Time Resolved Spectroscopy

with advanced CMOS single photon detector arrays for disease diagnosis in the distal lung

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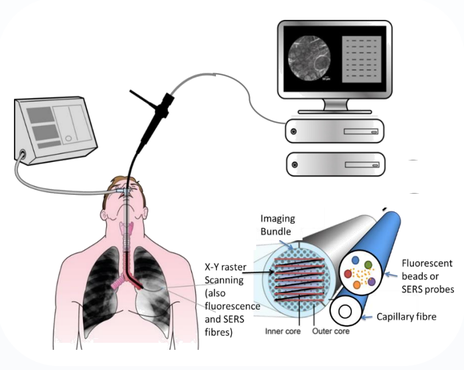
Introduction

With present diagnostic methods, identification of respiratory illnesses are inexact resulting in an often inaccurate multi-drug treatment. The Proteus project aims for a fibre-based sensing and imaging system to improve disease diagnostic in the distal lung for critically ill patients.
In this poster, a fibre based sensing methodology for physiological parameters like pH through exogenous fluorophores which varying their fluorescent properties with its biological environment is presented. The system uses a line array of CMOS Single Photon Avalanche Diodes (SPAD) which enables us for single photon detection through Time-Correlated Single Photon Counting (TCSPC).



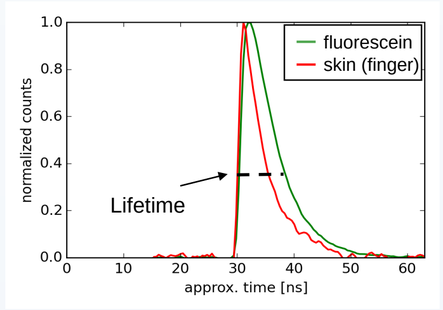
Aims

- Recording full TCSPC histograms for 256 pixel simultaneously.
- Distinguish between the tissue autofluorescence and fluorescence from fluorophores in the 'green' spectrum.
- Remove the scattering background from the optical fibre in the 'red spectrum'.
- Sensing of pH variation through changes in the fluorescence lifetime.

Fluorescence Lifetime Spectroscopy

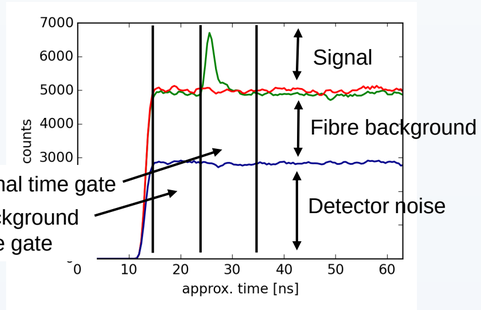
- measuring intrinsic tissue properties and accurate measurement of fluorescent probes in the distal lung.
- Fluorescence lifetime is an intrinsic parameter of fluorophores.
- Independent of fluorophore concentration, hence fluorescent intensity, and not affected by photobleaching.

'**Green' spectrum**
500nm – 600nm



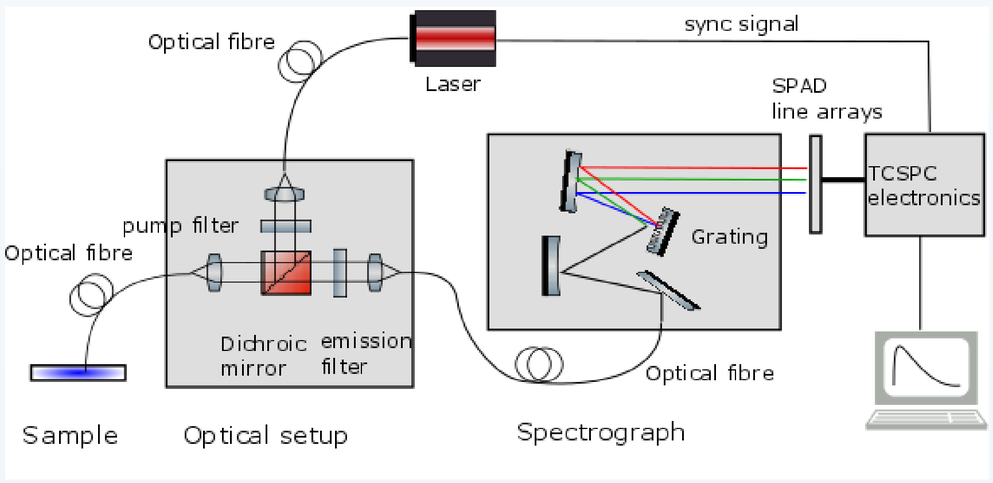
The autofluorescence of tissue can be resolved and may be used for label free sensing. The fluorophores with longer fluorescence lifetime can be distinguished from tissue.

