# One photon at a time – CMOS SPAD imagers for FLI(M) and beyond


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- Advanced Quantum Architecture Laboratory


HILIGHT 2026, London, Mar 4-5 2026

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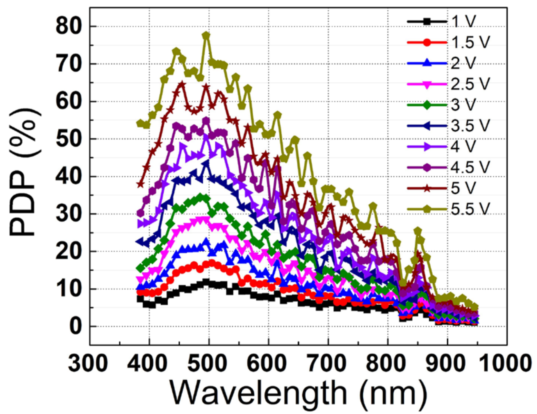
# SPAD Building Blocks, Key Metrics & Strengths

Detect/time-stamp single optical photons with CMOS Single-photon Avalanche Diodes (SPADs)

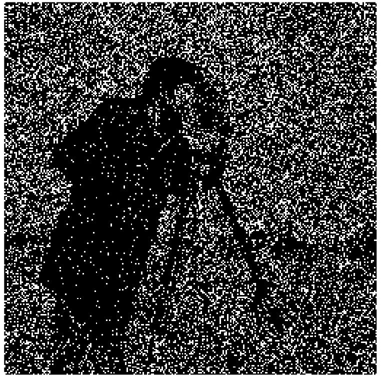
High sensitivity (up to 90% PDP)
Low noise (10-100 counts-per-second / pixel)

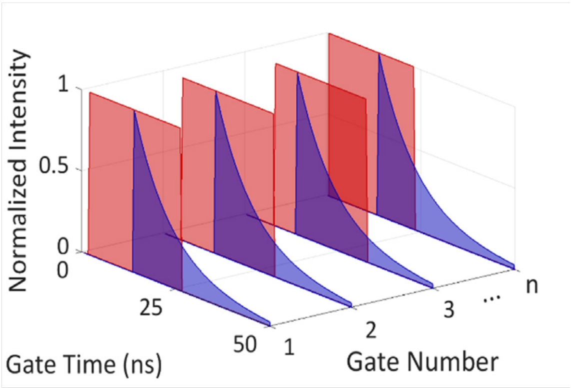
Excellent timing resolution (10-100 ps)

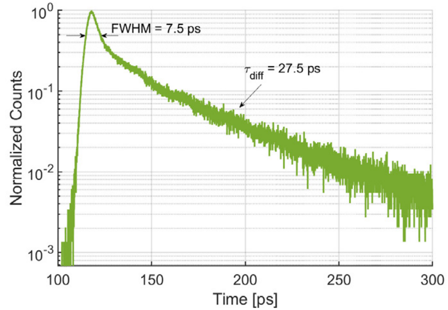
Increasing spatial resolution (kpx - Mpx)




U. Karaca, et al, IISW 2023
FSI 110 nm (monolithic)



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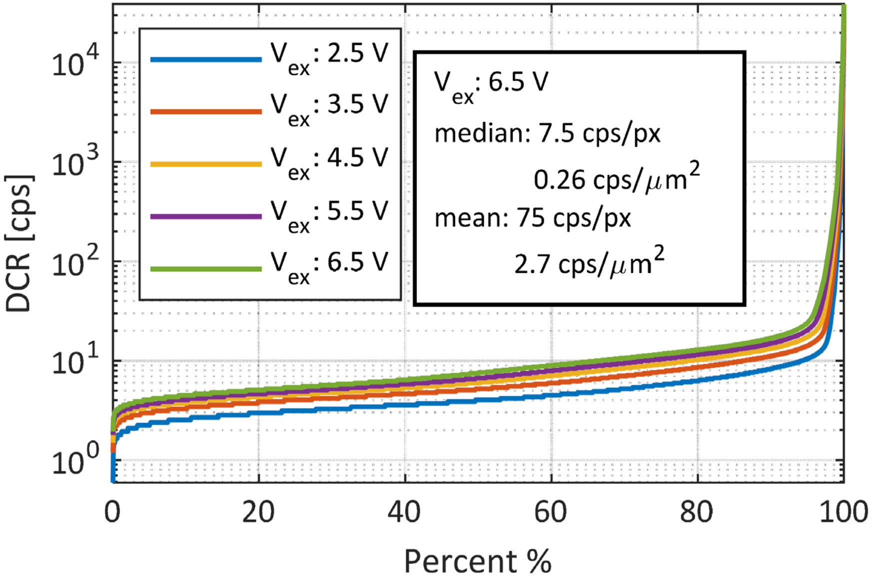
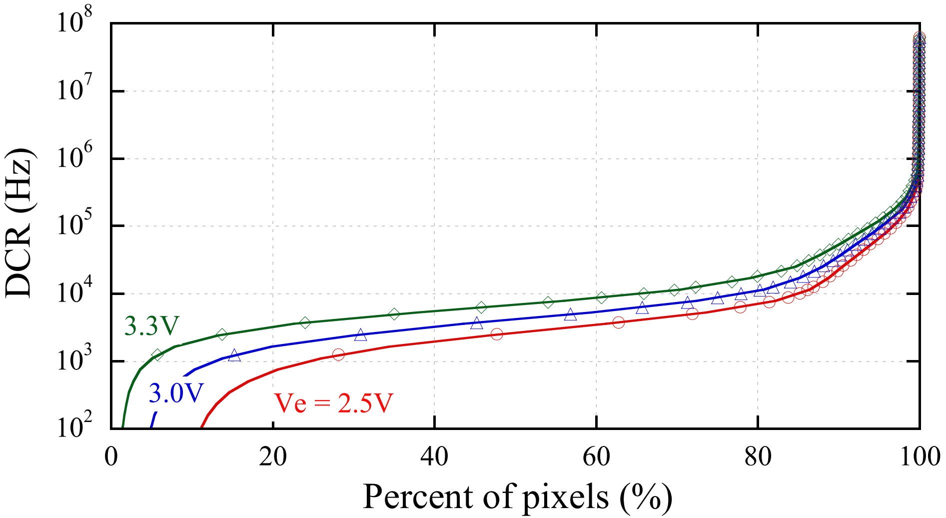
# From Pixels to Arrays & Imagers

# From single pixel to array properties: DCR example

- DCR (Dark Count Rate) population examples:
  - Left: SwissSPAD2 512x512px, 16.38 μm pitch, 10.5% fill factor native
  - Right: older 0.35 μm node
- Process dependent – not easy to obtain the corresponding statistics (large population)




Courtesy: Yuki Maruyama

- A Ulku, et al., JSTQE 2019

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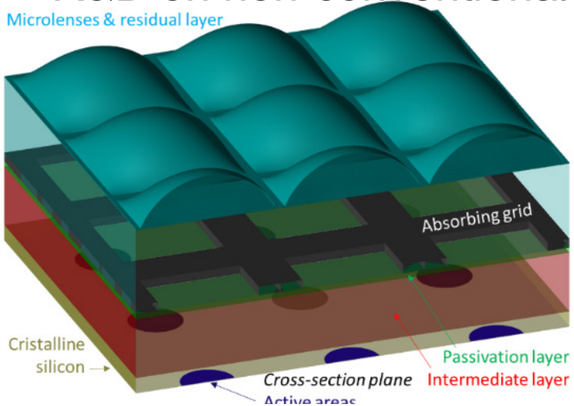
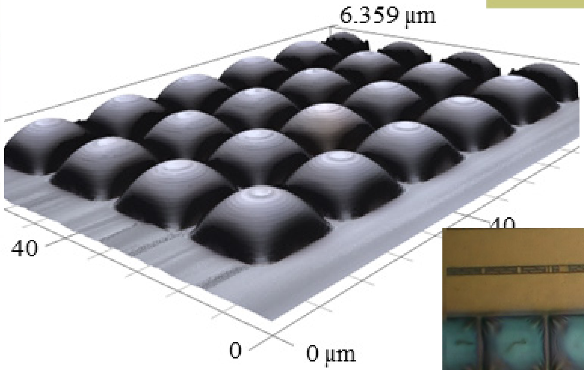
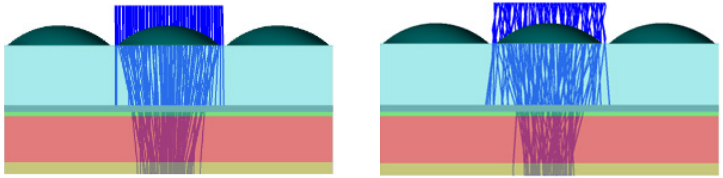
# Sensitivity: Fill Factor Recovery (Microlenses)

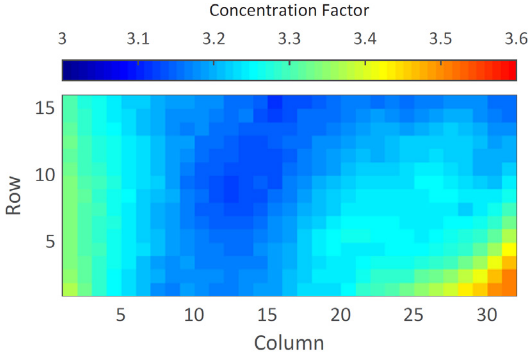
- (by far) Not all foundries support microlensing
- Optimised imprints possible on small quantities (sag/residual height)
- R&D on non-conventional geometries.

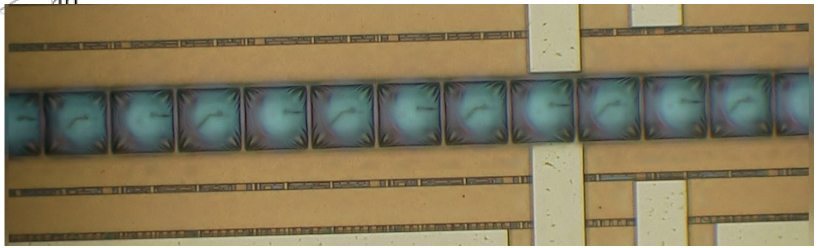


Low NA vs. high NA
→ Issues with scintillators!



R&D, die or reticle level, imprint (collaboration with CSEM)

