclones isolated from Chinese hamster cells were found. The cells were irradiated with 0.5, 1, and 2 Gy of acce-

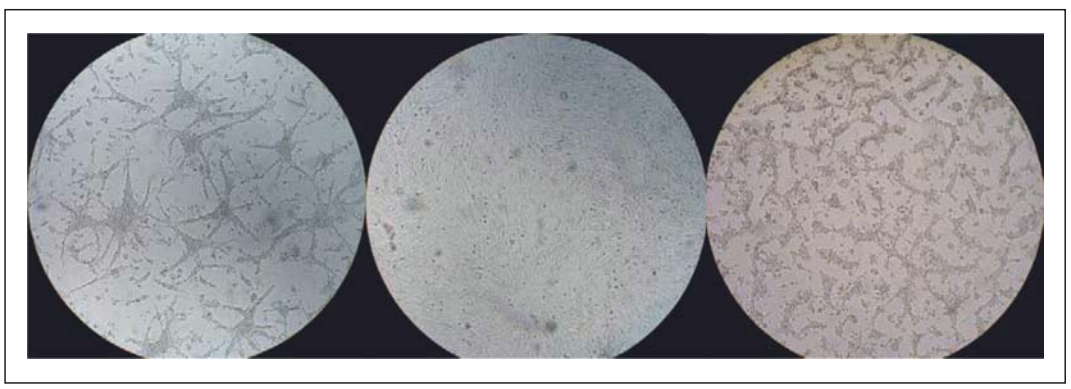

Fig. 7. Nonstandard types of mutant subclone growth

Irraditation influence on hematopoiesis and immunity ($M \pm m$) in CD-1 mice 24 hours after Bragg peak

Group	Number of mice (n)	Body mass, g	Thymus mass		Spleen mass		Bone marrow cellularity, $n \cdot 10^6$ nucleus-containing cells per thigh		Number of leukocytes in peripheral blood, $n \cdot 10^9$/l
			Absolute mass, mg	Index, %	Absolute mass, mg	Index, %	Absolute mass, mg	Per 1 g of the body mass	
γ	6	30.1±0.8	25.0±2.7	0.08±0.01	48.6±4.1	0.16±0.01	32.6±2.9	1.08±0.10	1.87±0.36
171 MeV protons	6	28.5±2.5	44.5±9.6	0.15±0.03	64.6±12.9	0.22±0.03	20±4.3 *	0.69±0.10 *	1.78±0.7
Bragg peak protons	6	27.8±2.0	40.6±13.4	0.14±0.05	55.8±7.2	0.20±0.03	14.7±0.2 *	0.53±0.09 *	1.04±0.25
Unirradiated control	12	29.4±1.0	52.9±10.4	0.18±0.04	103.5±10.2	0.35±0.03	63.4±4.2	2.15±0.12	4.47±1.75

* Statistically significant difference from the γ group by Student's test, $t = 5.7-12.6$; $P < 0.01$.

lerated ^{18}O ions with a LET of $\sim$ 130 keV/μm. Under the same growth conditions, some mutants show unusual morphological signs compared with the control cell population: a chain and stellar characters of growth (Fig. 7) [3]. Also, the emergence of colonies was observed before the formation of a dense monolayer of mutant subclone cells. These signs may indicate the initiation of the malignant transformation of cells.

In experiments on yeast cells, a cycle of studies on genetic stability control was performed. It was found that CDK1/CDC28 — the central protein kinase of the cell cycle — participates in chromosome and mitochondrial DNA stability control and in the checkpoints controlling genetic material inheritance. It was shown that the cdc28-srm mutation affects the G1 checkpoint, but not the S and G2 checkpoints, which control genetic material inheritance [4].

In cooperation with JINR's Medical Technical Complex staff, technical conditions were provided at the Phasotron to study the effect of the whole-body irradiation of experimental animals (mice) with Bragg peak protons. Photorecording of proton beam transmission through the animal's body was made. A pilot project was realized on studying the effect of extended Bragg peak protons on hematopoiesis in mice 24 hours after irradiation at 5 Gy. Separate groups of mice were irradiated with 5 Gy of ^{60}Co gamma rays at the Rocus-M facility and 5 Gy of 171 MeV protons. The experiment was conducted on four CD01 mouse groups. 24 hours after irradiation, a pronounced hematopoiesis disorder was observed.

In particular, the number of nucleus-containing cells per thigh was $63.4 \cdot 10^6$ in the control group, $32.6 \cdot 10^6$ in the gamma-irradiated group, $20 \cdot 10^6$ in the group irradiated with 171 MeV protons, and $14.7 \cdot 10^6$ in the group irradiated with Bragg peak protons. The number of peripheral blood leukocytes was, respectively, $4.47 \cdot 10^9$, $1.87 \cdot 10^9$, $1.78 \cdot 10^9$, and $1.04 \cdot 10^9$/l. These data show that Bragg peak protons have a more damaging effect on hematopoiesis than protons entering the object and ^{60}Co gamma rays (Table).

