MULTISCALE IMAGING OF DEVELOPING HEART DYNAMICS: ROLE OF THE CARDIAC JELLY AND THE ENDOCARDIUM

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As the heart undergoes major remodeling during its development, its complex mechanical and resulting physiological properties change. The early embryonic heart is valve-less and made of three layers: the myocardium, the muscle cell layer generating force; the cardiac jelly, an extracellular matrix present only in the embryonic heart; and the endocardium, a single cell layer which underlines the cardiac jelly and encloses blood flow. A complete picture of the interplay and the mechanics of these cardiac constituents is still lacking as the dynamic and molecular regulation of heart development can only be studied in the live, beating embryonic heart.

With its peripheral heart location and translucency during early development, the zebrafish Danio rerio has become an important cardiac research model and is ideal for imaging studies. However, resolving moving objects, such as in vivo beating hearts, is technically challenging. Our lab has developed state-of-the-art light sheet (or selective plane illumination microscopy, SPIM) [1] instruments and protocols tailored to live zebrafish imaging [2]. Recently, we have imaged and reconstructed beating zebrafish hearts *in vivo* in 3D across time with a dedicated instrument and post-acquisition synchronization of movie stacks [3].

Here we present our findings on how the early heart pumps blood in the absence of valves. With ultra-fast light sheet microscopy and advanced 5D (3D + time + colors) post-acquisition movie reconstruction, we show that when the myocardium contracts, it applies pressure on the incompressible but mobile cardiac jelly, thus propagating forces to the endocardium. Through live 3D imaging and analysis, we reveal how the endocardium prevents backward flow and allows efficient pumping. This study illustrates nicely how a custom-built light sheet microscope and dedicated analysis tools reveal previously unseen details in the fragile, rapidly moving heart.

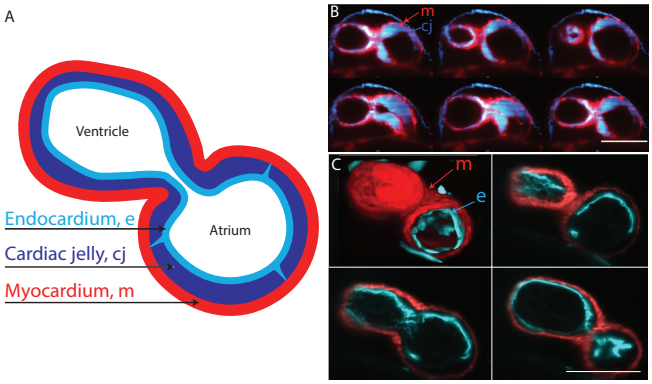

Figure 1: 48h zebrafish embryonic heart. A) Scheme of the 48h ZF heart. B) One heart contraction, with CJ and myocardium labeled. C) 3D reconstruction and 2D planes of one heart contraction, endocardium and myocardium labeled. Scale bar: 100µm.

Keywords: custom-built light sheet microscope, live imaging, image analysis, 5D, heart, zebrafish

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