

Special Issue on Nonthermal Medical/Biological Treatments Using Electromagnetic Fields and Ionized Gases

I. INTRODUCTION

THE INTERACTION of electromagnetic fields with biological cells often has a negative connotation. We think of effects such as electric shocks and electric burns. There is the fear that exposure to electromagnetic fields may cause cancer and the opinion that electromagnetic radiation is a kind of pollutant. Much of the research on biological/medical effects of electromagnetic fields has therefore concentrated on potential *hazards* of electromagnetic radiation, on a better understanding of damage mechanisms and how to protect against them.

However, more recently, the *beneficial* effects of electromagnetic interaction with biological cells are receiving more attention, particularly nonthermal effects. For example, for a long time now electric pulses have been used to save lives in cases of heart failure, but now we are finding that they can also be used to diagnose and even help to treat cancer. There are clearly effects of electric field/cell interactions, which have a positive effect on our well-being. Pulsed electric fields have also been shown to be useful in bacterial decontamination, an effect used, for example, to make our food and our drinking water safer. Furthermore, they have the potential to protect us against the threats of bacterial contamination in biological warfare.

Pulsed power is the enabling technology in many of these new applications. Cancer treatment using electroporation, which is already in clinical trials, is based on the application of high-power electrical pulses to malignant tumors. Bacterial decontamination of liquid food and drinking water with pulsed electric fields successfully utilizes microsecond and submicrosecond high-power pulses. Research in both medical and biological applications is moving toward the use of shorter and more intense pulses where interaction with cell substructures becomes likely, and consequently exciting new effects are expected.

Resonant effects of low-power microwave and millimeter waves on micro- and macroorganisms are topics of intense study, mainly in Europe. High-power microwave and millimeter waves allow one to similarly explore and utilize nonlinear processes on the molecular level, with the potential to someday selectively modify molecular structures in cells. In the short wavelength range of the electromagnetic spectrum, the ultraviolet (UV) and the X-ray range, research on the effect on cells has already led to applications of pulsed power ultraviolet and X-ray sources for bacterial decontamination.

Equally exciting is the growing field of research into the application of plasmas for chemical and biological sterilization and decontamination. A number of industrial and university research groups have already demonstrated the remarkable ability of relatively cold ionized gases to rapidly kill bacteria cells while avoiding the excessive heat and/or harsh chemicals associated with current conventional sterilization techniques. This new approach poses major advantages for both defense and commercial medical applications.

In order to provide a forum for the exchange of information and ideas in these emerging research and technology fields, the First International Symposium on Nonthermal Medical/Biological Treatments Using Electromagnetic Fields and Ionized Gases (ElectroMed99, for short) was held on April 12–14, 1999, in Norfolk, VA. The symposium was sponsored by the U.S. Air Force Office of Scientific Research, the National Science Foundation, the IEEE Nuclear and Plasma Sciences Society, the Bioelectromagnetics Society, Old Dominion University, the Eastern Virginia Medical School, and the College of William and Mary. One hundred and thirty-five scientists from 12 countries attended.

In order to introduce the audience (which consisted of engineers, physicists, biologists, and clinicians) to these research areas, we invited prominent scientists to give tutorials and reviews on the important research areas in nonthermal treatments and on the supporting plasma, pulsed power, and microwave technology. Eighteen invited talks were given in the first two days of the meeting, covering a range of topics from basic microbiology to pulsed power technology. Approximately 60 contributed papers were presented in a poster session. The largest research and development area represented in the poster session was bacterial decontamination using pulsed electric fields, UV radiation, and nonthermal plasmas. The second largest area dealt with basic studies and medical applications of pulsed electric fields. The relatively large number of papers on pulsed field generators, mainly presented by scientists from the former Soviet Union, provided the audience with a good overview of leading-edge pulsed power systems.

We have placed the papers in this special issue in generally the same sequence in which they were presented at the symposium. Contributed papers are placed in topic groups following the respective lead papers. In some cases, however, we have deviated from the symposium sequence. In such cases we had the feeling that a particular sequence might make it easier for the reader to grasp a new research field.