'**Red' spectrum**
650nm – 750nm



Time gating allows for an easy subtraction of the background from detector noise and optical fibre.

The Experimental Setup

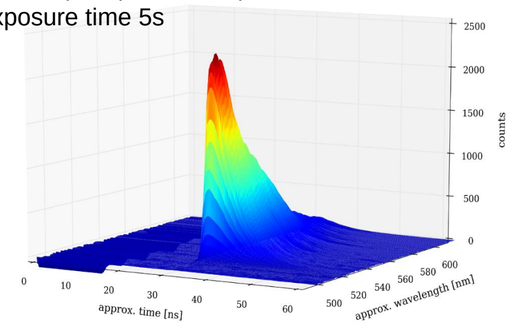


- Point detection of fluorescence using an optical fibre
- Dispersive element to separate the emitted light into its wavelengths
- TCSPC technology for recording dynamical processes

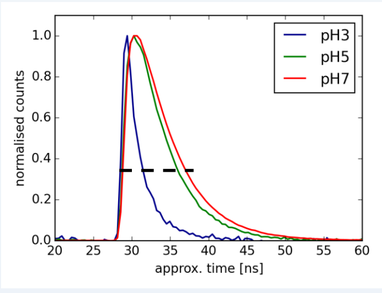
pH Sensing

- pH as a potential marker of tissue acid-base status
- a sensing methodology in inflammatory environments

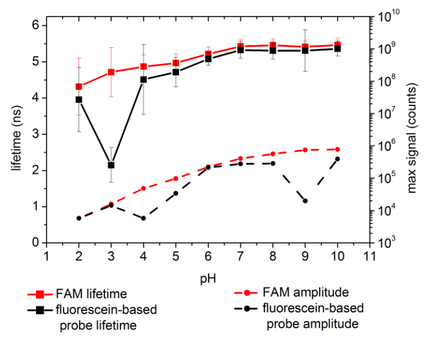
Fluorescence decay of Fluorescein amidite (FAM) solved in pH 7
Exposure time 5s



Single Exponential Fit with a Least-Square-Method to determine the fluorescence lifetime pixelwise

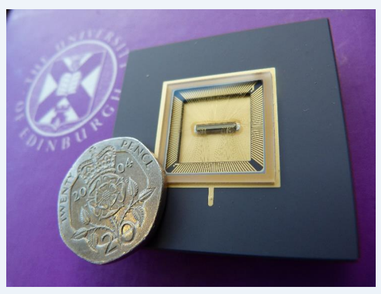


Small changes in the fluorescence lifetime can be measured and used for point sensing of pH in the distal lung.

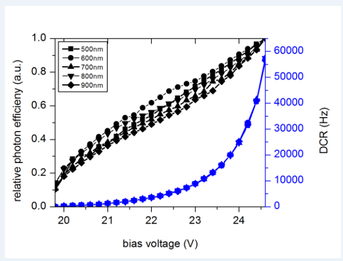


Line Sensor Ra 1

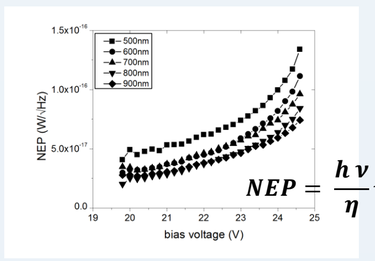
- 256 x 2 pixel, each pixel 4 Single Photon Avalanche Diodes (SPADs)
- Line rate 700 Hz
- Time-to-Digital conversion 0.42ns
- Timing jitter: IRF ~1ns



Dark count rate (DCR)



Noise-Equivalent Power



References
[1] J. R. Lankowicz. *Principles of Fluorescence Spectroscopy*. 3rd edition, Springer, 2010
[2] N. Krstajic et al. "256x2 SPAD line sensor for time resolved fluorescence spectroscopy", Optics Express 23.5, 2015

Acknowledgements
The author would like to thank the Heriot-Watt University for funding through the James-Watt Scholarship. We would like to thank the Engineering and Physical Sciences Research Council (EPSRC, United Kingdom) Interdisciplinary Research Collaboration grant EP/K03197X/1 for funding this work. We would like to thank the OPTIMA CDT for the Fianium laser and STMicroelectronics for Ra 1, further, all members of PROTEUS.