An Electrophysiologic Computational Model of the Zebrafish Heart

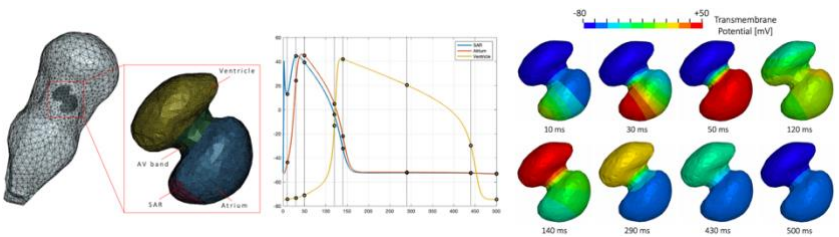
Ludovica Cestariolo*, Giulia Luraghi, Pierre L'Eplattenier, Jose F Rodriguez Matas

Department of Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, MI, IT

Aims: Recent studies suggest that the physiology of the zebrafish heart resembles that of the human in many aspects, namely: spontaneous heart rates are found to be similar, its cardiac action potential much more closely resembles that of the human, and QT-interval in electrocardiograms is heart rate dependent. Thus, zebrafish has been proposed as a potential model for genetic and pharmacological screening of factors affecting heart function. However, despite this rising interest, very few studies concern the development of computational models of the zebrafish heart.

Methods: This work develops a full electrophysiology model of the heart + body of a zebrafish 3 days post fertilization. The model is based on the geometry reported in *Crowcombe et al., 2016* and is composed of three main parts: body, heart chambers, and heart myocardium. The latter is, in turn, divided into four regions: ventricular wall, atrio-ventricular band (AV band), atrial wall, and sinoatrial region (SAR), where the stimulus is delivered. The action potential of the different regions of the heart has been simulated using the four-variables minimal model proposed by *Bueno-Orovio et al., 2008*. The model has been adjusted to fit experimentally reported action potentials of the zebrafish together with restitution curve data in order to reproduce a correct heart-rhythm dependence of the QT. The bidomain model has been used to model the electric propagation in the heart, whereas the body has been modeled as a volume conductor. The full set of equations have been solved in the software LS-DYNA (ANSYS, Canonsburg, PA, USA).

Results: The activation times and the activation sequence were found to be in line with experimental data. Furthermore, with this model, a dipolar ECG can be obtained to be compared to *in vivo* recordings found in literature.



Left: model geometry. Middle and right: transmembrane potentials.