Title	**Single cell analysis using surface enhanced Raman scattering (SERS) tags**
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Abstract	Fluorescence is a mainstay of bioanalytical methods, offering sensitive and quantitative reporting, often in multiplexed or multiparameter assays. Perhaps the best example of the latter is flow cytometry, where instruments equipped with multiple lasers and detectors allow measurement of 15 or more different fluorophores simultaneously, but increases beyond this number are limited by the relatively broad emission spectra. Surface enhanced Raman scattering (SERS) from metal nanoparticles can produce signal intensities that rival fluorescence, but with narrower spectral features that allow a greater degree of multiplexing. We are developing nanoparticle SERS tags as well as Raman flow cytometers for multiparameter single cell analysis of suspension or adherent cells. SERS tags are based on plasmonically active nanoparticles (gold nanorods) whose plasmon resonance can be tuned to give optimal SERS signals at a desired excitation wavelength. Raman resonant compounds are adsorbed on the nanoparticles to confer a unique spectral fingerprint on each SERS tag, which are then encapsulated in a polymer coating for conjugation to antibodies or other targeting molecules. Raman flow cytometry employs a high resolution spectral flow cytometer capable of measuring the complete SERS spectra, as well as conventional flow cytometry measurements, from thousands of individual cells per minute. Automated spectral unmixing algorithms extract the contributions of each SERS tag from each cell to generate high content, multiparameter single cell population data. SERS-based cytometry is a powerful complement to conventional fluorescence-based cytometry. The narrow spectral features of the SERS signal enables more distinct probes to be measured in a smaller region of the optical spectrum with a single laser and detector, allowing for higher levels of multiplexing and multiparameter analysis.
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