- Bruschini et al., OpEx(31) 2023

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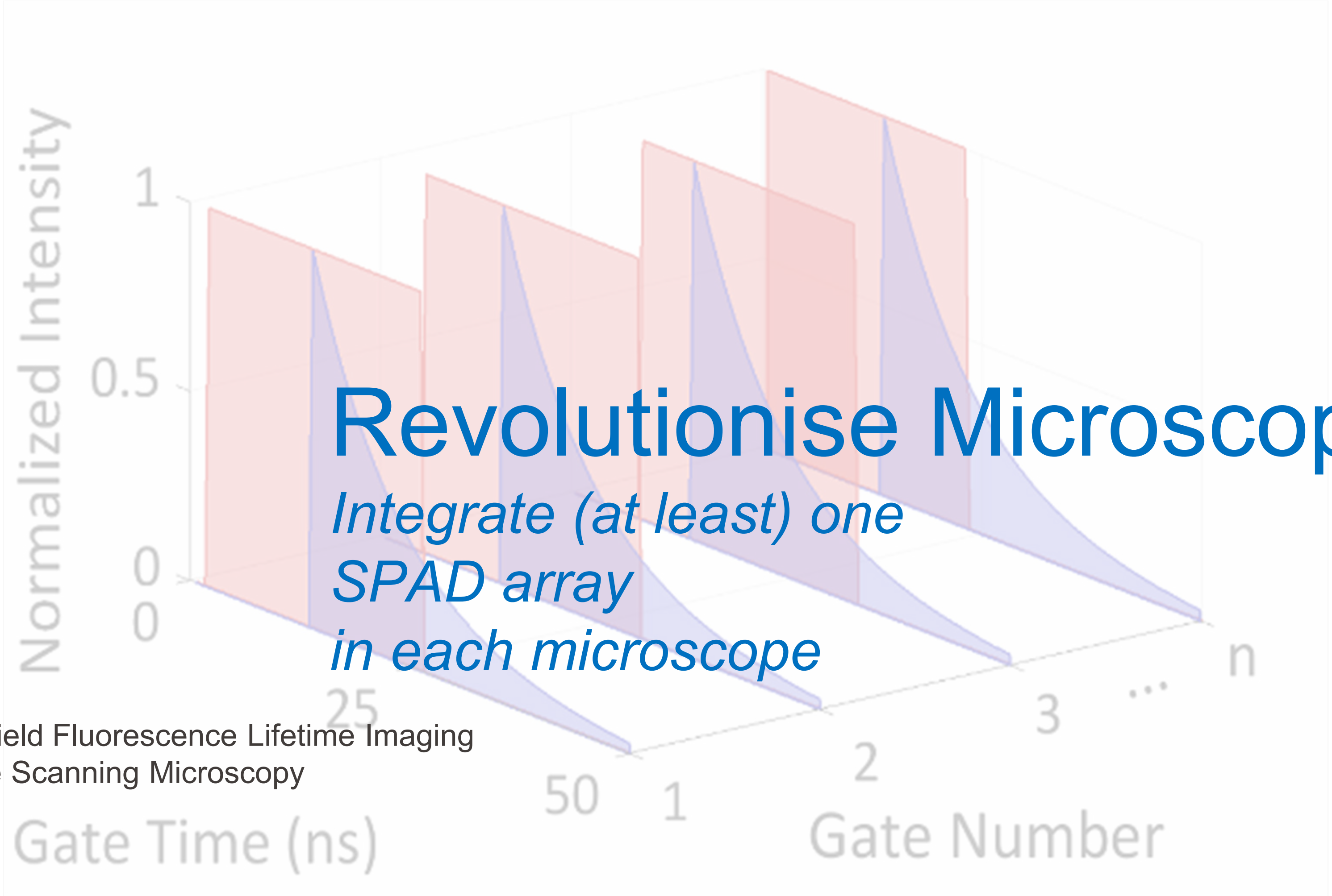
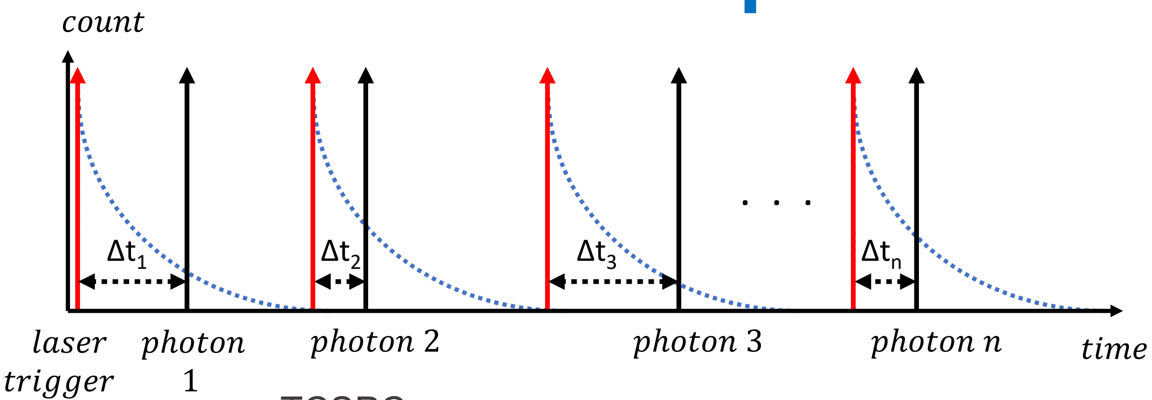


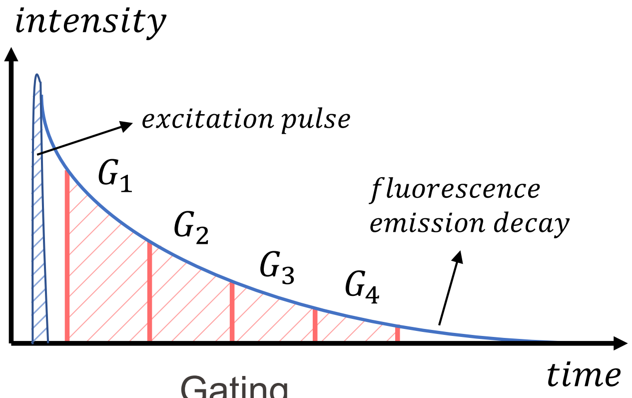

# Revolutionise Microscopy

*Integrate (at least) one SPAD array in each microscope*

Widefield Fluorescence Lifetime Imaging
Image Scanning Microscopy
…

# Data acquisition: TCSPC vs. gating



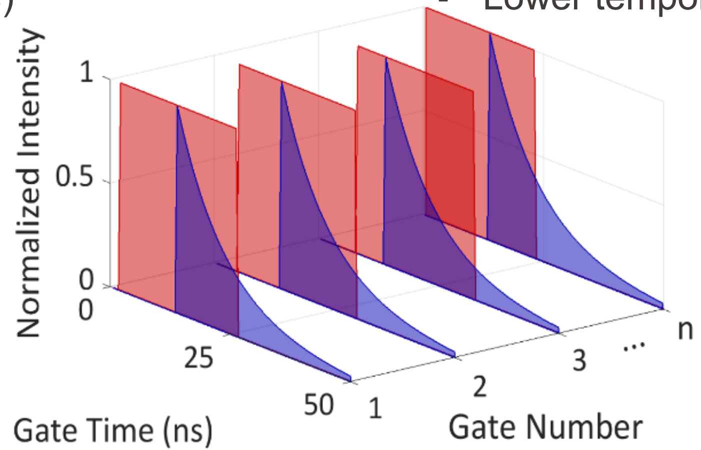




TCSPC
(time-correlated single-photon counting)

- \+ High temporal resolution (10-50 ps)
- \- Global photon count rate limitation

Gating

- \+ Simpler in-pixel implementation/high GCR
- \- Lower temporal resolution (large width)




**[A. Ulku, EPFL, PhD, 2021]**

(A. Ulku et al., MAF, 2020)

**Gate shifts as small as 18 ps!**

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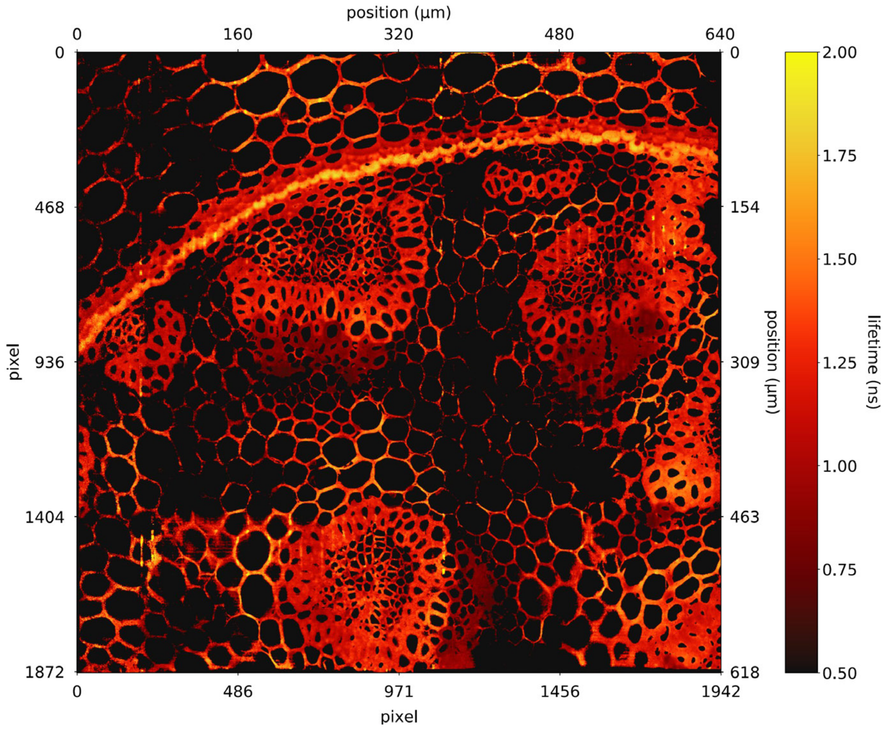
# Widefield (gated) vs. scanning (TCSPC) FLIM



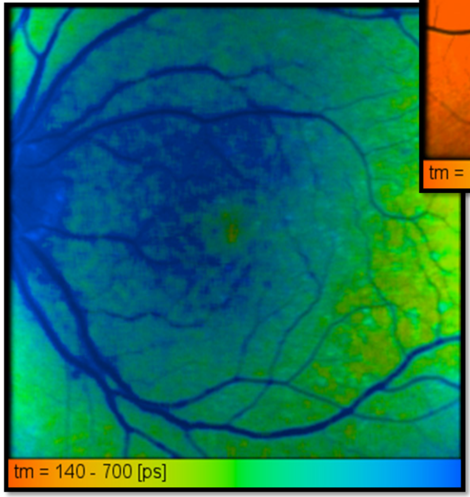
- Widefield, stiched (3.64 Mpx)+ ANN




**Zickus, Ma, et al, Sci Rep 2020**

Fundus Images, healthy vs. diabetic patient

(scanned, single-SPAD TCSPC)


*The final Frontier: in-vivo FLIM of endogenous Fluorophores*

**[M. Hammer, Univ. Hospital Jena, 2015]**



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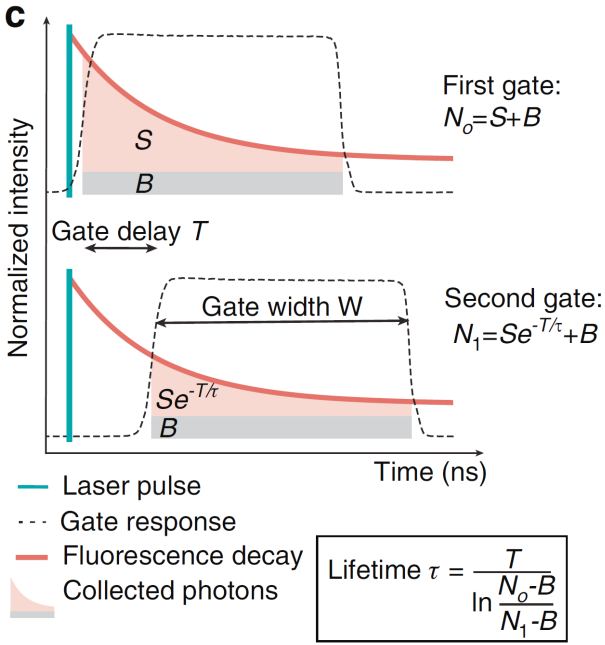
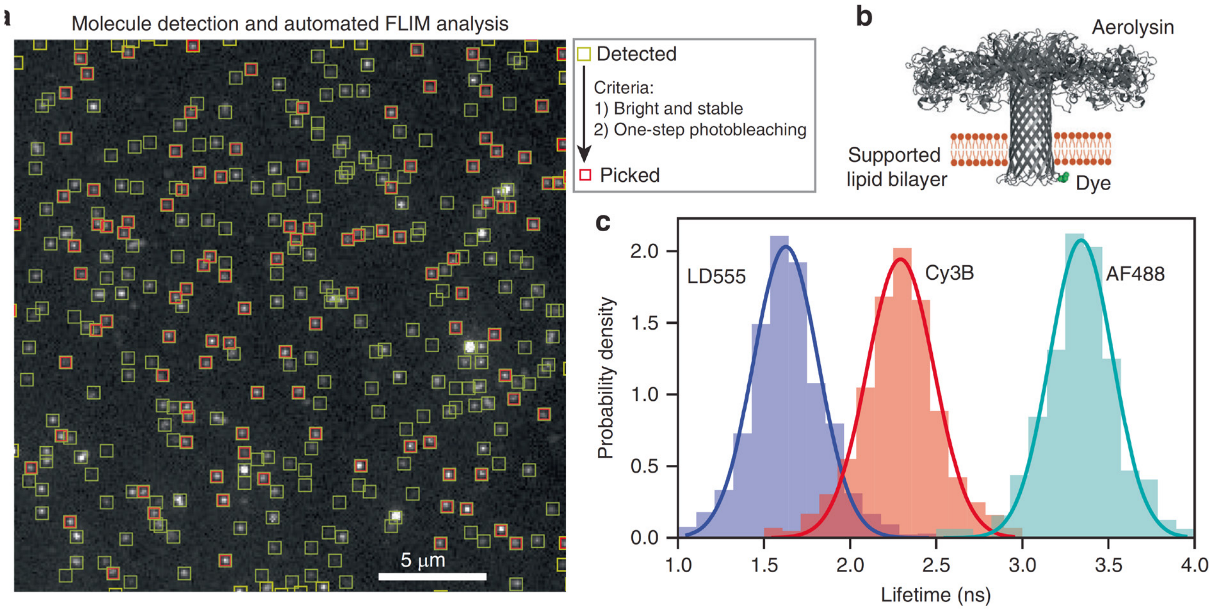
# More widefield FLI(M) / 1: less gates & RLD




