DIVISION OF RADIATION AND RADIOBIOLOGICAL RESEARCH

The research programme of DRRR is determined by the first-priority theme that focuses efforts on two main directions: radiation and biophysical. The radiation line is traditionally connected with radiation shielding, gamma and neutron spectrometry, and radiation monitoring at JINR basic nuclear facilities and in environment. The scientific line on biophysics joins genetic research at heavy charged particle beams, investigation of molecular photo- and radiobiological processes in eye structures, research in the field of molecular dynamics.

RADIATION RESEARCH

The work concerning the design and development of the radiation protection system of the Slovak cyclotron complex (Bratislava) was continued. The dose rate levels from the induced radioactivity in the accelerator structures were predicted for different modes of operation. The individual doses of the personnel at technical services of the accelerator were estimated.

The physics support of the biological experiments was carried out. Two experiments with carbon ions (480 MeV/nucleon) at the Nuclotron and two experiments with boron and lithium ions (32 and 33 MeV/nucleon accordingly) at the U400M were performed.

The radiation protection conception for the SAD installation was developed. The calculations of the SAD shielding, induced radioactivity of the materials, soil and air, radiation situation in environment and so on were done in cooperation with the specialists from the planning organizations. The investigations of the present radiation situation around the Phasotron were continued.

The calculations of multisphere neutron spectrometer response function were carried out in widest neutron energy range for detailed spectrometer geometry and different spatial distributions of the radiation field.

The activities in the framework of the participation in the planet surface research programme in collaboration with the Institute for Space Research (Moscow) and FLNP were continued [1]. The real geometry calculation of neutron detection efficiency of the Russian HEND neutron spectrometer on the basis of stilbene detector was finished. The DRRR specialists took part in the design of the instruments for water search of the Martian rover and the Moon spacecraft.

BIOPHYSICS RESEARCH

Radiation Genetic and Radiobiological Research

Radiation genetic research was continued at the accelerators of heavy ions. One of the specific characteristics of genetic effects of accelerated heavy charged particles is the induction of clustered DNA damages. Such lesions are the result of significant energy deposition in genetic structures. In this case the repair of single- and double-strand breaks (DSB) of DNA

may be strongly suppressed, which reflects on different radiation-induced genetic effects. It was established that DNA damages by the physical factors and different chemical mutagenes induce two kinds of cell response. The first kind is the repair of DNA damages and the second is the apoptotic cell inactivation. The specific character of DNA damages due to heavy charged particle irradiation can reflect on the damage repair kinetics and influence the frequency of apoptotic cell inactivation.

In order to study the regularities of DSB repair in human cells after heavy-ion irradiation, the DNA comet assay method was developed. This simple, rapid and sensitive technique allows determining the level of DNA damages in individual cells. In the comet assay, the cells are embedded in a thin agarose gel on a microscope slide. The cells are lysed to remove all cellular proteins and the DNA subsequently allowed unwinding under alkaline/neutral conditions. Following unwinding the DNA is electrophoresed and DNA stained with a fluorescent dye. During electrophoresis, broken DNA fragments (damaged DNA) or relaxed chromatin migrate away from the nucleus. The ability to detect specific lesions opens up a new area of investigation — cellular DNA repair. By looking at the removal of DNA damage over a period of time, comet assay can reflect the DNA repair that is taking place in the damaged cells.

The purposes of the investigation were the following: the study of DSB formation in human lymphocytes after irradiation with gamma rays and heavy ions with different energy and linear energy transfer (LET); the research of kinetics of DSB repair after irradiation with gamma rays and heavy ions. The boron, lithium and carbon ions were used in experiments. The energy and LET of the particles were 32 MeV/nucleon (LET = 55 keV/μm), 33 MeV/nucleon (LET = 20 keV/μm) and 480 MeV/nucleon (LET = 10.6 keV/μm), respectively. It was shown that the relationship of DSB induction as a function of the dose is described by the linear function for all the types of radiation (Fig. 1).

