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Title: Ultrasensitive Characterization of the Prion Protein by Surface-Enhanced Raman Scattering:

Selective Enhancement via Electrostatic Tethering of the Intrinsically Disordered Domain with

Functionalized Silver Nanoparticles

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Keywords: Ultrasensitive

> Characterization Prion Protein Surface-Enhanced

Issue Date: 2021

Publisher: **ACS Publications**

Citation: Journal of Physical Chemistry Letters, 12(12), 3187-3194.

Abstract:

Surface-enhanced Raman scattering (SERS) circumvents the inherent insensitivity of Raman spectroscopy and offers a powerful tool for the ultrasensitive detection and characterization of biomolecules at low concentrations. Here we show that SERS via electrostatic tethering between surface-modified negatively charged silver nanoparticles and highly positively charged intrinsically disordered N-terminal domain of the prion protein allows highly sensitive and reproducible protein detection and characterization at as low as hundreds of nanomolar protein concentrations. These measurements preferentially illuminate a selective part of the protein due to a sharp dependence of the near-field intensity on the distance between the nanoparticle surface and the protein. We also demonstrate that by shortening the length of the disordered tail it is possible to achieve a domain-selective Raman enhancement to study the C-terminal globular domain. Our tetherlength-dependent SERS methodology will serve as a potent, noninvasive, and label-free strategy to detect and characterize a wide range of proteins possessing disordered segments.

Description: Only IISERM authors are available in the record.

URI: https://doi.org/10.1021/acs.jpclett.1c00240 (https://doi.org/10.1021/acs.jpclett.1c00240)

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