chemistry proceedings

MDPI

Proceeding Paper

The Sers Analysis of the Interaction Between AG_8 Cluster and Adenine for Optical Sensor Applications Using DFT Calculations

Tuong Lam Vo Pham, My Phuong Nguyen Thi, Huy Phu Chu, Thuy Duong Nguyen Thi, Nhu Y. Duong Thi, Quoc Dat Ho and Van Hong Nguyen *

Department of Chemistry, Faculty of Education, An Giang University, Vietnam National University Ho Chi Minh City, Vietnam; lam_dhh220408@student.agu.edu.vn (T.L.V.P.); ntmphuong@agu.edu.vn (M.P.N.T.); phu_dhh220410@student.agu.edu.vn (H.P.C.); duong_dhh220401@student.agu.edu.vn (T.D.N.T.); y_dhh230719@student.agu.edu.vn (N.Y.D.T.); dat_dhh240703@student.agu.edu.vn (Q.D.H.)

* Correspondence: nvhong@agu.edu.vn; Tel.: +84-827998989

† Presented at the 29th International Electronic Conference on Synthetic Organic Chemistry (ECSOC-29); Available online: https://sciforum.net/event/ecsoc-29.

Abstract

The Raman spectrum of adenine and the surface-enhanced Raman spectrum (SERS) upon adsorption of adenine on an Ag_8 cluster in aqueous solution were calculated using the DFT/PBE0/Def2-TZVP method with the IEF-PCM solvent model. TD-DFT calculations were performed to determine the excitation wavelengths of adenine and the Ag_8•A complex, thereby selecting excitation wavelengths compatible with available experimental Raman spectroscopy instruments. In addition, excitation wavelengths with the maximum oscillator strength were chosen to propose characteristic spectra for experimental studies. The calculated Raman activities were converted into Raman scattering intensities, and the enhancement factor EF_int was determined. The results show that an excitation wavelength of 325 nm gives the strongest and most distinct SERS signal, 532 nm provides stable signals suitable for commercial instruments, while 442 nm significantly reduces several characteristic vibrational bands. Moreover, the Ag_8 cluster exhibits excellent enhancement of the Raman signal for adenine. This study provides a basis for selecting excitation wavelengths and characteristic vibrational modes to identify adenine, supporting the development of label-free biosensors based on silver clusters.

Keywords: DFT; cluster; SERS; characteristic vibrational; enhancement factor

Academic Editor(s): Name

Published: date

Citation: Pham, T.L.V.; Thi, M.P.N.; Chu, H.P.; Thi, T.D.N.; Thi, N.Y.D.; Ho, Q.D.; Nguyen, V.H. The Sers Analysis of the Interaction Between AG_8 Cluster and Adenine for Optical Sensor Applications Using DFT Calculations. *Chem. Proc.* **2025**, *volume number*, x. https://doi.org/10.3390/xxxxx

1. Introduction

Adenine is an aromatic base that makes up DNA and RNA, and is slightly soluble in water. When adsorbed on nanoparticles or precious metal clusters such as silver, gold, etc., adenine gives a strong SERS (Surface-enhanced Raman scattering) signal, which is useful in disease detection, DNA hybridization, and many biomedical and agricultural applications, etc. [1,2]. Adenine has become one of the most studied biological molecules in the field of SERS recently, and studies have combined both experimental and computational studies on clusters such as gold, silver, or bimetallic silver and gold to sense adenine [3,4]. Therefore, understanding the vibrational characteristics and Raman spectrum

of adenine is not only important in theoretical chemistry but also has practical significance in molecular biology. SERS spectra not only help determine characteristic molecular vibrations but also provide valuable information about the interaction between adenine and metal surfaces. These insights form the basis for the development of highly sensitive biosensors for the detection of biomolecules at low concentrations.

2. Methodology

Structure and vibrational frequency of Ag_8 and adenine in water solvent were optimized using DFT method with PBE0 hybrid function and Def2-TZVP basis set, model solvent IEF-PCM, using software Gaussian 16 [5]. The calculated results were analyzed using software Multiwfn 3.8 [6]. The PBE0 function is combined with Hartree–Fock and PBE exchange along with the basis set Def2-TZVP allows accurate simulation of complex interactions between silver clusters and adenine in water solvent. [7].

