

# Application Note

## Imaging the *deep* brain with infrared light



The field of brain imaging uses various techniques to image the structure and function of the nervous system. It is an emerging discipline crossing the boundary of medicine and neuroscience that has seen tremendous advances in recent years.

### Technical challenge

Optical microscopy is a valuable tool for in-vivo studies of the brain due to its non-invasiveness and relatively simple implementation. For example, confocal microscopy is routinely used as a research tool to investigate the brain function of living mice [1].

However, scattering and absorption of light in biological tissue is non-negligible, limiting the imaging depth achievable: for visible light, the propagation distance at which light intensity decreases to half its original value (attenuation length) is around 300  $\mu\text{m}$ .

Longer attenuation length allows access to structures that are deeper in the brain; this is beneficial for brain imaging, and has only been achieved using multiphoton microscopy thus far. In multiphoton microscopy, two or more photons are used to excite fluorescent markers. This requires the use of expensive and complex pulsed-laser systems, limiting their application.

### Solution

A strategy that allows deeper imaging works at a wavelength wherein the attenuation length is longer [1]. Fig. 1 depicts the effective attenuation length of light in biological tissue, where two optimal wavelength regions can be found: one around 1300 nm and another around 1700 nm. These ranges lie in the so-called short-wave infrared (SWIR) region of the spectrum.

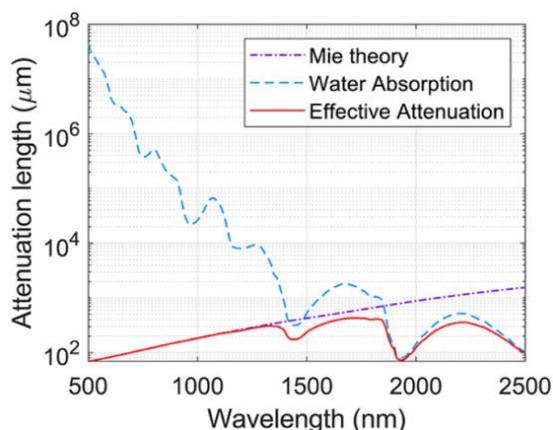


Fig.1: Attenuation length curve for brain tissue in the visible and SWIR range. The contribution of water absorption and scattering (Mie Theory) is shown. Reprinted (adapted) with permission from [1]. Copyright 2021 American Chemical Society.

Imaging in the SWIR can only be successful when efficient detectors are available. Superconducting nanowire single-photon detectors (SNSPDs) provide remarkable detection efficiency in this range (>80 % in 1550 nm - 1700 nm), in combination with high time resolution (<25 ps) and low dark counts (<100 cps), making them ideal detectors for SWIR confocal imaging applications.

### Experiment and results

Prof. Xu's group at Cornell University, in collaboration with Single Quantum, recently performed in-vivo confocal microscopy using laser excitation at 1310 nm and commercially available quantum dots (QDs) as emitting agent in the window of low attenuation around 1700 nm. This new configuration allowed them to achieve comparable imaging depths to that which multiphoton microscopy provides, with the advantage of using only easily available continuous-wave lasers.

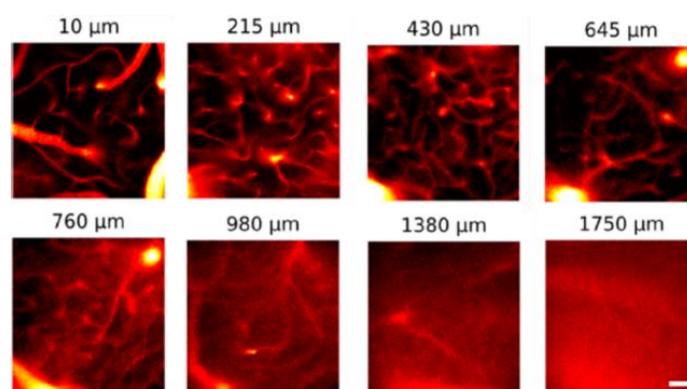


Fig.2: *Imaging the brain at SWIR range*. Confocal images of the intact mouse brain using SNSPDs as detectors. Scale bar: 50  $\mu\text{m}$ . Reprinted (adapted) with permission from [1]. Copyright 2021 American Chemical Society.

Fig. 2 presents the obtained images using an SNSPD detector. Note that at a depth of more than 1600  $\mu\text{m}$  imaging is still possible with a signal-to-noise ratio of 1, which is conventionally taken as the limit to resolve structures in an image [1].

In summary, the use of SNSPDs coupled to a confocal microscope operating in the SWIR opens up the possibility of imaging biological structures 2 to 4 times deeper than previously possible with one-photon confocal fluorescence microscopy.

**Reference:** [1] F. Xia, et. al. "Short-Wave Infrared Confocal Fluorescence Imaging of Deep Mouse Brain with a Superconducting Nanowire Single-Photon Detector". ACS Photonics 2021, 8, 9, 2800–2810 (2021).

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