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Singlet oxygen luminescence detection with a superconducting nanowire single-photon detector

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***Abstract*—Superconducting nanowire single photon detectors (SSPDs/SNSPDs) are a highly promising infrared single photon detection technology, with free running operation, low dark counts and high timing resolution. We have applied SNSPDs to a new application in the life sciences and medicine, namely the direct monitoring of singlet oxygen luminescence at 1270 nm wavelength. Singlet oxygen is an excited state of the oxygen molecule, a crucial intermediate in many biological processes. We recorded luminescence from a photosensitizer solution using a fiber-coupled SNSPD optimized for 1270 nm wavelength installed in a practical closed-cycle refrigerator. Narrow band spectral filtering and chemical quenching was used to verify the singlet oxygen signal, and lifetime evolution with the addition of protein was studied. Furthermore, we demonstrated the detection of single oxygen luminescence through a single optical fiber, a marked advance for dose monitoring in clinical treatments such as photodynamic cancer therapy.**

Keywords—superconducting detectors, infra-red detectors, single-photon detectors, singlet oxygen, luminescence spectroscopy

I. INTRODUCTION

Singlet oxygen ($^1O_2$), an excited state of the oxygen molecule, is a crucial intermediate in many biological processes. In the clinical domain, it is generated in most applications of photodynamic therapy (PDT) via photoactivation of a photosensitizing drug. Accurate dosimetry is needed to ensure that optimum treatment is delivered. Direct detection of the $^1O_2$ luminescence at 1270 nm wavelength is extremely challenging, due to the high reactivity of $^1O_2$ that results in very low emission probability (~10^{-8}) and short lifetime (<<1 µs) in biological media. About a decade ago, singlet oxygen luminescence dosimetry (SOLD) became technically feasible for the first time [1], using specialized photomultiplier tubes (PMTs) with extended near infrared (NIR) sensitivity, but significant limitations remain. The size and cost of NIR PMT detectors limits their widespread adoption, while their low quantum efficiency (~1%) restricts their utility, in particular making it impossible to achieve single optical fiber-based light collection from biological samples and limiting their clinical utility. Superconducting nanowire single-photon detectors (SNSPDs) [2] offer high infrared single-photon sensitivity, combined with picosecond timing resolution, low dark count rates and free running operation. We report the first demonstration of SNSPDs for $^1O_2$ luminescence detection [3].

II. EXPERIMENT

We employed a fiber-coupled cavity-enhanced SNSPD with >20% practical detection efficiency at ~1300 nm [4], representing a 20–fold improvement in efficiency over NIR PMTs used to date for SOLD. The singlet oxygen signature was isolated via time-resolved and spectrally-filtered luminescence measurements performed on Rose Bengal (RB) in solution as a model photosensitizer (fig. 1).

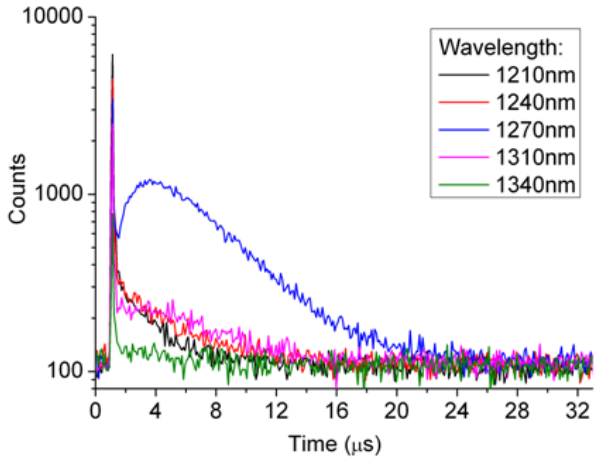

Fig. 1. Representative TCSPC histograms with a SNSPD from Rose Bengal photosensitizer solution (250 µg/ml, 0.257 µM) with bandpass filters (20 nm spectral width) centred at 1210, 1240, 1270, 1310 and 1340 nm [10 min acquisition time, 0.1024 µs bin size]. Short-lived fluorescence (occurring within the first µs) is present at all wavelengths studied; the key signature of $^1O_2$ is the onset and decay that is observed only at 1270 nm.

Quenching of the $^1O_2$ luminescence was demonstrated using sodium azide (fig. 2). Bovine serum albumen (BSA) was employed to simulate a proteinaceous biological environment; the evolution of the RB triplet and $^1O_2$ singlet-state lifetimes was successfully observed as the BSA concentration was increased.