Determine the total enhancement factor of the SERS signal [8]:

$$EF_{int} = \frac{R^{tot}_{Ag_8\text{的}}}{R^{tot}_{Adenine}} = \frac{\sum_k R^{k}_{Ag_8\text{的}}}{\sum_j R^{j}_{Adenine}} \tag{1}$$

EF_{int} (Integrated Enhancement Factor)–the total enhancement factor of the SERS signal.

$R^{tot}_{Adenine}$, $R^{tot}_{Ag_8 \bullet A}$ —Raman intensity of adenine and $Ag_8 \bullet A$;

$\sum_j R^{j}_{Adenine}$, $\sum_k R^{k}_{Ag_8 \bullet A}$ —the sum of all vibrational states corresponding to the same symmetrical representation in the symmetry point group of adenine and $Ag_8 \bullet A$;

Convert Raman scattering intensity from Raman activity [6]:

$$I_i = C \frac{(\nu_0 - \nu_i)^4}{\nu_i \left[1 - e^{-\frac{hc\nu_i}{kT}}\right]} R_i \tag{2}$$

I_i—Raman scattering intensity of vibration mode i.

C—normalization constant to bring the entire spectrum to the same scale. In Multiwfn 3.8 default $C=10^{-12}$;

ν_0—wavenumber of the excitation laser;

ν_i—wavenumber of vibration;

h—Planck constant;

c—speed of light;

k—Boltzmann constant;

T—absolute temperature (K);

$e^{-\frac{hc\nu_i}{kT}}$ —exponential component from the Bose–Einstein distribution;

R_i—Raman activity (unit A^4/amu).

3. Results and Discussion

3.1. Excited State Calculation TD-DFT (Time-Dependent Density Functional Theory)

The calculation results of the excited state show that adenine absorbs strongly in the region of 124.57–247.03 nm (radiation deep UV to near UV), Ag_8 has a range from 235.70–515.33 nm (near UV to visible green), while the $Ag_8 \bullet A$ complex extends from 243.76–

545.80 nm (near UV to blue-green visible). This synthetic wavelength range (≈124–546 nm) is suitable for commercial multi-laser Raman systems, typically such as Horiba LabRAM HR Evolution (325, 405, 442, 457, 488, 514, 532, 633, 785 nm) [9] and Renishaw inVia Qontor (325, 405, 532, 633, 785 nm) [10]. As a result, many important electronic states predicted by Multiwfn can be experimentally excited with the nearest laser in energy, helping to obtain optimal Raman spectra and ensuring consistency between theoretical simulations and laboratory measurement data.

Table 1. Excitation energy value (E_{exc}, eV), excitation wavelength (λ_0, nm) and intensity oscillation f.

Substance	E_{exc}	λ_0	f
Adenine	5.019	247.03	0.463
	6.244	198.57	0.620
Ag_8•A	2.300	539.01	0.547
	2.803	442.37	0.915
	2.897	428.02	1.482
	3.869	320.50	0.003

3.2. Raman Spectrum Analysis of Adenine and SERS of Ag_8•A

From the TD-DFT calculation results and the wavelength values established from experimental Raman spectrometers, the excitation wavelengths (λ_0) are chosen to be closest to the calculated values, specifically 325 nm close to 320.5 nm of Ag_8•A, 442 nm close to 442.37 nm. In addition, a wavelength corresponding to the maximum value of the corresponding oscillation intensity f of adenine will be selected as 198.57 nm and of Ag_8•A is 428.02 nm, and finally the wavelength is 532 nm is the wavelength that many Raman spectrometers have established.

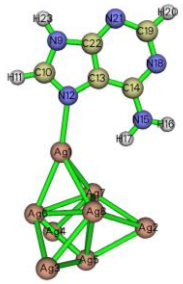


Figure 1. The most stable structure of Ag_8•A.

