UDC 534

RESEARCH IN FACULTY OF ELECTRICAL ENGINEERING, LABORATORY OF BIOCYBERNETICS, CHAIR OF BIOMEDICAL ENGINEERING UNIVERSITY OF LJUBLJANA

Maša Blažič, študentka, Katja Ružič, študentka
Scientific advisor - Prof. Damijan Miklavčič
+386 1 4768 456 e-mail:damijan.miklavcic@fe.uni-lj.si
University of Ljubljana, Faculty of Electrical Engineering,
Trzaska 25, 1000 Ljubljana, Slovenia

Since its foundation in 1963, the Laboratory of Biocybernetics has been involved in the study of interaction between electromagnetic fields (EMFs) and biological systems. This includes both the *i*nvestigation of harmful effects of EMFs on organisms and the exploitation of beneficial effects of EMFs for therapeutic and diagnostic purposes. During the period from the mid-1960s to the end of the 1970s, the major research topic was Functional Electrical Stimulation(FES) for the restoration of motor functions impaired by different types of injuries or neuromuscular diseases.

Biomedical engineering is a very diverse interdisciplinary field of study linking engineering with medicine and biology. Biomedical engineering strives to expand and deepen our knowledge of the composition and functioning of complex biological systems in different environments by employing engineering approaches and methods. Biomedical engineering continually develops new technologies, devices and procedures for the monitoring, maintenance and improvement of health and the quality of life; it is among the most rapidly evolving areas and will have an important impact on our future lives.

Since 1980s, our main field of research are the investigations of the influence of electric currents and electromagnetic fields on the physiological state of cells, tissues, organs, and the body as a whole, Fig. 1.

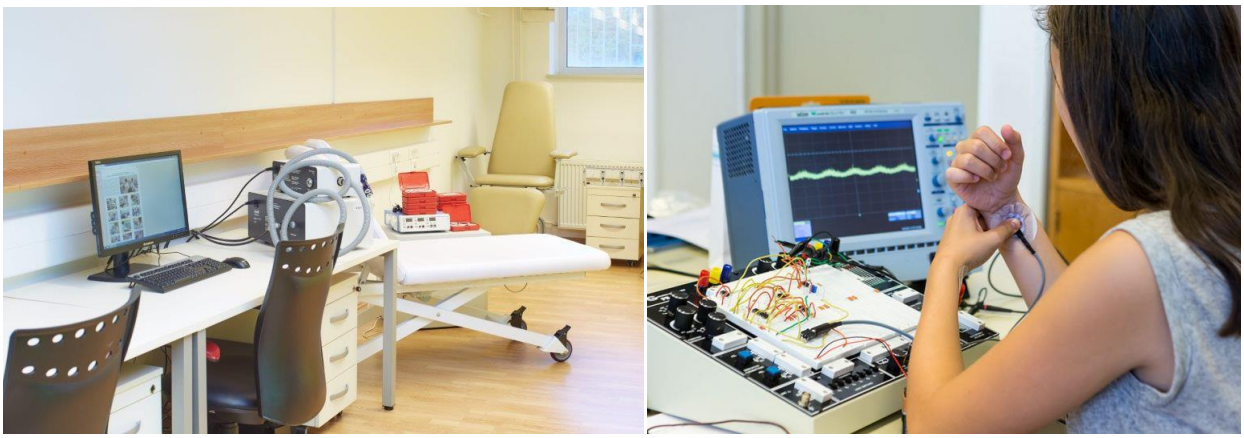

Fig. 1 – Investigations of the influence of electric currents and electromagnetic fields on the body

Since 1990s, our investigations gradually focused on cell membrane electroporation with its applications in biology, biotechnology, and medicine, particularly electrochemotherapy of tumors (ECT) and electrogene therapy (EGT), where we are among the leading research groups in the world.

At the Laboratory of Biocybernetics the infrastructural centre “Cellular Electrical Engineering” is located. Main parts of infrastructural centre which enable the research are the Unit for electric pulse generator development and the Unit for lipid bilayers, biological and microbiological research, Fig. 2.