PHOTORADIOBIOLOGICAL RESEARCH

A model was proposed of the chaperone-like functioning of lens α-crystallin. It is suggested that the damaged protein forms a temporary complex with α-crystallin, which breaks up into α-crystallin of a smaller size. The condition when the damaged protein (βL-crystallin) does not aggregate is determined by the low-molecular complex and the damaged protein, in which conformational restructuring takes place under exposure to its polar surrounding, and the aggregation sites are hidden in the molecule. The proposed scheme fits better into the pathogenetic process chain leading to cataract development [5].

The effect of genotoxic factors (methylnitrosourea (MNU) and ionizing radiation) on the mouse retina was

studied. It was found that up to 15 Gy of gamma or accelerated proton irradiation causes neither structural nor functional changes in the retina. An MNU dose of 70 mg/kg leads to the irreversible loss of retinal activity and photoreceptors' morphological degeneration. An MNU dose of 35 mg/kg has no cytotoxic effect: a reversible decrease in electroretinogram indicators is observed. It was established that there is an adaptive response of the retina's physiological activity to genotoxic agent introduction: after two consecutive exposures to MNU doses of 17 and 70 mg/kg, the mouse electroretinograms recovered in six hours. These results point to the effect of retinohormesis, which is similar to neurohormesis. The latter is observed for exposure to ionizing radiation and some chemicals. The response of retinal Müller glial cells, which play an important role in tissue regeneration, to genotoxic exposure was described [6].

A comparative molecular modeling study of the molecular dynamics of native rhodopsin and its mutant form E181K, which is typical of pigmented retinitis, was performed. It was shown that the stable covalent bond between 11-cis-retinal and the Lys296 residue is not formed in the chromophore center of rhodopsin's mutant form E181K. Such lesions have to result in disorder in visual pigment regeneration during dark adaptation. At the same time, in opsin's cytoplasmic domain, the active center of opsin binding with transducin is not blocked [7].

MATHEMATICAL MODELING OF RADIATION-INDUCED EFFECTS

Mathematical modeling studies were continued of the biological effect of heavy charged particles at different levels — from disorders in molecular mechanisms to changes in functions of separate physiological systems.

A model approach was formulated to the description of the main pathways of DNA double-strand break (DSB) repair by nonhomologous end joining. On the basis of kinetic equations, three main stages of DSB repair were described, which correspond to synaptic complex formation, end processing phases, and ligation. The model adequately reproduces repair kinetics in a culture of HSF42 human skin fibroblasts for irradiation with 1 Gy of ^{137}Cs gamma rays and 1 GeV/nucleon accelerated O, Si, and Fe ions (Fig. 8). The proposed approach generalized a great amount of experimental data on the kinetics of separate stages of radiation-induced DNA DSB repair in mammals and humans. Using this model, it is possible to predict time characteristics of DNA DSB repair for ionizing radiations of different physical quality [8, 9].

A new field of research was established: mathematical modeling of the effect of heavy charged particles on the structures and functions of the central nervous system (CNS). The first results were obtained of the mathematical modeling of the expression of NMDA glutamate receptors. These receptors are present in hippocampus synapses; they play an important role in the realization of the learning and memory functions. A dynamic model was proposed that characterizes the synthesis of receptor subunits, their assembly, and further transport to the postsynaptic membrane. Mathematically, these mechanisms are described by a system of ordinary differential equations. Within the framework of the model,

