June 23 to 27, 2002, Québec City, Canada

24nd Annual Meeting of the Bioelectromagn

by Jörg Reißenweber

1 Preface

There is still strong controversy in the public over the health damaging potential of electromagnetic fields. Aiming to do its share towards clarifying this issue, the 24nd Annual Meeting of the international Bioelectromagnetics Society provided a whole lot of new insights into the issue of biomedical effects of power supply low-frequency electric and magnetic fields as well as high-frequency electromagnetic fields used in mobile communications and by the new UMTS technology (see REFLEX program). Again, human health issues - directly or indirectly - related to electromagnetic field effects, were the focus of many presentations, of lectures as well as posters. And again, there was a quite remarkable number of German contributions to the topic.

A lot of stir was caused by the lecture of the group around D. Leszczynski of the STUK Radiation and Nuclear Safety Authority, Helsinki, Finland. In cooperation with other European researchers, the group claimed to have found evidence that mobile radio radiation might modify expression of different genes playing a part in the organism's stress response: alterations of gene expression have been discovered for different field exposure periods, SAR values, and cell systems (see below). Since the relevance of these results had not been thoroughly evaluated yet, media interest was huge: so, for example, Leszczynski did a much-noticed interview to the American news channel CNN.

Again, much space was given to medical aspects of electromagnetic field applications, both in the area of diagnostics as well as of therapy (see also Plenary Sessions I and II, and Special Symposium III within session 10: „Emerging Therapies"). Obviously, certain progress has been made in cancer therapy (through use of static magnetic fields) and in pain treatment (also using static magnetic fields), as well as, for example, in the treatment of the arm lymphedema after breast removal surgery (using pulsed high-frequency fields). However, these applications still are in their infancy.

Contrary to past meetings, this time the sessions of the sub-committee SCC 28 of the Institute of Electrical and Electronics Engineers (IEEE), as well as those of the IEEE working groups COMAR and ICES did not take place prior to but after the congress, on June 27 to 30, 2002.

2 Plenary lectures

All four days of the meeting began with plenary sessions:

- **Plenary Session I:**

Transcranial Magnetic Stimulation

(chaired by Shoogo Ueno, Japan, and Frank Prato, Canada)

– Shoogo Ueno, Japan, gave an overview

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of the present knowledge about transcranial magnetic stimulation (TMS) that has become an important tool for examining human brain functioning, on the one side, and for the treatment of diseases of the central nervous system, on the other side. So, for example, he could show that TMS can disrupt associative learning. Additionally, he emphasized the importance of repetitive stimulation for the recovery of damaged hippocampal neurons of rats.

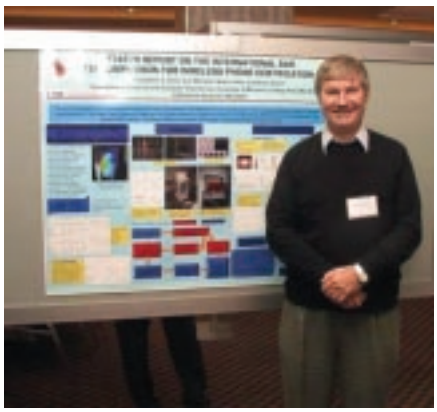
– John Rothwell, England, gave a detailed account of TMS effects on the human brain. He concluded that TMS is the best tool for affecting brain activity. In particular, applications of diagnostic techniques like positron emission tomography, magnetic resonance imaging and electroencephalography would be promising in reaching a better understanding of TMS effects.

– Eric Wassermann, USA, again explained in detail how TMS of the brain has been combined with different techniques for measuring brain activity in order to characterise local mechanisms of different TMS effects, and to find correlations between the stimulated area and other brain regions. These techniques include measures of the cerebral blood flow (magnetic resonance imaging and positron emission tomography), as well as of brain matter alterations (positron emission tomography with induced 18-fluorodeoxyglucose), and the electroencephalogram. In detail, the author dealt with the advantages and drawbacks of all these techniques. He concluded with the remark that TMS, when refined and extended to other application areas, will gain even more importance – above all, in combination with other measurement techniques.

• Plenary Session II:
Pain – Etiology and treatment
(chaired by Michael McLean, USA)

– Ravi Menon, Canada, spoke about neutral substrates of pain perception in humans studied using functional magnetic resonance imaging. As a result of this study, he claimed that there are identifiable brain areas that may exacerbate psychophysical pain perception in acute and chronic pain. According to Menon, the search for possibilities of intervention to specifically activate such brain regions thus could open up new opportunities for the treatment of chronic pain.

