

## **Metal plasmon-coupled fluorophore: a probe for single molecule detection on cell image**

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We studied metal-enhanced fluorescence (MEF) at ensemble and single molecule level. Numerical simulations by Finite-Difference Time-Domain (FDTD) method and radiative decay engineering (RDE) approach were used to interpret the experimental results. Based on the experiment results and theoretical predictions, we developed metal plasmon – coupled fluorophores (PCFs) as the molecule reagents for the cell fluorescence imaging. The emission properties of PCFs were investigated depending on the size of metal particle and excitation and emission wavelengths of fluorophore. Compared with the conventional organic fluorophores, PCFs were observed to display significant increases of emission intensity over 1,000 times and decrease of emission lifetime below 1/10. In addition, PCFs displayed better photostability and less photoblinking. The dye-labeled protein molecules were conjugated on the metal particles and the protein-metal complexes were site-specially bound with the target molecules on the cell surfaces. The cell fluorescence images were collected on the confocal microscopy in either the emission intensity or lifetime. Compared with the metal-free protein conjugates, the protein-metal complexes were observed to display a stronger emission intensity, shorter lifetime, and better photostability. It was noticed that the protein-metal complexes bound on the cell surfaces could be identified as the isolated emission spots distinct from the cellular autofluorescence. The emission intensity over the cell image was increased with an increase of the number of avidin-metal complex on the cell surface but the lifetime was decreased. A quantitative regression curve was achieved between the amount of protein-metal complex on the cell surface and the emission intensity or lifetime over the entire cell image. Based on this curve, we expect to develop an approach that can be used to quantify the amount of target molecules on the cell surfaces using the cell intensity and lifetime images at the single cell level.