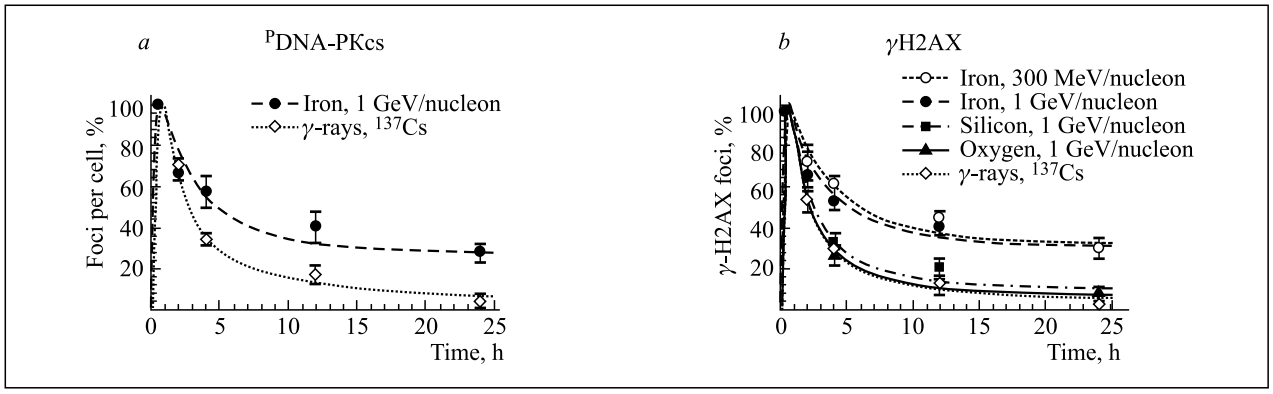

Fig. 8. Kinetics of changes in the level of phosphorylated DNA-dependent protein kinase (*a*) and γH2AX foci (*b*) in a culture of HSF42 human skin fibroblasts for exposure to 1 Gy of ionizing radiations of different physical characteristics. The curves show calculation results; the dots are experimental data (Asaithamby et al., 2008)

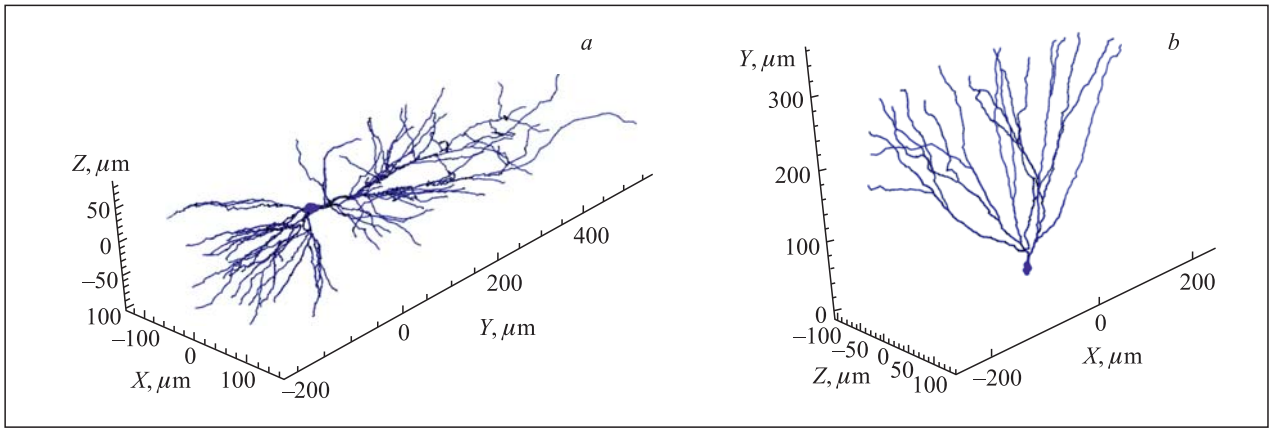

Fig. 9. *a*) A spatial model of a pyramidal neuron of the CA1 rat hippocampus field. *b*) A spatial model of a granular cell of the dentate gyrus of the rat hippocampus. The results were obtained with the use of the developed algorithm

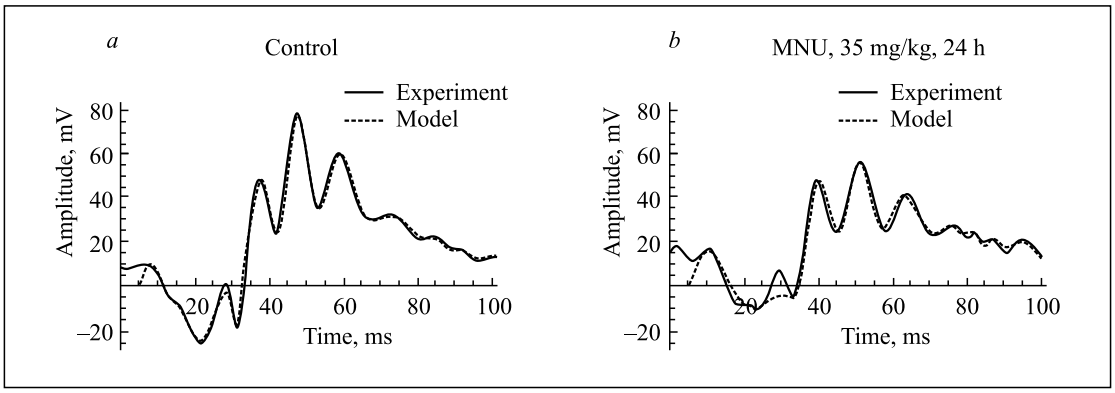

Fig. 10. Modeling results describing changes in the functional activity of the mouse retina 24 hours after exposure to MNU at a dose of 35 mg/kg. The calculated curves are shown in comparison with experimental data (M. A. Ostrovsky et al., 2011)

possible ways are suggested of taking into account the radiation factor, which determines changes in the level of NMDA subunits in rat hippocampus synapses after exposure to relatively low doses of irradiation with accelerated heavy ions. Approaches were formulated to the evaluation of the dose load on different types of brain neurons in comparison with other cells that do not have such complicated geometry. For this purpose, an algorithm was developed that allows the construction of spatial models of different types of neurons for microdosimetry calculations (Fig. 9). As input data, results of comparative experimental research on brain cell morphology are used.

