Ocean Optics

# Application Note

### Keywords


- SERS
- DNA
- HIV
- MRSA


### Techniques

- Raman spectroscopy

### Applications

- Biosensing
- Medical diagnostics

# SERS for Label-Free Biosensing


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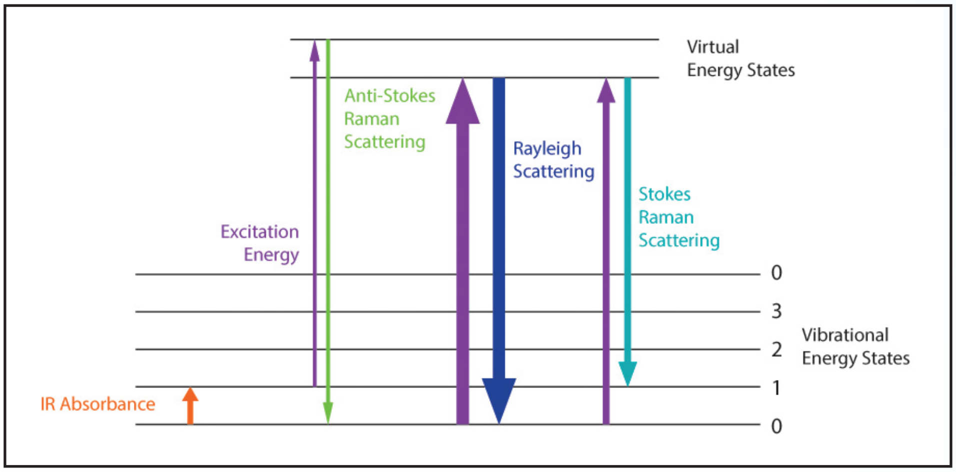
Surface enhanced Raman sensing (SERS) has expanded the applications of Raman spectroscopy to include trace analysis of materials such as explosives residues, evidence at crime scenes, chemical warfare agents and pesticides. As a label-free technique, SERS is also well suited to biosensing, from blood glucose to diagnosis of diseases like cancer, Alzheimer's and Parkinson's. A new variant of SERS developed by a group at Jackson State University in Mississippi, U.S., uses a hybrid probe composed of graphene oxide attached to a popcorn-shaped gold nanoparticle to achieve ultrasensitive sensing of HIV and MRSA DNA characteristics.

## Background

SERS allows extremely low levels of analyte to be detected via Raman spectroscopy through adsorption of the analyte onto a metal substrate. Localized surface plasmons are generated by an electromagnetic resonant effect between the substrate and the Raman excitation laser, interacting with the analyte to enhance Raman emission by a factor of up to $10^{10}$.




SERS can be performed on a substrate, or using colloids suspended in solution. While metals like gold, silver and copper are the most common materials used for SERS, novel options like graphene, semiconductors and quantum dots are also being explored. Graphene oxide, a chemically treated version of graphene, has a number of properties particularly suitable to biological applications.

Unlike most SERS substrates, the enhanced Raman signal observed with graphene oxide substrates is believed to be due to a chemical effect. By combining graphene oxide and a more traditional gold nanoparticle into a hybrid SERS probe, the group at Jackson State University has harnessed both the chemical and electromagnetic enhancement effects to maximize sensitivity when detecting two especially pernicious pathogens: the human immunodeficiency virus (HIV) and methicillin-resistant *Staphylococcus aureus* (MRSA).

