Plasmon-enhanced fluorescence on mass-produced biosensor chips

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Fluorescence assays has become an important tool for the detection of low concentrations of analytes in a wide range of analytical applications including medical diagnostics, food safety and environmental monitoring. Conventionally, end-point fluorescence measurements are conducted after the incubation and rinsing steps by a scanning device. Then, valuable affinity information, encoded in the binding kinetics of fluorescence labeled biomolecules, is typically not accessible due to low sensitivity because of large background fluorescence and weak fluorescence signal. This work addresses these issues by using tailored nanostructured surfaces for plasmon-enhanced fluorescence within a microfluidic cartridge. The surface consists of a multi-diffractive gold grating that couples the excitation and emission light to surface plasmon modes. Tight confinement of the electric field intensity of the excitation light in the immediate vicinity of the metallic surface boosts the excitation rate of fluorophores used in the assay, thus improving the signal to background ratio. Additionally, the optical collection efficiency is improved by plasmon-coupled emission with diffractive outcoupling to narrow angles in the far field. The combined effects can enhance the sensitivity by several orders of magnitude. In order to exploit this optics in real world applications, the scaled up manufacturing of plasmonic structures is an imperative. Here, all components are produced by industrial scale roll-to-roll (R2R) processes. The master molds are prepared by laser interference lithography (LIL), a method to rapidly produce large areas of homogeneous holographic gratings, and transferred to a roller by metal plating. Large numbers of substrates are then produced by R2R UV nanoimprint lithography followed by thermal evaporation of gold. After the chemical functionalization of the surface, the substrates are assembled with microfluidic covers to form a biosensor cartridge. Time resolved affinity assays on arrays of functionalized spots are then performed in an imaging reader designed to take full advantage of the plasmonic enhancement and more than 300-fold fluorescence intensity enhancement was observed compared to flat substrates which allowed reaching limit of detection of about 80 fM in immunoassay-based detection scheme.