

## Optical Detection of Small Charged Molecules via Surface-enhanced Raman Spectroscopy for Biological Conversion

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Real-time monitoring of small charged molecules during biological conversion holds great importance for the optimization of conversion efficiency and reproducibility of the bioprocess. In general, chromatography-based detections such as HPLC and GC are used for the detection of such molecules during the bioconversion. However, these methods are time-consuming, typically taking more than 10 minutes due to the retention time for separation. Furthermore, off-line sampling is necessary for the analysis which has a risk of causing contamination. For these reasons, a novel method for real-time monitoring for bioconversion is required. Here, we propose the optical detection of small charged molecules in biological conversion via surface-enhanced Raman spectroscopy. Such molecules are attracted by the surface ligands of plasmonic nanostructure. As a result, molecules are preconcentrated on the surface of the nanostructure, increasing the number of molecules affected by strong field enhancement at the proximity of the surface. The effect of electrostatic attraction is systematically studied through the measurement of zeta-potentials and Raman signals.