Plasmonic Mesoporous Gold for SERS Biosensor for Clinically Relevant Biomarkers

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Surface-enhanced Raman spectroscopy (SERS) is a potent biosensing tool known for its precise identification, heightened sensitivity, and real-time monitoring of disease biomarkers even at ultra-low concentrations. While previous research has explored the use of bimetallic (gold/silver) or trimetallic (gold/silver/copper) compounds to enhance signals, recent advancements show that simply introducing mesopores, especially in gold nanostructures, significantly enhances SERS signals.[1] These pores create engineered spaces that amplify the signals, facilitating the detection of disease-specific biomarkers with remarkable sensitivity. We have synthesized mesoporous Au (mAu) NPs with large, tunable pores, concave/convex features, and abundant kinks using a soft-templating strategy. Electron tomography measurements showed that the pores were distributed throughout the interior and exterior of the particle. The mAu NPs support multipolar plasmon resonances that penetrate deep into the interior pores of the NP. The mesopores affect the local optical conductivity of the NP by subdividing it into tiny nanoscale junctions that redshift the plasmon modes without changing the overall size or shape of the NPs.[2] Large pores promote symmetry breaking, causing the quadrupolar and dipolar modes to overlap and form strongly hybridized plasmon modes, enabling sensitive quantification. The mAu NPs with a rough surface create numerous local electromagnetic hotspots due to plasmonic effects, resulting in higher Raman signal enhancement, and improved loading of SERS probe molecules and antibodies, enabling highly sensitive detection. We have utilized such mAu NPs to develop an extracellular vesicle (EV) detection assay, which showed highly sensitive detection down to 100 EV per milliliter, with good reproducibility. The assay design is simple, requiring no amplification steps. The assay was validated using a small cohort of clinical samples obtained from ovarian cancer patients and successfully distinguished ovarian cancer patients from healthy and benign control groups. Moreover, the m Au NPs were also integrated into a microfluidic device to demonstrate the high feasibility of such NPs for point-of-care diagnostics. The integration of microfluidics with mAu-based SERS probe allows for highly sensitive and multiplexed detection of three viral proteins. The developed platform demonstrates rapid, sensitive, and semi-automated capabilities, showcasing its potential for translation to clinical settings for real-life applications.

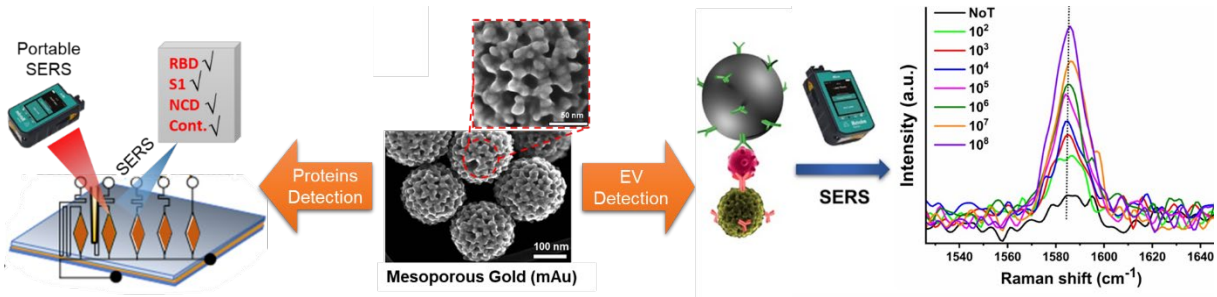

Figure 1. Schematic demonstration of mAu NPs-based biosensor development. In the middle, SEM image of mAu NPs; on the left, mAuNPs integrated microfluidic platform; and on the right, EV detection assay.

References:

[1] Li et al., *Nature Communications* **2015**, *6*, 6608
[2] Asep et al., *Chemistry of Materials* **2022**, *34*(16), 7256-7270