– Stefan Lautenbacher, Germany, gave a vivid overview of the role of pain perception of chronic pain development, and of the reasons for gender specificities. He concluded that women more strongly than men tend to develop chronic musculoskeletal pain like fibromyalgia, myofascial pain, tension-type headache, pain in the area of the temples and the jaw because of a weaker pain inhibitory control system. In women, this leads to a more intense pain per-



ception and to a heightened risk of developing chronic pain.

– Alex Thomas, Canada, spoke about pain therapies and diagnostic techniques based upon magnetic field application. He concluded that, at present, many physicians refer their chronic pain patients to non-pharmacological therapies, in other words, to complementary or alternative medicine. In his view, this includes treatment with low-frequency magnetic fields which, together with other therapies, could help to reduce annual costs per patient for pain treatment (in the USA, for example, 10,000 to 15,000 dollars per year). Recent studies have shown that pulsed magnetic fields could help to effectively soothe acute pain.

• Plenary Session III: Epidemiology (chaired by Joachim Schüz, Germany)

– Maria Feychting, Sweden, gave an overview of advantages and limitations of epidemiologic approaches for investigating health effects of electromagnetic fields. So, according to her, epidemiology provides very clear evidence determining whether exposure used by environmental medicine contributes to health hazards. In detail, she dealt with the issues of „misclassification" and „confounders". She concluded with the assertion that it is a misapprehension to believe that epidemiologic studies are easily understood or easy to perform.

– Leeka Kheifets, WHO, Switzerland, spoke about electromagnetic fields in public health care. The World Health Organization (WHO) has published several basic surveys on this issue, partially in cooperation with the International Agency for Research on Cancer (IARC) in Lyon (on cancer), and the National Radiological Protection Board in the United States (on neurodegenerative diseases). In 2003, the WHO will present a rigorous health risk assessment from magnetic fields including a description of field sources and dose-response relations; there will be further risk calculations for other, non-cancerous diseases. This evaluation will be published as a WHO Environmental Health Criteria (EHC) monograph.

– Mary McBride, Canada, gave an overview of epidemiologic studies having been performed to investigate high-frequency fields and/or microwaves focusing on potential health risks in the area of wireless communications. Her conclusion is that, at present, epidemiologic data are inadequate for the evaluation of health risks related to exposure to high-frequency fields and/or microwaves. Most of the earlier epidemiologic studies are of limited use, mainly because of methodologic limitations, in particular with respect to risk assessment. Moreover, at times, information on confounders is lacking; there is a lack of statistical power, or there are problems in exposure assessment and other aspects of study design. According to the author, more recent studies, including the ongoing large mobile phone study of WHO, will produce more definitive results. This study will examine the risk of brain and salivary gland tumors, as well as leukemia risk, involving 13 countries in Europe, North America, and the Pacific Rim, and is overseen by the IARC.

• Plenary Session IV: Mechanisms of Interaction (chaired by Abraham Liboff, USA)

– Stefan Engström, USA, gave an overview of the present state of knowledge about physical interaction mechanisms for electromagnetic field transduction in biological systems. He emphasized that transcranial magnetic stimulation could be useful in treating behavioral disorders and epilepsy, as well as in dealing with the radical pair mechanism, resonance models, ferromagnetic effects, and light as an electromagnetic phenomenon.

– Martin Blank, USA, spoke about the various potential effects of fields on biological systems from simple enzyme reactions to gene induction and protein biosythesis, and, among other things, dealt with his previous studies investigating transcription processes during stress response to fields. He suggested that these processes are caused by fields interacting with electron transfer in the DNA.

– Dean Astumian, USA, presented possible effects of high-frequency low-intensity electromagnetic fields on repair mechanisms during DNA synthesis. He emphasized that there is strong evidence for said fields not being capable to directly affect most biological processes. One single exception could be DNA reading during transcription where a protein repeatedly interrogates a certain DNA base sequence before another, corresponding protein is synthesized. Possibly, a weak oscillating field could slightly modify this moving back and forth over the DNA hypothetically leading to less fidelity of transcription and, subsequently, to health effects. However, threshold values for such effects still would be many orders of magnitude larger than the field strengths typical in environment.

