Perspectives on electroporation

Electroporation is connecting science, industry and medicine. Three experts from different fields, Professors Damijan Miklavčič and Javier Raso and Dr Georgeta-Mihaela Moisescu share their experiences using the method.

How did you become interested in the field?

DM: I first heard about electroporation during my undergraduate studies as a means to transform bacteria. At that time it was considered a crude, yet efficient, means of gene transfer that could only be used in bacteria. At the 1989 World Cancer Congress in Hamburg, Germany, however, I spotted a poster by Drs Jean Belehradek Jr, Stephan Orlowski and Lluis M Mir. They demonstrated the 1,000-fold cytotoxicity of bleomycin (an antibiotic) when combined with electroporation. I decided we needed to bring it to our patients in Ljubljana, Slovenia. In a way, that was the start of my more than 25-year long, fruitful and rewarding scientific journey!

Despite the wide-ranging potential of the technique, why is electroporation proving slow to bring to market?

MM: A medical treatment’s safety and efficacy are more important than its ‘speed to

The potential of pulsed electric fields

Short high-voltage electric pulses can be used to alter cell membrane properties. This technique, called electroporation, is beginning to reach its potential and is coming into common use, partly thanks to a recent drive from a COST initiative to streamline research and facilitate inter lab communication.

THE CELL MEMBRANE is a selectively permeable phospholipid bilayer that surrounds and separates a cell’s contents from its extracellular surroundings. Everything that enters or exits a cell must do so via its membrane. Proteins embedded in the membrane allow the transfer of specific ions and molecules into and out of the cell. It has been shown that by exposing cells to an electrical field to such membranes their permeability can be increased. This change in permeability can be reversible or irreversible depending on the parameters of electric pulses applied. This technique, termed electroporation, is a powerful method for introducing molecules that would not otherwise cross the membrane into cells.

Electroporation can also be used to do the reverse; increased permeability can allow the extraction of molecules from cells. Additionally, it is sometimes used to introduce foreign proteins into cell membranes, or even to induce neighbouring cells to fuse. Irreversible electroporation is an effective way to kill cells and can be particularly useful for non-thermal pasteurisation, food treatment and eliminating harmful bacteria in a clinical setting, especially those that have become immune to many antibiotics.

This powerful and diverse tool has been implemented in a wide variety of settings. For example the labelling of neurons with fluorescent dyes for imaging, transfection of cells with novel genes, targeted cancer treatments, food and biomass processing, and microbial inactivation in water treatment, to name but a few. Although its applications...
A COST TD1104 Action has established redundancy in the field, forming a barrier using similar techniques, and this has created interaction between researchers from different fields. There has been a lack of interaction in many fields, simply poor knowledge of why electroporation has not yet taken centre stage in many fields.

It has been suggested that one of the reasons electroporation works, and for the development of new techniques optimised for their applications. There is also a need to implement the technique at an industrial scale and bring it from the scientific periphery into common use.

COMMUNICATION IS KEY
It has been suggested that one of the reasons why electroporation has not yet taken centre stage in many fields is simply poor knowledge transfer. There has been a lack of interaction between researchers from different fields using similar techniques, and this has created redundancy in the field, forming a barrier to progress.

A COST TD1104 Action has established an international network of researchers, institutions and industries that will aid the development of electroporation-based technologies and treatments. The main objective of this Action is to streamline European (and wider) research on electroporation, ranging from basic research to industrial and medical applications, by collecting, pooling and transferring knowledge to partners,” explains Professor Damijan Miklavčič of the University of Ljubljana, Slovenia. The project, also known as EP4BioMED, seeks to advance basic mechanistic understanding of electroporation, overcome the limitations of existing applications and facilitate the development of new technologies.

EP4BioMED
To date, the project comprises 575 individual participants from 240 institutions in 43 different countries. These are divided into five working groups, each focusing on a different arm of the COST TD1104 Action’s objectives. Over half of the participants are focused on basic research under the guidance of Marie-Pierre Rols at the Institute of Pharmacology and Structural Biology at the French National Centre for Scientific Research. The goal is to understand and model the biological, physical and chemical mechanisms of electroporation. By better understanding how electroporation works at this level, the researchers hope to design improved technology and methods for use in other areas. Thanks to COST’s interconnectivity, this work can readily inform the remaining four working groups, which focus on different applications of electroporation.

Genome therapy holds marked potential for the next generation of cancer therapies. What are the unique qualities of electroporation treatments?

DM: Electroporation is a noninvasive means of delivering DNA and RNA fragments into cells in situ. This is being tested in clinical studies—primarily for cancer treatments—but we can soon expect efficient DNA vaccination against other diseases. This will be feasible with the use of electroporation.

What are the short-term scientific missions (STSMs)?

MM: STSMs support the mobility of researchers who want to learn new techniques and methods not available in their own laboratory or foster or strengthen collaborations with complementary teams. In total, 64 missions have been funded by COST TD1104 Action over three years, while 68 research and academic institutions from 18 European and two North African countries, as well as Israel, New Zealand and the US, have been connected by human and scientific bridges.
COST TD1104 ACTION

OBJECTIVES

- To provide effective steps to increase European expertise in electroporation
- To improve communication between international groups through interdisciplinary knowledge exchange on electroporation-based applications

KEY COLLABORATORS

For a full list of participating countries and working groups, visit: www.electroporation.net

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Group four is led by Wolfgang Frey of the Karlsruhe Institute of Technology, Germany, and aims to make electroporation technologies that are economically competitive and efficient for environmental applications, particularly the processing of biomass. Finally, group five led by Stefan Toepfl of the German Institute of Food Technologies is dedicated to developing new technologies, disseminating technical knowledge and ensuring that safe and reliable electroporation systems are developed for both industrial and clinical use.

This makes it much easier to share with other researchers and to remain informed about what their collaborators are working on.

COST TD1104 Action continually invests in education and support for its members through the organisation and provision of funding for meetings, training schools, knowledge dissemination and ‘short-term scientific missions’. This educational drive includes several annually held training schools, including ‘Electroporation-based Technologies and Treatments’ in Ljubljana (www.ebt.org). “Based on our experience we have organised a similar school in the field of food processing, ‘pulsed electric field (PEF) school’,” Miklavčič explains. “This took place for the first time in Zaragoza, Spain, in 2014 and then in Salerno, Italy, this year. Next year it will be held in Dublin, Ireland. COST TD1104 is also organising the first world congress on electroporation in Portorož, Slovenia, in September. The idea is that this will be the first of many, and will include over 350 participants and provide an additional platform for the exchange of ideas.

Another key success measure for the researchers has been the introduction of a unifying terminology for describing electroporation. “In the biomedical field the technique is termed ‘electroporation’ and in food processing it is known as PEF,” Miklavčič explains. “The participation of experts from various disciplines in this COST Action has contributed to standardising the terminology.” What is particularly exciting is that this already fruitful technique is still in its early stages. With improved knowledge infrastructure, electroporation, via COST, is now poised to reach its promised potential.