Fluorescence Lifetime Opthalmoscope
A Theoretical Study

P2.16

Jakub Nedbal°, Brice Thurin°, Ahmet Erdogan•, Robert Henderson•, Alistair Bounds°

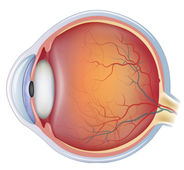
occuity

DISEASE

Need: Non-invasive early-detection methods for diseases like Alzheimer's and diabetes.

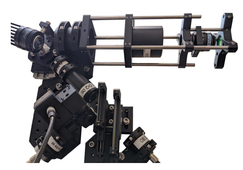
HUMAN EYE

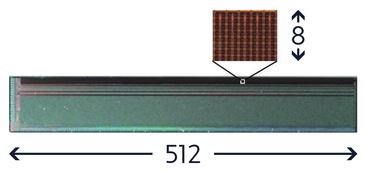
Opportunity: Diseases influence fluorescent properties of the human eye, specifically retina and lens.



TCSPC INSTRUMENT

Goal: Clinical scanning ophthalmoscope measuring human eye fluorescence using a linear SPAD array.





PROBLEM

Eye safety: Restriction on the laser excitation light dose reaching the eye limits the obtainable fluorescence signal.
Eye fluorescence is dim: Natural eye fluorescence is dim compared to engineered fluorescent dyes.
Eye fluorescence is given: It is not possible to add or remove autofluorescence of the eye for separate examination.
Eye fluorescence is mysterious: Each eye has different amounts of fluorescent compounds in different locations.
Ethics: Every experiment on human eye needs to be justified and minimise the risk of harm.
Cost: Large time expense to measure the eye fluorescence data, process them, and analyse them.

SOLUTION

Simulation: Monte-Carlo model of fluorescent photons originating in the retina and lens of the eye.
Realistic: Experimental data underpin the Monte-Carlo modelling.
SPAD array-specific: Model of SPAD, quenching circuit, OR-tree, and TDC behaviours.
Flexible: Model parameters can be altered at will and the outcomes studied.
Ground thruth: The input parameters are known and can be used to validate data analysis results.

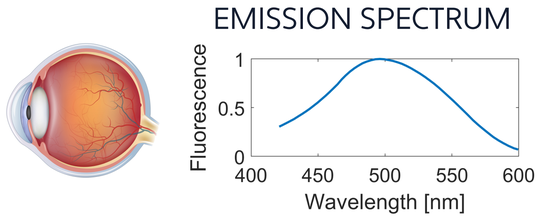
HUMAN EYE
Dimension, λ_{lens}, τ_{lens}, λ_{retina}, τ_{retina}

OPHTHALMOSCOPE
Idealised optical system relaying eye fluorescence

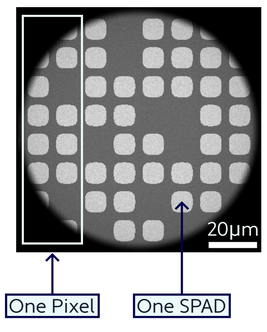
SPAD ARRAY
Active area, DCR, PDP, IRF, dead time, pile-up