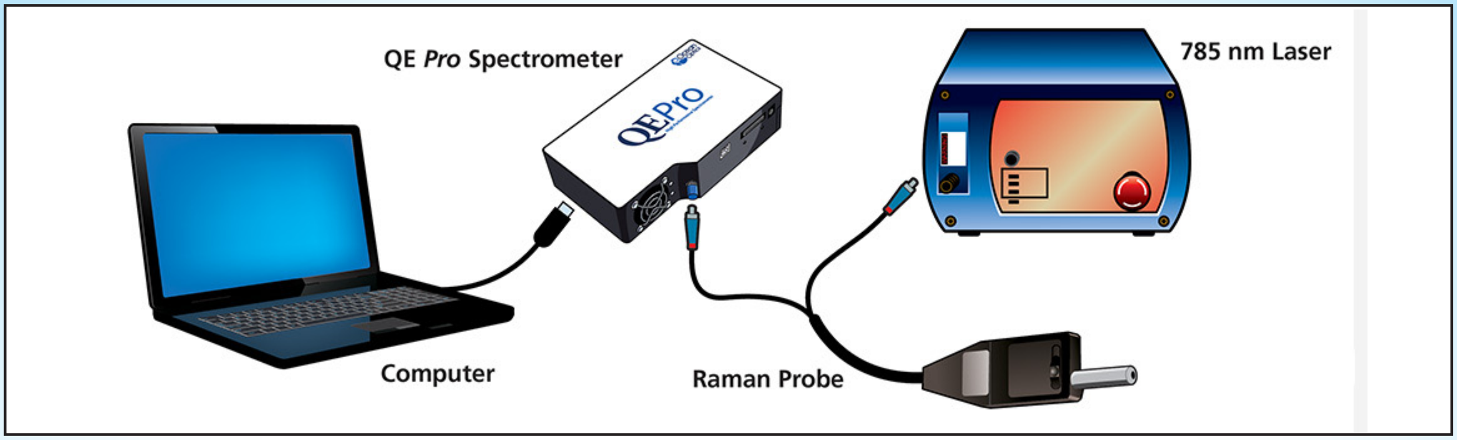



Figure 1: Modular fiber optic Raman spectroscopy system for SERS detection.

## Experimental Details

The researchers first tested gold nanoparticles of varying shapes to determine which would show the greatest electromagnetic enhancement. Spherical, cage and popcorn-shaped gold nanoparticles were tested using Rhodamine 6G dye, a well-known Raman-active compound. The system used to make the measurements was composed of an Ocean Optics QE series spectrometer, a 670 nm excitation laser and InPhotonics fiber optic Raman probe (Figure 1). The popcorn-shaped nanoparticles resulted in >50x more electromagnetic enhancement of the Raman signal than the other conformations, most likely due to the sharp tips on the nanoparticle creating a "lightning rod effect" in addition to the known surface plasmon excitations.

Once selected, the popcorn-shaped gold nanoparticles were conjugated to graphene oxide fragments less than 50 nm in diameter to create a hybrid SERS probe (Figure 2). These hybrid probes were studied for their ability to detect HIV and MRSA in low concentrations.

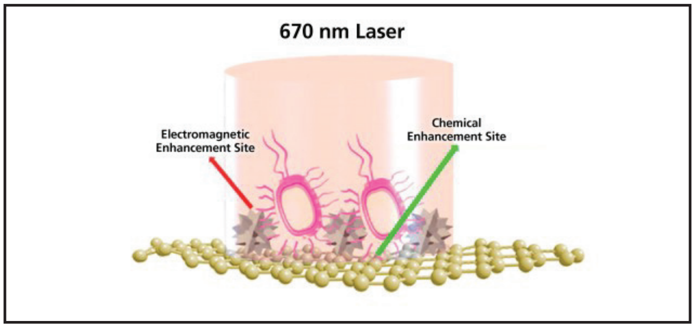



Figure 2: In a hybrid SERS probe for ultrasensitive biosensing, popcorn-shaped gold nanoparticles (spiked balls) result in electromagnetic enhancement of the SERS signal, while conjugated graphene oxide (grey mesh) provides chemical enhancement.

## Results

HIV was chosen as the first pathogen of interest due to its prevalence as a cause of death in Africa, Asia and the Middle East. Previous work on SERS for detection of HIV has typically used labels or tags, which must attach to specific genetic sequences. This work, in contrast, used a segment of the HIV gag-gene as the probe DNA (a DNA segment popularly targeted by anti-HIV therapies). Each peak in the observed Raman spectra could be assigned to the literature-reported data, confirming that the Raman spectra observed were attributable to the presence of HIV in the sample (Figure 3).

