# Beyond Diffraction Limit by Local Photon Statistics Evaluation

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Enhancing spatial resolution remains a fundamental objective in modern biological and medical research. While pioneering techniques such as STimulated Emission Depletion (STED) microscopy and Single-Molecule Localization Microscopy (SMLM) successfully bypassed the optical diffraction limit in the early 1990s, their practical application in live-cell imaging is often hindered by significant photodamage. These intensity-related issues have raised concerns regarding the long-term reliability and biocompatibility of such methods for sensitive biological samples.

To address these limitations, Super-resolution Optical Fluctuation Imaging (SOFI) emerged as a more biocompatible alternative, utilizing the stochastic fluctuations of fluorophores without requiring extreme illumination levels [1]. However, SOFI relies on a classical light model that treats intensity as a continuous variable, failing to account for the discrete nature of photons. In low-light environments, where photon quantization becomes dominant, a comprehensive quantum framework is essential to achieve peak imaging performance.

Building upon super-resolution strategies designed for the restricted case of single-photon emitters emitters [2, 3], here we introduces a full quantum model for super-resolution integrating the quantum characteristics of light labelled Quantum Super-resolution Imaging by Photon Statistics (QSIPS) [4]. Unlike approaches based on the parametric estimation of distances between emitters — which are often hindered by model-dependency — QSIPS is a direct imaging technique. Consequently, it maintains high performance in realistic scenarios where multiple emitters are located at sub-diffraction distances and in the presence of experimental non-idealities. We present a full quantum model that demonstrates a clear advantage over traditional SOFI techniques. Furthermore, through both numerical simulations and experimental validation, we demonstrate the integration of QSIPS with Structured Illumination Microscopy (SIM), a combination that pushes resolution capabilities significantly further beyond the classical diffraction limit.

**References**

[1] T Dertinger, R Colyer, G Iyer, *et al.*, Proc. Natl. Acad. Sci. USA **106**, 22287 (2009)

[2] O Schwartz, J M Levitt, R Tenne, *et al.*, Nano Lett. **13**, 5832 (2013)

[3] D Gatto Monticone, K Katamadze, P Traina, *et al.*, Phys. Rev. Lett. **113**, 143602 (2014)

[4] F Picariello, E Losero, S Ditalia Tchernij, P Boucher, M Genovese, I Ruo-Berchera and I P Degiovanni, Optica **12**, 490 (2025)