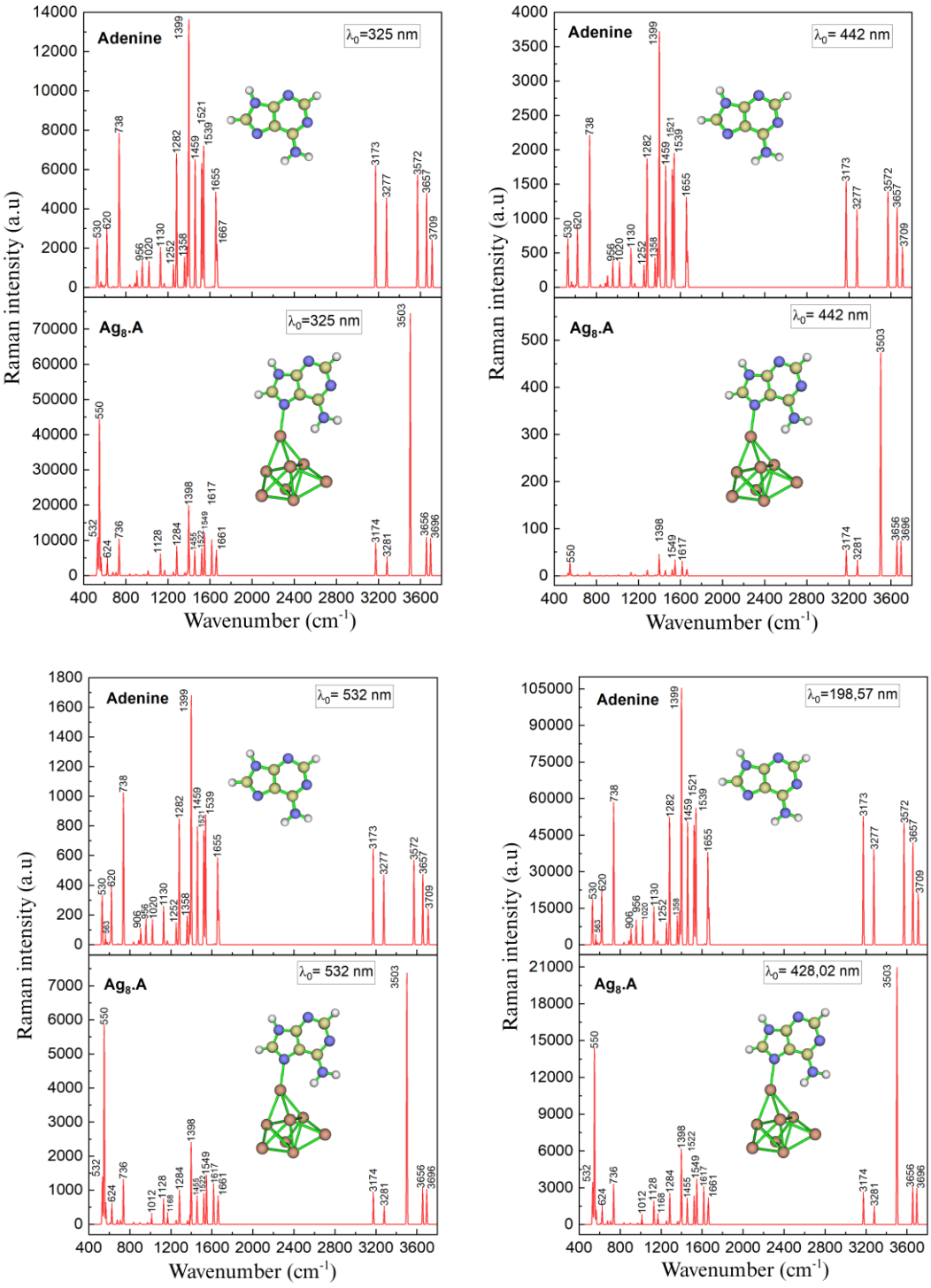


Figure 2. Raman spectrum of adenine (**above**) and SERSof Ag8•A (**below**) at different excitation wavelengths.

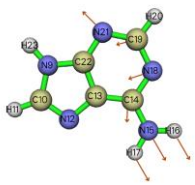
The above Raman and SERS analysis results show that the initial excitation wavelengths of 325 nm and 532 nm give clear and easy-to-follow characteristic spectral peaks. In which the 325 nm wavelength helps increase the Raman scattering intensity very high for both adenine and Ag8•A.This can be explained by the fact that the excitation wavelength of adenine when analyzing TD-DFT is quite small, only ranging from 124.57 nm to 247.03 nm.When the excitation wavelength increases from 325 nm, 442 nm and up to 532 nm, the Raman scattering intensity will gradually decrease.

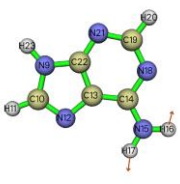
When using an excitation wavelength of 442 nm, the characteristic vibrations of adenine in the Ag_8•A complex will lose a lotfrom 550–1300 cm^{-1}, this makes it difficult toanalyzeadenine recognition sensor. Selecting the excitation wavelength according to TD-DFT calculations that has the maximum oscillation intensity f will obtain the clearest spectral peak signals.