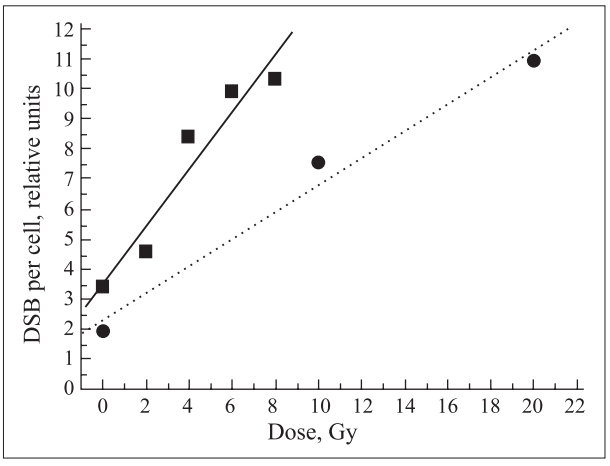

Fig. 1. The induction of DSB in human lymphocytes after irradiation with gamma rays and carbon ions with energy 480 MeV/nucleon: ■ — ^{12}C ($Y = 3.49 + 0.96^{*}X$, $R = 0.96$); ● — γ rays ($Y = 2.28 + 0.45\,X$, $R = 0.99$)

The efficiency of DSB induction by carbon ions with an energy of 480 MeV/nucleon is higher in comparison with gamma rays. The incubation of the lymphocytes after irradiation reveals the decreasing of DSB amount after gamma and heavy-ion irradiation (Fig. 2). But after 6-hour cell incubation at carbon ion irradiation the relative amount of DSB increases again. This fact may be connected with growth of cell population that is inactivated by damages induced by the apoptosis in the living cells. The experiments with comet assay and with the other heavy charged particles are planned at the Nuclotron and U400M.

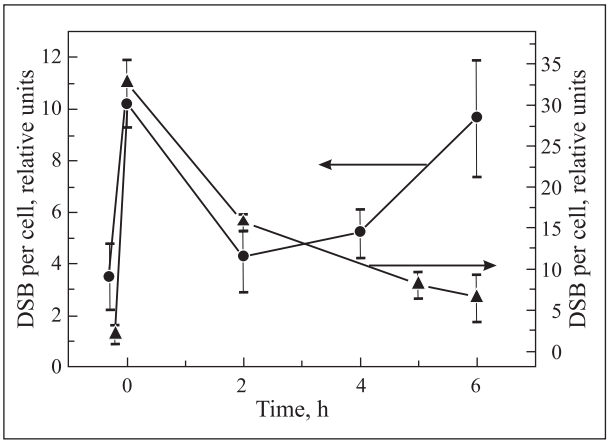

Fig. 2. The dependence of the relative amount of the double-strand breaks of DNA in human lymphocytes and their repair on the time of irradiation with 480-MeV/nucleon carbon ions (●, 6 Gy) and gamma rays (▲, 80 Gy)

The study of low-dose radiation cytogenetic effects in human peripheral blood lymphocytes and Chinese hamster cells exposed to X and γ rays, carbon ions (LET 10.6 keV/μm), magnesium ions (LET 43 keV/μm) was continued. Nonlinear dose-response dependences in the range from 0.01 to 0.5–0.7 Gy were demonstrated for the four samples of donor's blood and Chinese hamster cells for all types of radiation by using various cytogenetic methods. In the dose range from 0.01 to 0.05–0.07 Gy the cells revealed the highest radiosensitivity mainly due to chromatide-type aberration induction. As dose increased, the frequency of aberrant cells and aberrations decreased significantly (in some cases to the control level). At the doses above 0.5–0.7 Gy the dose-effect curves become linear, but their slope decreased compared to initial one (by a factor of 5–10 depending on the cytogenetic criteria used) reflecting the higher radioresistance of cells. This hypersensitivity increased radioresistance phenomenon (HRS/IRS) is revealed for all types of radiation.