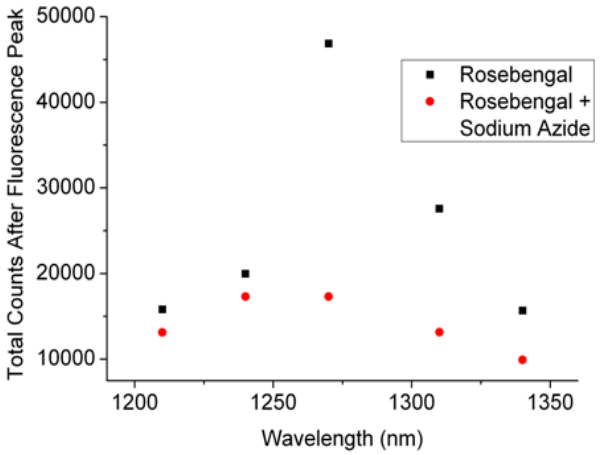

Fig. 2. Total counts within 3 min histograms (after fluorescence peak subtraction) from Rose Bengal (0.257 μM), using band pass filtering, before and after the addition of quencher sodium azide (2 M).

Finally, and most compellingly, an optical fiber delivery and collection scheme was demonstrated as a breakthrough advance in SOLD for *in vivo* preclinical and clinical applications. The laser beam is launched into a collimation package attached to a 62.5 μm core diameter multimode graded index fiber. A collimation package on the other end of the fiber then produces an expanded beam (3 mm diameter) that is directed into the cuvette. A separate collimator/focuser collected the emitted light into 9 μm core diameter single-mode fiber. The light is then sent through the bandpass filters, before being coupled into the telecom fiber connected to the SNSPD. Once again, the signal was confirmed through spectral filtering and sodium azide quenching. While about 60% (~30 mW) of the free-space pump power was delivered to the sample, the collected signal was approximately 2 orders of magnitude lower than with free-space collection, requiring long acquisition times (~30-60 min) to obtain a reliable measurement. In order to improve the signal-to-noise we reduced the current bias on the SNSPD, operating at 5% detection efficiency and a background (dark) count rate of <10 cps. Under these conditions, the system detection rate of the nominal $^1O_2$ signal was estimated to be ~0.6 cps.

III. Conclusion

In this study we have employed SNSPD technology in SOLD for the first time. The importance of this optical fiber delivery and collection advance lies in the potential for greatly widening the applications of SOLD to encompass effective *in vivo* SOLD monitoring, even in a clinical context: for example, fiberoptic-based detection would allow $^1O_2$ measurements in minimally-invasive endoscopic and intraoperative treatments, which are commonly used in photodynamic therapy of solid tumors (fig. 3).

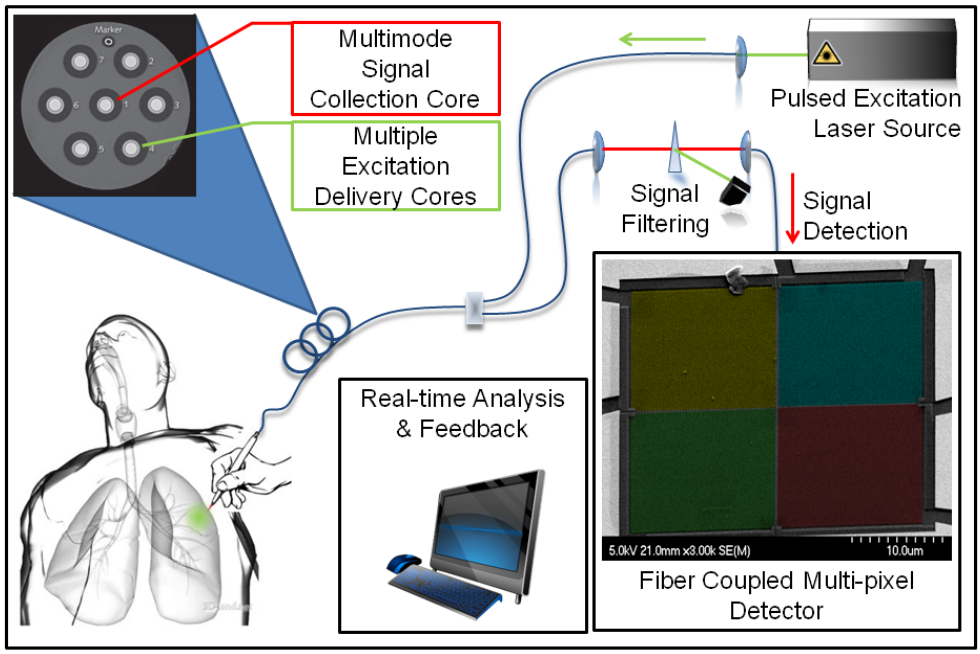

Fig. 3. An example of the future application of the system described. A Multiple core fiber delivery and collection system allows the detector to be housed remotely from the operating theatre. Next generation multiple pixel detector systems will allow the coupling of multimode fiber vastly increasing collection efficiencies and allowing real-time feedback to clinicians.

IV. REFERENCES

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