2 Short summaries of selected sessions and lectures

– M. Fedrowitz, Hannover, Germany, dealt with magnetic fields effect in the DMBA breast cancer model using different substrains of Sprague-Dawley (SD) rats. She pointed to the unsuccessful attempts of the American Battelle Institute to replicate earlier results of the Hannover work-

ing group (tumor co-promoting effect of 50-Hz fields in the mT range on breast cancer in the rat), in the following seeking to explain these contradictory results: the test presented here consciously applied different substrains of SD rats because genetic differences between individual substrains are seen as the cause of conflicting test outcomes. The speaker concluded that the different reactions of mammary gland tissue in the SD-1 and SD-2 substrains confirm earlier studies suggesting that substrains markedly differ in their sensitivity to the carcinogen DMBA, and to 50-Hz magnetic field exposure in the mT range.

– J. Silny, Aachen, Germany, spoke about state-of-the-art knowledge about perception, adaptation, and pain thresholds triggered by electromagnetic fields and associated current densities induced in tissue. The aim was to determine internal current densities in the tissue at the perception threshold as a measure for receptor sensitivity in the skin compared to non-adequate stimulation. The result was a value of 170 mA for the perception threshold at a current strength of 50 Hz. Based upon this value, there is a tissue current density of 30 mA/cm² at the site of the excited mechanical receptors as a result of a worst-case scenario. The speaker concluded with the assertion that for threshold value determination current density is more adequate than current strength since it is not dependent on the individual test design, as is the case with current strength. Moreover, current density mirrors the real situation within an organ.

– J. Silny held two other lectures, one dealing with the effect of GSM signals of different frequencies on interference thresholds of cardiac pacemakers, the other dealing with the assessment of pacemaker responses to low-frequency fields.

– W. Sontag, Karlsruhe, Germany, spoke about induction of heat shock proteins in HL-60 cells by low-frequency magnetic fields. He emphasized that the treatment of these cells with thermal stress (30 min at 43° C) leads to a 2,5-fold induction of the heat shock protein (hsp) 72 with a maximum at 2 hs after treatment. Interestingly, a 15-min exposure to a magnetic 50-Hz flux density of 1 mT showed a similar result: the hsp-72 level increased to a maximum value 2 hs after heat treatment, afterwards decreasing below control value. In the frequency range between 0 and 60 Hz, the hsp-72 protein level only at 20 Hz (decrease) and at 50 Hz (increase) showed statistical differences from control tests. The lecturer concluded that magnetic field exposure of HL-60 leukemia cells, dependent on frequency, modifies hsp-72 expression, even though field treatment under the given conditions (15 min at 1 mT) is less effective than thermal brain induction.

– F. Thoss, Leipzig, Germany, reported spectacular findings of research done in the visual system. So he found out that alterations of the geomagnetic field may affect the sensitivity of the human eye, measured by means of the differential threshold. When the direction of view was related to the direction of the geomagnetic field, human visual sensitivity was affected; when the direction of the artificially produced geomagnetic field was changed, visual sensitivity changed as well.

• Session 11: Animal Studies II (chaired by Bernard Veyret, France, and Ronald Seaman, USA)

– L. Gatta, ENEA, Biotechnology Unit, Rome, Italy, reported on in vivo experiments performed in peripheral lymphocytes of C57BL/6-mice being exposed in a TEM

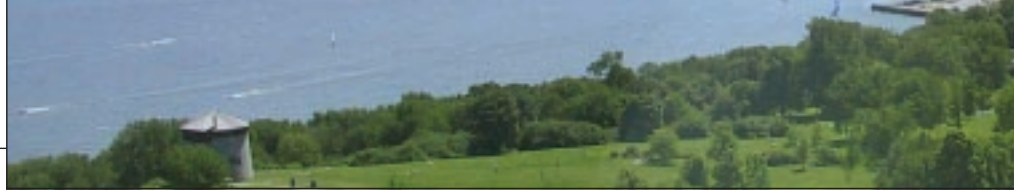
cell over 1, 2 or 4 weeks to fields of 900 MHz (GSM; 1 or 2 W/kg). Parameters tested were cell counts, cytokine production, cell phenotype, as well as the expression of the early activation markers CD 69 and CD 25. Under these experimental conditions, results failed to demonstrate any field effect on peripheral lymphocytes.