The reader is introduced to the field of bioelectrics, the interaction of pulsed, high electric fields with cells, through five invited papers by Polk (University of Rhode Island), Foster (Uni-

versity of Pennsylvania), Weaver (MIT/Harvard), Zimmermann *et al.* (University of Wuerzburg, Germany), and Dev *et al.* (Genetronics, Inc.), respectively. They cover the range from fundamental effects to medical applications. Effects on cells can also be achieved with low-intensity electric field as discussed in the first contributed paper by Liu *et al.* (University of Chengdu, China). The enabling technology for bioelectrics, pulse power technology, is introduced in an invited paper by Kristiansen and Mankowski from Texas Tech University. This paper is followed by an overview of the bioelectrics research at the Efremov Institute in St. Petersburg, Russia, by Burtsev *et al.*

An attractive application of bioelectrics is the treatment of drinking water and liquid food with pulsed electric fields (PEF's). PEF research activities in the Netherlands (van Heesch *et al.*, University of Eindhoven), the United Kingdom (McGregor *et al.*, University of Strathclyde), and Japan (Katsuki *et al.*, Kumamoto University) are discussed in three following papers. Related to these methods is biofouling prevention using pulsed electric fields, a topic discussed by Ghazala and Schoenbach (Old Dominion University). Pulsed electric discharges as a means to decontaminate water is discussed in a paper by Efremov *et al.* (Trinity, Troitsk, Russia). Experimental observations on biological effects of high-power microwaves are presented in an invited paper by Kiel *et al.* (Brooks AFB). This is complemented by a review of low-intensity micro- and millimeter-wave effects by Pakhomov (McKesson BioServices) and Murphy (Brooks AFB). Biological effects of electromagnetic fields on the molecular level are discussed in an invited paper by Blank and Goodman (Columbia University).

The ElectroMed99 Symposium focused on biological effects of nonionizing radiation. However, there is strong interest in the scientific community and in the public on the effects and applications of ionizing radiation. This field is represented in four papers: an invited paper on structural changes in cell membranes due to ionizing radiation by Hannig and Lee (University of Chicago) and three contributed papers on bacterial decontamination by means of pulsed light and X-rays. The papers are authored by Anderson *et al.* (University of Strathclyde, U.K.), McDonald *et al.* (University of Missouri), and R. Curry *et al.* (University of Missouri).

Thirteen papers in this special issue are devoted to medical/biological applications of nonthermal plasmas. The invited papers presented at ElectroMed99 by Kunhardt, Montie, and Birmingham remain in their symposium sequence, although four new papers are inserted before Birmingham's. Readers will find Kunhardt's work to be a detailed review paper on the physics of air plasma generation. His discussions on the various techniques are important to anyone who would seek to apply air plasmas to medical/biological purposes. Montie's paper then provides a detailed description of just such an application; namely, the use of an atmospheric pressure air plasma for the destruction of biological pathogens. The next two papers, those of Laroussi *et al.* and Efremov *et al.*, then describe the results they achieved with similar atmospheric pressure approaches. The paper by Kondrashova *et al.* is a bit of a change of pace. It is inserted at this point to remind the reader of the long history of low-level air ionizers used for therapeutic (and sometimes

pseudotherapeutic) purposes. Importantly, the Kondrashova team specifically demonstrates how professional medical/biological studies can move such "faddish" applications into the realm of legitimate medical therapy for the improvement of air in modern closed working environments. The paper by Kelly-Wintenberg *et al.* then maintains the theme of air-quality improvement in its discussion of the novel "Volfilter" concept. This forms a convenient transition into the commercial world considerations, which Birmingham's and Hammerstrom's paper elaborates on in its presentation of various industrially oriented air plasma applications. In this similar commercial vein, the paper by Farrar *et al.* discusses large-surface air plasma decontamination/sterilization techniques. The papers by Roth *et al.* and Namihira *et al.* then go on to describe interesting plasma chemistry-related concepts that rely on the longevity of some of the plasma-generated active species in order to impose spatial distance between the plasma source and the desired treatment objective. In the paper by Kotov *et al.*, results are presented that indicate how air plasma chemistry can dramatically enhance the effectiveness and utility of existing approaches using e-beams for sterilization. Finally, the papers by Zengliang and Dubinov *et al.* discuss the possible mechanisms for the observed positive effects of ion bombardment of agricultural seeds.