The data obtained point to the existence of HRS/IRS in response to ionizing radiation with wide range of

LET and confirm the idea that the direct linear extrapolation of high-dose effect to low-dose range — the procedure routinely used to estimate genetic risk of low-dose irradiation — is incorrect and leads to underestimation of chromosome damage produced by low radiation doses [2].

Comparative analysis of individual radiosensitivity of peripheral blood lymphocytes exposed to radiation with different LET was continued. The experiments were performed with lymphocytes of few healthy donors, male and female from 20 to 55 years.

Unstable chromosome aberrations *in vitro* in human peripheral blood lymphocytes exposed to sparsely and densely ionizing radiation (γ-ray ^{60}Co, protons with an energy of 170 MeV and ^{12}C ions with an energy of 480 MeV/nucleon) were analyzed. The differences between donors were revealed. The interexperimental variability of total aberration frequency in some donors was observed for all types of radiation. The obtained results indicate correlations between sensitivity to low-LET and high-LET radiation in the dose range from 1 to 3 Gy. The data show that heavy ions are more effective than γ rays and protons.

The study of chromosomal damages in the cells on the model of human blood lymphocytes after irradiation with the initial 170-MeV proton beam at the entrance of an object and in the Bragg peak region has been performed, which corresponds to the irradiation of surrounding tissues along the beam path and tumour tissues [3]. High biological efficiency of the Bragg peak protons has been shown. RBE values were ~ 1.25 within the dose interval from 1 to 4 Gy, while protons at the entrance did not differ from the γ radiation. Because the therapeutic proton beam dose to a tumour is formed by patient irradiation from several (up to 7) directions, the level of cytogenetical damages of cells in surrounding tissues along the initial proton beam path decreased by an order. So, about 80% of tumour cells will obtain the damages after irradiation by a dose of 3 Gy, but in surrounding healthy tissues it will not exceed 10%. The data confirm high biological efficiency of proton beams for radiotherapy.

The study of induction of mutations of different nature by ionizing radiation in yeast *Saccharomyces cerevisiae* was continued. Mutagenic property of ionizing radiation was characterized by using four different mutator assays.

They were a forward mutation rate assay that detects mutations inactivating the arginine permease gene (Can^r mutations) and reversion assays detecting mutations that revert a 4-base insertion in the LYS2 gene or that revert a +1T insertion in a stretch of 6 T's in the HOM3 gene. The reversion to Lys$^+$ and Hom$^+$ is due to deletion of a single nucleotide predominantly. Induction of mutations by γ rays was studied earlier. Now the induction of mutations by heavy ions is investigated. Induction of mutations in haploid yeast cells by Li ions with LET = 17 keV/μm was tested. We did not show efficient induction of frameshift mutations. The curve had maximum at a dose of about 25 Gy.

Moreover, a plasmid system for quantitative analysis of small deletion (about several kbp) formation by ionizing radiation was used. We are getting straight this system using UV light. The heavy ions (Li, 17 keV/μm) also did not induce efficiently this type of mutation. The curve had maximum at a dose of about 75 Gy.

The study of checkpoint control, genetic control of DNA damage-induced arrest of cell cycle progression, was continued together with the Institute of Molecular Genetics (Moscow, Russia). It is planned to study interactions between the known checkpoint genes and SRM genes using such a property as the radiosensitivity. It was determined that CDC28 and RAD53 genes define two epistasis groups. CDC28 and RAD53 define two branches of the pathway controlling the radiosensitivity. Now the interactions between these two branches and RAD52-repair pathway are studied. Earlier it was shown that CDC28 and RAD52 interact epistatically. We show that triple mutant rad52 rad53 cdc28-srm was sensitive as double mutant. So, there are two branches determining radiosensitivity — CDC28-dependent and RAD52-, RAD53-dependent.