– J. Buschmann, Fraunhofer Institute of Toxicology and Aerosol Research, Hannover, Germany, spoke about effects of pulsed high-frequency radiation at a carrier frequency of 890 MHz (modulated with 1.733 kHz, 217 Hz, 2 Hz, and integer multiples therof) during pregnancy on Winstar rat offspring. The following reproductive parameters were determined: uterus weight, number of corpora lutea, implantation sites, number and localisation of early or late resorptions, number and position of living and dead fetuses, gender, position and individual weight of living fetuses, and, further, the individual placenta weight and externally visible anomalies of the fetuses, as well as skeletal and visceral anomalies. Result: Statistically significant field effect on whole body weight increase and weight increase of mother animals could not be found, with the exception of uterus weight, though values in the exposed group were smaller than in the sham-exposed group. The animals showed no unusual clinical symptoms during the study; neither mortalities nor abortions or premature births were seen in exposed and non-exposed females. However, the observed – statistically non-significant – effects, especially on weight gain of mother animals, on egg loss before and after implantation, on fetus weight (in male fetuses significant!), and on placenta weight could be seen as evidence for the onset of unspecific adverse effect of field exposure on prenatal development.

– M. La Regina, Division of Comparative Medicine, Washington University School of Medicine, St. Louis, USA, held a lecture on effects of chronic exposure to typical mobile radio fields (835.62 MHz EMCW, or 847.74 MHz CDMA) on spontaneous tumor incidence in F344 rats. Subject of postmortal macroscopic and histopathological examinations were nearly all organs including heart, brain, spinal cord, nasal cavities, salivary glands, esophagus, stomach, intestines, liver and pancreas, adrenal glands, thyroid, kidneys, urinary bladder and reproductive organs, lungs and trachea, spleen, thymus, and cervical lymph nodes. Here, numbers and types of tumor and incidence of hyperplasia for each organ were compared with the control group. The result showed that chronic exposure to above mentioned high-frequency fields had no influence on survival rate, body weight, or on spontaneous tumor incidence in F344 rats.

– L. De Jager, School of Health, Bioemfontain, South Africa, held a lecture on effects of a 50-Hz magnetic field in the flux density range of 0.5 to 77 mT (average value: 2.75 mT) on the immune status of the mouse (mus musculus) during long-term or short-term exposure. Exposure duration was 1 week, 14 weeks or 12 months. Result: There were statistically significant differences between the numbers of cells in lymphocyte subpopulations in the exposed as well as in the control group. Other discernible differences between immune parameters, however, were not significant. The lecture concluded with the suggestion that immune system response to magnetic fields probably depends on exposure length.

– R.L. Seaman, Microwave Bioeffects Branch, Brooks AFB, Texas, USA, spoke about single exposure of 12 Sprague-Daw-



ley rats to pulsed microwave radiation in the 1.25-GHz frequency range (duration: 6 ms; specific absorption rate: 0.6 W/kg) showing no effect on locomotor activity and/or acoustic startle immediately after exposure. Only one of the behavioral variables, the overall duration of stereotypy activity, as well as the colon temperature of the rats were altered differently in the exposed and in the control group. The conclusion is that field exposure is not capable to measurably affect the majority of neuronal circuits (underlying most behaviors).

• Session 13: Special Symposium IV A: Combined Effects of Electromagnetic Fields and other Agents (chaired by Vijayalaxmi, USA, and Junji Miyakoshi, Japan)

During this session, only few new insights were presented; most lecturers focused on interpreting already known results. All in all, we can say that to-date results of the REFLEX program point to possible effects of exposure to high-frequency electromagnetic fields on biological systems. However, replication is still to be done.

• Session 14: Special Symposium IV B: Presentation of REFLEX Results (chaired by Franz Adlkofer, Germany)

– In his introduction, F. Adlkofer, VERUM foundation, Munich, Germany, in brief presented the REFLEX program and the 12 research partners participating in it. Their task was to resolve open questions related to the effects of electromagnetic fields at cellular, subcellular and molecular levels condensed into five work packages. Each of these work packages included direct and indirect genotoxic effects of electromagnetic fields, as well as field effects on differentiation and function of embryonic stem cells, effects on protein biosynthesis and gene expression, and, further, field effects on cell transformation and apoptosis. The last work package included quality control; exposure conditions of different cell lines in electromagnetic fields, as well as dose measurement and temperature were recorded to obtain replicable and reliable data.

In the following, some subprojects of the REFLEX program were particularly referred to:

– S. Schuderer, ITIS, Zurich, Switzerland, spoke about exposure systems and dosimetric quality control within the REFLEX program: According to him, to date five HF and four ELF setups have been installed in the laboratories of the VERUM research group which he described in detail. One aim was to keep to the minimal requirements for test setups of bioexperiments defined in 2000 by Kuster.