*Wide-field fluorescence lifetime imaging of single molecules with a gated single-photon camera*

*SwissSPAD2: 512x512 binary gated imager @100kfps*

*RLD: rapid lifetime determination*

Ronceray et al. Light: Science & Applications (2025) 14:258
doi: 10.1038/s41377-025-01901-2

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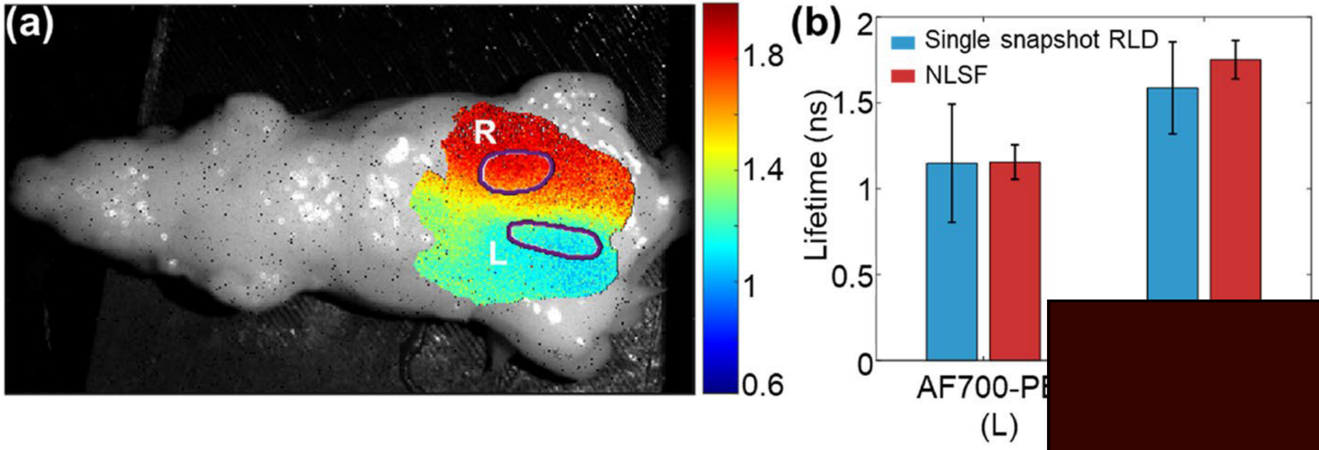
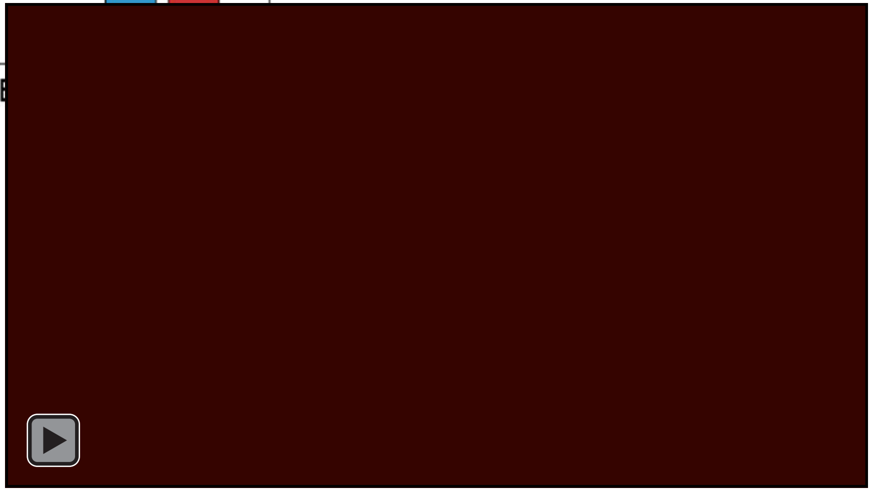
# More widefield FLI(M)/2: dual gate "snapshot"





*Real-time wide-field fluorescence lifetime imaging via single-snapshot acquisition for biomedical applications*

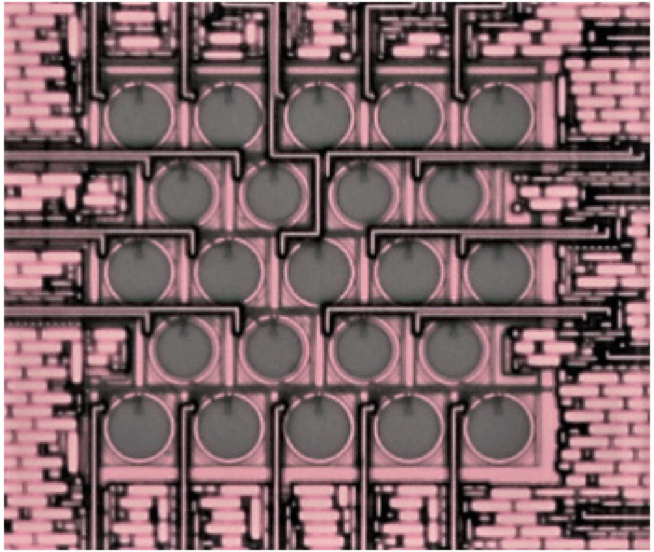
*SwissSPAD3: 500x500 px dual gate binary imager @50kfps*

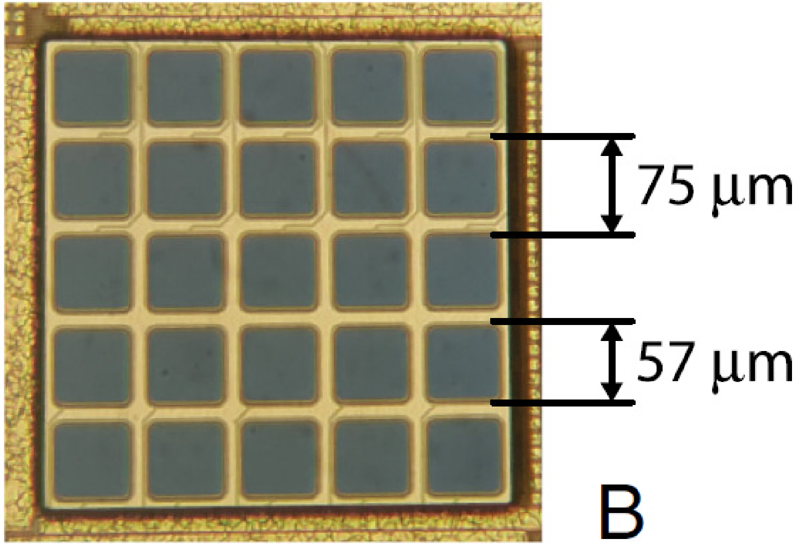
Pandey *et al. PhotoniX (2025) 6:5*
doi: 10.1186/s43074-025-00216-0

# Confocal - Next gen small-format high-performance SPAD imagers



Asynchronous readout (event-driven) of the individual pixels - excel in confocal applications

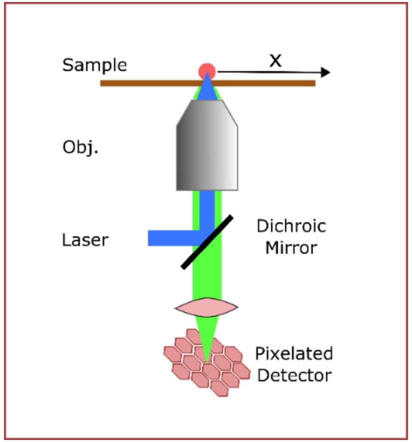




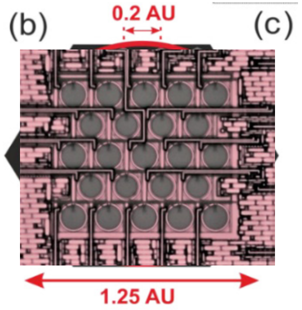

**Antolović et al, Optics Express 2018, FOM 2019 - 0.18 μm**
SPAD23 array (Pi Imaging Technology)

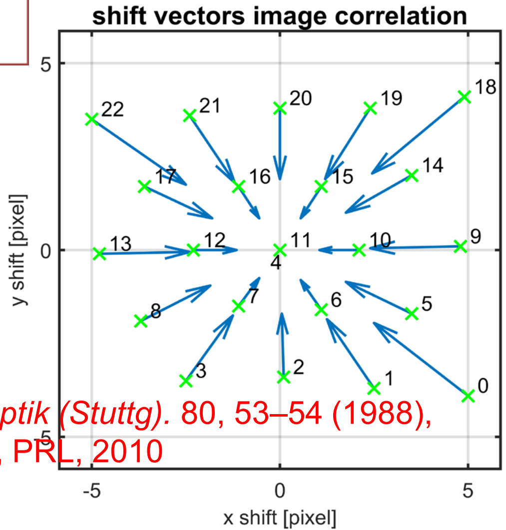
**Buttafava et al, Optica 2020**
**0.16 μm BCD**

# Image Scanning Microscopy (ISM)

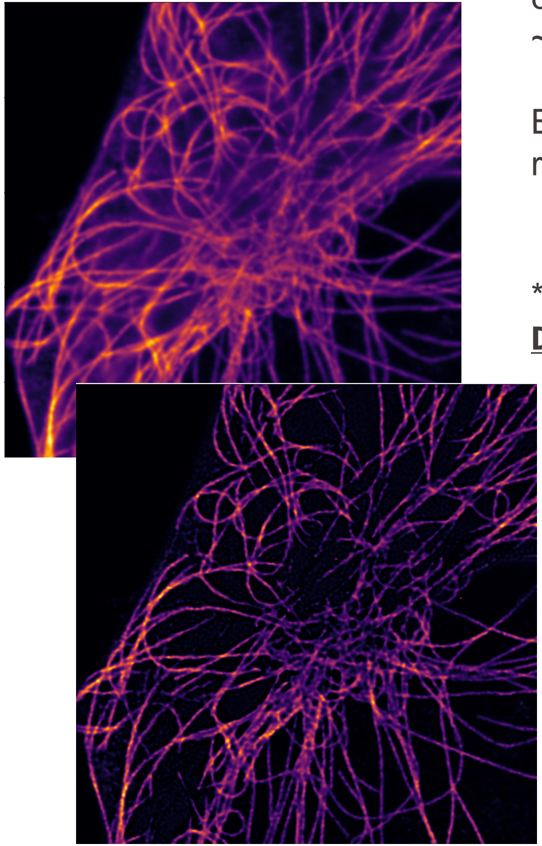



A pixelated confocal detector




Sheppard, C. J. R. *Optik (Stuttg).* 80, 53–54 (1988),
Muller and Enderlein, PRL, 2010



Top: pseudo-confocal (sum23) → ~190nm

Bottom: LC-DCV, reg. GR* → ~120nm

*deconvolved with **DeconvOptim.jl**

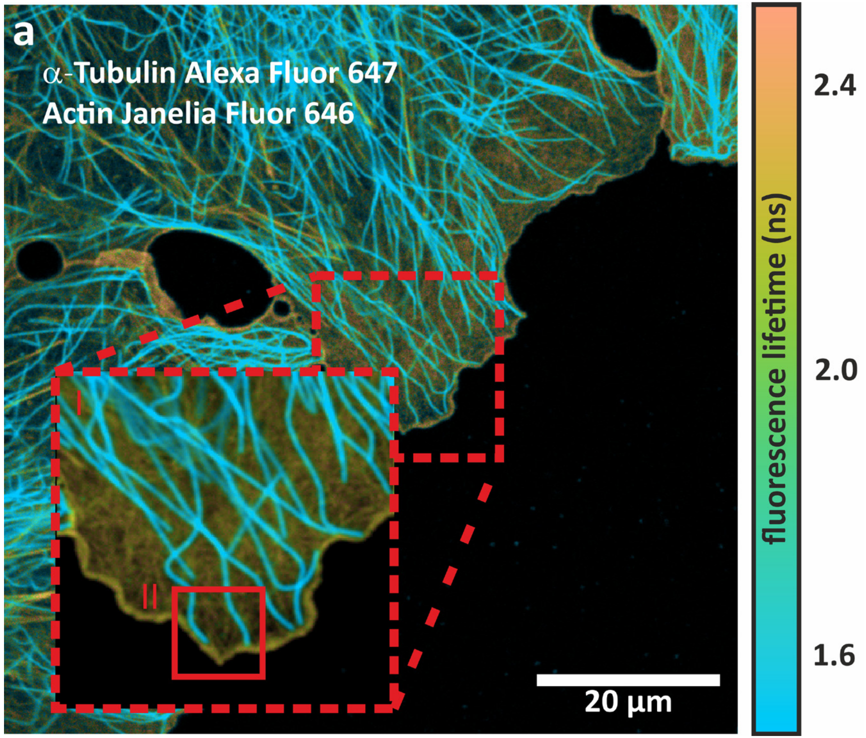
35nm/px, 512px x 512px
$\lambda_{ex} = 485$nm, NA1.45
100x oil,
Gattacell U2OS, α-tubulin AF488