A computational method was developed that allows calculating the numerical values of some physiological parameters of the mouse retina based on electroretinographic study results. A comparative analysis was made of photoreceptors' response and sensitivity after exposure to the chemical agent methylnitrosourea (MNU), which in certain concentrations causes degenerative changes in the retina (Fig. 10).

In cooperation with the Far Eastern Federal University (Vladivostok, Russia), a model approach was developed that describes the physical mechanisms of the formation of DNA lesions of different types under exposure to heavy charged particles. Using Monte Carlo-based TRIOL, Geant4, and RITRACKS codes, which describe particle transport in matter, the primary acts of accelerated carbon and iron ion (3.3 MeV/nucleon and 1 GeV/nucleon, respectively) interaction with a short double-stranded DNA sequence in an aqueous medium were modeled. On the grounds of the obtained results, the most likely initial localizations of the charge introduced by a particle were determined. To describe further stages of radiation interaction with DNA, a charge migration model was constructed, which allows finding the most probable sites of the emergence of primary DNA lesions of different types (Fig. 11). The proposed approach can explain the quantum mechanics nature of the origination of clustered DNA damage of different complexity [10–12].

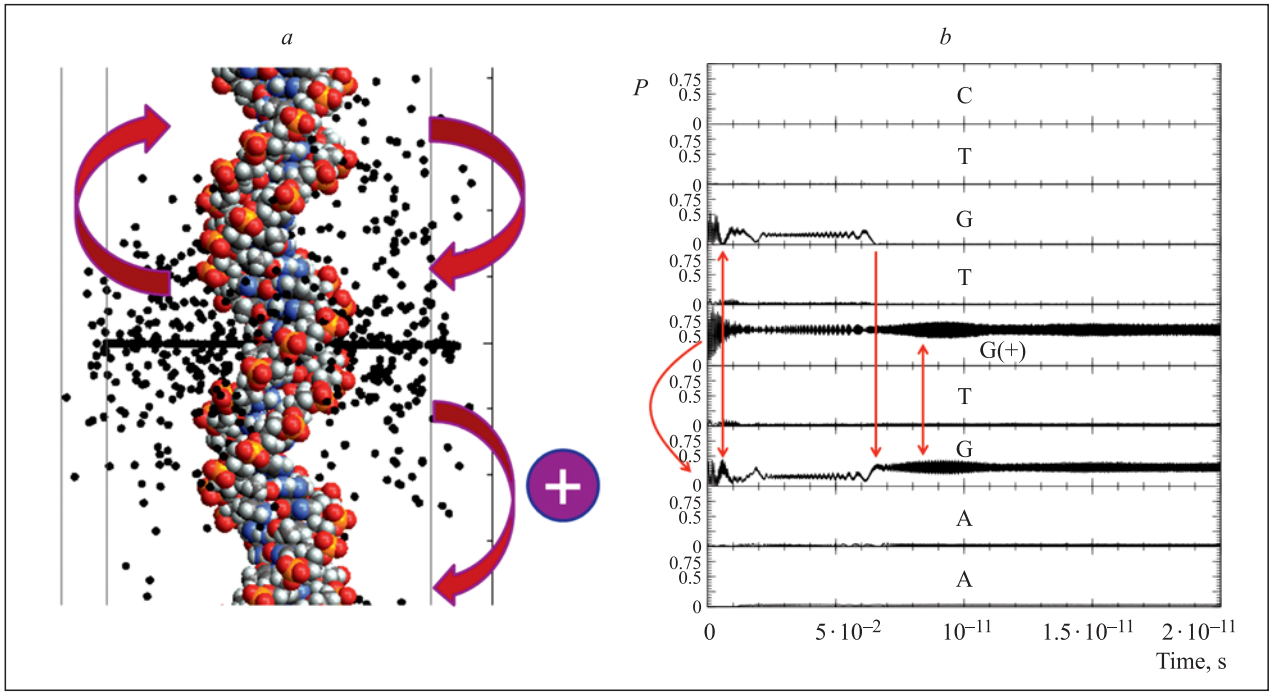

Fig. 11. *a*) A spatial DNA model superposed with a model of a 3.3 MeV/nucleon carbon ion track. *b*) The time dynamics of charge localization on a strand of the DNA short sequence CTGTGTGAA