– H.W. Rüdiger, Div. for Occupational Medicine, University of Vienna, Austria, spoke about genotoxic effects of low-frequency electric and magnetic fields (50 Hz; 24 h; flux density: 1000 mT) on human cells in vitro. For identification of DNA single- and double-strand breaks, the alkaline and the neutral comet assay were applied. The speaker emphasized that low-frequency intermittent field exposure could produce replicable and dose-dependent clastogenic effects, mostly double-strand breaks; the dose-response relation began to show at 70 mT (the most effective exposure pattern being 5 min on/10 min off). Contrary to this, there were no DNA single- or double-strand breaks at continuous exposure.

– C. Maercker, Center for Genome Research, Heidelberg, Germany, spoke about studies on gene expression at exposure to low-frequency electric and magnetic fields with different on/off time patterns (50 Hz; 2.3 mT; 5 min on, 30 min off over a period of 6 hs; or 50 Hz; 1000 mT; 5 min on, 10 min off over a period of 24 hs; or 50 Hz; 100 to 2000 mT; 5 min on, 5 min off over a period of 16 hs; or 100 mT; continously over a time period of 42 hs). Human fibroblasts; embryonic stem cells of mouse (wildtype and p53 deficient), human promyelocytic cells (HL 60), human neuroblastoma cells (NB 69) were exposed. Results showed evidence that ELF fields may positively affect NB-69 cell proliferation. As well, genes of the nicotinic receptor gene family were shown to be potentially affected by fields. These experiments presently are repeated at the level of protein biosynthesis. Apparently, further experiments with RNA from different cell lines using even more refined techniques for examination will be necessary to take a closer look at possible up- and down-regulation of genes like egr-1, p21 and c-jun, etc., by EMF fields.

– F. Adlkofer (see above) reported on results of the Berlin working group from the Department of Clinical Chemistry, Klinikum Benjamin Franklin, Freie Universität Berlin (K. Schlatterer, R. Tauber, R. Fitzner) on genotoxic effects of high-frequency fields. Cells of the human promyelocytic cell line HL 60 were exposed to a continuous 1800-MHz fields at 37° C (SAR: 1.3; 1 W/kg/24 hs). DNA double-strand breaks were measured by the comet assay. Result: There was evidence for the existence of cells with an increased sensitivity to genotoxic field effects. According to the author, there could be an association with repair enzyme alterations.

– B. Billaudel, PIOM, École Nationale Supérieure de Chimie et de Physique, Bordeaux, France, presented knowledge ob-

tained from in vitro tests investigating effects of mobile radio radiation on gene and protein expression. The aim was to expose a human endothelial cell line, on the one hand, and rat glioma cells as well as pluripotent embryonic stem cells, on the other, to different field patterns at three different research sites (900 MHz GSM singal [SAR: 0.2 W/kg and/or 2 W/kg], 1800 MHz GSM signal [SAR: 1.5 W/kg and/or 2 W/kg]). Gene expression was determined by polymerase chain reaction. Results provided evidence for mobile radio radiation being able to modify the expression of different genes involved in the regulation of stress response. Gene expression alterations were discovered for different field exposure lengths, SAR values and cell systems.

– Moreover, B. Billaudel spoke on the topic: „Do low-frequency or high-frequency fields affect apoptosis?“ His conclusion is that overall results of the REFLEX program so far do not provide evidence for a possible association between high- or low-frequency fields and apoptosis in cell cultures.

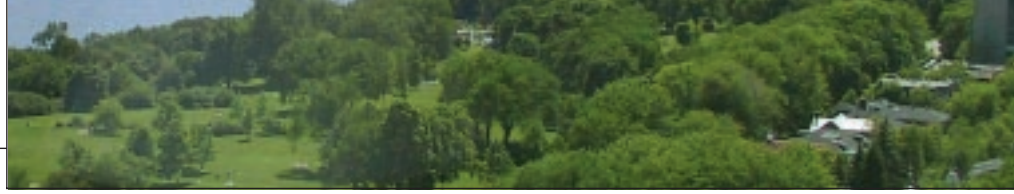
– Finally, F. Adlkofer in short summarised to-date available results of the REFLEX program: Though only the first half of the REFLEX research period has passed, there is sufficient evidence for a possible field influence on cells at the DNA level. In this context, he primarily referred to DNA strand breaks and genotoxic effects concluding that the search for molecular, subcellular and cellular mechanisms that may be affected by electromagnetic fields, in any case should be continued. Since the relevance of these mechanisms for human health is still unclear, the question remains whether they are relevant at all for the whole organism and for disease pathogenesis. One of the aims may be to identify genes which respond to field exposure.

