Real-time Recurrent Neural Network-based Fluorescence Lifetime Imaging with SPAD Sensors

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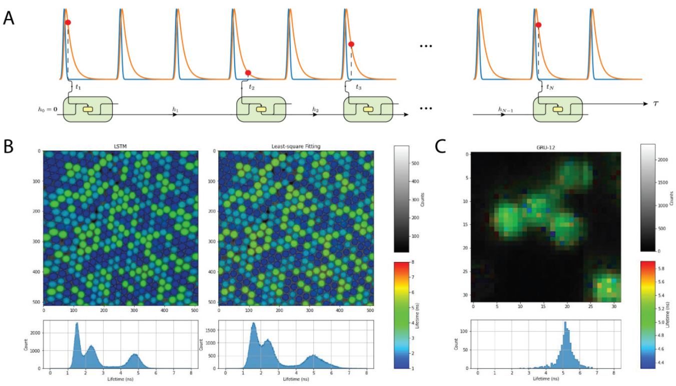
Abstract

Fluorescence lifetime imaging (FLI) has been receiving increased attention in recent years as a powerful imaging technique in biological and medical research. However, existing FLI systems often suffer from a tradeoff between processing speed, accuracy, and robustness. In this paper, we propose a recurrent neural network (RNN) based FLI system that accurately estimates fluorescence lifetime *directly* from raw timestamps instead of histograms. This process is done on the fly, in real time, as shown in Figure A. We train two variants of the RNN on a synthetic dataset and compare the results to those obtained using the center-of-mass (CMM) and least squares fitting (LSF) methods. The results demonstrate that two RNN variants, gated recurrent unit (GRU) and long short-term memory (LSTM), are comparable to CMM and LSF in terms of accuracy and outperform CMM and LSF by a large margin in the presence of background noise. We also looked at the Cramer-Rao lower bound and detailed analysis showed that the RNN models are close to the theoretical optima. The analysis of experimental data shows that our model, which is purely trained on synthetic datasets, works well on real-world data, as shown in Figure B. We build a FLI microscope setup for evaluation based on Piccolo, a 32x32 SPAD sensor developed in our lab. Four quantized GRU cores, capable of processing 4 million photons per second, are deployed on a Xilinx Kintex-7 FPGA. Powered by the GRU, the FLI setup can retrieve real-time fluorescence lifetime images at up to 10 frames per second (Figure C). The proposed FLI system is promising for many important biomedical applications, ranging from biological imaging of fast-moving cells to fluorescence-assisted diagnosis and surgeries.



A: Schematic of RNN-based real-time fluorescence lifetime estimation. Upon the detection of the photon, the arrival time is sent to and processed by RNN immediately, and the estimated lifetime is updated. B: Comparison of lifetime estimation of fluorescent beads with our model (LSTM) and commercial software (Least-square fitting). The beads have a diameter of 6.5 µm and the reference lifetime of 1.7, 2.7, and 5.5 ns. C: Real-time lifetime estimation of fluorescent beads with our setup.

References

1. Zhang, Chao; Lindner, Scott; Antolovic, Ivan Michel; Wolf, Martin; Charbon, Edoardo (2018): A CMOS SPAD Imager with Collision Detection and 128 Dynamically Reallocating TDCs for Single-Photon Counting and 3D Time-of-Flight Imaging. In Sensors (Basel, Switzerland) 18 (11), p. 4016. DOI: 10.3390/s18114016.
2. Wu, Gang; Nowotny, Thomas; Zhang, Yongliang; Yu, Hong-Qi; Li, David Day-Uei (2016): Artificial neural network approaches for fluorescence lifetime imaging techniques. In Optics letters 41 (11), pp. 2561–2564. DOI: 10.1364/OL.41.002561.
3. Li, Day-Uei; Rae, Bruce; Andrews, Robin; Arlt, Jochen; Henderson, Robert (2010): Hardware implementation algorithm and error analysis of high-speed fluorescence lifetime sensing systems using center-of-mass method. In JBO 15 (1), p. 17006. DOI: 10.1117/1.3309737.