*data taken with a non-cooled prototype*

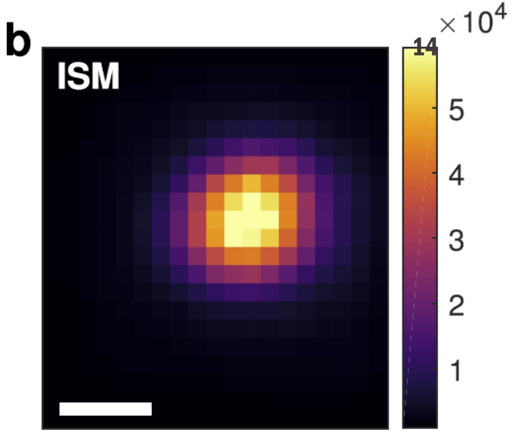
Data courtesy PicoQuant GmbH

# Image Scanning Microscopy and Beyond

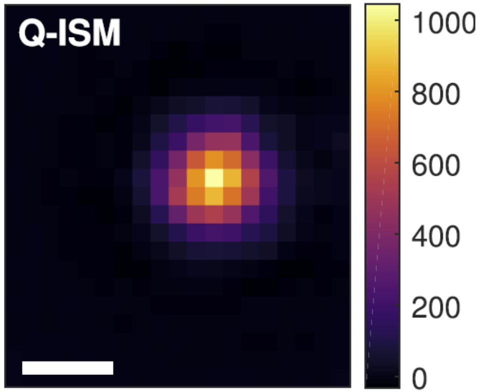
Image Scanning Microscopy + Fluorescence Lifetime
Single Molecule Localization Microscopy




Tenne et al, SPIE PW 2019; Lubin et al OpEx (23) 2019




Q-ISM: exploit quantum correlations




- Radmacher, …, Enderlein, NatPhot(18) 2024

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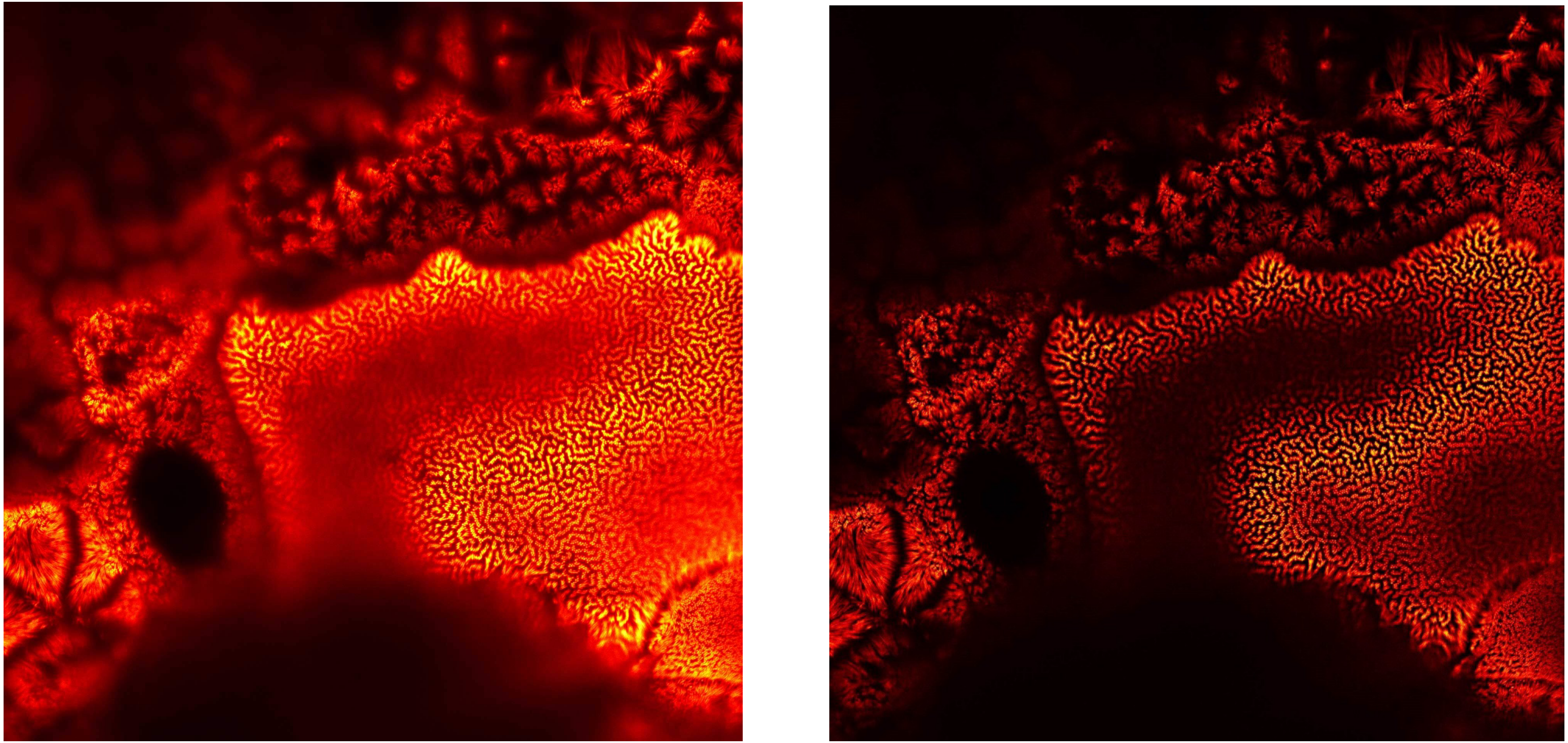
# Superresolution: STED & Background removal

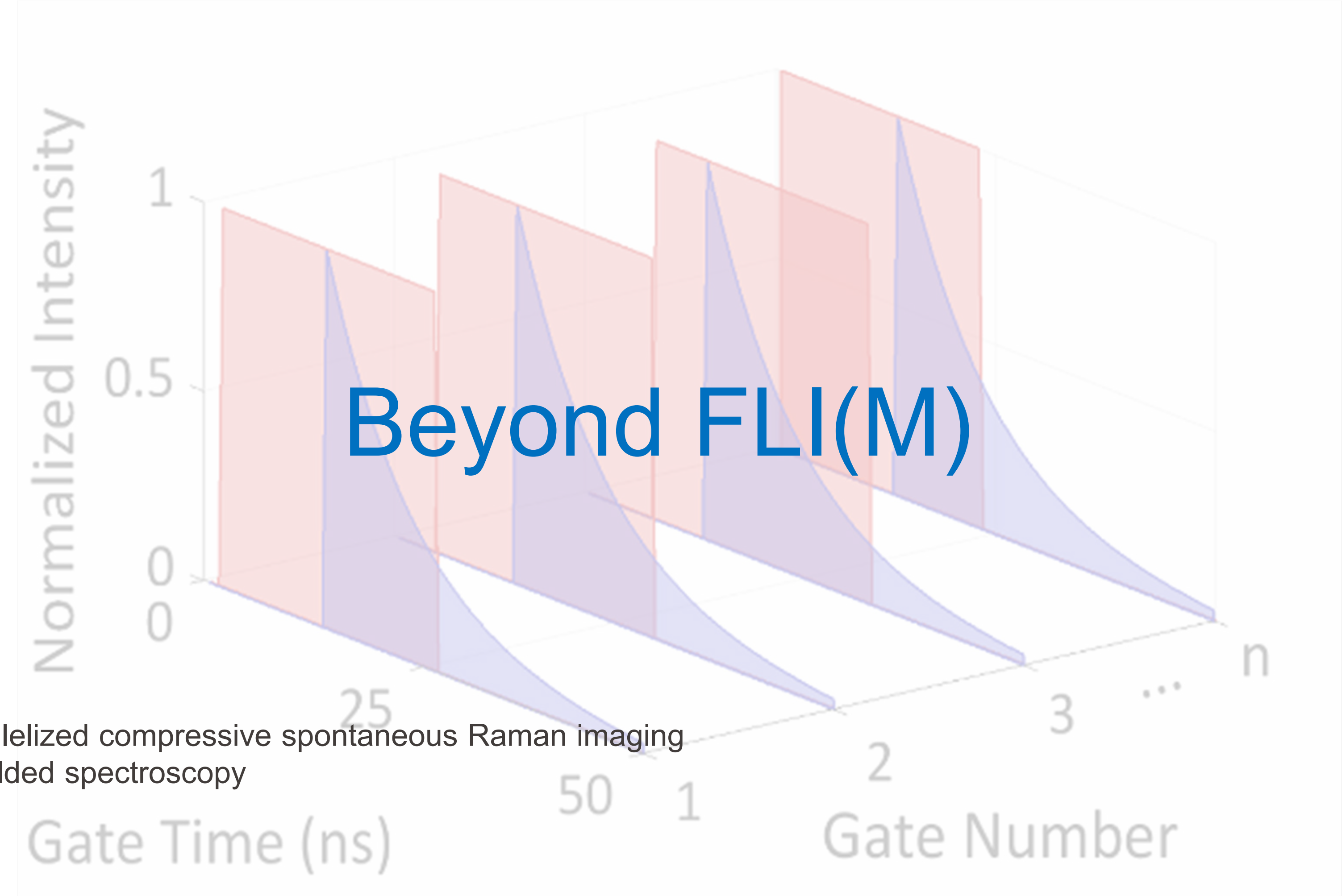




Abberior 2D STED, samples: Charité –Berlin

- Actin in microvilli of Caco2 cells. Fixed cells were stained with abberior STAR RED phalloidin. *MATRIX* detection -> background signal removal and optical sectioning improvement (2D-STED).

# Beyond FLI(M)




Parallelized compressive spontaneous Raman imaging
Heralded spectroscopy
…

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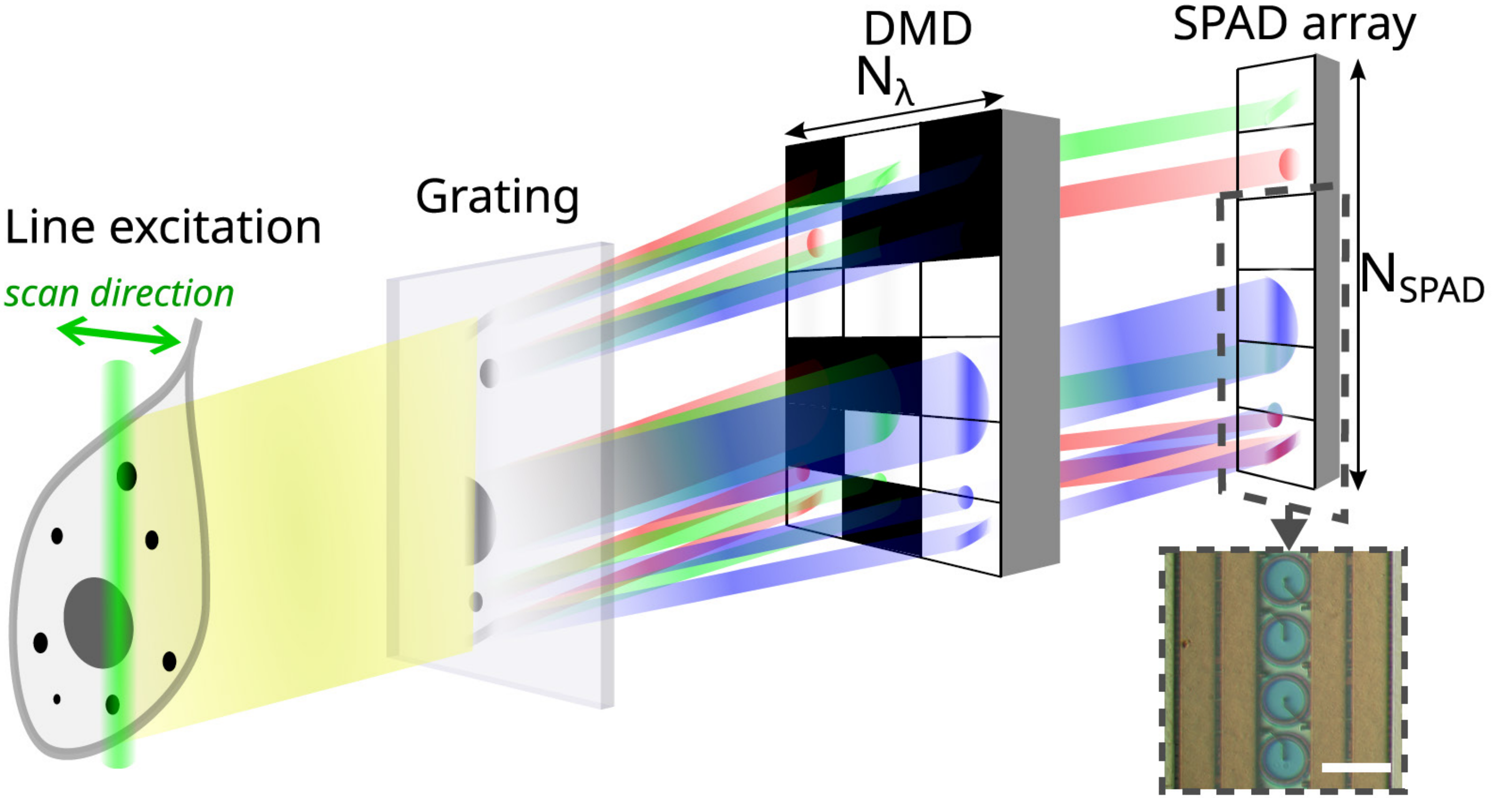
# Parallelized compressive spontaneous Raman imaging