II. CONCLUSION

The ElectroMed99 Symposium and this special issue are intended to help bridge the gap between disciplines that in the past were not considered compatible: on one side, pulsed power and microwave physics and engineering, as well as plasma physics; and on the other side, biology and medicine. As in any new encounter between research areas that seem fundamentally different, the language barrier between the disciplines needs to be overcome first, in order to initiate communication. Biologists and clinicians need to learn about the basics of pulsed power, electromagnetic fields, and plasma physics in order to recognize the potential of these technologies for their research. Our colleagues in the pulsed power, microwave, and plasma science areas, on the other hand, will be confronted with unfamiliar biological and clinical terms in some of the papers that follow.

We refer readers of this special issue to publications that emphasize biological and clinical research through the bibliographies of a series of introductory review papers. We have also asked the authors of these papers to express and explain their methods and findings in terms understandable to all readers. We understand, however, that this is not always possible. There is the danger that through oversimplification papers lose some of their scientific value. Therefore, reading and understanding these papers requires more effort than most of our other special issues in the IEEE TRANSACTIONS ON PLASMA SCIENCE. However, we hope that the reader feels that it is worth the effort. The contributions on biological and clinical issues open, in our opinion, a fascinating new research area for engineers and physicists, an area where they can make a strong impact. The Second International Symposium on Nonthermal Medical/Biological Treatments using Electromagnetic Fields and Ionized Gases, to be held in Norfolk, VA, in spring of 2001, will again

serve as forum for discussions and exchange of information on new developments in this research field.

It is our sincere hope that this special issue (and the ElectroMed99 Symposium that spawned it) can succeed in imparting to our colleagues in the physics and electrical engineering communities some measure of the true professional and personal enthusiasm that we now hold for this exciting field of "electromedicine." Research in this area affects the life and health of human beings. There is no more fundamental concern. We sincerely believe that the future opportunities in this field, whose dim outlines can already be perceived, are nothing short of staggering. The potential for the treatment of cancer without surgery, chemotherapy, or X-rays is, by itself, earth-shaking. When one also factors in the opportunities for rapid nonthermal sterilization/decontamination as well as possible intracellular repair, it is easy to become perhaps overawed.

Therein also lies a danger—"electromedicine" has been and remains a fertile field for medical charlatans. We have all heard of cases of individuals and groups who, through technical naiveté or greed or both, have sought to exploit the hunger for hope that fills the terminally ill and suffering. Nevertheless, the therapeutic effects of electromedicine are real; they simply require the serious studies and dynamic collaboration of electrical engineering/physics and medical/biological professionals in order to conclusively determine the true scope of those positive effects. The papers that appear in this issue reveal the early fruits of some pioneering collaborations. Much remains to be done. Many people are awaiting the answers.

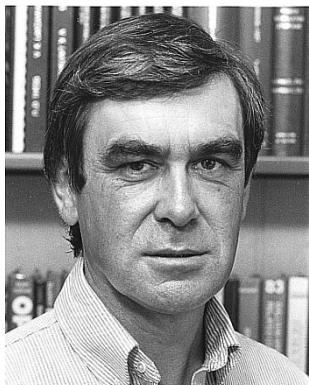
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Karl Schoenbach (F'94) received the diploma and Dr.rer.nat. degrees in physics from the Technische Hochschule Darmstadt (THD), Germany, in 1966 and 1970, respectively.

From 1970 to 1978, he was working at THD in the areas of high-pressure gas discharge physics and on dense plasma focus. From 1979 to 1985, he held a Faculty position at Texas Tech University, where he was involved in research on fast opening switches, especially electron-beam and laser-controlled diffuse discharge opening switches. In 1985, he joined Old Dominion University, Norfolk, VA. He was active in research on photoconductive switches until 1993 and has now concentrated his research efforts on high-pressure glow discharges and on environmental and medical applications of pulsed power technology. He has organized a number of workshops and conferences, most notably the 1991 IEEE International Conference on Plasma Science.



Robert Barker (M'89–SM'95–F'97) received the B.S. degree in physics from the Stevens Institute of Technology, Hoboken, NJ, in 1971, and the M.S. and Ph.D. degrees in applied physics from Stanford University, Stanford, CA, in 1972 and 1978, respectively.

