A Giga-Event Throughput TCSPC System for Real-Time FLIM: Achieving Lifetime Estimation within 1 µs

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Advanced medical imaging requires minimally invasive light-probing techniques capable of extracting fluorescence signatures that provide subcellular structural mapping. In this context, Time-Correlated Single-Photon Counting (TCSPC) provides sub-picosecond temporal resolution and extremely high sensitivity. However, pile-up distortion caused by the detection system dead time historically limited photon count rates to ≈5% of the excitation frequency, restricting operation at high illumination power [1]. To address this limitation, we introduced a novel TCSPC measurement paradigm that removes these constraints and enables operation in previously inaccessible count-rate regimes [2].

In this context, high-performance electronics, including ultra-low-dead-time photodetectors and high-throughput conversion systems, are essential. Although previous studies [3] demonstrated TCSPC operation beyond the classical 5% limit, system-level constraints persist due to the limited capability of acquisition electronics to sustain the throughput of modern photodetectors and the computational burden of processing time-tagged data. In this work, we introduce a comprehensive strategy for fluorescence lifetime measurements, achieving lifetime estimation within 1 µs and photon count rates up to 500% of the excitation rate (Fig. 1a). This performance relies on a custom single-photon detection module based on a 250 µm × 250 µm SiPM developed by FBK, featuring an output pulse with a FWHM of only 250 ps. By interfacing a commercial event timer with an external FPGA, we implemented custom firmware for near-real-time distortion correction, sustaining a throughput of 1.2 Gevents/s. The resulting giga-event-throughput system (Fig. 1b) pushes TCSPC-based fluorescence imaging toward a new generation of instruments suitable for hospital integration, enabling real-time clinical diagnostics and surgical guidance.

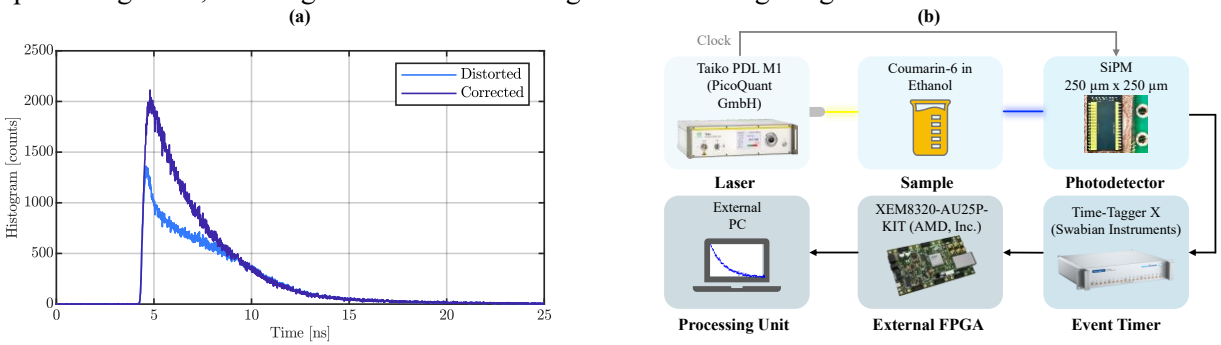

Fig. 1: *Real-time TCSPC-FLIM measurement (a) obtained with the developed giga-event-throughput system (b).*

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References

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[3] Fratta, Gennaro, et al. "Up to 200% of the excitation frequency in compressive FLIM: a constraint-free pile-up correction methodology for advanced biomedical imaging." *Optics Express* 33.12 (2025): 26444-26460.