Methodological Perspectives on Modeling Photo-Induced Interactions at the Silver Nanoparticle-Bio Interface

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The application of silver nanoparticles (AgNPs) in targeted therapies relies strongly on their optical response under controlled irradiation, particularly within the blue light spectrum (400-480 nm). At bio-nano interfaces, the interaction between metallic surfaces and biomolecules is governed by complex electronic phenomena that remain challenging to describe using standard computational protocols [1]. These limitations become especially pronounced under photo-activation, where plasmonic excitations and interfacial chargetransfer processes jointly determine the stability and reactivity of hybrid bio–nano systems [2] (Figure 1).

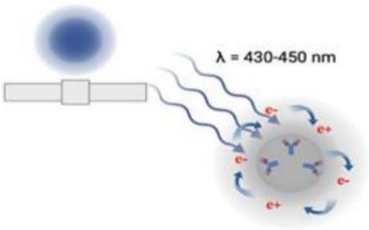

Figure 1: Schematic representation of localized surface plasmon resonance (LSPR) and biomolecular interactions at the AgNP interface under 430–450 nm irradiation (Created in BioRender (2026)).

In this context, the present work proposes a systematic benchmarking framework aimed at assessing the reliability of theoretical methods for modeling photo-activated AgNP–biomolecule assemblies. Due to the size, flexibility, and chemical heterogeneity of these systems, accurate modeling requires not only robust excited-state methodologies but also extensive structural sampling and multi-scale treatment of the interfacial environment [3]. Particular attention is given to systems involving DNA, where photosensitization and aggregation phenomena play a critical role in governing electronic processes and photochemical outcomes [4].

The methodological challenges addressed in this framework are structured as follows:

• Spectral Sensitivity: Assessing the capability of time-dependent density functional theory (TD-DFT) and related excited-state approaches to accurately reproduce electronic transitions of AgNP-based systems in the visible region (400-480 nm), particularly when functionalized with biological ligands, where plasmonic resonances and metal-ligand coupling strongly influence excitation profiles [1, 2].

• Confinement and Charge Transfer: Evaluating how spatial confinement at nanoparticle surfaces modulates charge-transfer pathways and energy transfer efficiency at the bio–nano

interface, with a focus on the photostability and reactivity of DNA-AgNP complexes under irradiation [2, 5].
• Methodological Benchmarking: Systematically comparing exchange–correlation functionals and excited-state methodologies to identify computational strategies that optimally balance accuracy and feasibility for largescale hybrid bio–nano models [1, 3].

• Implementation and Preliminary Experimental Insights

Wavelength-Dependent Modulation of Cell Fate: Our findings demonstrate that 433 nm irradiation, when combined with AgNPs, predominantly biases cancer cell fate toward programmed mitochondrial apoptosis, whereas 450 nm irradiation results in a cell death profile dominated by non-programmed, necrosis-associated mechanisms.

• Irradiation Dynamics and Temporal Profile: We observed that at 433 nm, even short irradiation durations are sufficient to trigger an efficient apoptotic response, while treatment under 450 nm requires more prolonged exposure to induce significant cytotoxicity.
• Differential Oxidative Stress Induction: Our results indicate that 433 nm light exhibits higher photochemical efficiency, leading to rapid and pronounced generation of intracellular Reactive Oxygen Species (ROS), while 450 nm irradiation produces a significantly slower and less intense oxidative response.
•Transcriptional Regulation and Gene Expression: Through qPCR analysis, we confirmed that the 433 nm + AgNP combination triggers a coordinated molecular cascade, significantly upregulating pro-apoptotic genes (such as BAX and CASP3), whereas 450 nm irradiation fails to consistently activate these structured apoptotic gene programs.

In conclusion, we have established a mechanistic framework demonstrating that the choice of blue light wavelength (433 nm vs. 450 nm) is a critical determinant that programs the specific intracellular stress-response pathway and the subsequent mode of cancer cell death.

• Conformational Sampling:
Implementing efficient global potential energy surface exploration and conformational sampling strategies on nanoparticle facets to identify representative interfacial structures and capture realistic molecular arrangements governing photo-induced behavior [3]. By addressing these interconnected challenges, this benchmarking framework directly contributes to the objectives of Working Group 1 and Working Group 4 of the COSY Action. The proposed methodological roadmap aims to support the rational design of photoresponsive silver-based nanomaterials while providing fundamental insight into the molecular mechanisms underlying light-driven processes at complex bio–nano interfaces.

References:

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