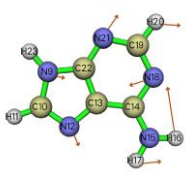
Table 2. Vibration modes, wave number(ν, cm^{-1}) Raman activity (R_i, $Å^4$/amu) of Raman spectrum of adenine and SERS of Ag_8•A, enhancement factor EF_{int}.

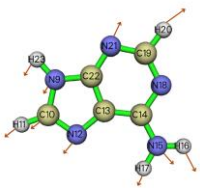
Symbol	Vibration	Raman Adenine		SERS Ag_8•A		EF_{int}
		ν	R_i	ν	R_i	
ν_1	ν_{b6}	530 (529 [a,b])	7.1	533 (537 [c])	37.8	5.3
ν_2	ω (NH_2)	580 (534 [e])	0.6 (0 [e])	550	223.4	359.1
ν_3	ρ (NH_2), ρ (CH), φ_6	620 (621 [a], 618 [b])	16.3	624 (689 [c])	21.3	1.3
ν_4	ν_b	738 (724 [d])	57.6	736 (709 [e])	67.3 (20 [e])	1.2
ν_5	γ_6 (CH)	906 (904 [b])	5.8	907	1.4	0.3
ν_6	ν_{b5}	956 (949 [b])	10.9	972 (950 [c])	3.8	0.4
ν_7	ρ (NH_2)	1020 (1019 [a])	11.6	1012	14.6	1.3
ν_8	σ_5 (NH, CH)	1130 (1127 [b])	22.4	1128 (1190 [c])	58.9	2.6
ν_9	ρ (NH, CH)	1282 (1276 [e])	95.4 (22 [e])	1284 (1299 [e])	98.6 (36 [e])	1.0
ν_{10}	σ_5 (NH, CH), ρ_6 (CH)	1399 (1397 [e])	217.1 (27 [e])	1398 (1392 [e])	295,8 (38 [e])	1.4
ν_{11}	ρ_5 (NH), ρ_6 (CH)	1459	94.3	1455 (1458 [e])	90.7 (32 [e])	1.0
ν_{12}	ν_{as} (C-N)	1521	108.3	1522 (1517 [e])	110.1 (60 [e])	1.0
ν_{13}	ν_{as5} (C-N), σ (NH_2)	1539	125.2	1549	194.7	1.6
ν_{14}	σ (NH_2)	1626 (1596 [e])	1.0	1617	164.9	163.9
ν_{15}	ν_{as6} (C-N), ω_5 (N-H)	1657	91,4	1657 (1609 [e])	71.0 (38 [e])	0.8
ν_{16}	ν_{as6} (C-H)	3173 (3160 [b], 3111 [e])	276.7 (120 [e])	3174	368.6	1.3
ν_{17}	ν_{as5} (C-H)	3277 (3269 [b])	210.3	3281	186.4	0.9
ν_{18}	ν_s (H-N-H)	3572 (3433 [b], 3451 [e])	306.0 (174 [e])	3503	3992.6	13.0
ν_{19}	ν_{as5} (N-H)	3657 (3497 [e])	260.7 (144 [e])	3656	536.0	2.1
ν_{20}	ν_{as} (H-N-H)	3709 (3550 [b], 3587 [e])	128.3 (46 [e])	3696	533.1	4.2

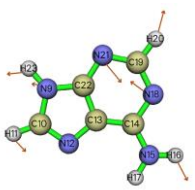
ν_s: symmetric stretching; ν_{as}: asymmetric stretching; ν_b: ring breathing vibration; γ: out-of-plane ring vibration; σ: scissoring vibration; ϱ: rocking vibration; ω: wagging vibration; φ: fanning vibration. The subscripts 5, 6 are for the five-membered imidazole and six-membered pyrimidine rings. [a] gExperimental value in water environment [11], [b] from [12]; [c] experimental adenine value-silver film [13]; [d] experimental adenine adsorption value-composite-nano silver [14]; [e] Ag calculation-adenine [15].

