SUPER RESOLUTION WITH SPAD IMAGERS

Ivan Michel Antolovic[1], Samuel Burri[2], Claudio Bruschini[2], Ron Hoebe[3], Edoardo Charbon[1,2]
[1]AQUA Lab, Department of Microelectronics, TU Delft, Netherlands
[2]School of Engineering, EPFL, Switzerland
[3]Academic Medical Centre, University of Amsterdam, Netherlands
E-mail: i.m.antolovic@tudelft.nl

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Localization super resolution microscopy (GSDIM, STORM, and other techniques) is based on accurately determining the center of sparsely activated point spread functions of single fluorophores. Since the number of detected photons determines image resolution, the cameras of choice have been EMCCDs because of their high quantum efficiency and built-in electron amplification. Lately, many researchers introduced sCMOS imagers in super resolution instrumentation, so as to take advantage of faster readout and absence of excess noise.

Alternatively, single-photon avalanche diode (SPAD) imagers can provide even faster frame rates and zero readout noise. We used a 1-bit 512x128 SPAD imager, called SwissSPAD, which enables a frame of 6.4 µs [1]. Variable sequences of 1-bit frames can be used to form gray level images of programmable resolution, while keeping the same time resolution information. The sensitivity of the imager, characterized as photon detection efficiency (PDE) has been boosted 12x using a microlens array mounted directly on the sensor [2].

We measured multicolor intensity florescence with SwissSPAD and compared its performance to a commercial EMCCD camera. Furthermore, the higher sensitivity enabled us to detect single fluorophores as required by GSDIM and to reconstruct super resolution images, while the 6.4 µs time resolution led to unprecedented accuracy in analyzing the blinking effects of the fluorophore independently in each pixel.

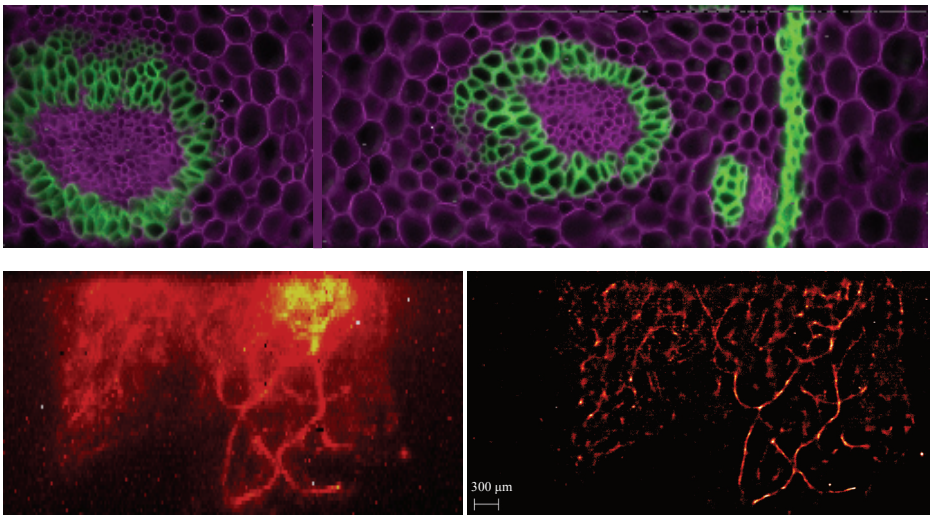

Figure 1: SwissSPAD multicolor fluorescence (top), widefield and super resolution (bottom).

[1] S. Burri, *et al*., "Architecture and applications of a high resolution gated SPAD image sensor," *Opt. Express,* **22**, 17573–89 (2014).
[2] J. Mata Pavia *et al.*, "Measurement and modeling of microlenses fabricated on single-photon avalanche diode arrays for fill factor recovery," *Opt. Express,* **22**, 4202–13 (2014).