**BOOK REVIEW**

**Synergistic Interaction and Cell Responses to Environmental Factors**

**Authors:** Vladislav G. Petin and Jin Kyu Kim (Head of Biophysical Laboratory, Medical Radiological Research Center, Obninsk, Kaluga Region, Russia, and Korea Atomic Energy Research Institute)

The current ecosystem adapted to the effects of natural factors has been increasingly affected with new biological, mechanical, chemical and physical anthropogenic factors unprecedented in their power and diversity. Combined or synergistic interactions of the abovementioned environmental factors which have become a reality can result in negative consequences both for humans and the environment. Therefore, publication of thorough scientific information regarding the regularities and mechanisms of synergistic interaction of various physical and chemical environmental factors seems especially important.

This point drew attention of a popular publishing company, Nova Science Publishers, whose books being traditionally characterized by relevance and novelty are stored in the Library of Congress of the USA, Cambridge University and some other world renowned institutions, has published the ingenious book. It came into being due to a close cooperation of Vladislav Petin (Head of Biophysical Laboratory, Medical Radiological Research Center, Obninsk, Kaluga Region, Russia) and Jin Kyu Kim (Korea Atomic Energy Research Institute, Republic of Korea) widely recognized by the international scientific community.

In the seven chapters of the monograph the authors presented and systematized basic results of their experimental studies and a mathematically sound ingenious concept of synergistic interactions of factors of different nature. The material is represented through a gradual transition from the data obtained for prokaryotes to the ones for eukaryotes including mammalian cells (both animal and human ones), and comparison of the proposed ideas with epidemiological materials of Chernobyl origin.

A sufficiently wide range of issues is exposed quite obviously and easy to understand thanks to a uniform scheme of presentation used for each chapter: first, an abstract, then an introduction containing the tasks of research work, the obtained results of the research, and the conclusions followed by references for each topic. An extensive illustrative material given in the form of graphs and tables makes the monograph high informational.

Quite reasonably, the book begins with the chapter in which the response of cells belonging to various genotypes and having various physiological states to ionizing radiation being one of the environmental factors most dangerous with respect to radiation hygiene is discussed in detail. This agent is widely used both in medicine and biology for different purposes like diagnostics, stimulation, inhibition or sterilization in the form of both densely and/or sparsely ionizing radiation of various relative biological efficiency (RBE) levels. The authors rightly point out that now the RBE problem is of utmost importance also with respect to aerospace missions and environmental problems emerged after the reactor accidents in Chernobyl and Fukushima. A mathematical model describing the cell responses to ionizing radiation which includes a target theory and a stochastic approach has been developed. In various versions it was used as a basis for predicting the combined effects observed in the experiments.

In Chapter 2, a characteristic of the radio-protective and sensitizing effect of various chemical compounds is given. The experiments using haploid and diploid cells of various radio-sensitivity levels and genotypes showed that the mechanisms of the radio-protective and sensitizing effects can work both through formation of primary radiation damage and biochemical processes including a diploid-specific recovery following radiation damage.
Quantitative consistent patterns of the combined effect of various physical agents like ionizing radiations, a visible or an ultraviolet light (UV), and a thermal factor are discussed in Chapters 3 and 4. Based from the results of the research of a large number of objects including mammalian cells of various origins, a simple mathematical model describing the synergistic interaction of environmental factors occurring in the biosphere was developed. As a basic postulate for the model, an assumption that the synergism is due to the formation of additional effective kinds of damage caused by interaction of sub-damages ineffective in case of a separate application of the agents is used. The model predicts maximal synergy values and the required conditions. Moreover, the model provides prediction of the synergism dependence on the intensity of the agents applied, and the proportion of irreversible damages following combined exposures.

The mathematical approach to synergism (namely, forecasting and optimization) is developed in Chapter 5. As a result, synergism general regularities were determined and demonstrated which, as the authors reasonably suggest, are universal and do not depend on biological objects, methods for their examination or physical & chemical factors applicable at combined effects. In accordance with the single biophysical concept as proposed by the authors, the synergistic effect of a combined impact of two agents is due to formation of additional effective damages from which cells fail to recover. Based on the new synergy mechanism concept, an ingenious mathematical model was developed providing a quantitative description and prediction of environmental factors synergy patterns. The qualitative correlation of model-based predictions and experimental results is shown for a variety of biological objects and tests.

Chapter 6 presents data regarding quantitative forecasts for synergistic effects of various biological objects including viruses, spores, bacteria, and various types of yeast cells exposed to various combinations of ionizing radiation, high temperature, UV light and/or ultrasound. Here the prediction of the synergy dependence on the intensity levels of the agents used is of importance, in particular, the range of the temperature levels synergistically acting together with some physical and/or chemical agents is shifted to lower temperatures at decreasing intensity of the agents used indicating the principal significance of synergistic effects at low intensity levels of the factors really occurring in the biosphere.

In Chapter 7, the authors prove the universalism of the experimentally confirmed patterns of the synergistic effect, which lie in the fact that the data obtained using isolated protozoan organisms, can be extended to cultured mammalian cells. The mechanism of inhibition of the regenerative process following a combined effect of ionizing radiation and hyperthermia or chemicals increasing cell radiosensitivity rate was shown to be associated with the increase in irreversible damage levels so that they did not allow cell recovery. Also, an opportunity of interpretation of certain synergistic effects in humans using the proposed model is discussed, and a qualitative correlation with the forecast model is determined.

In general, the experimental and theoretical materials as observed in the monograph arrive at a fairly comprehensive picture of the features, regularities, mechanisms and interpretation approaches of diverse manifestations of synergistic phenomena at combined effects of harmful environmental factors on biological objects in the contemporary world.

The complex of the newly obtained results presented in this work is of fundamental importance with respect to understanding the mechanisms of synergistic effects and the ways of the acting agents
optimization to maximize the synergism, and be also useful for a number of practical applications in biomedical technology and environmental research.

This monograph, which is based on the latest achievements of up-to-date biological science, will certainly be useful for experts in radiation biology, medicine, ecology, environmental protection, and high school students interested in synergy issues.

Review provided by Professor V.A. Budarkov, Doctor of Biology, Chief Researcher, State Research Institution National Research Institute for Veterinary Virology and Microbiology of Russia (SRI NRIVVaMR), Russian Academy of Agricultural Science, Pokrov, Vladimir region, Russia