**Anomalous power dependence of lanthanide-doped upconversion nanoparticles for super-resolution multiphoton microscopy**

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The optical resolution of confocal microscopy can be improved through multiphoton excitation, which typically offers a factor of √*s* improvement when imaging nonlinear probes with emission depending on the excitation intensity to the power of *s*, i.e. the slope in the log-log plot. However, conventional fluorescent probes provide a mere slope of 2 or 3 (corresponding to 2-photon and 3-photon excitation, respectively) – as a result, multiphoton microscopy has not been considered a super-resolution technique.

We show that sub-diffraction imaging can be achieved in confocal/multiphoton microscopy using lanthanide-doped upconversion nanoparticles (UCNPs) exhibiting super-linear power dependence with a slope as high as 6.2 [1]. The UCNPs employed were NaYF4 doped with Yb3+ and Tm3+, which emit 4-photon upconversion luminescence at 455 nm under 980 nm excitation. While it has been articulated that the slope of upconversion luminescence is at maximum equal to the number of photons involved in the upconversion process [2,3], our experiments revealed slopes over 6 from UCNPs with Tm doping concentration at 8% or higher (and 20% Yb). Based on rate equation modelling [4], the observation is ascribed to the intense cross-relaxation among Tm3+ dopants, which leads to the photon-avalanche-like process in individual UCNPs, and consequently the anomalous high-order nonlinearity at excitation intensity close to the photon-avalanche threshold. By imaging NaY0.72F4:Yb0.2,Tm0.08 nanoparticles functionalized with colominic acid and taken up in *E. coli*, we demonstrated optical resolution of 210 nm and 450 nm in the lateral and axial direction, respectively. This new approach, coined super-linear excitation-emission (SEE) microscopy, will open vast opportunities for 3D super-resolution imaging using common confocal setups, whereby low-cost laser diodes instead of expensive femtosecond lasers can be used to facilitate multiphoton microscopy for longitudinal studies at biological-friendly excitation intensity.

**References**

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