ABSTRACT TESI DI DOTTORATO
di
ELIA SIMONA

The activity of this thesis is devoted to modelling the electromagnetic behaviour of complex biological structures and in particular of nerve cells and the study of nanotechnology applications to these structures for therapeutic, diagnostic and investigative purposes.

The 'design' of artificial nanoscale devices is the chance to accurately understand and manipulate the phenomena that occur inside biological structures. Until a few years ago, the most widely accepted technology was that of MEA (Micro Electrode Arrays), which indeed is characterized by several limitations, such as microelectrodes whose sizes are very larger than individual cells, lack of local control of electrical activity, etc. In recent years, new possibilities have arisen due to the increasing development of nanotechnology. In particular, the Carbon Nanotubes (CNTs) are very compatible as systems capable of interfacing with the Central Nervous System (CNS). This paves the way for neuro-implantable devices for vision, hearing, taste, movement, elimination of seizures, repair and improvement of brain functions. Increasingly, attempts are being made to try to integrate CNTs with other technologies to develop biochips that can help repairing damaged tissues of the CNS. MEA with electrodes coated with CNTs have recently been proposed. Further progress is being made in the direction of the nanoarray electrode (the so-called NEA - Nano Electrode Array), to have greater spatial and temporal resolution.

It is within this very broad and extremely complex scenario that this thesis is placed, investigating Finite Element Method (FEM) modelling and design issues of a neurostimulation system at nanoscale. The apparatus is an array consisting of vertically-aligned CNTs acting as nano-electrodes to provide a signal electrical stimulation. In particular, the application considered is the neurostimulation of the retina, where the spatial resolution is a crucial factor and a sensitivity analysis proves to be very useful in studying system performances dependences on different main setup parameters.

The electromagnetic modelling of the system is performed in a FEM multiphysics environment used to couple in an efficient way the non linear differential equations related to biological system with Maxwell equations.

One of the peculiar characteristics of this study is the approach proposed to obtain the dynamics of Action Potential (AP), the basic unit of the nervous message, inside a neuron membrane without the use of the "transmission line" equation, widely adopted in literature. Starting from the Hodgkin and Huxley (HH) model (the nonlinear partial differential equations describing the chemical transport through the nerve membrane) a translation in terms of suitable equivalent electric parameters is obtained for different pieces of the neuron and in a model describing soma, axon hillock and initial axon segment. The HH equations are coupled with those of Maxwell (in quasi-static formulation, due to the considered range of frequencies) and, exploiting the high nonlinearity of the membrane domain, the triggering and propagation of the AP is simulated. A comparison between two proposed modelling approaches is carried out investigating the trade-off between accuracy and numerical burden.

Moreover, a systematic determination of the most significant parameters and design variables is also carried out (e.g. AP triggering and its promptness as well as AP duration), allowing to maximize the effectiveness of the artificial stimulation of the biological cell. The optimization of system parameters (in terms of stimulus and electrode geometrical features) in order to maximize the selective initiation of APs on one neuron or on clusters of several neurons can be effectively accomplished to boost the spatial resolution of the device.

Finally, conclusions are drawn and possible future developments are discussed both in terms of model implementation and further studies of the neuroelectrical stimulation and analysis.