Together with the University of Perugia (Italy), mutagenesis, cellular aging and apoptosis using *S. cerevisiae* as a model system were investigated. In particular, effects of nutrient starvation on yeast life is under study. Starvation-associated mutations (SAM) are considered as genetic changes that arise in nondividing or slowly dividing cells during long-term cultivation under selective conditions. There are many situations in nature where cells are not actively dividing; indeed, it may be that the majority of cells, whether free-living or components of multicellular organisms, are in this «resting» state most of time. These mutations are distinct from spontaneous mutations and arise by a mechanism independent of standard DNA replication. The precise mechanism that produces mutations in these conditions is not understood. Little is known about the genetic control of this phenomenon. It is planned to investigate the participation of checkpoint genes and polymerases in SAM. It was shown that the main replicative DNA polymerases δ and ε are involved in starvation-associated mutagenesis and survival of cultures.

Photoradiobiological Research

Study by the Ultraviolet Testing Method of Damage Action of Heavy Charged Particles on the Lens Proteins — Crystallines. It is considered that the main cause of cataract disease (lens dimness) of astronauts is irradiation by high-energy heavy particles [4]. One of the reasons of cataract disease development may be radioactive damage of the lens soluble proteins of cytoplasm fibrous cells — crystallines. This damage may produce latent damages of protein molecules. UV light may serve for amplifying aggregation factor. In our

work, UV irradiation was used for detection of latent radioactive damages of crystallines. The goals of the research were: to study the changes of bovine lens crystallines, appearing by heavy nuclei bombardment of the protein solution; to determine the borders of the dose responsible for changes in crystallines stability.

Solutions of α and β_L crystallines of bovine lens obtained by gel filtration were subjected to bombardment of B, C and Li nuclei, whereupon the structure functional changes of proteins were investigated. Stability of β_L crystalline with respect to heat- and photo-induced melting (denaturation), and also chaperon activity of α crystalline with respect to heat- and photo-induced melting (denaturation) of β_L-crystalline were studied. Structural changes of proteins were characterized with the help of analysis of triptophane and non-triptophane fluorescence, methods of gel filtration and electrophoresis in PAAG in denaturating and reducing conditions.

Irradiation with nuclei of B^{11} (32 MeV/nucleon) did not produce evident changes in stability of β_L crystalline to heat melting (denaturation), whereas the dose 8 Gy brought to 30% decreasing of lag period of the process of photoaggregation under the action of UV light (at 37 °C). At the same time, data of electrophoresis did not show changes in the polypeptide structure of samples under the action of irradiation. Exploration of the spectra of fluorescence is evidence of some conformative reorganizations in molecule of β_L crystalline already appearing at irradiation dose 4 Gy.

Exploration of α crystalline showed that irradiation with nuclei of B^{11} does not produce significant changes neither in size nor in form of molecule (gel filtration, small-angle X-ray scattering); it also did not find formation of lacings between subunits of protein (electrophoresis in PAAG). Changes in chaperon activity with respect to heat-induced melting (denaturation) of β_L crystalline were not observed as well; however, little decrease was found in chaperon activity of protein with respect to photoaggregation.

Irradiation with C nuclei (480 MeV/nucleon) of α and β_L crystallines was carried out twice, however it did not find significant changes.

Irradiation with nuclei of Li (33 MeV/nucleon) did not have an influence on stability of β_L crystalline to heat melting (denaturation). Exploration of protein stability to photoaggregation under the action of UV light (at 37 °C) showed that irradiation decreases lag phase and increases speed of aggregation. However, dose dependence was essentially nonlinear — the maximum effect of acceleration of photoaggregation was at the dose 4 Gy, whereas the dose 16 Gy did not differ from the control. Electrophoresis data also did not show changes in polypeptide structure of the samples under the action of irradiation. Exploration of spectra of fluorescence showed that significant changes in spectrum of molecule are absent. Exploration of α crystalline found out that the irradiation does not produce significant changes in size of molecule (gel filtration); it also did not find lacings between subunits of protein (electrophoresis in PAAG). Changes in chaperon activity with respect to heat-induced melting (denaturation) of β_L crystalline were absent. However, with respect to photoaggregation, as in the case of irradiation with nuclei of B^{11}, observed was some decrease of chaperon activity of protein.

