

Optical gating for cardiac imaging in dynamic samples, from milliseconds to days

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Sample motion represents a major challenge for *in vivo* imaging on many different timescales, and nowhere is this more prominent than in the heart itself. Flow dynamics change on millisecond timescales, the full heart cycle is completed several times per second, mobile cells such as immune cells interact on timescales of minutes, and developmental processes unfold over the course of days. Our goal, through optical gating, is to synchronize imaging such that imaging in the heart is as stabilized and routine as imaging in any other tissue.

We have developed a system, now in routine use for 24h timelapse zebrafish cardiac imaging studies, to actively trigger image acquisition in time with the heartbeat [1,2]. This permits “stroboscopic” 3D image acquisition with minimal light exposure, avoiding measurable phototoxic effects in a live sample and saving researchers from drowning in a sea of data acquired way faster than it can be analyzed. We will show recent example applications in studying immune response to injury, and cell fate studies in the developing embryonic heart.

Within a single heartbeat, optical gating is the key to obtaining accurate, quantitative measurements of rapidly-changing blood flow fields in the cardiovascular system [3]. These measurements are crucial for precision measurement of biomechanical quantities such as wall shear stress and actual pumped volumes in the presence of flow regurgitation. We will discuss how our optical gating approach has enabled us to accurately fuse information across multiple images (each representing one sampling of flow), to obtain reliable flow profiles in the face of raw data that is inevitably compromised by limited light levels and low tracer densities.

Together, these approaches are beginning to open up interesting possibilities to use *in vivo* microscopy to directly explore the coupling between structure, flow and electrical activity in normal and diseased hearts.

- [1] J. M. Taylor *et al.*, “Hybrid optical gating for long-term 3D time-lapse imaging of the beating embryonic zebrafish heart”, *bioRxiv* (2019).
- [2] C. J. Nelson *et al.*, “Imaging the Developing Heart: Synchronized Timelapse Microscopy During Developmental Changes”, *Proc. SPIE* **10499** 104991F (2018).
- [3] V. Zickus *et al.*, “3D + time blood flow mapping using SPIM-microPIV in the developing zebrafish heart”, *Biomedical Optics Express* **9** 2418-2435 (2018).