To assess the chemical enhancement effect of the graphene oxide, SERS spectra were acquired for both the hybrid probe and popcorn-shaped gold nanoparticles alone. Taking into account differences in concentration

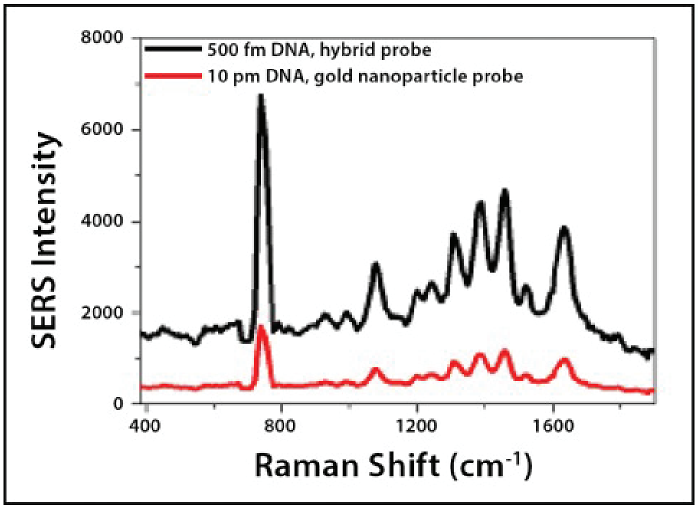



Figure 3: SERS-based detection of a segment of the HIV-1 gag-gene using popcorn-shaped gold nanoparticles conjugated with graphene oxide (black) and with the gold nanoparticle alone (red).

of the samples, the hybrid probe was found to be ~100x more sensitive than the gold nanoparticle probe alone, showing the power of employing both chemical and electromagnetic enhancement simultaneously in the same SERS probe.

The second pathogen of interest to be studied was MRSA. Approximately 100,000 MRSA infections occur each year in the United States, with 20,000 lives lost. Sensitive detection of this pathogen has the potential to catch infections at the early stages. The researchers modified the graphene oxide used in the hybrid probe with the aptamer APTSEB1 to achieve selective detection of *Staphylococcus aureus*, with MRSA aggregating inside the graphene oxide sheet.

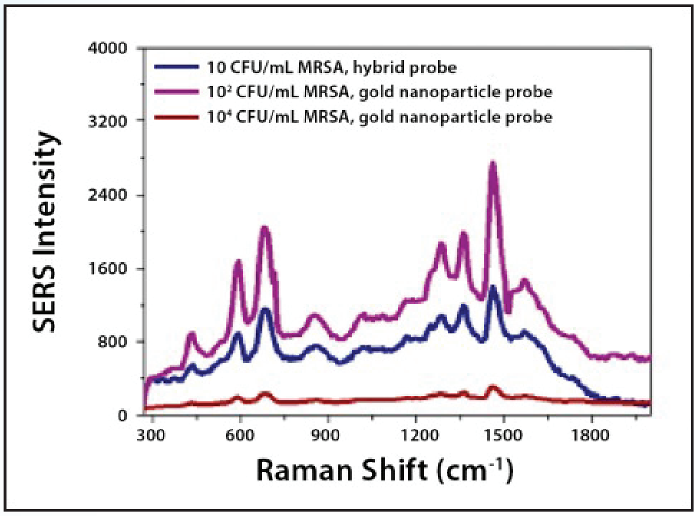



Figure 4: SERS-based detection of MRSA using popcorn-shaped gold nanoparticles conjugated with graphene oxide (purple), with the gold nanoparticle alone (blue) and with graphene oxide alone (red).

SERS data collected compared the enhancement effect of gold nanoparticles and aptamer-modified graphene oxide alone to the hybrid probe (Figure 4). All were shown to provide some enhancement, with the electromagnetic enhancement of the gold popcorn-shaped nanoparticles exceeding the chemical enhancement of aptamer-modified graphene oxide. The hybrid probe displayed significantly higher SERS signal than either single-component probe alone, allowing detection of MRSA down to 10 CFU/mL (colony-forming units per volume of solution).

## Conclusions

By combining the chemical and electromagnetic enhancement effects available from graphene oxide and gold nanoparticles, respectively, a highly sensitive SERS probe can be created for the detection of pathogens like HIV and MRSA. Use of a portable modular spectroscopy system for detection further increases the viability of this method for practical clinical diagnostics.