Thus, on the basis of the obtained results we can conclude that high-energy nuclei (480 MeV/nucleon) at a dose rate of 4 Gy/h do not have an influence on crystallines, whereas nuclei with an energy of about 30 MeV/nucleon at a dose rate of 4 Gy/h can damage both the molecules of α crystalline and β_L crystalline. But the obtained results are contradictory enough and need further explorations.

Exploration of Crystalline Structure by the Method of Small Angle X-ray and Neutron Scattering.

By the method of small-angle X-ray scattering the influence of irradiation with nuclei of B with LET = 55 keV/μm on the structure of α crystalline was investigated. In the experiments we used solutions of α crystalline obtained from bovine lenses. Concentration of α crystalline in the solution was fixed by the microbiuret method came on the irradiation and small-angle X-ray scattering measuring to 11 mg/ml. Small-angle X-ray scattering was measured by diffractometer with linear coordinate detector at IBPH RAS in Moscow. Curves of small-angle X-ray scattering were analyzed with the help of the program «Gnom» using Fourier method. Angle X-ray scattering measurements of α-crystalline solutions irradiated with B nuclei with dose rates of 4 and 16 Gy and two control (unirradiated) solutions of α crystalline were carried out.

Curves of small-angle X-ray scattering solutions of α crystalline irradiated with nuclei of B with dose rates of 4 and 16 Gy and control solutions in limiting error of experiment were identical. The radius of gyration and the maximum size irradiated and control solutions of α crystalline were (6.2 ± 0.2) nm and (18 ± 1) nm, accordingly. Decrease in intensity of small-angle scattering, which might be expected at the partial precipitation of protein, was not observed.

Thus, after B nuclei irradiation with a dose of up to 16 Gy, no considerable structural changes of α crystalline (neither changes of size nor of molecular weight and shape of macromolecules of α crystalline) take place.

The obtained data show high radioactive stability of α crystalline, which is obviously an important condition of this protein function in the lens over a long period of time throughout the life.

Spadework was done for investigating crystallines structure with the small-angle neutron scattering method including search and analysis of literary data, discussion and planning of experiment. With the purpose of preparing for experiments of neutron scattering by using the method of variation contrasts, a start has been

made on exploration of the influence of heavy water on α- and β_L-crystalline structure (comparative analysis of α- and β_L-crystalline structure by the small-angle X-ray scattering method in buffer containing common and heavy water).

Exploration of Influence of Heavy Charged Particles on Eye Pigment Molecule — Rhodopsin (in vitro). During 2004, two experiments of irradiation of digitonin extract of rhodopsin were carried out on the atom-smasher U400M with boron nuclei (LET = 55 keV/μm) and lithium nuclei (LET = 20 keV/μm), and also two experiments at the Nuclotron with 480-MeV/nucleon carbon nuclei. For understanding the damage action of heavy charged particles on rhodopsin, the following tests were carried out:

• *Investigation of spectral properties of rhodopsin.* It is shown that, independently of dose rate (4, 8, 16 Gy) and nature of heavy particles, the spectral properties of rhodopsin after its irradiation practically did not change.

• *Determination of the native degree of rhodopsin protein part — opsin.* It is shown that regeneration ability of opsin obtained from irradiated rhodopsin with added 11-*cis*-retinal did not change distinctly and was commensurable with control unirradiated samples irrespective of dose rate and nature of particles.

• *Determination of the ability to react of the protein SH groups by Ellman's method.* For samples irradiated at the Nuclotron with carbon nuclei, the test for available SH groups for titration by DTNB did not show any activity changes of sulfhydryl groups for irradiated samples with different doses (4 and 16 Gy) as compared with control.

