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Implications of Single-Particle Experiments for Track Theory, Therapy and Radiation Protection

Robert Katz

University of Nebraska-Lincoln, rkatz2@unl.edu

Francis Cucinotta

NASA Johnson Space Center, francis.cucinotta@unlv.edu

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EXTENDED ABSTRACTS

Proceedings of the 5th International Workshop: Microbeam Probes of Cellular Radiation Response

Stresa, Lago Maggiore, Italy, May 26–27, 2001

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Università degli Studi di Milano, Dipartimento di Fisica, Milano, Italy
Università degli Studi di Pavia, Dipartimento di Fisica Nucleare e Teorica, Italy

The extended abstracts that follow provide a summary of the Proceedings of the 5th International Workshop: Microbeam Probes of Cellular Radiation Response, held in Stresa, Lago Maggiore, Italy, on May 26–27, 2001, which was organized by INFN, Laboratori Nazionali di Legnaro, Italy and Università degli Studi di Milano, Dipartimento di Fisica, Italy.

There is increasing interest in the use of microbeam systems (1, 2), which can deliver beams of different radiations with a spatial resolution of a few micrometers or less, for radiobiological research. Single-particle microbeams can be used to address such questions as the relative sensitivities of different parts of the cell (e.g. nucleus compared to cytoplasm) and the effects of irradiation on non-hit neighboring (bystander) cells. For particle (e.g. α -particle) beams, irradiation with exactly one (or more) particle per cell can be achieved, allowing questions of risks of very low doses of ionizing radiations, such as radon, to be addressed. Several microbeams are now in operation, and others are being developed. The workshop provided a forum to assess the current state of microbeam technology and current biological applications and to discuss future directions, both technological and biological.

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tical beamline of the AVF cyclotron at JAERI-Takasaki, was used for cell irradiation. The number of ions traversing the sample was detected and counted with a plastic scintillator-photomultiplier tube assembly, and the irradiation was terminated with a beam shutter actuator, which was governed by a preset counter module. The cells were attached to a CR-39 ion track detector (100 μm thick) and then irradiated with 17.5 MeV/ μm ^{20}Ne or 11.0 MeV/ μm ^{40}Ar ion beams. Just before irradiation, the medium was removed to allow the ions to penetrate the cells and the CR-39 film. The beam was collimated with a 20- μm -diameter aperture, and the each cell was irradiated with 10 counted ions. Immediately after irradiation, the cells were re-covered with medium; then the CR-39 film was etched from the side opposite to the cell with an alkaline-ethanol solution at 37°C for 15 min. After a rinse with distilled water, the etched samples were observed under a phase-contrast microscope. The cell samples were then incubated continuously at 37°C to observe the effect of this etching treatment on the cell growth.

After 15 min of the etching treatment at 37°C, we could observe the ion-track pits on the CR-39 film. At each irradiation point, 9 to 12 ion-track pits were observed. Almost all ion-track pits were concentrated within the collimated diameter range. No significant effect of the etching treatment on cell growth was observed.

These results indicate that this method will provide us accurate information about the spatial distribution of the radiation from the ions. This means that, with this method, we can observe the position and the number of ion hits within and around the target cells at the beginning of the postirradiation incubation of cell samples. When studying low-dose effects, especially the effects of hits by single ions, the accuracy of information about the radiation is quite important. Therefore, this method will be quite useful in studies of the cellular effects of low-dose irradiation, especially in single-ion hit experiments.

Implications of Single-Particle Experiments for Track Theory, Therapy and Radiation Protection

R. Katz^a and F. A. Cucinotta^b

^aUniversity of Nebraska and ^bNASA Johnson Space Center

“Because the predominant exposure of cells in humans is to single isolated tracks, a critical question is what effects a single track is capable of producing and with what probabilities.” “Most of the current biophysical models. . . make the clear prediction that a single track can produce virtually all of the detrimental stochastic effects of interest.” “But one model, in particular (the amorphous track model of Katz and co-workers), disagrees fundamentally that a single low LET track has the ability to cause the cellular changes.” “This model leads to very dramatic differences in the predicted risk at low doses. . . ” “Because of the very major implications this would have if true, there may be strong grounds for critical evaluation of the model” (1).

That critical evaluation is now possible in single-particle experiments that are the subject of this workshop. Thus far, calculations from published equations, from published radiosensitivity parameters, and thus from predictions in real time have yielded agreement with measurements of cell survival after proton and α -particle bombardments, as well as with single α -particle-induced oncogenic transformations (2). From their experiments, the authors have concluded that “the measured oncogenicity from exactly one alpha particle was significantly less than for a Poisson-distributed mean of one alpha particle, implying that cells traversed by multiple alpha particles contribute to most of the cancer risk” (3).

Recall that our predictions are based on the application of the theory to high-fluence experiments with a variety of bombarding ions, up to argon, at energies up to 10 MeV/nucleon.

This theory also provides the motivation for ion-kill dosimetry (4), now being investigated as the basis for evaluation of the qualitative effects of high-LET radiations. Ion kill is also suggested as the basis for the differences in tissue response, for the loss of the benefits of fraction-

ation, and for late effects in neutron and high-LET radiation therapy (where overdose can be ruled out as the cause) and also as a basis for space dosimetry in regard to the protection of astronauts from the deleterious effects of cosmic rays. For these purposes, experiments based on the Biostack principle offer the greatest versatility in projectile type and energy (5, 6). Since the physical parameter that determines single-particle response is z^2/β , we propose that the response of a tissue or cell to different particles should match at the same value of this parameter.

Single proton bombardments in particular are needed to test both Katz's theory and the assumption that a single (electron or proton) track has the ability to cause cell killing, and transformation, as demanded by the linear, no-threshold extrapolation to low dose which forms the basis of radiation protection affirmations. This is an excellent opportunity for experiment to test both theory and the conventional wisdom.

There is frequently a hidden agenda in physical units and measurements. Thus dose, energy per unit mass, implies multiple random transits of charged particles through a designated target. Cross section is a probabilistic concept, not a geometric concept. It relates to the probability of an interaction between randomly placed targets and random trajectories of projectiles within a channel. The theory of RBE requires knowledge of cellular properties and the full particle energy spectrum in a radiation field, and it is not restricted to a sub-class of secondary interactions, like all secondary protons. Heat and temperature imply thermal equilibrium, which is not achieved in a “thermal spike”.

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Session IV

Chair: E. J. Hall

Center for Radiological Research, Columbia University,
New York, New York

Upgrading of the Gray Laboratory Soft X-Ray Microprobe with Aluminum K-Shell X Rays and Measurement of the Effect of a Carbon K-Shell X-Ray Beam of Different Size Focused into V79 Cell Nuclei

G. Schettino, M. Folkard, K. M. Prise, B. Vojnovic and B. D. Michael

Gray Laboratory Cancer Research Trust, Mount Vernon Hospital,
Northwood, Middlesex, HA5 2JR, United Kingdom

The X-ray microprobe developed at the Gray Laboratory was originally designed to produce carbon K-shell X rays (278 eV) by electron bom-