DECAY FITTING
Levenberg-Marquardt non-linear least squares

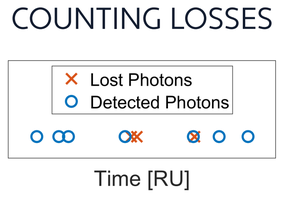
EMISSION SPECTRUM



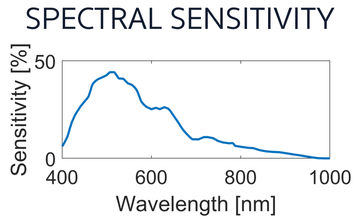
FLUORESCENCE PHOTONS FORMING A SPOT OF LIGHT ON THE SPAD ARRAY



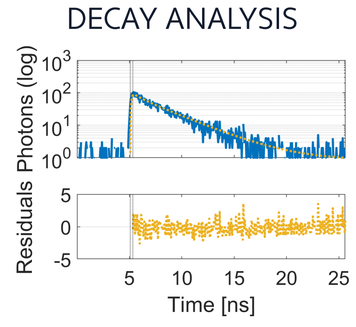
COUNTING LOSSES



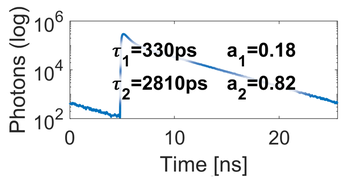
SPECTRAL SENSITIVITY

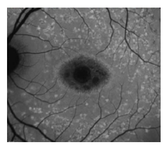


DECAY ANALYSIS

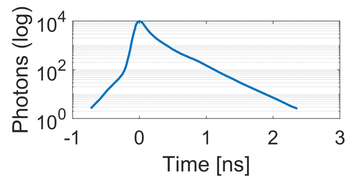


FLUORESCENCE LIFETIME





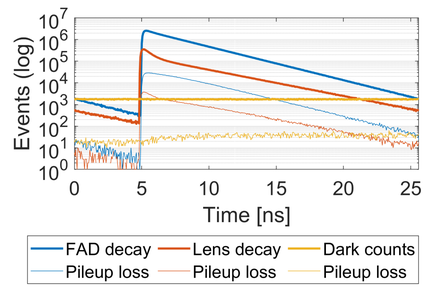
INSTRUMENT RESPONSE FUNCTION

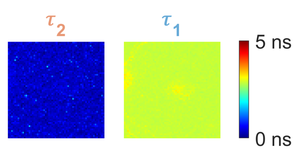
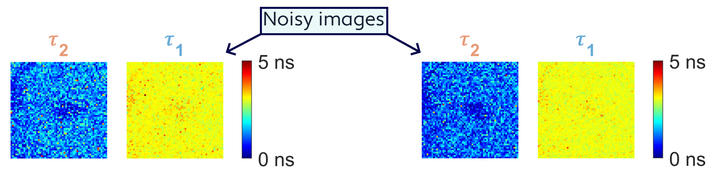
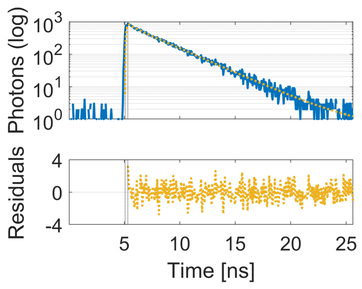
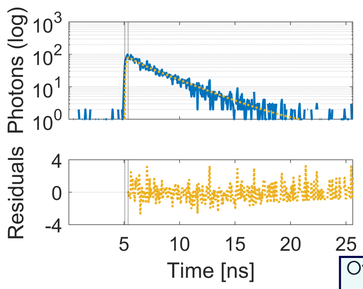
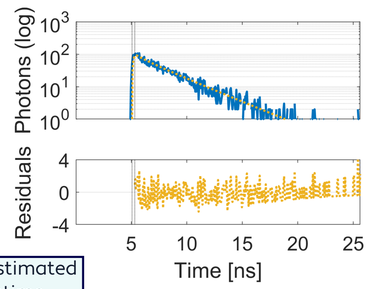
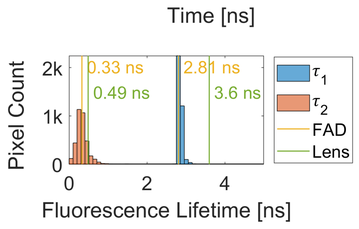
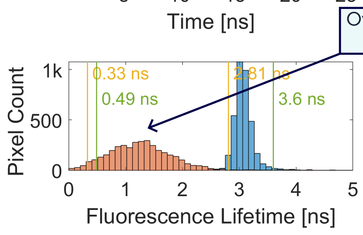
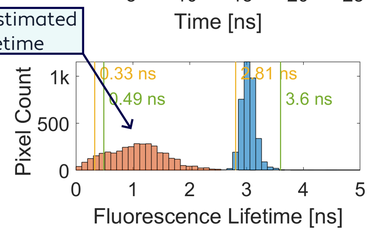


RESULTS

Decays: Pixel-by-pixel fluorescence decay data.
Images: Fluorescence lifetime and fractional contribution contrast.
Histograms: Pixel distribution of fluorescence decay fit results.
Informative: Separates SPAD count events of different origin.
Useful: Optimized fit conditions to match the ground truth.

DCR, PILE-UP & INDIVIDUAL DECAY ANALYSIS



Spot diameter	96 µm	96 µm	48 µm
Photon rate	36.3 MHz (4.71 MHz)	3.63 MHz (0.478 MHz)	3.63 MHz (0.534 MHz)
Dark count rate (after losses)	25.3 kHz (24.8 kHz)	25.3 kHz (24.8 kHz)	5.53 kHz (5.51 kHz)
Images 60×60 pixels 36 seconds			
Decays Single pixel			
Histograms Fluorescence lifetimes			

DISCUSSION

Summary: Monte-Carlo model of SPAD-based fluorescence lifetime ophthalmoscope for instrument development.
Benefit: Known ground truth, separation of SPAD events by their origin, in-depth analysis of losses and noise.
To-do: Model of data-transfer bottlenecks, on-chip histogramming, global fluorescence lifetime analysis, parametrization with real human eye data.
Weakness: Uncertain parametrization, high RAM demand.

° Occuity Ltd, The Blade, Reading, RG1 3BE, United Kingdom | • School of Engineering, University of Edinburgh, King's Buildings, Edinburgh, EH9 3FF, United Kingdom