In the case with rhodopsin irradiation with nuclei of boron and lithium at the U400M accelerator we found dose dependence reactivity of SH groups of the molecule's protein part. It is shown that at rhodopsin irradiations with heavy charged particles the number of SH groups available for titration increases, as compared with control, with increased dose rate (4, 8, 16 Gy). As is well known, after visible-region light action on the rhodopsin the increase of SH groups available for titration is due to conformational reorganizations of the protein part of the molecule and tertiary structure loosening. It may be supposed that in the case of heavy charged particle irradiation, transgressions take place in tertiary (possibly secondary and primary) structure of molecule. Molecular mechanism of increasing of available rhodopsin SH groups after irradiation with heavy charged particles is being investigated.

• *HPLC analysis of the state of rhodopsin chromophore group — retinal.* Analysis was performed of retinal conformation state in the rhodopsin irradiated with nuclei of boron on the atom-smasher U400M. It is shown that, in comparison with control sample, three extra peaks appear on the chromatogram which belong to more polar compounds rather than to any retinal isomers. It may be supposed that these are either fragments of retinal polyene chain or its oxidized form (epoxide). It is necessary to mark that percentage of all-*trance*-retinal in the irradiated sample does not change. In other words, at the heavy charged particle action on the rhodopsin molecule the isomerization of chromophore does not take place as it takes place at absorption of the light quantum by visual pigment.

Computer Molecular Modeling of Biophysical Systems

At the beginning of 2004, a new research unit CMMG (Computer Molecular Modeling Group) was created at DRRR. Having spent a bulk of time of the establishment period for the computational network, computing facilities and other related equipment, the CMM sector, headed by Professor Kh. Kholmurodov, began working in the field of the computer molecular dynamics simulations for the biomolecular structures (DNA, RNA and proteins) and studies related to the material and biological fields, with special emphasis on the problems of the cell and radiation biology. Molecular Dynamics (MD) simulations were performed to investigate the structural conformation of the rhodopsin and prion proteins. The effect of specific disease-related amino acid mutations on the dynamics and conformational changes has been estimated.

Retinal proteins (rhodopsins), a super family of the membrane receptors (known as GPRCs, G-protein-coupled receptors), are involved in conversion of light to chemical energy and vision. The correlation of rhodopsin conformational dynamics and its activation process at later stages are the most challenging targets in computer molecular modeling. The relative movement of the rhodopsin helices could be part of its light-activated photocycle. The experiments reveal that the movement of rhodopsin helices plays a key role in its activation. This evidently motivates the extremely time-consuming atomic modeling for biomolecular rhodopsin.

The structural and functional properties are known often to correlate well for a number of proteins. This fact can be obviously observed, for example, for the prion proteins. It is well understood that the misshapen prion protein (today cell biology's challenging topic) is generally associated with its disease-related form. In the normal human prion protein the prion molecules are coiled into helix and help to maintain the integrity of the nerve cells. As theoretical and experimental observations show, the infectious prion proteins are more sheet-like and coax normal prions to fold into infectious (disease-related) form. Thus, a central question of the physiological functionality of the normal prion protein and its aberrant form has closely to be connected with their structural transformations. The MD simulations were performed on the human PrP to elucidate the effect of point mutations related to the inherited Creutzfeldt–Jakob disease.

As a first computational problem, a model of the interaction of the flexible polyethylene chain has been investigated. For different types of heating the simulations have been performed on a special-purpose MDGRAPE-2 computer (provided in the joint cooperation with CAL RIKEN, Japan) [5]. The study on the polyethylene chain is an important task, being considered with a close relationship in the construction of *in vitro* and *in vivo* diagnostics tools, the development of new means for radiobiological protection and the designing of new materials. The simulations showed that the dependence of a final polyethylene ball configuration is effectively governed by a speed of the heating modes. The folding states and dynamical hydrophobic phases were directly captured and estimated from the computer simulations. The molecular simulation results obtained for the flexible polyethylene systems can provide a new insight on the development of nontrivial polyethylene aggregates with prescribed surface interaction properties, and so on.

