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Duration of the experiments: 60 min

Max. number of participants: 4

Location: Laboratory of Biocybernetics

Level: Advanced

## PREREQUISITES

Basic to advanced knowledge of finite element modeling.

## THEORETICAL BACKGROUND

The effects of various physical phenomena can be investigated by separately analyzing each individual phenomenon, with no respect to interaction between them. However, often we are dealing with two or more interacting, simultaneously occurring phenomena, such as heat transfer in tissue due to resistive heating. This coupling may give rise to tissue conductivity changes (due to temperature increase), which in turn changes the magnitude of electric current. When constructing a model, we have to estimate such interactions and, if needed, in order to obtain accurate results, include mutual dependencies. To do so, we need data on how the material properties significant for one field (such as the electric field) vary with the value of another field (such as temperature) and vice versa.

The equation frequently used in the modeling of heat transfer in living tissue is Pennes' bioheat equation which includes the contributions from blood flow and metabolic heat production. However, these contributions can often be neglected, and simpler, conduction heating equation can be used:

$$\rho c \frac{\partial T}{\partial t} - \nabla(k \nabla T) = Q, \quad \text{where}$$

$T$  is the temperature,  $\rho$  is the material (tissue) density,  $c$  is the specific heat capacity of the tissue,  $k$  is its thermal conductivity, and  $Q$  is the heat source, in our case the resistive heating of the material:

$$Q = \sigma |\nabla V|^2, \quad \text{where}$$

$\sigma$  is electrical conductivity of the material and  $V$  is electric potential.

**The aim** of the experiment is to become familiar with the modeling of coupled physical phenomena and to evaluate the rise in tissue temperature during the application of different electric pulses. Also, we would like to demonstrate the usefulness and necessity of such numerical models for the planning of experiments and treatments as well as the analysis of the results.

## EXPERIMENT

Theoretical evaluation of different pulse parameters and tissue-electrode geometrical setups is becoming commonplace in electroporation-based treatments, however, thermal aspect is mostly overlooked. Since the amount of resistive heat is different for every specific

application, thermal effects should be considered in such theoretical models, as merely a general estimation is often not sufficient.

The application of electric pulses will be investigated on a numerical model of a homogeneous tissue with needle electrodes. The model will be constructed in COMSOL Multiphysics (COMSOL AB, Sweden), based on finite electrode method.

Temperatures above 43-45 °C cause denaturation of proteins and destruction of cell structures, eventually resulting in cell necrosis. The duration of exposure needs to be in the order of minutes to hours in order to cause tissue damage at this temperature. However, only about 1 s of exposure is needed at 70 °C.

We will evaluate temperature increase in tissue caused by resistive heating by coupling the electrical and the thermal quantities, for different parameters of electrical pulses.

- We will experiment with different amplitudes and lengths of a single electric pulse to estimate the temperature increase within the duration of one pulse.
- If we use trains of pulses, with intervals between them when there is no current flow, the cooling of the tissue takes place, which should be taken into account during the simulation. In this way we can investigate the effect of pulse repetition frequency on tissue heating.

#### **FURTHER READING:**

Davalos RV, Rubinsky B, Mir LM. Theoretical analysis of the thermal effects during in vivo tissue electroporation. *Bioelectrochemistry* 61(1-2): 99-107, 2003

Becker SM, Kuznetsov AV. Thermal in vivo skin electroporation pore development and charged macromolecule transdermal delivery: A numerical study of the influence of chemically enhanced lower lipid phase transition temperatures. *International Journal of Heat and Mass Transfer* 51: 2060-2074, 2008

Lacković I, Magjarević R, Miklavčič D. Three-dimensional finite-element analysis of joule heating in electrochemotherapy and in vivo gene electrotransfer. *IEEE T. Diel. El. Insul.* 15: 1338-1347, 2009

Pavšelj N, Miklavčič D. Resistive heating and electropermeabilization of skin tissue during in vivo electroporation: A coupled nonlinear finite element model. *International Journal of Heat and Mass Transfer* 54: 2294-2302, 2011

#### **NOTES & RESULTS**

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