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Single-Molecule SERS: Still a Needle in the Haystack?

Surface-Enhanced Raman Scattering (SERS) remains one of the few available techniques capable of detecting and characterizing individual molecular species at the single-molecule (SM) level. Despite the first successful observation of single-molecule SERS (SM-SERS) over 25 years ago, achieving reliable SM detection for new molecular systems continues to pose significant challenges. This is primarily due to the inherent complexity of the SERS effect, which arises from the interplay of multiple physical and chemical phenomena occurring simultaneously. The enhancement process involves both electromagnetic and chemical contributions, which are highly dependent on the local nano-environment, molecular orientation, and the specific electronic properties of the analyte. As a result, developing a universal, molecule-independent approach to controlling or optimizing SM-SERS remains elusive. In this presentation, we will discuss the underlying difficulties in extending SM-SERS to novel molecular species, highlight key parameters influencing successful detection, and explore strategies for improving reproducibility and control in SERS-based single-molecule experiments.