

Plasmonic-Photonic Hybrid System for Enhanced Fluorescent-based Digital Resolution Biosensing

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Plasmonic and photonic technologies have attracted strong interest in the past few decades toward several interdisciplinary applications stemming from unique light-matter interactions fostered by materials at the nanoscale. The versatility of plasmonic and photonic sensors for ultrasensitive, rapid, analyte sensing without extensive sample pre-treatment steps or sophisticated optics have resulted in their strong foothold in the broad arena of biosensing. Fluorescence-based bioanalytical techniques are widely used in liquid-biopsy diagnostics applications, but require many labeled target molecules to combine their emission output to achieve a practically useful signal-to-noise ratio. Approaches capable of amplifying fluorescence signals can provide signal-to-noise sufficient for digitally counting single emitters for ultrasensitive assays that are detected with simple and inexpensive instruments. [1]. Plasmonic and nano-photonics can function in synergy to amplify fluorescence signals. By concentrating optical energy well below the diffraction limit, plasmonic nanoantenna provide spatial control over excitation light, but their quality factor (Q) is modulated by radiative and dissipative losses. Photonic crystals (PC) as dielectric microcavities have a diffraction-limited optical mode volume despite being able to generate a high Q-factor. Here, we demonstrate a plasmonic-photonic hybrid system to produce a much stronger fluorescent enhancement for digital resolution biosensing. With an optimized dielectric spacer layer, around 200 Alexa-647 fluorophores have been coated over heterometallic Ag@Au core-shell plasmonic nanostructures with minimized Ohmic losses and quenching effects [2]. The target-specific molecule capture events enabled this plasmonic fluor to attach to the PC surface, forming a Plasmonic-Photonic hybrid mode. With much stronger local field enhancement, far-field directional emission, large Purcell enhancement, and high quantum efficiency, we report a two-orders signal enhancement from PC-enhanced plasmonic-fluor (104-fold brighter than a single fluorophore). This improved signal-to-noise ratio enabled us to perform single molecule imaging even with a 10x (NA=0.2) objective lens while offering 3 orders of magnitude boost in the limit of detection of Interleukine-6 (common biomarker for cancer, inflammation, sepsis, and autoimmune disease) compared with standard immunoassays in human plasma [3].

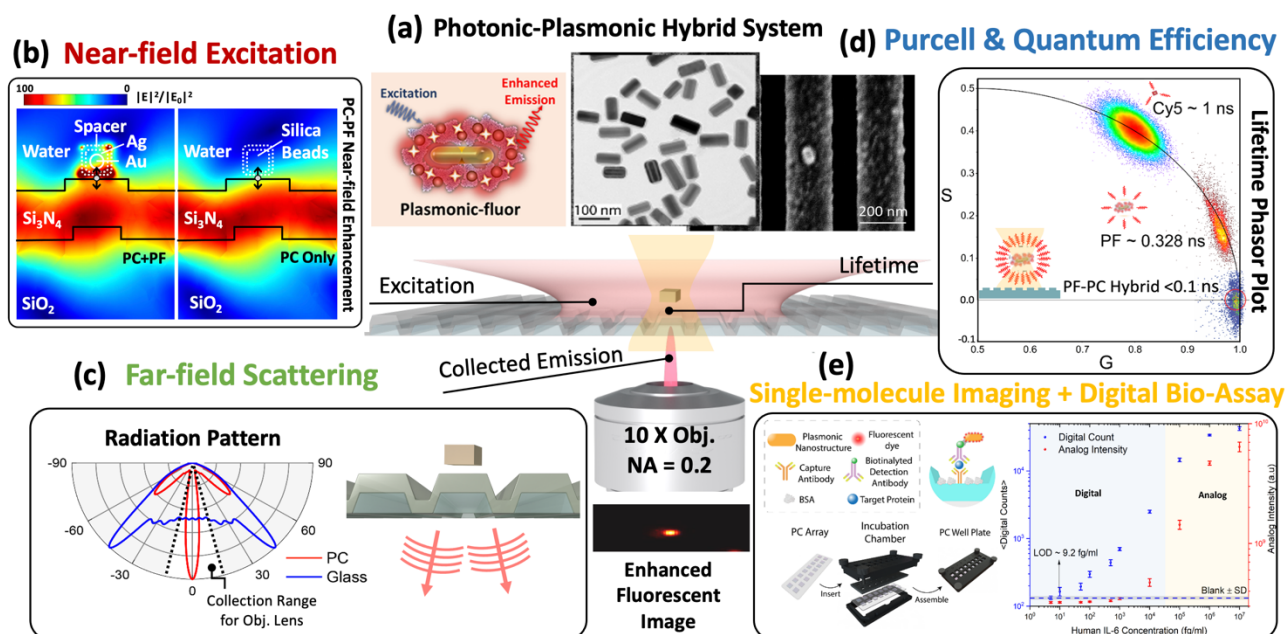


Fig. 1 Principle of plasmonic-photonic hybrid for fluorescence enhancement applied towards a digital resolution immunoassay. (a) Photonic-Plasmonic hybrid system. (b) Near-field excitation enhancement. (c) Improved collection efficiency with a low-NA objective lens. (d) Purcell effects in spontaneous emission and improved quantum efficiency. (e) Enhanced digital resolution detection assay for IL-6.

References

- Xiong, Y.; Huang, Q.; Canady, T. D.; Barya, P.; Liu, S.;...Cunningham, B. T., Photonic crystal enhanced fluorescence emission and blinking suppression for single quantum dot digital resolution biosensing. *Nat Commun* **2022**, *13* (1), 4647.
- Luan, J.; Seth, A.; Gupta, R.;...Singamaneni, S., Ultrabright fluorescent nanoscale labels for the femtomolar detection of analytes with standard bioassays. *Nature Biomedical Engineering* **2020**, *4* (5), 518-530.
- Barya, P.; Xiong, Y.; Shepherd, S.; Gupta, R.;...Singamaneni, S.; Cunningham, B. T., Photonic-Plasmonic Coupling Enhanced Fluorescence Enabling Digital-Resolution Ultrasensitive Protein Detection. *bioRxiv* **2022**, 2022.10.29.514360.