Separation, denoising, and reconstruction of multi-dimensional embryonic cardiac microscopy datasets for improved visualization and flow analysis

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Heart development is a highly dynamic process since the heart is beating long before it has reached its final shape. Currently there is a need for novel image processing techniques for image component separation, denoising, and reconstruction of high frame-rate, high resolution, multi-dimensional cardiac datasets acquired during live (in-vivo) imaging of the embryonic heart. Such methods would help quantifying blood flow and tissue deformation during cardiac development, thus facilitating a better understanding of the interplay between genetic and epigenetic factors that contribute to cardiac morphogenesis.

The first part of this thesis deals with capturing the dynamics of individual structures in the embryonic heart using label-free, high speed brightfield (BF) microscopy. To improve the specificity in these images, we propose a motion-based separation algorithm to decompose a single-channel 3D+time (3D+T) volume into three channels showing cyclic heart-wall, static support structures, and transient blood cells. The technique is based on non-uniform temporal synchronizing, selecting, and combining images from multiple cardiac cycles and z-sections to produce 3D+T image volumes of one full cardiac cycle that are highly suitable for velocity analysis and 3D-visualization.

In the second part, a novel computational noise reduction technique is proposed to restore optical coherence tomography (OCT) datasets of cyclically moving structures. This allows imaging dynamic structures and fluid flow within scattering tissue like the embryonic mouse heart, while preserving temporal and spatial resolution.

In the final part, we discuss reconstruction of a 3D+T cardiac volume from multiple high-speed 2D+T sequences that are sequentially acquired along multiple heart beats. Current methods overcome the limitation of low frame-rates in direct 3D+T imaging either by synchronizing the 2D+T sequences using complex triggering hardware during acquisition or by image-based retrospective temporal registration of the 2D+T sequences which accumulates registration errors. We propose a technique that uses image-based retrospective gating for temporal alignment but mitigates the cumulative registration errors by using a second set of 2D+T sequences acquired at an angle different from the first. By globally minimizing an objective criterion that depends on the similarity between the data present at the intersecting slices, the two sets are registered and fused to get a high-resolution multi-dimensional reconstruction of the heart. This method enables inference of 3D optical flow by combining the 2D flow (a projection of the 3D flow on to the plane of observation) from each 2D+T sequence.

In summary, this thesis contributes along three folds: a motion-based separation algorithm to improve specificity in high-speed cardiac BF microscopy images; a denoising method for cardiac OCT that preserves spatial and temporal resolution; and a reconstruction technique for creating 3D volumes from multiple 2D slices. The tools developed have been adopted for the quantitative study of cardiac morphogenesis.