**Title: Computational Models to support Cardiac Electrohpysiology: development and improvement of human atrial and ventricular models**

In the last decades a huge amount of mathematical models of cardiomyocyte electrophysiology have been developed, and due to the increase of the available experimental data the complexity of these models has raised progressively.

Sudden cardiac death is one of the main death causes all over the world, and it is correlated with the basic pro-arrhythmic mechanisms at the level of ion currents and single atrial/ventricular myocyte action potential (AP). To understand these mechanisms, and taking advantage of the increasing availability of specific data on ionic currents gathered from human cardiomyocytes, several mathematical models were developed to describe the biophysical mechanisms underlying the human APs.

The quantitative description of the electrical signal propagation in the cardiac muscle and the subsequent contraction-relaxation process consists of the following components:

- the excitation-contraction coupling (ECC) model of the cardiomyocyte, i.e. a stiff system of ordinary differential equations (ODEs), describing the flow of the ionic currents through the cellular membrane;

- the active tension or active strain models, consisting of non-linear systems of ODEs, describing the cross bridges binding, which results either in a local force or in the shortening of fibers;

- the electrical current flow model of the cardiac tissue, i.e. the Bidomain model, which is a degenerate parabolic system of two non-linear reaction-diffusion PDEs, describing the evolution in space and time of the intra- and extracellular electric potentials;

- the finite elasticity model for the deformation of cardiac tissue, derived from a strain energy function which characterizes the anisotropic mechanical properties of the myocardium.

All these components will be separately exploited for both the atrial and ventricular chambers by taking into account their specific electrophysiological, anatomical and mechanical properties.

**Piano attività**

This research will be part of the PRIN project “*Modeling the heart across the scales: from cardiac cells to the whole organ*” with the following steps:

1. standard cell models will be improved to correctly reproduce the electrical behavior of cardiomyocyte when in vivo extracellular electrolyte concentrations, as measured from blood tests, are considered.
2. improve the currently used ECC models for human cardiac cells by adding the stretch-activated currents models, to account for the mechano-electric-feedback (MEF).
3. Validation of the new models, consisting of systems of ODEs, against experimental data available in the literature.
4. As a further crucial step for a bottom-up approach (from cells to organ) towards realistic electro-mechanical modeling, we plan to develop detailed models for active contraction of cardiac cells based on cooperative interactions of myofilaments and myosin heads, which are capable of reproducing physiological steady-state force-calcium and force-length relationships