SERRS AS A RELIABLE ANALYTICAL TECHNIQUE – NEW APPROACHES AND NEW DIMENSIONS

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Abstract: In the last few years, SERRS has been transformed from a difficult technique to use, to one which is ready to be exploited to provide new analytical techniques with real advantages to meet the demand for fast, informative and ultra-sensitive analysis. This has been achieved by a combination of the more widespread availability of effective spectrometers, improved surface attachment of ligands, improved understanding of the effect, and new sampling methods.

Using colloidal SERRS, the analysis of DNA has been shown to be quantitative for eight different labels [1] with detection limits more than three orders of magnitude better than those obtained from two fluorescence spectrometers used routinely for DNA detection. Quantitation has been achieved by ensuring that the probe sequences adhere strongly to the silver colloid used as substrate and by using a colloidal suspension which by its nature averages the single molecule responses. In addition, this approach protects the surface from photo-degradation since Brownian motion ensures regular exchange of particles in and out of the interrogation volume.

The progress of this work is facilitated by a better practical and theoretical understanding of the effect. Using colloidal suspensions, no aggregating agent, and dyes which either assist aggregation or prevent it, single particle SERRS was demonstrated and found to be at a maximum with excitation at the plasmon resonance frequency [2]. The single particle enhancement is confirmed by studies of isolated particles. These studies also show different concentration dependence for SERS and SERRS. There is still much to be done to fully understand the theory, and there are concerns that the single molecule enhancement is inconsistent (We have found it vary from colloid batch to batch). However where an average of many single molecule events is taken, quantitation can be obtained.

The use of modern microscope and fibre optic coupled spectrometers enables developments of sampling methods to improve sensitivity and reliability. Micro fluidics (lab on a chip), cells give flowing streams on a small scale within a lamellar flow regime [3]. This enables the colloid to be prepared in situ and the aggregation procedure to be controlled. The result is an improvement in sensitivity of about 2 orders of magnitude. In a separate development, colloidal particles have been incorporated into a polymer and the signal detected using a small portable instrument at up to 20 metres [4]. The sharp molecularly specific nature of SERRS means that it is possible to write codes into these polymers. New SERRS polymer beads have been created in which SERRS active silver nanoparticles labelled with dye are incorporated within a polymer. The advantages of these beads are that thousands of labels are detected for every bead and hence the signals are intense, the aggregation state is reproducible, and the polymer protects the matrix, which might be a biological fluid, from any contact with silver particles.

New methods include the use of SERRS in optical tweezers and SERRS beacons. Tweezed SERRS active microparticles give extremely intense scattering easily observed as a flash of emitted radiation with a video camera. Conventional beacons use a loop of single stranded DNA with a fluorophore at one end and a quenching agent at the other so that the fluorescence is quenched. Addition of a complementary strand of DNA (the analyte) breaks the loop causing fluorescence.
With a beacon attached by one end to the silver particles, when the loop breaks both SERRS and fluorescence are observed and the efficiency of quenching, molecular specificity and sensitivity of SERRS is clearly illustrated.

References