C. Gentner, et al., OptLett 49(22) Nov 2024
C. Gentner, et al., SPIE PW 2023

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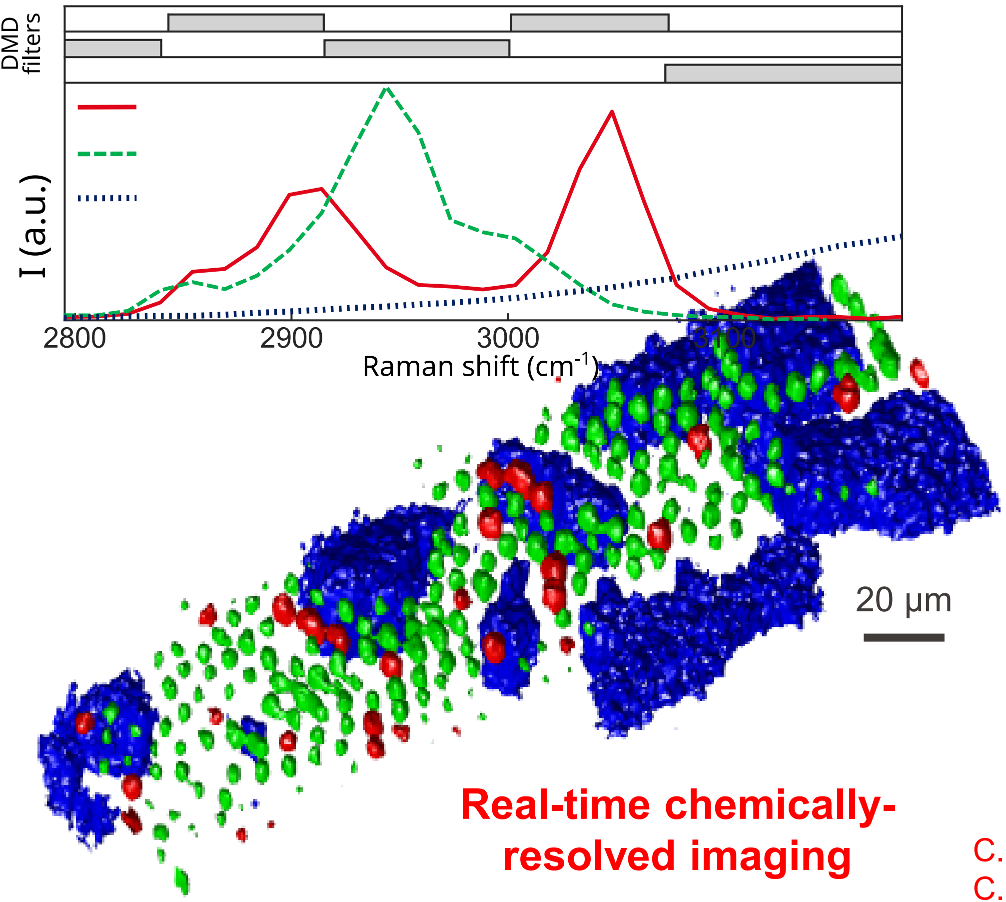
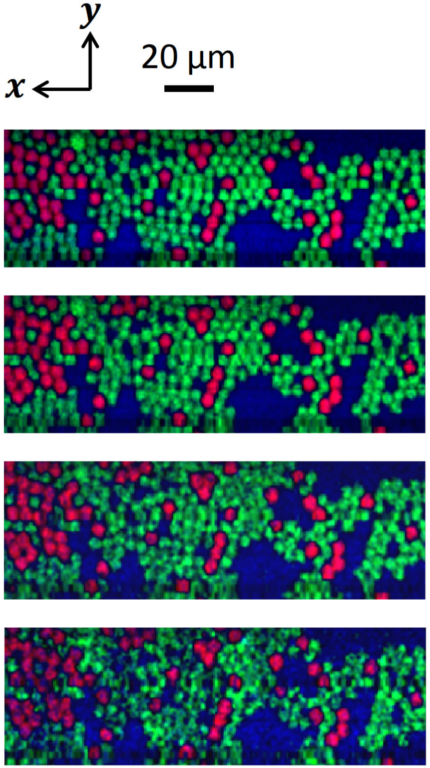
# Parallelized compressive spontaneous Raman imaging




| $\tau_{pdt}$ : | $f$ : |
|---|---|
| 33 µs | 0,4 Hz |
| 8,3 µs | 2 Hz |
| 1,7 µs | 11 Hz |
| 0,8 µs | 24 Hz |

**Real-time chemically-resolved imaging**

C. Gentner, et al., OptLett 49(22) Nov 2024
C. Gentner, et al., SPIE PW 2023

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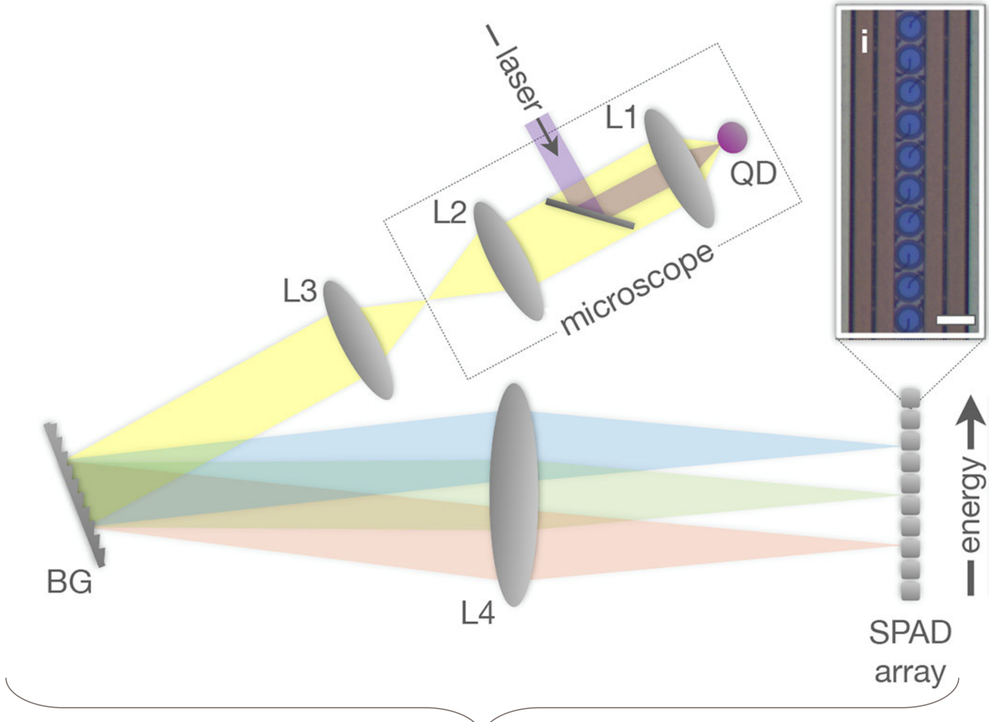
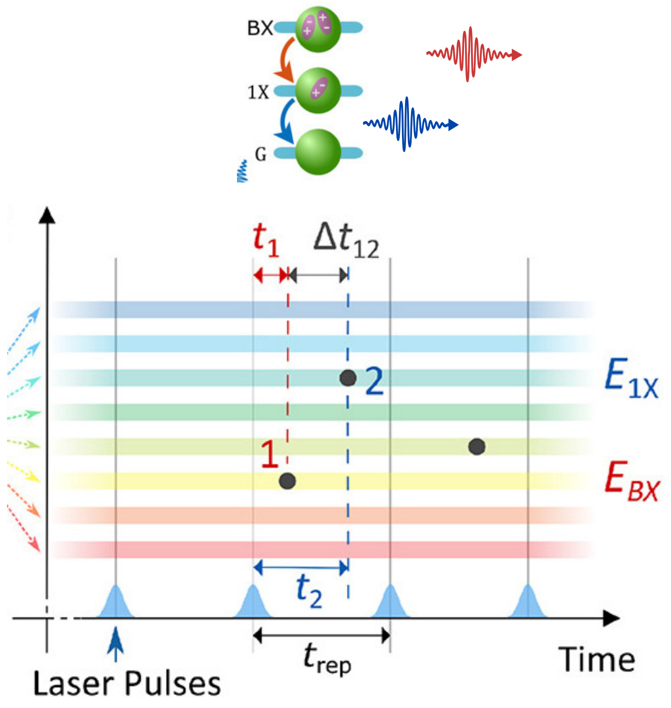
# Heralded spectroscopy




spectroSPAD apparatus




Heralded Spectroscopy post-analysis

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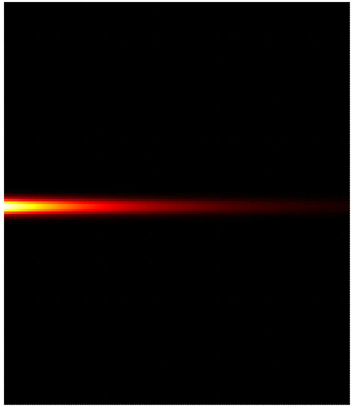
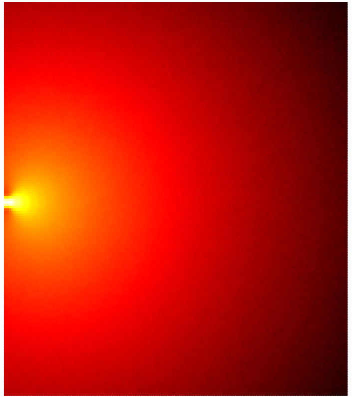
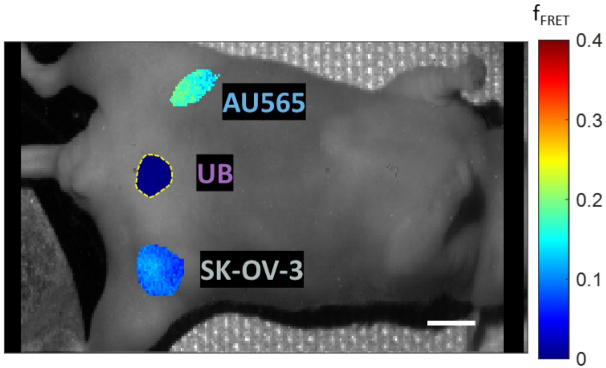
Lubin *et al., ACS Nano 15.12 (2021)*

