

Photonic Crystal Enhanced Fluorescence for Digital Resolution Biosensing

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Abstract—Photonic crystals are used to amplify the fluorescence emission and collection efficiency from quantum dots and plasmonic fluor nanoparticles to enable miRNA and proteins to be detected from plasma with single molecule precision, with simple 1-step assays.

Keywords—photonic crystal, biosensor, fluorescence, liquid biopsy, microscopy

I. INTRODUCTION

Harnessing nanoscale light-matter interactions for bioanalytical applications has hitherto been challenged by the exigencies of high numerical aperture objectives and sophisticated optics, particularly for single-molecule resolution assays. In this integrated study, we amalgamate the distinct yet complementary attributes of Photonic Crystal (PC)-enhanced Quantum Dots (QD) and Plasmonic-Photonic hybrid systems, thereby surmounting limitations in sensitivity and signal-to-noise ratio. Utilizing the multiplicative benefits of the PC framework, we demonstrate an approximately 3,000-fold enhancement in QD-based fluorescence emission through concerted mechanisms of excitation enhancement, directional emission, quantum efficiency improvement, and blinking suppression. Concurrently, we exploit a Plasmonic-Photonic hybrid system to achieve 10^4 orders of magnitude enhancement in fluorescence signals, comparing single fluorophore, from Plasmonic-fluor (PFs) mediated by optimized dielectric spacer layers and heterometallic core-shell nanostructures. Notably, these unprecedented enhancements facilitate single-molecule assays for cancer-associated microRNA and Interleukin-6 biomarkers, even when employing low-NA optics. Our composite system thus holds significant promise for advancing the frontier of ultrasensitive, high-throughput bioanalytical assays, thereby having broad implications in liquid biopsy diagnostics and personalized medicine.

II. RESULTS

Before By quality factor engineering, we achieve a ~ 3000 times enhancement in photon intensity from single QD tags on PC vs glass using experiments supported by simulations to attribute a 23X gain to enhanced excitation, a 39X gain to enhanced extraction (including both photon extraction rate improvement and quantum efficiency change via the Purcell effect), and 3.5X of enhanced collection efficiency [1]. Moreover, the blinking suppression capability of the PC improves the QDs “on-time” from 15% to 85%, provides a novel method to ameliorate signal intermittency issues encountered during ultrasensitive measurements and fast motion tracking at a single particle level. Herein, by exploiting those synergistic properties, we show the PC-QD system can achieve single QD sensitivity with high signal-to-noise ratio (~ 59) using a low NA lens (NA=0.5, 50X) without TIRF or high gain electron-multiplying camera.

We developed a QD-tagged “bridge” assay for cancer-associated miRNA biomarkers from a 45 μ l sample volume with single-molecule resolution, single-base mutation selectivity, 10 aM (10⁻¹⁷ Molar) detection limit, and linear dose-response over a 9-log concentration range with two steps, room temperature workflow. The direct counting capability yields linear dose-response across a target concentration range of 10aM to 1nM with 10,000X detection limit improvement compared to analog ensemble intensity measurement.

REFERENCES

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