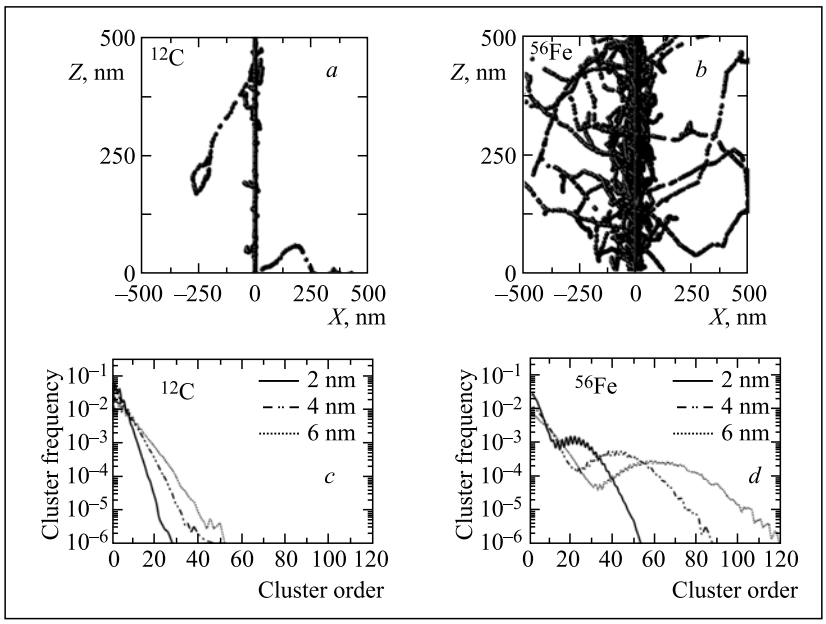

Fig. 12. Two-dimensional projections of 100 MeV/nucleon carbon (*a*) and iron (*b*) ion tracks obtained with the Geant4 code and the corresponding ionization cluster distributions for different target sizes (*c*, *d*)

Joint research was continued with the National University of Mongolia (Ulaanbaatar). An improved algorithm was proposed for the cluster analysis of the tracks of heavy particles that produce a great number of ionizations in a medium. The developed method was used to perform a comparative analysis of the frequency of ionizations produced in biological targets with a size of 1–6 nm by accelerated protons, alpha particles, and nuclei of carbon and iron with an energy of 3.5–100 MeV/nucleon (Fig. 12) [13, 14].

In cooperation with Cairo University, Egypt, results were obtained of the theoretical study of the mismatched base repair (MMR) role in the realization of the ultraviolet-induced mutation process in *E. coli* bac-

terial cells. For this purpose, a mathematical model of this type of repair was developed, within which the key pathways of error removal with the participation of DNA endonucleases are described. The results of the performed calculations fall in line with the hypothesis that MMR is responsible for the removal of nucleotides that were mistakenly substituted by DNA polymerase V during SOS response (Fig. 13) [15, 16].

A model was developed of the collective dynamics of proton tunneling in the hydrogen bonds between DNA bases. The probability was calculated of tautomeric DNA base formation depending on temperature, the degree of DNA structure deformation, and charge distribution. The dynamic mechanism of the direct excitation of tautomeric DNA bases was studied. In the considered case, the tautomeric transition can be determined by the following two factors: resonance tunnel transitions of protons or hydrogen bond deformation under exposure to terahertz electromagnetic fields [17].

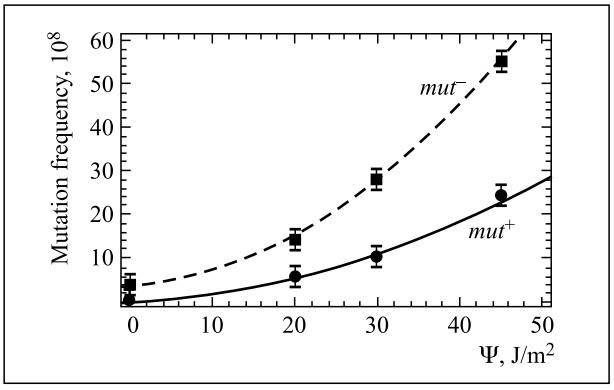

Fig. 13. Dependence of mutations in the *lacZ* gene of *E. coli* on ultraviolet radiation energy fluence. The calculations were performed for strains with the normal MMR function (*mutS*+) and in its absence (*mutS*–). The dots are experimental data (Hongbo et al., 2000)

COMPUTER MOLECULAR MODELING OF BIOPHYSICAL SYSTEMS

A molecular dynamics simulation of a DNA photolyase enzyme was performed to study the conformational behavior of the photoactive cofactor flavin adenine dinucleotide (FAD) inside the enzyme pocket. DNA photolyase is a highly efficient light-driven enzyme that repairs the ultraviolet-induced cyclobutane pyrimidine dimer in damaged DNA. The conformational and dynamic changes of FAD were studied in the whole DNA photolyase structure (containing FADH, MTHF, and DNA molecules) in a water solvent. The conformational changes of the FAD cofactor and other constituent fragments of the molecular system under consideration were compared [18].