Lubin*, Tenne* *et al., Nano Letters 21.16 (2021)*








J. T. Smith, et al., Optica(9) 2022

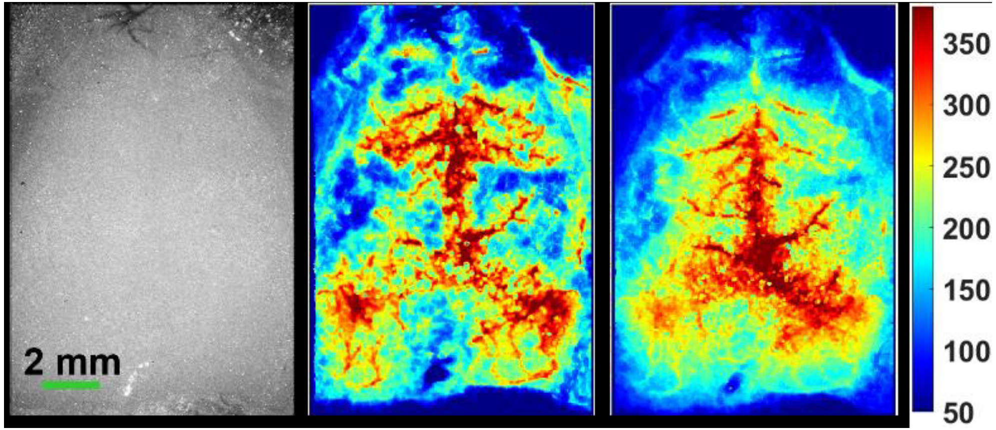
# Biophotonics /Molecular Imaging

*Pave the way for new use cases & eventually push SPAD imagers into clinical use*

# Deep Tissue Imaging



Raw intensity image | Gated mode | Intensity mode




Neuroimaging - 2D mapping of cerebral blood flow index (BFI) at different depths of the head – SwissSPAD2 + gated imaging

Time-resolved laser speckle contrast imaging

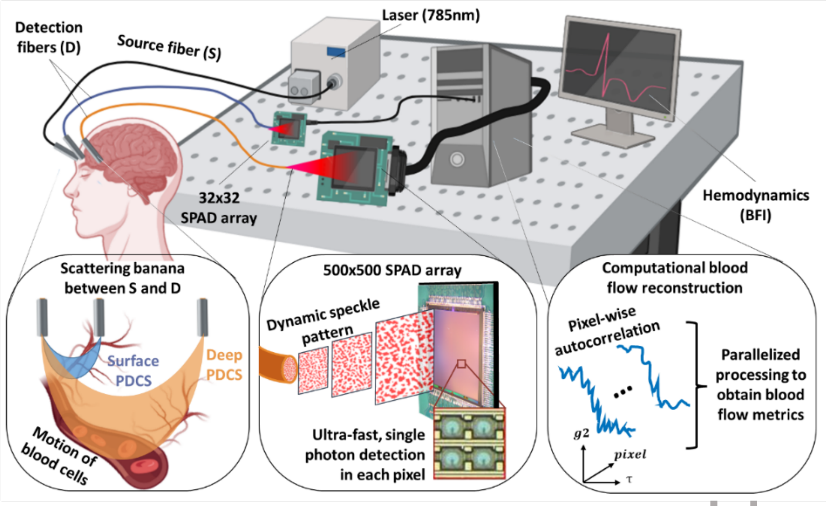
$$BFI \sim \frac{1}{K_s^2} = \frac{\sigma_s}{\langle I \rangle} = \frac{\sqrt{\langle I^2 \rangle - \langle I \rangle^2}}{\langle I \rangle}$$

F. Fathi, et al., IEEE TMI(44) 2025

$$g^2(\tau) = \frac{\langle I(t) \cdot I(t+\tau) \rangle}{\langle I(t) \rangle^2}$$

Parallelized DCS to measure cerebral and muscular blood flow. One pixel → one speckle.

Multispeckle Diffuse Correlation Spectroscopy

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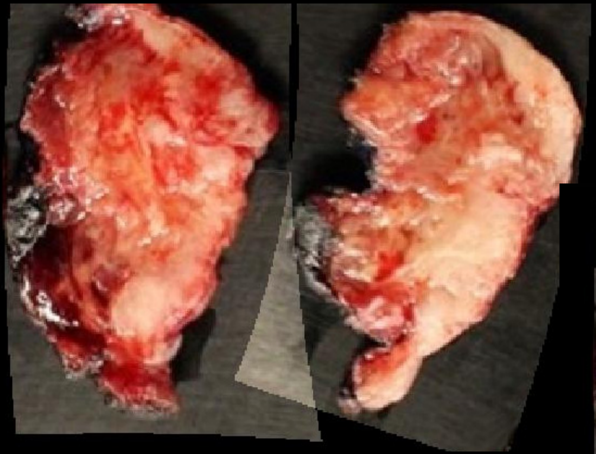
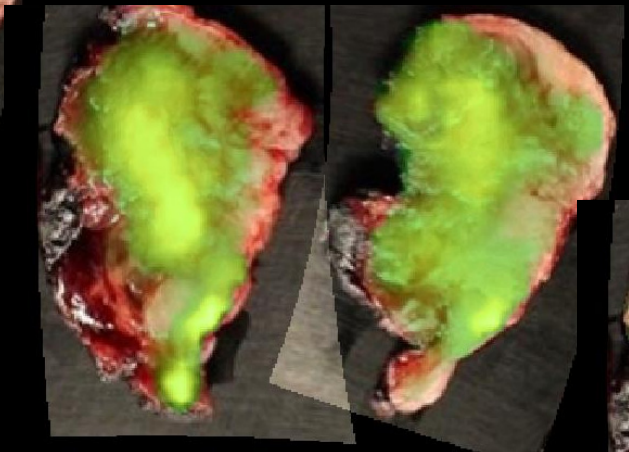
L. Kreiss, et al., Neurophotonics(12) 2025

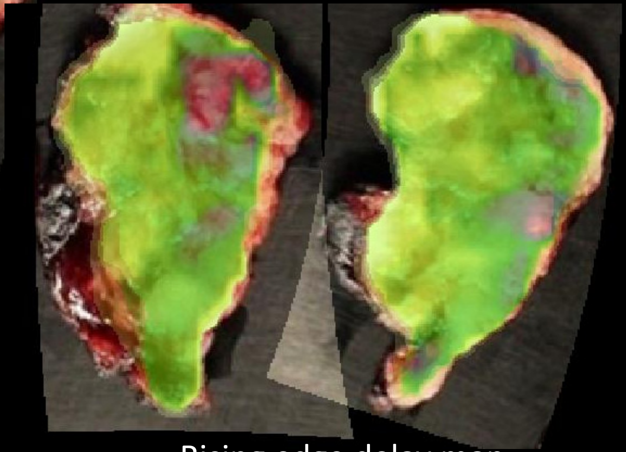
# First ex-vivo fluorescence LiDAR data with SPAD – head & neck tumor

ABY-029 (anti-epithelial growth factor receptor Affibody molecule coupled with IRDye 800CW, 0.63 ns lifetime)





Integral fluorescence intensity map

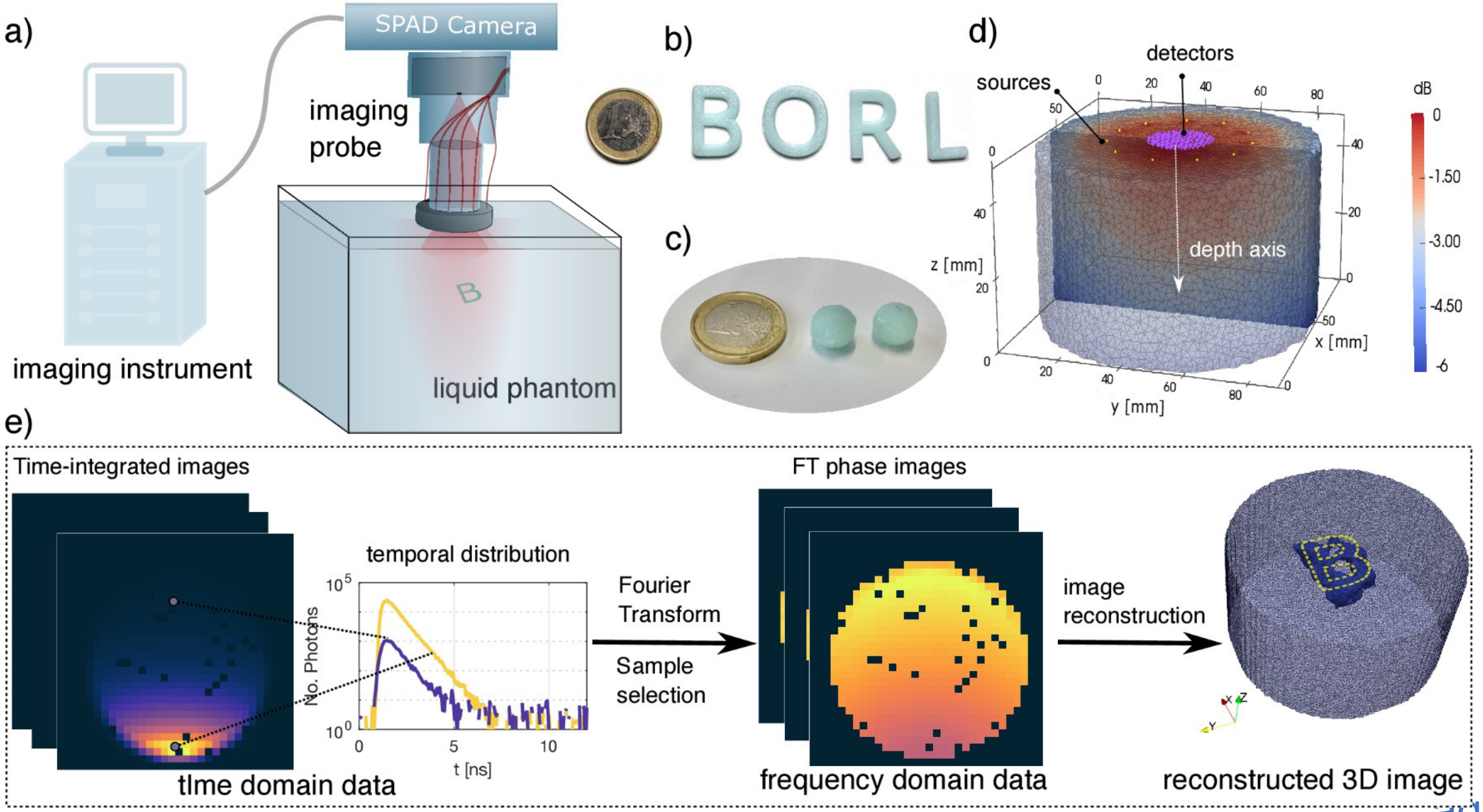



Rising edge delay map



Bruza P, et al. Optica 8(8), 2021.

# Near-infrared optical tomography (NIROT)



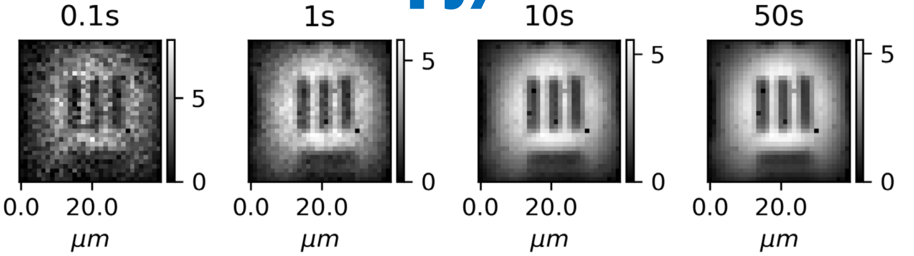

J. Jiang, et al., Bio OpEx 13 (2022)

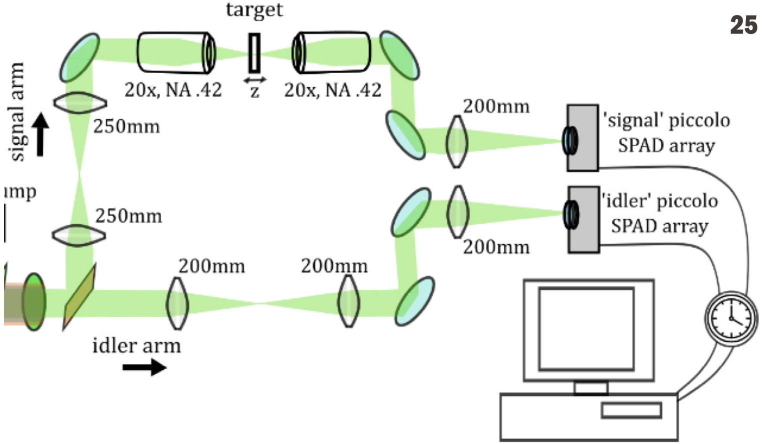
# Single-photon Quantum Imaging

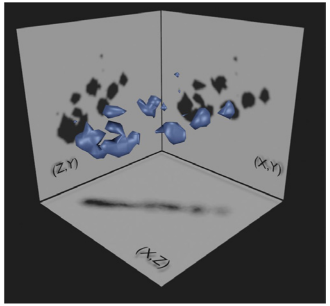
*Advance fundamental science and unlock new quantum use cases*