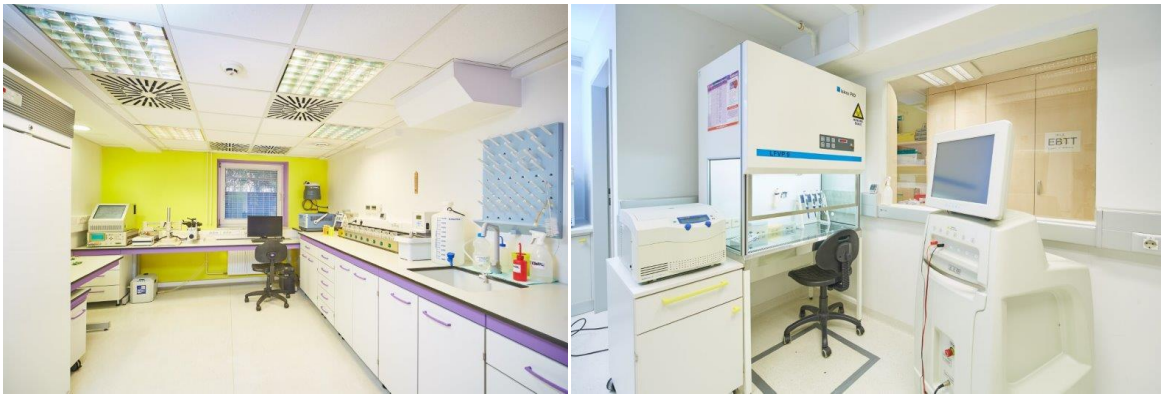

Fig. 2 – Infrastructural Centre «Cellular Electrical Engineering»

The main purpose of infrastructural centre is the study of interactions between electromagnetic fields and living organisms. Main areas of research supported by infrastructural centre are:

a). cell and tissue electroporation and its use in electrochemotherapy of tumors and gene electrotransfection

b). development of electrical equipment and electrodes for research and clinical work

c). design of microelectrodes, microchambers and microstructures that enable application of electric pulses and monitoring of their effects on level of lipid bilayers, lipid vesicles, cells and microorganisms.

We are studying the electroporation phenomenon using both theoretical and experimental approaches, and on scales ranging from atomic-molecular (MD simulations), membrane-level (lipid bilayers and vesicles), organelle- and cell-level (cells in suspension, attached cells, and clusters of them), up to tissues and organs (experiments on animals in cooperation with the Institute of Oncology Ljubljana), and we also collaborate in clinical studies (again in cooperation with the Institute of Oncology Ljubljana). Our work encompasses analytical derivations, numerical computations and simulations, experiments *in vitro* and *in vivo*, treatment planning, and we are also developing devices for research an clinical use, as well as information technology for clinical trials. A more detailed description of our work in each field can be obtained by following the links in the research tab.

The membrane electroporation of a biological cell has been well known as a convenient, multipurpose and universal way of temporarily increasing its permeability in a pulsed electric field (PEF) with certain parameters. The influence of this field on the cell leads to reversible perforation or irreversible membrane rupture depend on applied field strength. The process and result of the membrane interaction with the PEF is greatly influenced by its heterogeneous biological structure, which has both native pores of various sizes and various protein inclusions. This leads to heterogeneity of the electrophysical properties.

Main research path in the areas of medicine and biology is the use of electroporation to enhance the transport of various substances into cells or to directly affect the cell viability. This mechanism can be used for various aims, such as treatment of cancer, insertion of genetic material for genetic modification of organisms or gene therapy, directly destroying target tissues, and protection of cells during freezing.

Electrochemotherapy is a cancer treatment modality which uses electroporation to increase the uptake of cytotoxic drugs into cells. This allows for a great potentiation of the effectiveness of these drugs, while simultaneously limiting side effects of the drugs. Laboratory of Biocybernetics (Faculty of Electrical Engineering, University of Ljubljana) is actively involved in development of numerical treatment planning methods for optimization of treatment delivery. This is used in clinical studies for electrochemotherapy of liver tumors and head and neck cancer. Irreversible

electroporation uses electrical pulses alone to destroy unwanted tissues, which has been used already in the treatment of liver, pancreas, kidney and brain tumors.

Electroporation can be used to introduce genetic material into cells, which leads to gene expression, enabling different basic research in biology. Simultaneously, we are researching electroporation for gene therapy, where different therapeutic endpoints are investigating, among those also treatment of cancer.

During freezing of cells, ice crystals form, which can damage the fragile cell membrane, so typically several toxic protective substances are used. However, using electroporation various natural sugars, which are used by cold adapted plants, can be introduced into the cells. In this way, cells can be protected using non-toxic materials, which is especially important for keeping of stem cells.

Our publications in the field have received over 10 thousand pure citations, we were the chairs of the COST action TD1104 – European network for development of electroporation-based technologies and treatments (EP4Bio2Med), that ran from 2011 until 2016, bringing together 581 researchers of electroporation from 243 research institutions and 28 hi-tech companies from 43 different countries. Since 2003 we are organizers (first bi-annually, and since 2011 annually) the workshop and postgraduate course Electroporation-Based Technologies and Treatments, attracting each year over 50 attendees, and in total over 700 participants from 39 different countries. Professor Damijan Miklavčič, the head of the laboratory, is the editor of the Handbook of Electroporation, published in 2017 by Springer, currently spanning almost 3000 pages, and available in print as well as online.

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