Identifying biological agents with surface-enhanced Raman scattering

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An analytical assay detects Category A and B bioterrorism agents.

The anthrax attacks which afflicted the United States in 2001 underscore the necessity of a quick response to biological terrorism agents. Optimal organization and capacity are critical to saving lives at minimal cost. Important to this effort is rapid biological agent identification aided by a field-ready analytical protocol. Given its capacity for unique molecular identification, Raman spectroscopy is uniquely poised to contribute to this need.

Although Raman spectroscopy readily detects chemical species, direct identification of biological materials is often difficult due to spectral complexity and low signal intensity. Several direct detection methods are available, including extraction and detection of a specific molecular marker, as well as surface-enhanced Raman spectroscopy (SERS) spectral generation by adsorbing an intact biological species onto a roughened gold or silver surface. Several indirect SERS detection methods are also available, such as labeling the analyte with a Raman-active dye and bringing it to the SERS substrate for readout. Nanometer-scale SERS-active tags conjugated with specific biological recognition moieties, thereby effecting direct binding to the analyte, is another possibility.

We developed an indirect biological detection system compatible with the Raman-based StreetLab Mobile. It employs SERS tags as unique labels for each target of interest in a sandwich immunoassay format. Unique spectroscopic signatures are generated with SERS tags consisting of individual glass-encapsulated gold nanoparticles and surface-bound Raman active reporter molecules, as depicted in Figure 1. These SERS tags are bound to a specific antibody and provide a strong, spectroscopically-consistent label. Superparamagnetic particles conjugated to the antibodies capture and concentrate the SERS-labeled complex at the focal point of the Raman laser using a magnetic field. The simple SERS readout confirms the presence or absence of the analyte (see Figure 2).

SERS tags are typically resistant to photobleaching. Our silica-encapsulated tags are also immune to changes in the detection medium, such as pH or temperature, which renders our assay amenable to field use. Another important advantage is rapid interaction between the capture particles, targets, and SERS tags in solution, resulting in low-level target detection within five minutes.

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Figure 2. Diagram of the SERS-based sandwich immunoassay. Antibody-conjugated SERS tags serve as labels for the biological analyte and are captured by superparamagnetic beads which are also functionalized with antibodies specific to the analyte. A Raman laser strikes the SERS tags, generating a unique spectrum that easily identifies analytes.

The ability to successfully detect very low levels of *E. coli* was fundamentally important for demonstrating assay capabilities. However, StreetLab Mobile is a rugged device intended for dealing with potential chemical or biological threat agents in real life. Our future work focuses on SERS-based sandwich immunoassays to detect potential biothreats, such as anthrax (*Bacillus anthracis*), ricin toxin from *Ricinus communis*, tularemia (*Francisella tularensis*), botulism (*Clostridium botulinum* toxin), plague (*Yersinia pestis*), and abrin toxin from *Abrus precatorius*.

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Frank J. Mondello received his PhD in microbiology from the University of Tennessee, Knoxville, in 1982. His research originally focused on microbial degradation of chlorinated aromatic hydrocarbons. He currently focuses on biosensor development and co-invented the SERS-based immuno-magnetic bioassay for StreetLab Mobile. He possesses eight patents and 20 peer-reviewed publications.

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Marie Lesaicherre received her MSc in chemical engineering from the Superior National School of Chemistry, France, and her PhD from the National University of Singapore. She is a chemical biologist and the biodetection program manager. Her experience includes over 10 years of research in biosensors, focusing on development and utilization of advanced detection technologies for DNA, RNA, and protein analysis for medical, water analysis, and security applications.

References