Embryonic Hearts: How Do They Pump?

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Background Congenital heart defects remain the most common birth defect in humans occurring in almost 1% of live births. The majority of the defects are believed to be influenced by both genetic patterning and mechanical stimuli such as the shear stress exerted by the blood flow on the developing heart (Hove et al., Nature, 2003) The major causes for changes in fluid mechanical environment are changes in the pumping of the heart itself.

The pumping mechanism of the embryonic heart has long been believed to be peristaltic. Recently however Forouhar et al. (Science, 2006) proposed dynamic suction as the driving force behind the pumping of hearts prior to valve formation. Their suggested mechanism is based on a single activation zone located at the pacemaker cells near the inlet of the heart. The contraction of this zone induces waves travelling alongside the heart wall. Those passive wall motions are believed to be the cause of the blood flow.

Our aim is to reveal the mechanism behind the intracardiac blood flow in order to provide more insight in cardiac development.

Methods and results Using transmission light microscopy in combination with high speed image recording modalities we succeeded in mapping hearts of zebrafish embryo's, a model frequently used in developmental cardiology.
Trying to understand the underlying players in the cardiac wall motion we compared normal pumping hearts with hearts where the pumping efficiency was reduced. To estimate the efficiency of the heart we developed an automated algorithm based on pattern recognition to derive the cardiac flow by tracking the motion of aortic blood cells in image sequences.

We used 2,3-butanedione 2-monoxime (BDM) to reduce the pumping efficiency. This drug decouples the electrical signal from the muscle. In relative low doses, we noticed a reduction in cardiac output without affecting the heart rate. This finding enable us to investigate the pumping mechanism by comparing the wall mechanics of a normal heart (control) with the wall mechanics of a heart with reduced efficiency (after using BDM in the same embryo), (figure 1).

Wall mechanics of embryos treated with BDM showed a group of cells not subjected to any form of motion whereas further on the hearttube cells responded normally. This suggest active contraction of muscle cells other then the pace maker cells emphasizing the pumping mechanism to be peristaltic instead of dynamic suction.

To further investigate this we plan to build a computer model of the embryonic heart. Zones actively contracting should be characterized as higher pressure zones on the wall.

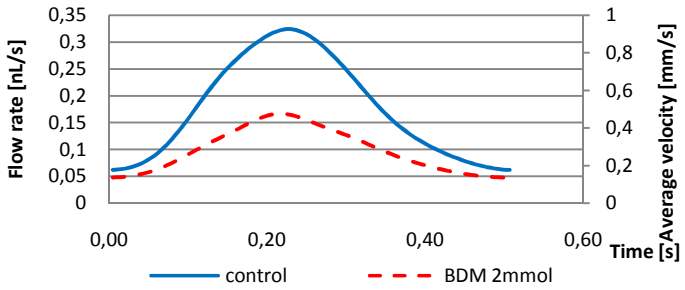

Figure 1. flow rate and blood velocity in a 30 hpf zebrafish aorta

Hove, J.R., et al., Nature, 421(6919): 172-177, 2003.
Forouhar, A.S., et al., Science, 312(5774): p. 751-753, 2006.