PROTECTION PHYSICS AND RADIATION RESEARCH

In cooperation with contractor Comet Corp., the radiation safety section of the NICA collider project was completed. The collider's radiation environment was finally calculated in detailed geometry. The calculation was based on a Monte Carlo technique and was performed using the Geant4 code customized for the accumulation and collision of 4.5 GeV/nucleon ^{197}Au nuclei.

Concerning the effective neutron dose, the calculations took into account the contribution of the following secondary radiation sources formed due to nuclear beam losses:

— local losses: all the beam catchers in both rings (24 in each);

— losses distributed uniformly over the rings;

— ion recombination on electronic cooling system electrons (additional local losses on several catchers);

— losses of nuclei in kickers (septum magnets) at beam injection into the collider.

Beam interaction points were not considered as secondary radiation sources.

As regards geometry, the calculations took into account the effective dimensions of the magnetic optics elements, their stacked arrangement in the rings observing the nucleus flux direction in each ring, the ion guide and cryostat design, the actual location of the rings in the collider tunnel and its dimensions, shielding thicknesses proposed by Comet Corp., the presence of annexes to the collider building and their shape, and the multiple scattering of leaked neutrons in the air and soil of the environment. The calculations yielded data on the contribution of each separate source (normalized to a nucleus lost in the source) to the effective neutron dose at the selected points beyond the collider shielding. It allowed modeling the radiation conditions beyond the

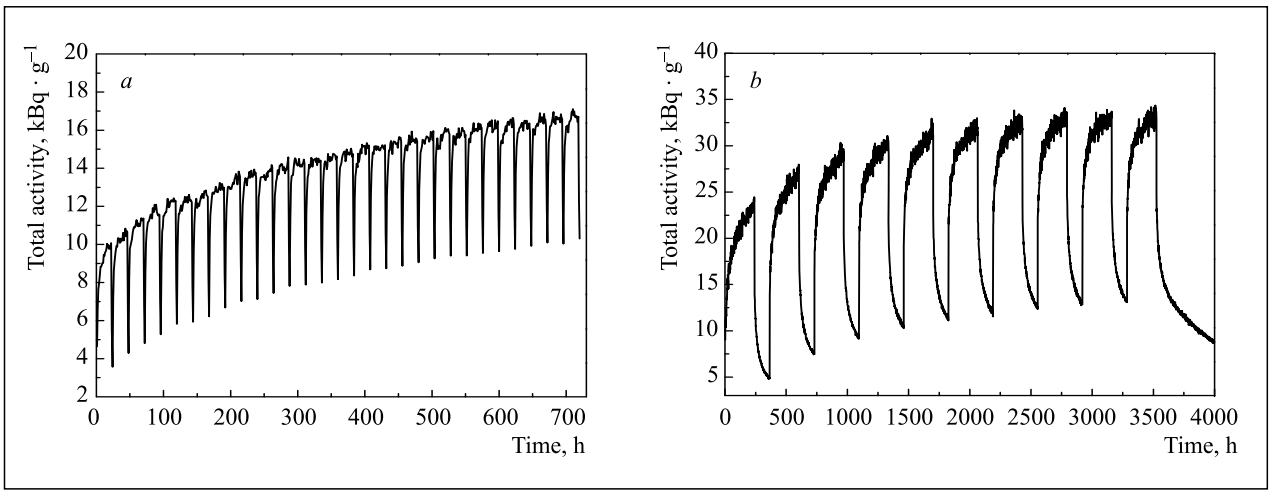

Fig. 14. The dynamics of induced activity accumulation in a beam catcher: a month-long operation at 22 hours of work and a two-hour break per 24 hours (*a*); 10-year operation at eight straight months of work and a four-month break a year (*b*)

collider shielding and in the environment for different collider operation scenarios and beam loss distributions. It was found that for a realistic collider operation mode and the most probable beam losses on different sources, the effective dose rates at the workplaces in the buildings around the collider (the A category staff), on the border of the prohibited access zone (the B category staff), and at the buffer area border (population) will not exceed the acceptable values with the specified safety factor [19, 20].

In predicting the radiation conditions around the collider, the main uncertainty is related to the imperfection of the physical models used to describe the nucleus–nucleus collisions in the nucleus mass and energy region typical of the NICA collider. To evaluate the possible error range, a comparison was made of calculations of the basic source term (differentiated twice with respect to the angle and energy of secondary neutrons for the collision of a 4.5 GeV/nucleon ^{197}Au nucleus and a $^{\mathrm{nat}}$Fe nucleus) performed using three acknowledged codes that are based on different physical models of nucleus–nucleus interactions: Geant4 (CERN), SHIELD (Russia), and MCNPX (the U.S.). The divergence of the results was not more than a factor of 2, which is acceptable from the point of view of radiation safety. The dynamics of induced activity accumulation in the beam catchers was modeled for a month-long operation of the collider and for its whole design service life (Fig. 14).

