A Computational-Experimental Study of Aptamer Recognition of West Nile Virus at Gold Interfaces

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Single-stranded DNA aptamers are promising molecular recognition elements for biosensors targeting viral pathogens, including West Nile Virus (WNV). However, surface immobilization can alter aptamer conformation, dynamics and target recognition. Here, we developed an integrated computational-experimental approach to design and optimize a sensitive diagnostic platform based on the Tr-WNV-37 DNA aptamer immobilized on functionalized gold surfaces, while elucidating recognition at the bio-nano interface.

Because the three-dimensional structure of Tr-WNV-37 remains experimentally unresolved, structural prediction and molecular docking were used to model the aptamer-WNV envelope (E) protein complex and identify key residues involved in molecular recognition. Multi-replica atomistic molecular dynamics simulations and MM-PBSA analyses then compared the aptamer-protein complex in solution and after immobilization on an Au(111) surface functionalized with a hexanol-thiol self- assembled monolayer and a six-thymidine (T6) spacer.

The simulations show that the T6 spacer maintains separation from the gold interface and that immobilization preserves the overall aptamer architecture while reducing conformational freedom, reorganizing the aptamer-protein interaction network and modifying the local ionic environment. Overall molecular recognition remains broadly comparable between free and surface-bound complexes. Complementary experiments using Tr-WNV-37-functionalized gold nanorods showed a preferential target-associated plasmonic response relative to control conditions, supporting the sensing concept.

This computational-experimental framework links molecular-level understanding of aptamer immobilization and target recognition with measurable nanoplasmonic response, supporting rational design and optimization of sensitive surface-bound aptamer biosensors for WNV detection.