SCHEDA RELAZIONE DOTTORANDI

Al collegio docenti del Dottorato in Medicina Molecolare

Dott. Giardini Francesco

Ciclo XXXIV° - Tutor Prof. Corrado Poggesi, Prof. Elisabetta Cerbai

Attività scientifica svolta nel 1° anno di Dottorato, Anno Accademico 2018/2019

Introduction

In my PhD project I want to increase our understanding in the relationship between heart structural remodelling and electrophysiological dysfunction found in a mouse model of hypertrophic cardiomyopathy. We are using a multi-side approach to investigate morphology and electrical propagation in several hearts.

Methods

We used high-performance imaging and analysis techniques to correlate the whole heart cytoarchitectonic organization with action potential kinetics recorded at mesoscale resolution. We use an ultra-fast wide-field mesoscope in combination with voltage sensitive dye to map the action potential propagation in Langendorff perfused hearts. Then, the same heart is structural investigated at sub-cellular resolution. To this end, we will combine advances in tissue clearing, immunostaining and high-resolution optical microscopy (light-sheet microscopy) to reconstruct the three-dimensional organization of myocardial tissue. During my first year of PhD, I developed a cytoarchitectonic analysis software to map myofilaments alignment in 3D using Structure Tensor Analysis, defining the conduction pathways of action potential propagation at intercellular level.

Results

I modified the architecture of the software that manage the optical wide-field mesoscope to improve the time resolution of the system. Several healthy and pathological hearts are investigated, highlighting differences in action potential propagation. To investigate the morphology of these hearts, the imaging protocol was optimized for the heart tissue. The new analysis software allow us to map the fiber orientation in 3D, managing the anisotropic resolution and the images defects. This fibers reconstruction will be use to extract myocardial architecture features. Action-potential propagation across the whole heart will be modelled on these structural data to allowing a directly comparison with functional data previously acquired on the same heart by means of optical mapping.

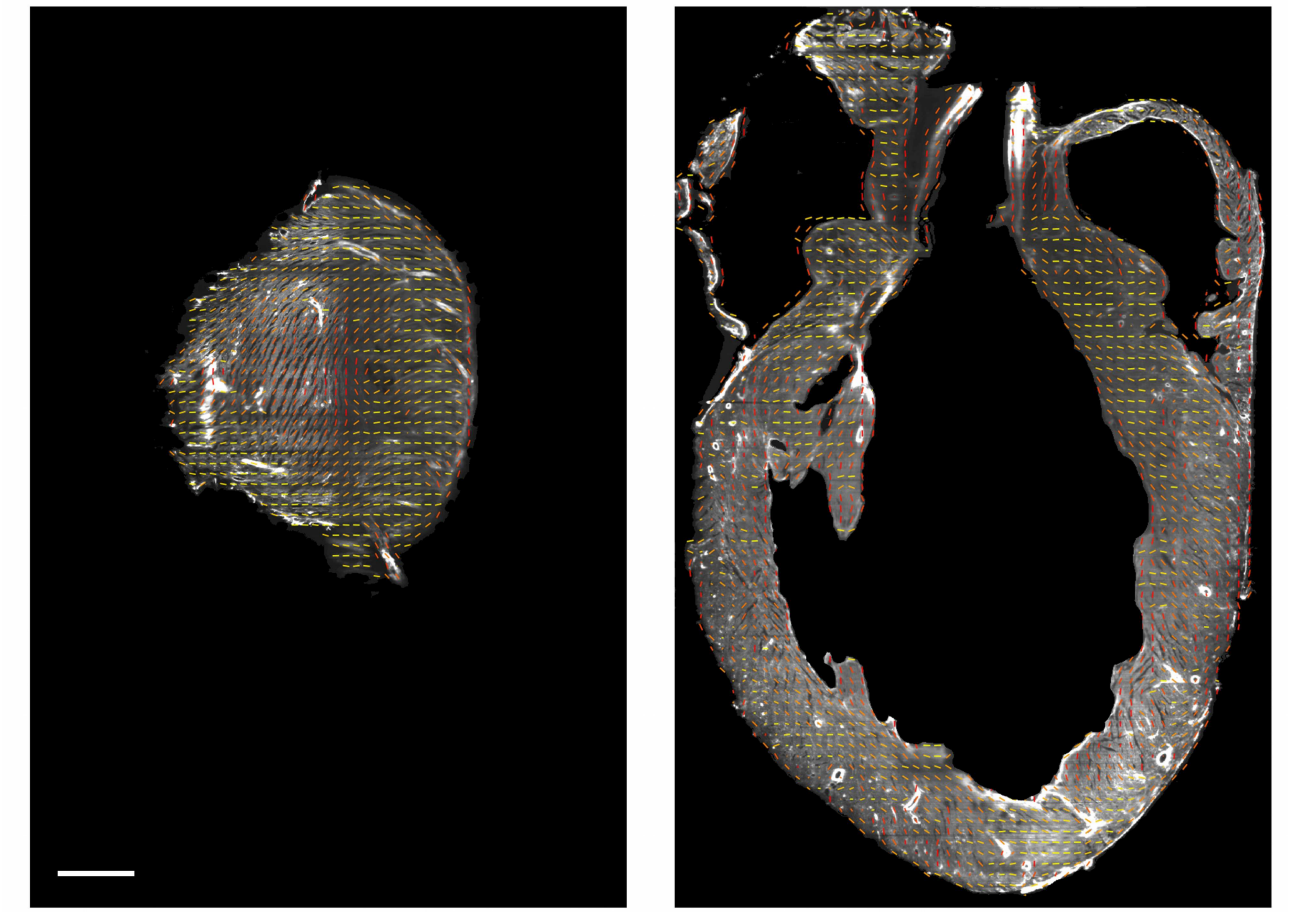

Figure 1 – Entire mouse reconstruction and orientation analysis of myocardial fibers *Two representative frames of cleared entire mouse reconstructed with lightsheet microscopy, pixel size (5.2 x 5.2 x 6) µm in x, y, z, depth 198 µm and 4950 µm respectively. The 3D orientation of myocardial fibers is extracted automatically with a resolution of 135 µm by structure tensor analysis. The 2D projection of orientation vectors are superimposed on the tissue. The vector length and color represent XY component and angle. Scale bar: 1 mm.*

Participation to meeting and workshop

2018 - Novel optics-based approaches for cardiac electrophysiology. Florence, Italy.
2018 - International Conference on Bio Sensing and Imaging. Florence, Italy.

Abstracts and Publications

2019 - Giardini F, Biasci V, Scardigli M, Pavone FS, Bub G, Sacconi L. A Software Architecture to Mimic a Ventricular Tachycardia in Intact Murine Hearts by Means of an All-Optical Platform. Methods Protoc. 2(1):7