In collaboration with JINR's Laboratory of Neutron Physics and the Institute of Space Research of the Russian Academy of Sciences, development of instruments was continued for planet surface research with nuclear physics methods [21]. The Dynamic Albedo of Neutrons (DAN) instrument, which was created with the active participation of LRB staff members, is efficiently working on the Mars surface on board NASA's Curiosity rover.

A portable version of the multisphere neutron spectrometer was designed and fabricated [22], as was the Genome irradiation facility for radiobiological experiments at nuclear beams of the U400M cyclotron of JINR's Laboratory of Nuclear Reactions [23].

CONFERENCES AND EDUCATION

In 2012, LRB staff members participated in nine scientific conferences in Russia and five — abroad.

Jointly with the Department of Physiology and Fundamental Medicine (DPFM) of the Russian Academy of Sciences (RAS), a visiting Session of the DPFM RAS Bureau was held. The Session focused on the issues of the effect of high-energy heavy charged particles on the structures and functions of the central nervous system, regularities and mechanisms of radiation cataractogenesis, visual reception disorders, and prediction of the danger of galactic heavy nuclei for manned interplanetary flights. Among the Session participants were nine RAS Full Members and nine RAS Corresponding Members. The Session was presided by RAS Academicians A. I. Grigoryev (RAS Vice-President), V. A. Matveev (JINR Director and Secretary Academician of the Department of Physical Sciences, RAS), and Yu. V. Natochin (Secretary Academician of the DPFM RAS). In the course of the discussion, Acad. A. I. Grigoryev made a special note of the im-

portance of solving space radiobiology problems with the use of JINR's potential.

The 5th Japan–Russia International Workshop «Molecular Simulation Studies in Materials and Biological Sciences» (MSSMBS 2012) was held. Scientists of Canada, France, Italy, Japan, Mongolia, the United States, and CIS countries presented results of their research. The Workshop topics extended over a wide range of modern molecular and mathematical modeling aspects, including the molecular dynamics simulations of proteins; protein folding research with generalized-ensemble techniques; mutation transition effects in protein structures; molecular dynamics (MD) and Monte Carlo simulations of radiation-induced mutations; modeling genetic regulatory networks in bacterial and mammalian cells; simulation of DNA damage induction by ionizing radiations; chemical and nanostructure design of crystals, liquids and polymers; drug design (molecular docking, enzymes, and inhibitory activities); novel MD computing methods (DFT, QM/MM, MD, MD/CFD, and hybrid approaches); and general- and special-purpose MD computers with modern communication architecture.

The Biophysics Department of Dubna University continued the educational process. Current total enrolment is made up of 58 students majoring in the specialty «Human and Environmental Radiation Safety» and 5 radiobiology specialty postgraduates. In 2012, the Department accepted 10 new students; 10 successfully competed their programs and received engineer-physicist diplomas. A molecular dynamics course is offered to Dubna University's senior students on the basis of the Departments of Chemistry, Geochemistry, and Cosmochemistry.