The important point of the cell biology is the resonant diagnostics and monitoring of biochemical reactions in radiofrequency and optical electromagnetic range. The first interest in this field is related to the energies and eigenfrequencies related to the DNA double-helix. Working in this direction, we start a research of the eigenfrequencies and the geometry of the nucleotide doublets, adenine-thymine and cytosine-guanine. The calculations have been performed using the Gaussian98 package [6]. The minimal energy geometry of the duplets, and the eigenfrequencies, including those in microwave regions, were calculated. The results may be useful to study the cell self-repair mechanisms that are common of the radiation-induced and electromagnetic damages, e.g., by high-density radiowaves, cell phones, etc.

Regardless of increasing performance of the modern supercomputers, the direct simulation of large biomolecules — long DNA and protein chains are still beyond their capacities, basically because of the quadratically increased CPU and memory demands for the electrostatic forces. Working in these direction, we have created an object-oriented fast multipole code (based on the Greengard–Rokhlin algorithm) that is unique in Russia and enables one to simulate an electrostatic force in 10^6 particle systems using the Pentium-IV without any special chipsets.

RADIATION PROTECTION

The radiation monitoring for occupational exposure at JINR nuclear facilities was carried out by the automatic systems of radiation control (ASRC) and by portable radiometers and dosimeters.

In 2004 the individual dosimetry service maintained dose control to 1663 persons, including 59 visitors. The average individual yearly dose at JINR was 1.3 mSv. The maximum individual yearly dose was at DLNP (14.4 mSv).

The regular environmental monitoring of soil, plants and water from the river basins in the Dubna vicinity confirmed the conclusion: the environmental radiation pollution around JINR has remained constant for a long time and is due to natural radioactivity and products of global fallout only. Any contribution to radioactivity pollution of the environment from JINR nuclear facilities was not found.

The exceeding of planned personal doses at JINR was not observed in 2004. The level of radiation protection and control at JINR corresponds to the federal rules and regularities, which was confirmed by regular inspections.

SCIENTIFIC MEETINGS AND EDUCATIONAL ACTIVITY

The III Sissakian readings took place in Armenia on 30 May – 03 June. It was organized by the Scientific Council of RAS on radiobiology, Bakh Institute of Biochemistry, SRC RF Institute for Biomedical Problems, Joint Institute for Nuclear Research, Yerevan State University and Institute of Biochemistry of Armenian AS. The readings were supported by the Venetian office of UNESCO (UVO-ROSTE). More than 40 physicists and radiobiologists from Russia, Armenia and JINR participated in the readings. The readings' programme included 20 plenary reports on different objects connected with the scientific heritage of Academician N. Sissakian: biochemistry, radiobiology and photobi-

ology, space biology and medicine. The Russian delegation was headed by Academician-Secretary of RAS, head of IBMP A. Grigoriev and head of IBCh Professor V. Popov. JINR was presented by Vice-Director Professor A. Sissakian, Academician of RAS M. Ostrovsky and Professor E. Krasavin. The Russian delegation was received by the speaker of Armenian parliament A. Bagdasarian.

The 1st international workshop «Molecular Simulation Studies in Material and Biological Sciences», organized by DRRR, was held from 8 to 11 September 2004 at the International Conference Centre. The workshop was one of the first ones held in Russia, devoted to the computer molecular dynamics simulations of the biological and chemical physics problems. The workshop was attended by leading research experts working in various branches of sciences — computer molecular simulations, biophysics and chemical physics, nanotechnology, etc., from Japan, USA and European countries, Russian research institutes and universities, JINR. The research topics covered at the workshop included molecular dynamics simulations of DNA and proteins, nanoclusters, membranes and lipids, quantum biophysics, parallel computing for biomolecular simulations.

The education process at the «Biophysics» chair of the International University «Dubna» was continued. A total of 56 students are studying now the specialty «Radiation Protection of People and Environment». Twenty new students were admitted in 2004 to the chair. The first graduation of the students will be in 2005.

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