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Solution-phase gold films for microarrays and molecular imaging

Researchers in Prof. Hongjie Dai's laboratory have developed a simple process to easily deposit plasmonic nanoscopic gold films on a variety of surfaces. These stable films can enhance the sensitivity and dynamic range of spectroscopic-based biosensing applications by orders of magnitude over unenhanced signals. Because the gold films are a physical enhancement, they do not require additional assay steps. The films can be modified with functional groups or biomolecules and used for a wide variety of research and diagnostic assays. Specific applications of this technology include SERS (surface-enhanced Raman scattering), MEF (metal enhanced fluorescence) in the near-infrared, and NIR-FE (near-infrared fluorescence enhanced) molecular imaging *in vitro*.

Stage of Research
The inventors have:
- developed the solution-phase, seed-based process and initially demonstrated deposition on a variety of surfaces, including a highly complex surface (protein coated bioassay)
- characterized the nanoscopic structure and localized surface plasmon resonances of such gold films
- used the gold films with SERS to detect a cancer biomarker in serum with a limit of detection ~5fM
- used the gold films with NIR-FE imaging and showed single-molecule imaging and tracking of single-walled nanotubes bound to cellular surface receptors
- used the gold films with MEF protein microarrays, enhancing near-infrared fluorescence ~100-fold, extending the dynamic range of detection by 3 orders of magnitude, to ~ 5fM, and detecting a cancer biomarker in xenograft-bearing mouse serum at ~30fM
- demonstrated proof-of-principle analyte detection in peptide and carbohydrate microarray assays based on MEF of the gold films.

Applications

- **Spectroscopic detection in biological assays** - for research and diagnostics of diseases such as cancer, viral infection or autoimmunity; assays include:
  - SERS - simple process to create gold film for surface-enhanced Raman scattering, for protein, peptide, DNA and carbohydrate sensing and quantification
  - MEF - metal enhanced near-infrared fluorophores for protein, peptide, DNA, and carbohydrate microarrays
  - NIR-FE - in vitro molecular imaging with near-infrared enhancement using both single-walled carbon nanotube or organic fluorescent labels (particularly for imaging low abundance cell membrane proteins and cell membrane/uptake dynamics)

Advantages

- **Simple, facile, solution-phase process** - for aqueous phase deposition over a large area on complex surfaces
- **Enhanced signal** of both fluorescence and Raman scattering in the near infrared, with enhancement factors of 107 observed uniformly and reproducibly (with SERS); 6 - 9x enhancement of molecular imaging (with NIR-FE); 100-fold enhancement of protein detection (with MEF)
- **Sensitive** - detection limits approximately 1 fM for protein analytes in sandwich assay format
- **Broad dynamic range** - extended by 3-4 orders of magnitude over unenhanced signal, enabling biological microarrays with ~7 decades of dynamic range
- **Simple bioassays** - gold film provides physical enhancement and does not require complex assay procedures, specialized equipment, or additional reagents
- **Easily modified surface** - to present a variety of functional groups or biomolecules
- **Variety of surfaces** - including glass, quartz, silicon, indium tin oxide, polyvinyl choride, poly dimethylsulfoxide, polystyrene, and amino-modified glass, quartz, or silicon

- **Spatial measurements** - fluorescence enhancement decays at distances greater than ~50nm, allowing spatial information to be gained based upon degree of fluorescence enhancement in real time without complex optical instrumentation and data processing (with NIR-FE)

Publications

- U.S. Published Patent Application 20130172207, "FLUORESCENCE ENHANCING PLASMONIC NANOSCOPIC GOLD FILMS AND ASSAYS BASED THEREON".
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- Scott M. Tabakman, Zhuo Chen, Hernan Sanchez Casalongue, Hailiang Wang, Hongjie Dai, A New Approach to Solution-Phase Gold Seeding for SERS Substrates, Small, Vol. 7, Issue 4, pp. 499-505, Feb. 8, 2011 (published online January 3, 2011).
- Scott M. Tabakman, Lana Lau, Joshua T. Robinson, Jordan Price, Sarah P. Sherlock, Hailiang Wang, Bo Zhang, Zhuo Chen, Stephanie Tangsombatvisit, Justin A. Jarrell, Paul J. Utz & Hongjie Dai, Plasmonic substrates for multiplexed protein microarrays with femtomolar sensitivity and broad dynamic range, Nature Communications, published online 13 Sep 2011. DOI: 10.1038/ncomms1477

Patents

- Published Application: 20130172207
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