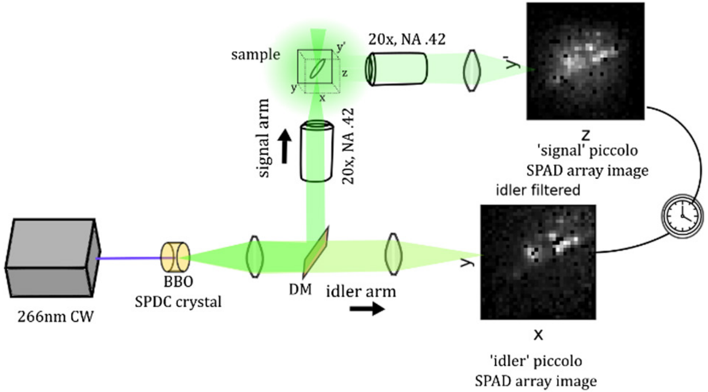
# Quantum ghost imaging microscopy/1

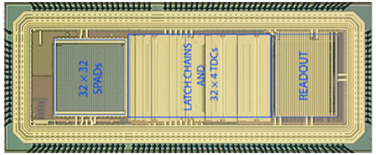





Paul Mos, Yang Lin

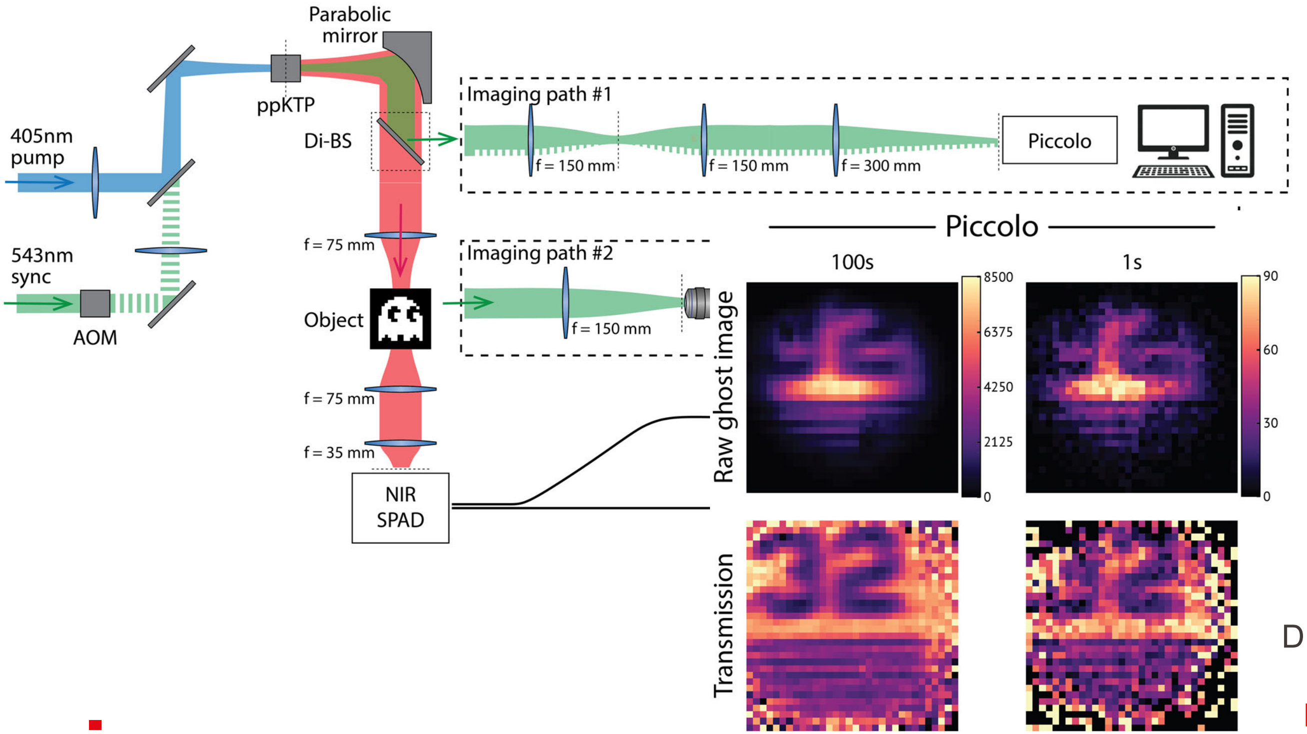
- Employs two 32x32 Piccolo SPAD arrays
- 3D quantum microscope: 3D image without scanning (standard image from one perspective / perpendicular ghost image)
- “Gentle” imaging – no photobleaching, e.g. biological samples

D. Davenport, et al, OpEx(32), 2024; A. Eshun, et al., Optica(12) 2025

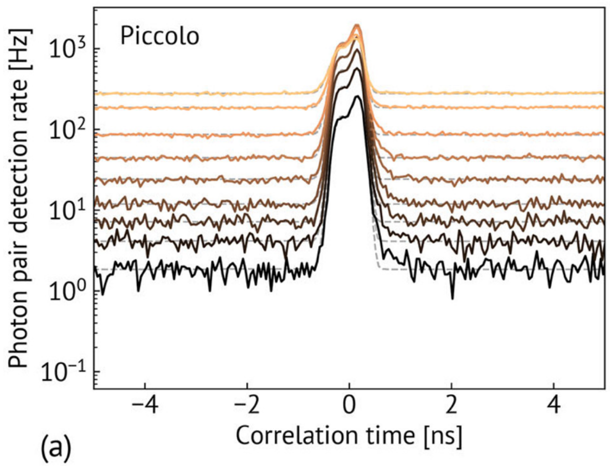
# Quantum ghost imaging microscopy/2



## Quantum ghost imaging – SPAD array & NIR bucket detector (LANL)



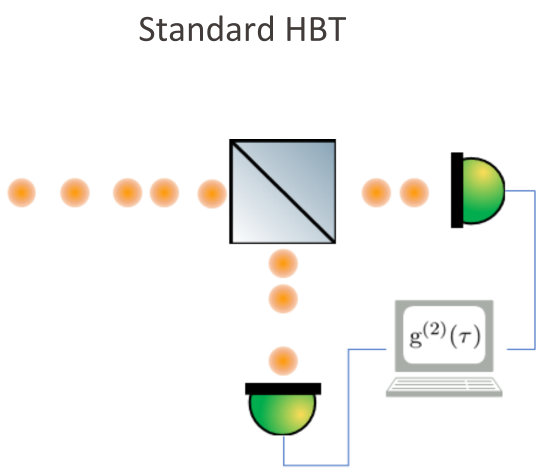

Correlation curve

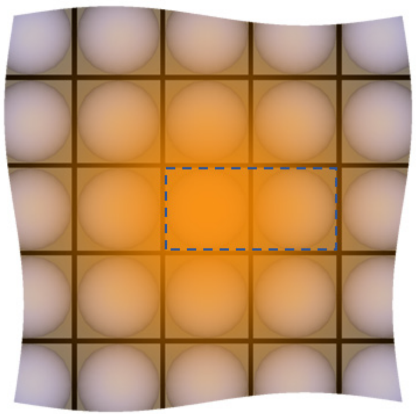


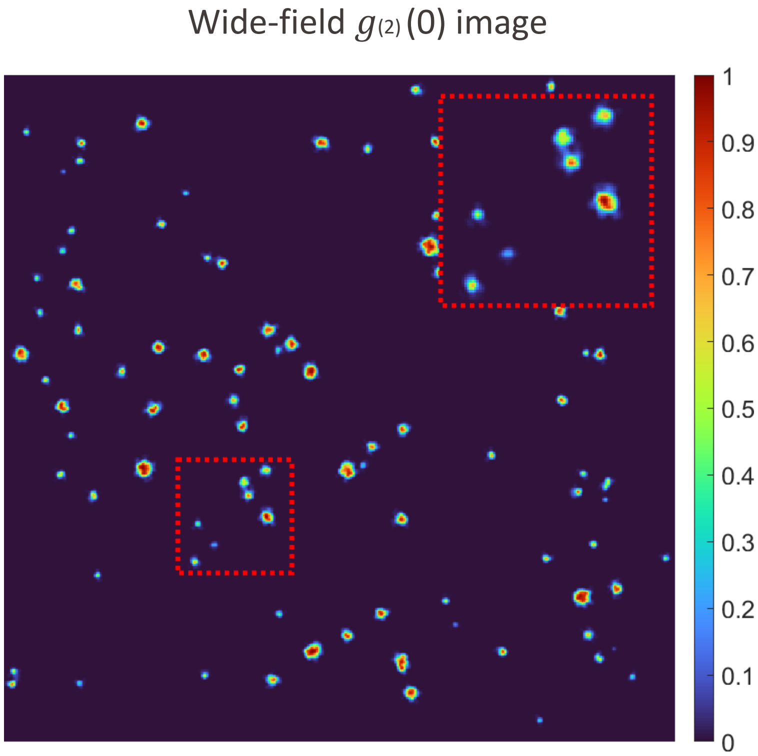

D. Ryan, et al., Eur. Phys. J. Plus (2025)

EPFL: Paul Mos, Yang Lin aqualab

# Massively parallel HBT



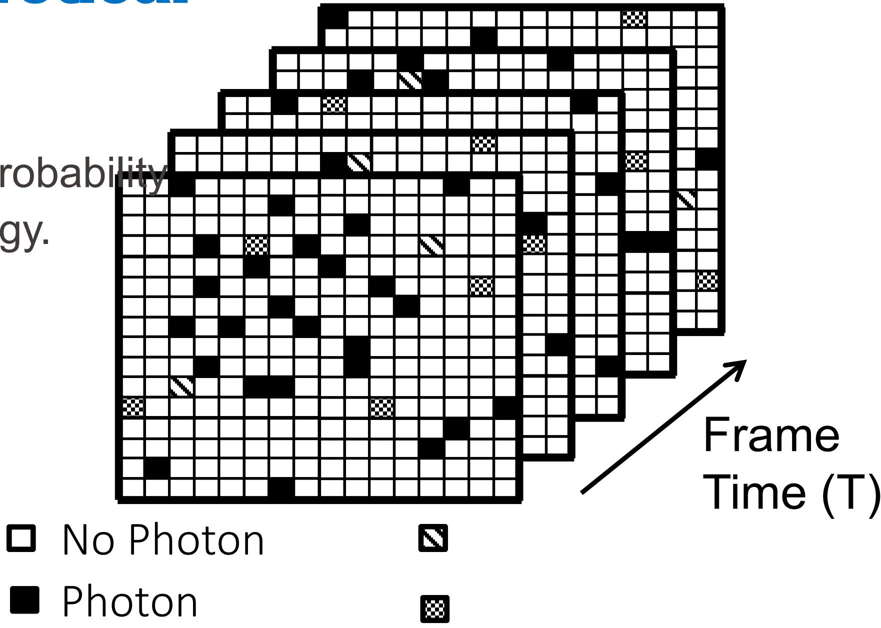

S. Elmalem, *et al.*, Optica(12) 2025

- SwissSPAD3 500×500 SPAD sensor
- Massively multiplexed wide-field photon correlation sensing
- Wide-field emitter counting and quantum-enabled super-resolution imaging (factor √2)

# Teaching & Training the next generation

# SPADs for Teaching – Theoretical

- *EPFL MICRO-428 Metrology MSc course*
  - Concept of measuring in different domains. Probability & statistics fundamentals, electrical metrology.



