A COMPUTATIONAL MODEL OF THE ZEBRAFISH HEART

Ludovica Cestariolo[1], Giulia Luraghi[1], Pierre L'Eplattenier[2], Jose Felix Rodriguez Matas[1]

[1] LaBS, Dept. of Chemistry, Materials and Chemical Engineering "Giulio Natta", Politecnico di Milano, Milan, Italy

[2] Livermore Software Technology Corporation, Livermore, CA, US

INTRODUCTION

The zebrafish's heart physiology resembles that of humans in several aspects. In particular, the heart of the zebrafish has similar spontaneous heart rates, the QT-interval is heart rate dependent [1], it has comparable action potential (AP) shape and duration, and it also shows the presence of orthologues of human ion channels. For these reasons, the zebrafish has been proposed as a potential model for genetic and pharmacological screenings of factors that could affect heart functions.

MOTIVATION OF THE STUDY

Despite the rising interest in the zebrafish in the last years, very few studies concern the development of a computational model of the zebrafish heart [2].

HYPOTHESIS

A consistent computational model of the zebrafish heart, can be useful to assess the main electrophysiological parameters and their correlation with pathologies and drug administration.

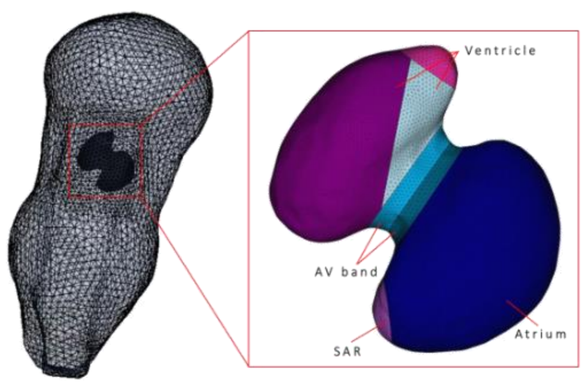
METHODS

Ansys LS-DYNA

A **full electrophysiological model** of a 3-days post fertilization (**3 dpf**) zebrafish (heart + body) has been modeled in this study. The complete set of equations has been solved using a **semi-implicit numerical scheme** with a **fixed time step** in the multiphysics simulation software **LS-DYNA (ANSYS, Canonsburg, PA, USA)**. The electric propagation in the heart was modeled using a **bidomain model**, while the body has been considered as a **passive volume conductor**.

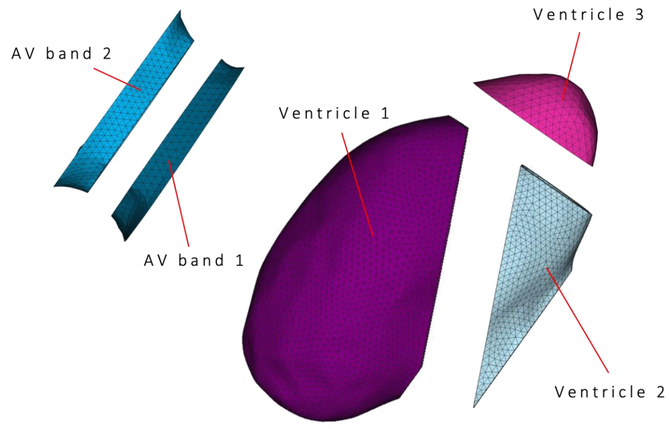
The geometry was created using **ANSA pre processor 22.0.0 (BETA CAE System, Luzern, CH)** and is composed of:

- Body
- Heart chambers
- **Heart myocardium**:
  - Sinoatrial region (SAR)
  - Atrial wall
  - Atrioventricular band (AVband)
  - Ventricular wall



ANSA PRE PROCESSOR

- 550974 elements
- 97307 nodes

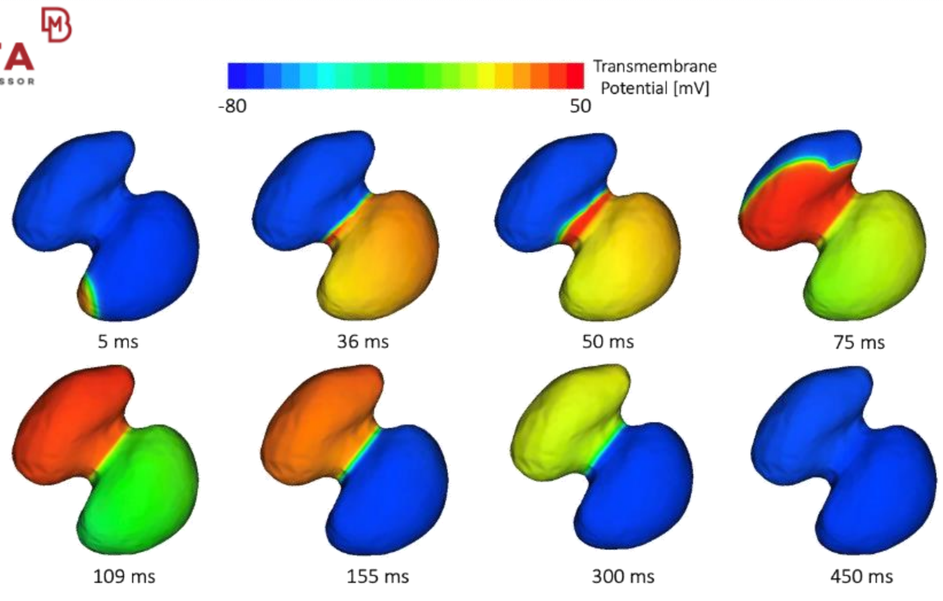


The **heart tissue** was considered as **isotropic** with different **conductance values** assigned to different parts in order to reproduce the activation pattern reported in literature.
The AV band is composed of two rings. To AVband1 has been assigned the action potential model of the atrium, and to AVband2 the action potential of the ventricle. On the contrary, the ventricular wall has been divided into three regions following the activation sequence experimentally reported.

