

# NANOMETER RESOLUTION IMAGING WITH MINIMAL PHOTON FLUXES

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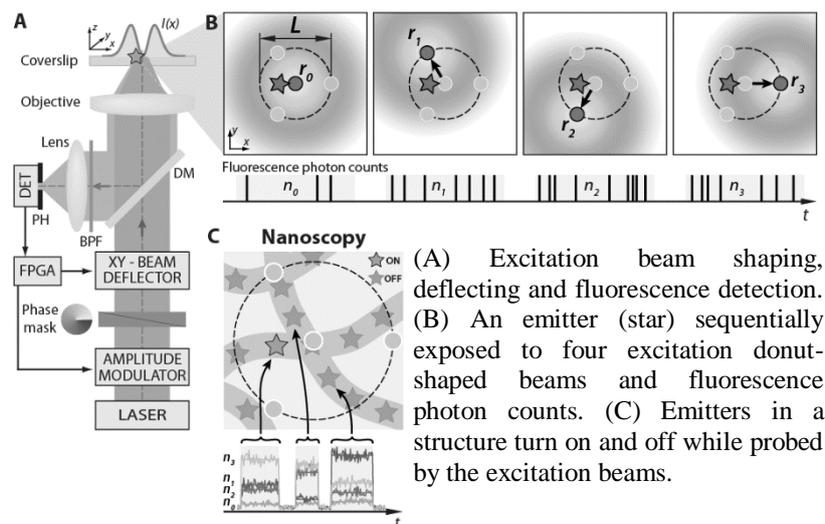
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Superresolution microscopy methods such as STED and PALM/STORM have revolutionized far-field optical fluorescence microscopy by manipulating state transitions of the emitters. In STED, a depleting beam featuring a zero of intensity switches off emitters everywhere except around said zero and fluorescence from emitters that remain in the on-state is assigned to originate from the position of the zero. In PALM/STORM, individual emitters switch on and off stochastically and their position is obtained from fluorescence emission imaged onto a camera. Though both methods offer potentially unlimited resolution, value below  $\sim 10\text{nm}$  have remained so far elusive, as it is the finite photon budget of fluorescent probes what ultimately limits resolution.

We present here MINFLUX [1], a technique that tackles the localization problem by rendering each fluorescent photon more informative. For a given photon budget, an improved localization precision is obtained by repeatedly probing with a zero of intensity the location of stochastically switching emitters, merging the strengths of both STED and PALM/STORM. Conversely, it is possible to attain a given localization precision by using fewer photon than conventional centroid-localization techniques.

Single emitter localization, as a proof of concept, attained a 22-fold reduction of the required photon detections compared to camera-based methods. Superresolution images of DNA origami labeled with Atto647N achieved  $\sim 1\text{nm}$  precision, resolving molecules only 6 nm apart.



[1] Balzarotti, F., Eilers, Y., Gwosch, K. C., Gynnå, A. H., Westphal, V., Stefani, F. D., Elf, J., Hell, S. W. (2016), “Nanometer resolution imaging and tracking of fluorescent molecules with minimal photon fluxes”, *Science*, 10.1126/science.aak9913