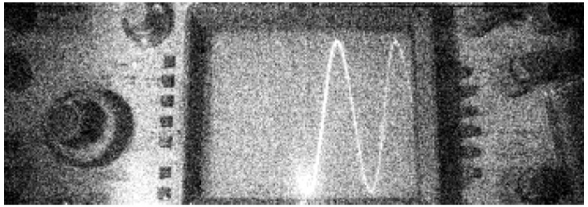

**Link concepts to practical examples, in this case:**

**Binomial Random Variable → Photon-counting statistics**

# of photons k at each pixel for n consecutive (independent) frames:

$$P\{n,k\} = \frac{n!}{(n-k)! \cdot k!} \cdot p_{ph}^{k} \cdot (1 - p_{ph})^{n-k} \; where$$

$$p_{ph} = 1 - P\{1,0\} = 1 - e^{-(\phi\tau\eta + r\tau)}$$



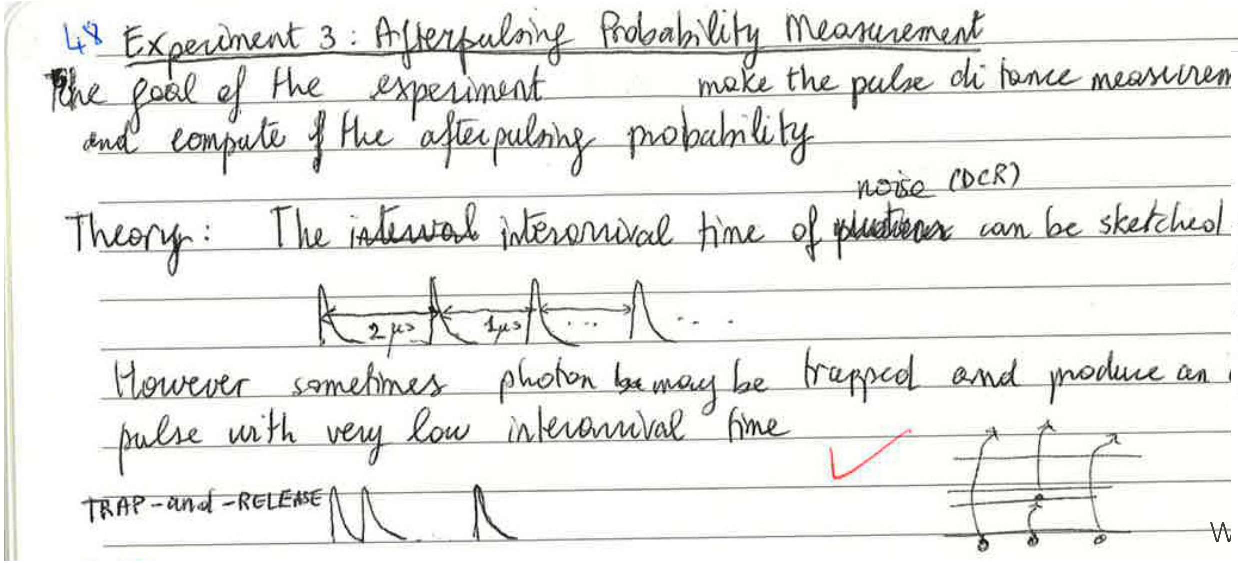
Y. Hirose, MDPI Sensors(18), 2018

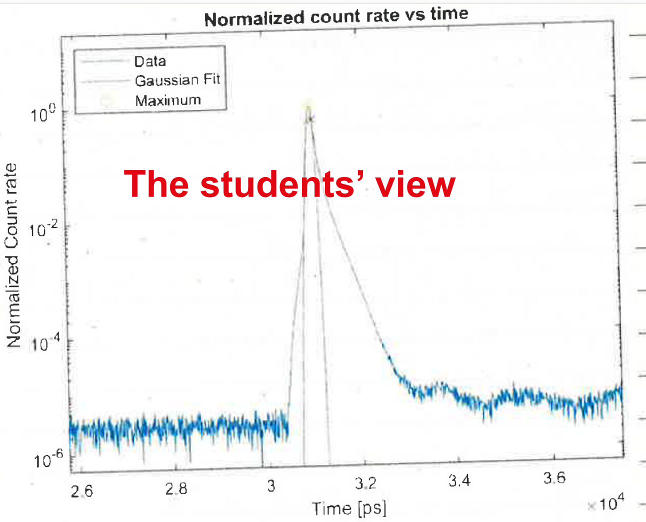
With Edoardo Charbon and Georg Fantner

EPFL

# SPADs for Teaching – Experimental

- *MICRO-429 Metrology Practicals MSc course*
  - Students get familiar with the techniques learnt in class and put them to practice with experiments in the laboratory.

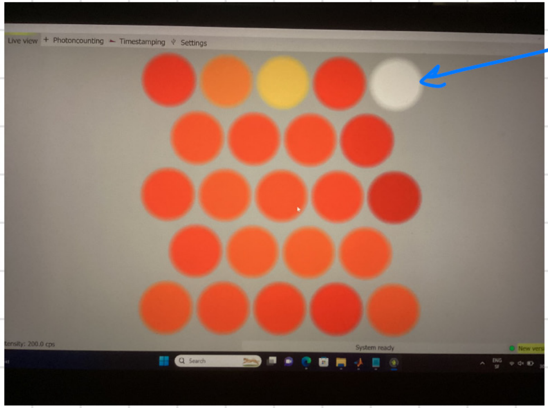


# Example: Dark count rate (DCR) and afterpulsing

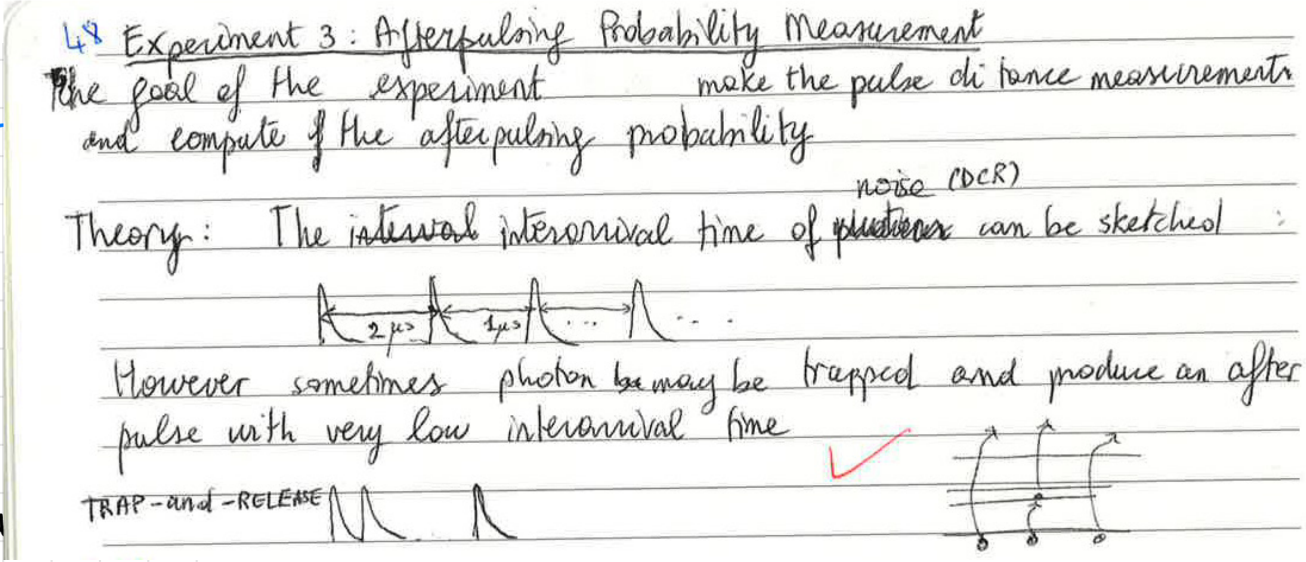


## The students' view




Picture of the live view menu. Pixel 4 is hot.

"hot pixel" (GUI)



48 Experiment 3: Afterpulsing Probability Measurement

The goal of the experiment make the pulse distance measurements and compute of the afterpulsing probability

Theory: The interarrival time of noise (DCR) can be sketched:



However sometimes photon may be trapped and produce an after pulse with very low interarrival time

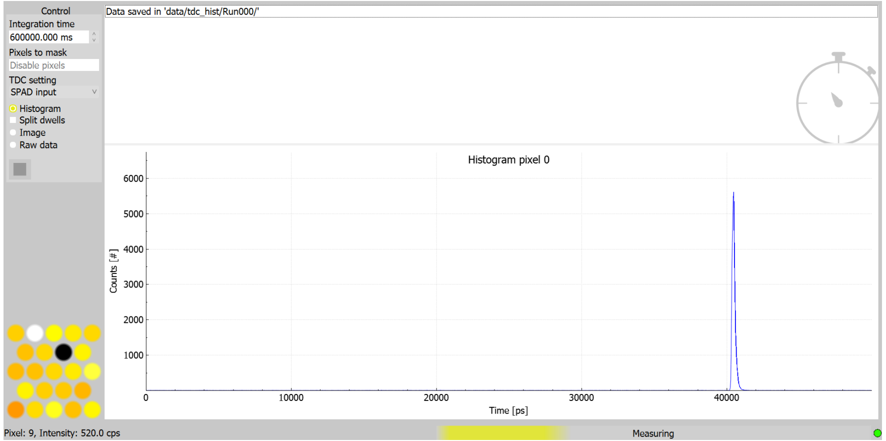
TRAP-and-RELEASE

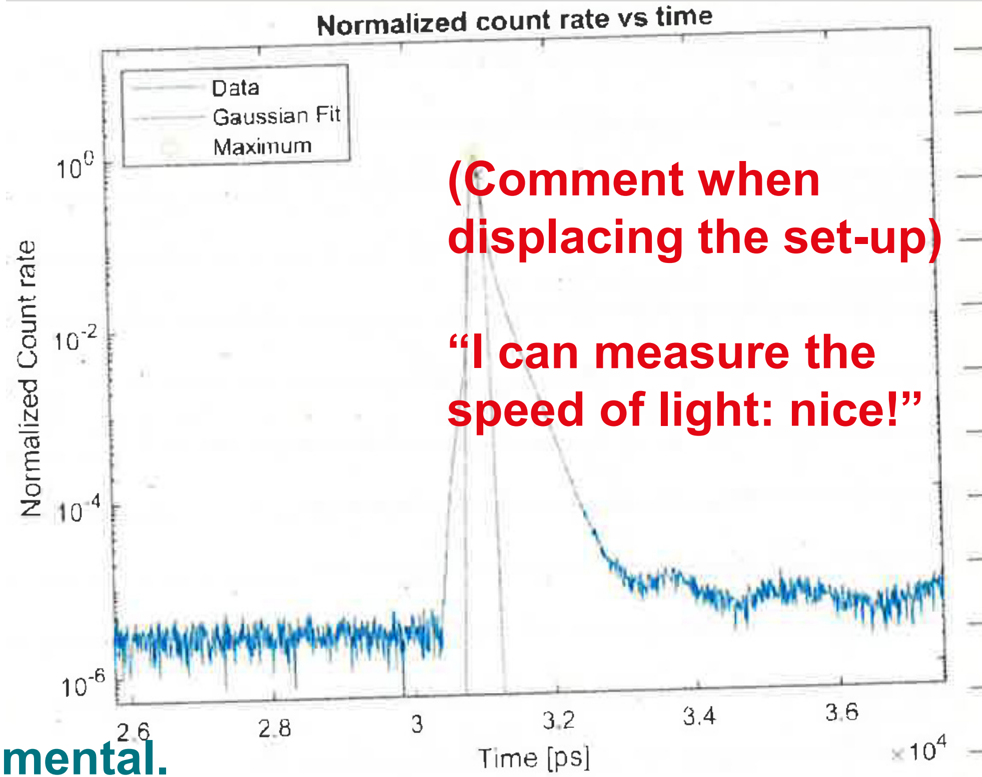
Afterpulsing explanation

# Example: Timing jitter measurements

**The students' view**

## From ideal…




**(Comment when displacing the set-up)**

**"I can measure the speed of light: nice!"**

## …to experimental.

# Final Considerations

# Final Considerations



- **Development of single-photon sensors for time-resolved imaging and applications**
  - *Expected impacts:*
    - Pave the way for new use cases, which are then adopted in the community and eventually industrialised as appropriate.
    - Advance fundamental science, unlock new (quantum) use cases, progressively displace other detectors and imagers, towards real-time implementations
    - Eventually push SPAD imagers into clinical use, for example to enable better tumor differentiation and/or earlier diagnosis.
- Exploit applications where there is an added value from the digital circuitry
  - *Higher granularity, spatial and/or temporal*
  - *Added functionality, like switching off noisy SPADs, or control hold-off time*
  - *"Ultimate" performance (e.g. timing)*
- To be improved: sensitivity in the red/NIR (3D-stacking?), scaling/tiling for specific applications, more on-chip/edge intelligence (e.g. correlations)

EPFL

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