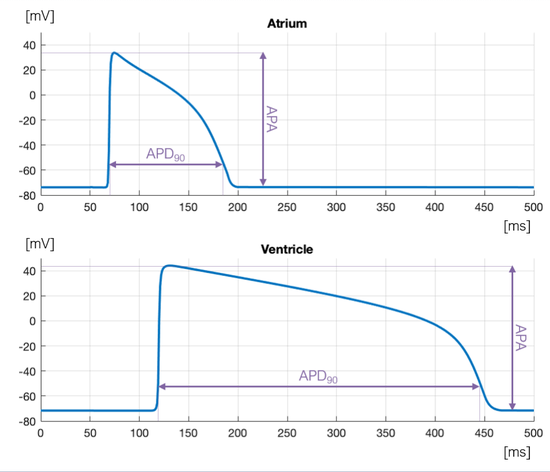
RESULTS

The analysis of the results focuses on the main **electrophysiological parameters** such as the **activation sequence**, **activation times**, and the main characteristics of the **action potential morphology** (i.e., AP duration, AP amplitude, max and min AP derivatives). Additionally, an in-silico **bipolar ECG** was computed between two electrodes located at the body surface in correspondence of the ventricular base (+) and apex (-). All the obtained results were then compared with experimental data [3][4].

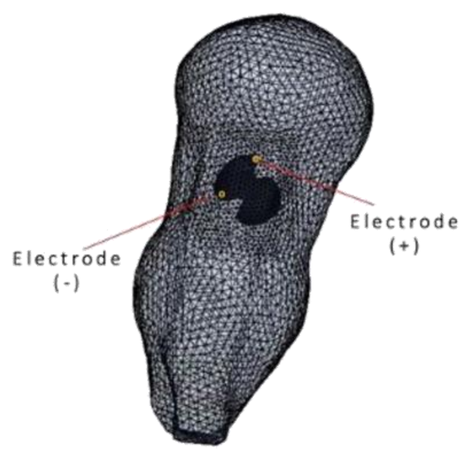
META POST PROCESSOR

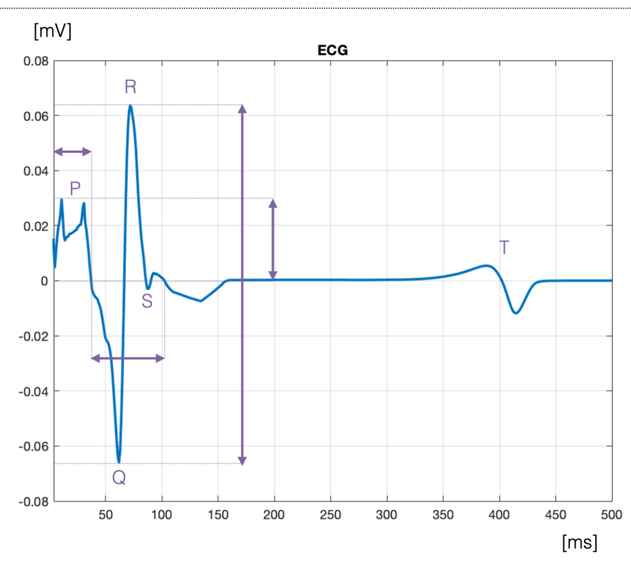


	Model	Experimental
Atrium	36 ms	35 ms [3]
AV band delay	14 ms	25 ms [3]
Ventricle	59 ms	75 ms [3]



Region	AP marker	Model	Experiment
Atrium	APD_{90} (ms)	122.48	166.00 ± 3.00 [4]
	AP amplitude (mV)	107.759	80.10 [1]
	Max. Derivative (V/s)	58.468	8.38 [1]
	Min. Derivative (V/s)	-3.758	-3.99 [1]
Ventricle	APD_{90} (ms)	348.40	272.00 ± 15.00 [4]
	AP amplitude (mV)	118.361	117.60 [1]
	Max. Derivative (V/s)	59.801	7.15 [1]
	Min. Derivative (V/s)	-2.149	-1.69 [1]





ECG parameters	Values
P width (ms)	~37 ms
QRS (ms)	~64 ms
P amplitude (mV)	29.594 μV
QRS amplitude (mV)	129.584 μV

CONCLUSIONS

The numerical results indicate that considering **conductance heterogeneity** in the ventricular tissue as indicated in experimental observations [3] may properly describe the correct activation of the zebrafish heart and gives a bipolar ECG in good agreement with experimental measurements from literature.
This model comprises a significant improvement with respect to the previous model developed in [2] not only in terms of the activation sequence, but also in terms of the resulting ECG. In general, comparison with the experimental data [3,4], we can consider the results as promising.

References:

[1] M. Vornanen and M. Hassinen, Channels, 2016.
[2] J. Crowcombe et al., PLoS One, 2016.
[3] D. Panáková et al., Nature, 2010.
[4] Y. Zhao et al., Cardiovasc. Res., 2021.

Contact address:
ludovica.cestariolo@polimi.it