REFERENCES

1. *Savelyeva M. et al.* The Effect of DNA Synthesis Inhibitors on the Induction and Repair of Double-Strand Breaks as Apoptosis Inductors under Ionizing Radiations // Proc. of 12th Intern. Workshop on Radiation Damage to DNA, 2–7 June 2012, Prague, Czech Republic. Prague, 2012. P. 98.
2. *Baranova E.* Comparison of DNA γH2AX/53BP1 Foci Formation, Nuclear Distribution and DNA Double-Stand Break Repair for Skin Fibroblasts and Lymphocytes Either Irradiated with Gamma-Rays or Incubated with Hydrogen Peroxide // Ibid. P. 72.
3. *Blaha P.* Influence of Accelerated ^{18}O Ions on the Growth of HPRT-Mutant Subclones of Chinese Hamster Cells // Ibid. P. 76.
4. *Koltovaya N.A.* Cell Cycle Regulation by the CDK1/CDC28 Cyclin-Dependent Kinase // Genetics. 2013 (in press) (in Russian).
5. *Muranov K.O., Poliansky N.B., Ostrovsky M.A.* Interaction of Alpha-Crystallin with UV Radiation-Damaged β_L-Crystallin // Proc. of XX Biennial Meeting of the Intern. Society for Eye Research. July 21, 2012. Berlin, 2012. P. 024.
6. *Tronov V.A. et al* Radioresistance Mechanisms in Terminally Differentiated Cells of the Mature Retina // Cytology. 2012. V. 54(3). P. 261–269 (in Russian).
7. *Feldman T. et al.* Model of Abnormal Chromophore-Protein Interaction for E181K Rhodopsin Mutation: Computer Molecular Dynamics Study // The Open Biochemistry Journal. 2012. V. 6. P. 94–102.
8. *Belov O.V., Lyashko M.S., Timofeeva I.L.* Dynamic Model of DNA Double-Strand Break Repair in Mammalian Cells // Symbiosis — Russia 2012: Proc. of the 5th All-Russian (with International Participation) Medical and Biological Congress of Young Scientists. Dec. 3–8, 2012, Tver, Russia. Tver, 2012. P. 250–252 (in Russian).
9. *Lyashko M.S., Belov O.V.* Mathematical Modeling of the Homologous Repair Mechanism in Human Cells // Proc. of the 16th Conf. of JINR's Young Scientists and Specialists. Febr. 6–11, 2012, Dubna, Russia. Dubna, 2012. P. 265–268 (in Russian).
10. *Belov O., Boyda D., Shirmovsky S.* Quantum Mechanical Nature of Complex DNA Lesions // Proc. of 12th Intern. Workshop on Radiation Damage to DNA. June 2–7, 2012, Prague, Czech Republic. Prague, 2012. P. 43.
11. *Belov O., Boyda D., Shirmovsky S.* Mathematical Model of DNA Lesions // Proc. of XXI Intern. Baldin Seminar on High-Energy Physics Problems. Sept. 10–15, 2012, Dubna. Dubna, 2012. P. 042.
12. *Aksenova S.V., Belov O.V., Lkhagva O.* Modeling the Spatial Distribution of Energy and Absorbed Radiation Dose in the DNA Structure under Accelerated Heavy Ions // Part. Nucl., Lett. 2012. V. 9, No. 1(177). P. 161–168 (in Russian).
13. *Batmunkh M. et al.* Cluster Analysis of the Highly Charged Particle's Tracks for the Space Radiobiology Studies // Proc. of 5th Japan–Russia Intern. Workshop MSSMBS'12 «Molecular Simulation Studies in Material and Biological Sciences». Sept. 9–12, 2012. Dubna–Moscow, 2012. P. 27–28.
14. *Bayarchimeg L. et al.* Heavy Ion's Track Structure by Geant4 // Proc. of Intern. Conf. «ICMS 2012», August 20–23, 2012, Ulaanbaatar, Mongolia. Ulaanbaatar, 2012. P. 2–4.
15. *Belov O. et al.* Modeling the Mismatch Repair System in Bacterial Cells // Proc. of 12th Intern. Workshop on Radiation Damage to DNA. June 2–7, 2012, Prague, Czech Republic. Prague, 2012. P. 74.

16. *Belov O. et al.* The Role of the Bacterial Mismatch Repair System in SOS-Induced Mutagenesis: A Theoretical Background. JINR Preprint E19-2012-96. Dubna, 2012. 19 p.
17. *Bugay A. N.* Interaction of Terahertz Radiation with DNA // Nanosystems: Physics, Chemistry, Mathematics. 2012. V. 3, No. 1. P. 51–55.
18. *Kholmurodov K., Dushanov E., Yasuoka K.* Molecular Dynamics Simulations of a DNA Photolyase Protein: High-Mobility and Conformational Changes of the FAD Molecule at Low Temperatures // Advances in Bioscience and Biotechnology. 2012. V. 3, No. 3. P. 169–180.
19. *Timoshenko G., Paraipan M.* Estimating the Main Radiation Source Terms for the NICA Collider // Part. Nucl., Lett. 2012. V. 9, No. 8. P. 643–647.
20. *Timoshenko G., Paraipan M.* Conceptual Data and Models for the NICA Collider Radiation Shielding Simulation // 2nd Eur. Nucl. Phys. Conf. Sept. 16–21, 2012, Bucharest (in press).
21. *Kotelnikov S. G. et al.* Protable Autonomous Version of the Multisphere Neutron Spectrometer with a Monitor Sensor for Measurements in Field Conditions // Instr. Exp. Tech. 2012. No. 4. P. 104–105 (in Russian).
22. *Bezbakh A. A. et al.* Upgrade of the Genome Facility for Radiobiological Experiments at Heavy Ion Beams // Part. Nucl., Lett. (in press) (in Russian).
23. *Litvak M. L. et al.* Calibration of a $LaBr_3$(Ce) Detector for Studying Planet Surface Elemental Composition with Gamma Spectroscopy // Theses of the 3rd Intern. Conf. «Scintillation Materials Engineering and Radiation Technologies», Dubna, Nov. 19–23, 2012. Dubna, 2012. P. 7 (in Russian).