
Petra Petrović Popović¹

Adriana Kendel¹, Tea Juračić¹, Nikša Krstulović², Dijana Pavlović Saftić³, Snežana Miljanić¹

¹University of Zagreb Faculty of Science, Horvatovac102A, Zagreb, Croatia

²Institute of Physics, Bijenička cesta 46, Zagreb, Croatia

³Ruđer Bošković Institute, Bijenička cesta 54, Zagreb, Croatia

ppetrovic@chem.pmf.hr

Gold-Based SERS Substrates for Label-Free Monitoring of G-Quadruplex Formation

G-quadruplexes (G4s) are non-canonical nucleic acid structures formed by guanine-rich sequences and are increasingly investigated as structurally and biologically relevant nucleic acid motifs. Surface-enhanced Raman scattering (SERS) spectroscopy offers a label-free approach for probing such structures through their intrinsic vibrational fingerprints, although the obtained spectral response strongly depends on the properties of the plasmonic substrate [1]. In this study, gold-based colloidal substrates with different morphologies and surface properties were investigated for label-free SERS monitoring of G-quadruplex formation. A human telomeric DNA Tel24 sequence was used as a model system and studied in its non-folded and G4 conformations. The gold nanostructures were characterized by UV/Vis/NIR spectroscopy, scanning electron microscopy, dynamic light scattering, and zeta potential measurements, providing insight into their optical, morphological, hydrodynamic, and surface properties. G4 formation in the presence of the investigated substrates was independently confirmed by circular dichroism spectroscopy. SERS spectra were acquired using 785 nm excitation and evaluated with particular emphasis on characteristic bands associated with adenine and guanine ring breathing vibrations, which provide spectral markers of structural rearrangement upon G4 formation [1,2]. Among the investigated substrates, citrate-stabilized gold nanoparticles provided the clearest spectral differentiation between the non-folded and G4 conformations, while ascorbate-stabilized gold nanostars also enabled successful monitoring of the structural transition. In contrast, laser-ablated gold nanoparticles provided only limited structural information. Spermine-stabilized gold nanoparticles were found to influence the conformation of the DNA analyte itself, limiting their suitability for monitoring G4 formation. Overall, the results demonstrate that surface chemistry and nanoparticle properties are critical considerations when selecting gold-based SERS substrates for label-free investigation of G-quadruplex DNA.

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References

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