Development of Oligonucleotide-Functionalized SERS Probes for Ultrasensitive Nucleic Acid Detection

Abstract: The accurate and early detection of nucleic acids plays a critical role in clinical diagnostics, forensic investigations, and environmental monitoring. Traditional methods such as PCR, while sensitive, require complex instrumentation and are prone to contamination. Surface-Enhanced Raman Scattering (SERS) presents a powerful alternative, capable of label-free, ultrasensitive detection—even at the single-molecule level. This proposal aims to develop a hybrid sensing platform by integrating synthetic oligonucleotides with plasmonic nanoparticles to enable SERS-based detection of specific DNA or RNA sequences. Short oligonucleotides will be synthesized using solid-phase phosphoramidite chemistry, incorporating functional end-groups such as thiols for nanoparticle attachment. These sequences will be conjugated onto silver or gold nanoparticles to form stable, bioactive nanoprobes. Raman reporter molecules may be co-adsorbed to enhance signal specificity and intensity. Upon hybridization with complementary target sequences—including those with single-nucleotide differences—the SERS spectrum is expected to exhibit distinct, analyte-specific changes. The sensor will be evaluated for sensitivity, selectivity, and stability, including performance in biologically relevant media. This approach is anticipated to achieve detection limits in the femtomolar range and distinguish even single-base mismatches. The successful development of this platform could lead to a new class of portable, ultrasensitive biosensors for point-of-care diagnostics, pathogen surveillance, and genetic screening. By harnessing the precision of synthetic oligonucleotides and the signal amplification of SERS, this project bridges molecular biology and nanotechnology for impactful, real-world applications.

Keywords: Oligonucleotide-functionalized nanoparticles, Surface-Enhanced Raman Scattering (SERS), Nucleic acid detection, Biosensor development, Single-nucleotide polymorphism (SNP) analysis