From 1978 through 1982, he was an on-site Computational Plasma Physicist with G. Cooperstein's Light Ion Fusion group at the Naval Research Laboratory, Washington, DC. During that period, his collaborations with S. Goldstein resulted in several important discoveries on the fundamental nature of charged particle flow in axial and radial relativistic electron-beam pulsed power diodes. He then joined Mission Research Corporation, working with B. Goplen on improvements to both the 2-D MAGIC and 3-D SOS plasma simulation codes. He successfully applied those codes to explore novel accelerator and microwave source concepts. In 1984, he began his current career as a Program Manager for Plasma Physics at AFOSR. In this capacity, he actively fosters and participates in research in the areas of pulsed power, electromagnetic/electrothermal launchers, microwave/millimeter-wave generation, air plasmas, charged particle beam generation and propagation, explosive power generation, computational physics, and wargaming. He is currently coediting (with E. Schamiloglu) an IEEE Press book reviewing the state-of-the-art in high-power microwave sources. He is a Colonel in the U.S. Air Force Reserves, assigned to the Directed Energy Directorate of the Air Force Research Laboratory in Albuquerque, NM.

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Shenggang Liu (F'98) graduated from Southeast University (formerly Nanjing Polytechnic Institute), China, in 1955. He received the Ph.D. degree in physical electronics from the University of Electronic Science and Technology of China (UESTC), Chengdu, in 1958.

He became a Lecturer, Associate Professor, and Professor at UESTC in 1961, 1964, and 1977, respectively. He became Vice-President of UESTC in 1984 and has been President since 1986. He is Chairman of the Vacuum Electronics Society of China, Vice President of the Chinese Institute of Electronics, Chairman of the Academic Committee of the Chinese National Key Laboratory on High Power Microwaves (Beijing), Chairman of the Academic Committee of the Chinese National Key Laboratory on Intense Radiation (Chengdu), and Chairman of the Academic Committee of the Key Laboratory of the Research Institute of Electronics, Chinese Academy of Sciences (Beijing). He was a Distinguished Visiting Professor of the University of Tennessee, Knoxville, in 1991 and 1992, the Philips Chair Professor of the Technical University of Hamburg, Germany, a Visiting Professor at Leeds Polytechnic University, U.K., and a Visiting Professor of Pohang University of Science and Technology, Korea. He is also Honorary Professor of many Chinese universities. He has lead various research projects on gyrotrons, free electron lasers, and plasma electronics since 1964. More recently, he has been the Principal Investigator of the National Key Research Project on "Basic research of microwave plasmas and their applications" funded by the National Science Foundation of China. He is presently a Distinguished Visiting Professor at Old Dominion University and the College of William and Mary, working in the field of microhollow cathode discharges, microwave plasma excited excimer lasers, and electromagnetic field effects on biological cells.

Prof. Liu was elected an Academician of the Chinese Academy of Science in 1980. He is a member of the International Electromagnetic Academy, Massachusetts Institute of Technology.

A magnetic field (MF) is a magnetic force that extends out from a magnet and can be either static or dynamic. These MFs are produced by electric currents and specifically as a result of electron movement. But what does that have to do with pain management? Biologic nonthermal means that a modality does not cause significant gross tissue heating. Physically nonthermal refers to being below the thermal noise limit at physiologic temperatures.² The energy level at thermal noise is much lower than that required to cause heating of tissue, so any physically nonthermal application is automatically biologically nonthermal. Some traditional applications that use electromagnetic radiation include the entire family of therapies known as electrophysical agents. Nonthermal biocompatible plasma (NBP) (or plasma) is produced by applying a sufficiently high-voltage electric field across the discharge gap to initiate a breakdown of gas at atmospheric pressure [24]. When NBP is generated, the major components of charged particles, neutral gas species, reactive species, electric field, and radiation are produced. NBP was first employed in antimicrobial applications, because it produces a variety of biotoxic agents that include reactive species, UV radiation, and charged particles. Initially, NBP was generated by ionizing neutral gases with high voltage. Advances in these technologies led to the organization of dedicated sessions at international conferences such as the IEEE International Conference on Plasma Science and to two international symposia on "Nonthermal Medical/Biological Treatments Using Electromagnetic Fields and Ionized Gases" (ElectroMed'99 and ElectroMed 2001). These conferences and symposia brought together scientists from around the world working in fields related to physics, electrical The dialogue among these groups generated new interest and excitement, fostered cooperation and collaboration among disciplines, and provided the basis to establish new research programs in the United States and abroad. Tangible examples of