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20th Anniversary of the Electroporation-based Technologies and Treatments International School and Workshop

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The use of electric fields and the effect on cells has been evident throughout scientific history. This includes evaluating treatments for headaches in the first century to evaluating the effects on animals, human skin, muscle contractions, and other aspects of electrical stimulation in the 18th century and evaluating electric fields as an antibacterial agent for liquids and food in the 19th century. However, it was not until the late 1950s and 1960s that this work focused on the effects of electric fields on cells and cell membranes. This early work essentially laid the foundation for many of the biomedical, food, environmental, and industrial applications of how pulse electric fields are used today.

There were several important milestones occurring in the early 1980s including demonstration of transient effects on phospholipid vesicles and small molecule uptake following administration of PEF. A major breakthrough was reported by E. Neumann et al. demonstrating that genes could be delivered to mammalian cells using electric pulses. In this paper, Neumann first used the term *electroporation*, which is still seen as the standard term for this technique 40 years later. Electrofusion of fibroblasts was demonstrated by Teissie et al. also in 1982. It is clear that this sequence of discoveries and events were key sparks to get many researchers in the biomedical field to become interested in this technology. In 1984, H. Potter was able to demonstrate a safe and standardized way of treating cells by reporting on the first electroporation cuvette. These studies were instrumental in opening the field for multiple biotechnical and biomedical applications, in particular, they were instrumental in the initiation of clinical applications such as electrochemotherapy, gene electrotransfer, and irreversible electroporation.

Following a similar timeline, PEF was being evaluated for other applications such as disinfection of foods and wastewater as well as a means to remove substances from fruits and vegetables. In the mid-1900s, studies demonstrated through a process called electroplasmolysis that AC fields could be used to disrupt fruit and vegetable cells. A key contributor moving the field forward in the 1960s-1980s was H. Doevenspeck. There have been many contributors in moving the field forward through stages of electroplasmolysis and electroextraction to now where electric fields are used for many purposes in food, environment, and industry.

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As the field of pulse electric fields/electroporation has moved towards maturation, as with most technologies there were obstacles. For non-biomedical applications it was scaling equipment and gaining acceptance of the process. For biomedical applications, it was overcoming the stigma that "electroporation kills cells" as well as the notion that this was just a laboratory technique for transfecting cells. For both areas it was also removing the notion that all substances, cells tissues or applications can be done using the same electric field characteristics. Early attempts to overcome these obstacles relied on publications or presentations and discussions at workshops. While helpful, this was not the solution.

In the early 2000s, D. Miklavčič proposed the notion that if the idea is to train and/or educate people to the proper use of the technology, then why not establish a school to do just that. So, in 2003, he and L.M. Mir became co-directors of the Electroporation Based Technologies and Treatments (EBTT) School. They recruited experts in the field to be faculty in the school and the week-long format included lectures from the faculty but also guest lecturers to bring the latest information. A key element was hands-on training for the attendees. While the concept was to establish a means to train students and young researchers the intricacies of the technology, the school provided much more. It was an opportunity to interact with experts in the field and establish collaborations and relationships and learn the latest innovations.

Clearly, EBTT has been a success, but it has been more than that. It has been a launching point for other schools to be established and to educate researchers in PEF technologies in food, environment, veterinary as well as others. These additional schools modeled themselves after EBTT and have also been successful in helping to move the field forward. While this accomplishment alone would be something to be proud of, it is not the major accomplishment of EBTT. For any concept to become established there needs to be an acceptance by the scientific community at large. The EBTT was a catalyst for the formation of a network of researchers to interact. Through this network, D. Miklavčič was able to successfully establish the COST action which included 581 investigators from 43 countries. As an end result of the COST action was the 1st World Congress on Electroporation. At this meeting, the International Society for Electroporation Based Technologies and Treatments (ISEBTT) was established. Since then, the ISEBTT has held 3 more World Congresses. There were on average 400 attendees at each Congress, and these meetings have become the place to go to find out the latest on this technology.

The use of pulse electric fields has certainly expanded and gained acceptance in many areas. Whether it is the approval of using PEF in food processing, wine making or decontamination of water or biomedical applications where over 250 clinical trials have shown the utility of this technology for treating various diseases leading to FDA approval of irreversible electroporation, acceptance of electrochemotherapy in Europe and most likely other applications not far from being approved including some using gene electrotransfer. As we look back on the 20 years of EBTT, we can draw a straight line for many of the advances that have occurred and the dissemination of the technology from the initiation of the school. All those that have participated in the EBTT can look back with pride, not just at helping to create a successful school, but contributing to moving a dynamic field forward, and the creation of a technology that impacts many fields. We all look forward to seeing the impact over the next 20 years.

A photo snapshot reaching way back to 2003 – the first edition of the EBTT School.

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