3 Short summaries of the posters presented by the Electropathological Research Center

– In his poster presented by J. Reißenweber, E. David, Electropathological Research Center, University Witten/Herdecke, Germany, dealt with new preliminary results on the issue of lymphocyte migration in 50-Hz magnetic fields. Seemingly, the percentage of moving lymphocytes with magnetic field exposure is higher than that without exposure, but not average migration velocity. There is discussion about a microthermal effect caused by the magnetic field possibly playing a part in leading to these findings.

– J. Reißenweber, Electropathological Research Center, University Witten/Herdecke, Germany, reported on the serious strain felt by persons being subjectively convinced of being electrosensitive. Therefore, he demonstrated another approach aiming to clarify the phenomenon of self-diagnosed so-called „electrosensitivity“ presently being the focus of the medical field of electropathology: the examination of microcirculation in subjectively so-called electrosensitive persons compared to healthy subjects, both at exposure to a magnetic 50-Hz field with a flux density of 96 mT, and without exposure. Results showed no significant differences in microcirculation between both groups, that is, so-called electrosensitive persons and healthy test persons. Thus, according to the author, we will continue to speak of them as „patients“ but of concerned persons since an official diagnosis „electrosensitivity“ is not yet justified.

– A. Wojtysiak, Electropathological Research Center, University Witten/Herdecke, Germany, presented a poster dealing with potassium currents affected by 1.9-GHz



fields in astrocytes as a non-thermal effect. He emphasized that the control of the ionic current through the cell membrane is one of the most important mechanisms for cell responses to environmental factors. Earlier experimental studies conducted in the cell membrane using weak electromagnetic fields had shown contradictory results, especially regarding non-thermal effects of high-frequency field exposure. The presented approach examined how the principally unachievable precondition of identical temperatures whether with or without high-frequency field exposure could be fulfilled. But the presented approach claims to nearly achieve just that by artificially producing the same temperature as well in control tests without field exposure: transient outward potassium currents were examined by means of the whole cell patch clamp technique, both at exposure to a high-frequency electromagnetic field and at conventional heating. The result showed that transient potassium transmembrane currents increase, dependent on temperature, both at heating and at high-frequency field exposure. Remarkably, potassium currents increase at 37° C in most cases is slightly reduced compared to conventionally heated samples, if this temperature level was achieved by field exposure. In the temperature range between 37° C and 40° C, reduction at field exposure can reach a maximum of 25% thus being statistically significant. The author concludes that, as an explanation for this discrepancy in test results with and without field exposure, a field influence on the open probability of the channel gate is more likely than effects on the diffusion behavior of ions in the membrane channel molecule. Differences in sample heating as a cause are excluded by the author.

4 Evaluation of the BEMS 2000 meeting from the perspective of the Electropathological Research Center

Dr. med. Jörg Reißenweber
Electropathological Research Center
Department of Medicine,
University Witten/Herdecke
(Chair: Prof. Dr. med. Eduard David)

Overall, we may say that the results presented during the meeting do not provide sufficient cause for public concern. There was a general tendency to objectify discussion concerning the topic of biomedical field effects based upon scientific knowledge. From a scientific – as well as a medical – perspective, further research aiming to resolve still open questions on potential health hazards and/or biomedical effects of electromagnetic high-frequency fields of mobile radio technology, as well as low-frequency electric and magnetic fields of energy technology, is necessary. It is by scientific research, also performed in the human whole organism, that fears ultimately can be put to rest where they obviously are unfounded: the medical field of psychoneuroimmunology has found convincing evidence that psychic distress like – even unfounded – fear, depression, etc., alone may favor a whole spectrum of diseases, starting with an increased susceptibility for infections caused by a weakening of the immune system via the central nervous system. This also sheds light on the phenomenon of subjectively perceived so-called electrosensitivity being associated with field exposure.

The fact that both diagnostic as well as therapeutical applications of electromagnetic fields in medicine were presented in a separate session, shows that the Bioelectromagnetics Society also in future will be prepared to even more strongly examine not only potential health hazards of low- and high-frequency fields but also to look at potential healing and soothing field effects. This is a general trend which has been observed for quite a few years now.