DNA probes for highly multiplexed, precisely quantitative, ultra-resolution imaging

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Living organisms are complex molecular systems. Imaging provides a natural and direct way to investigate such systems and is thus becoming a central tool for biomedical science. However, due to limitations of current microscopy, scientists face three crippling changes when attempting to visualize biology on the molecular scale: *blurred vision* (i.e. inability to visualize individual molecules clearly, especially for crowded targets), *partial color blindness* (i.e. only a small number [typically 3 or 4] of colors are used to simultaneously track distinct molecular species), and *ambiguous quantification* (i.e. the inability to precisely count the number target molecules in a resolution limited area). Using programmable fluorescent DNA probes (*Nature Methods*, 11:313, 2014; *Science* 344:65, 2014), we present a highly multiplexed (10× demonstrated), precisely quantitative (>90% precision), and ultra-high resolution (sub-5 nm) optical imaging method that simultaneously addresses these challenges, and hence promises to broadly transform biomedical research.