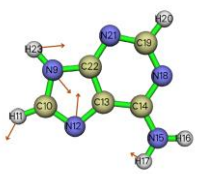

ν_1

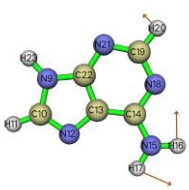

ν_2

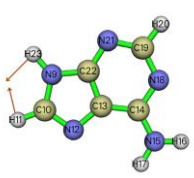

ν_3


ν_4


ν_5


ν_6


ν_7


ν_8

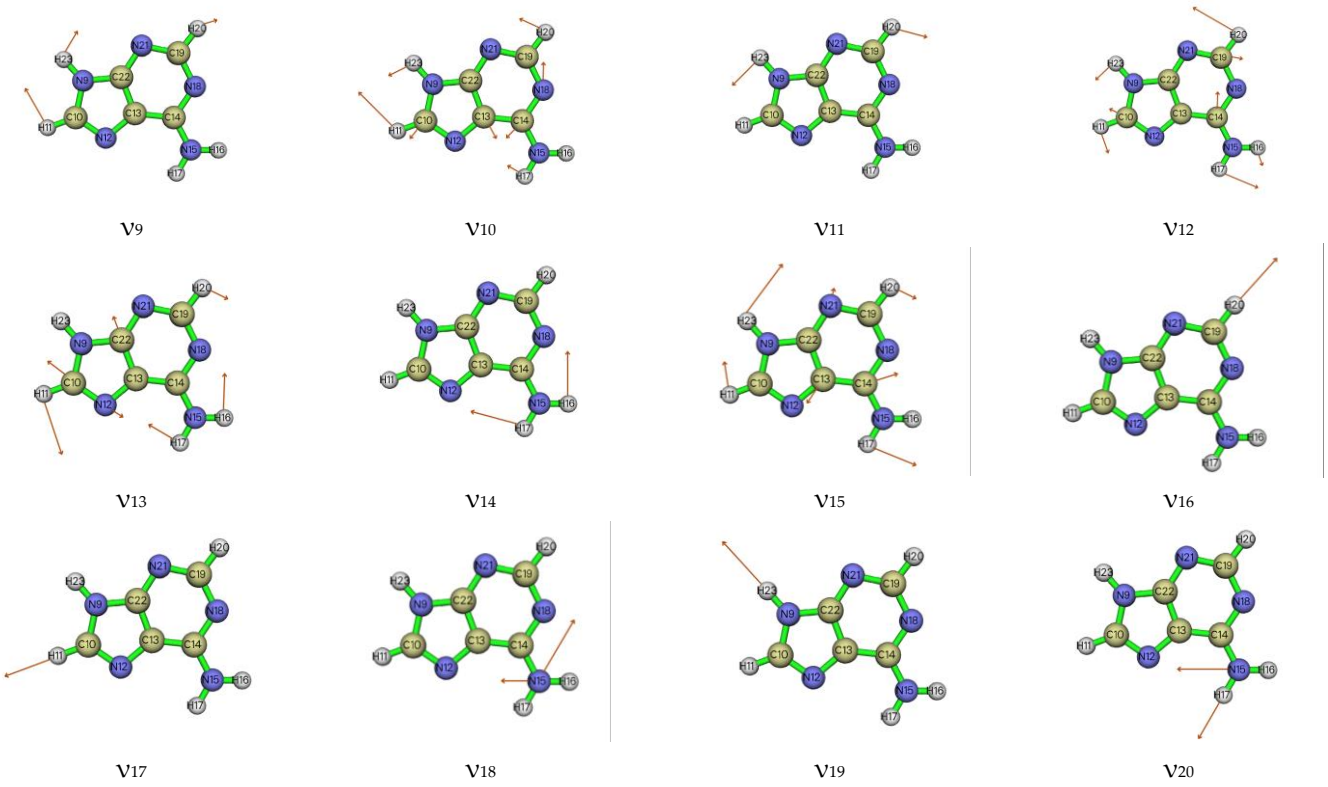


Figure 3. Types of adenine vibrations.

Research results show that the characteristic spectral peaks of adenine are quite consistent with published experimental studies, however at wave numbersgreater than 3000 cm^{-1} of the stretching vibrations of the C-H, N-H groups when adenine is bonded to the metal substrate have not been published.

Among the enhanced peaks, there is a peak at 580 cm^{-1} of the Raman spectrum of adenine shifted down to 550 cm^{-1} in the Ag_8•A complex, this is the vibration with the highest total enhancement factor with EF_{int} can reach 359,1. And at the peak of 1626 cm^{-1} similarly, there is a decrease in wave number to 1617 cm^{-1} corresponding to EF_{int} is 163.9. Both of these characteristic vibrations are related to the NH_2 group are scissoring and wagging vibrations, the reason is that the NH_2 group is outside the ring of adenine, the electron pair on the N atom is freer, when adenine forms a bond with Ag_8 through the N atom of the imidazole ring, from the surface plasmon effect of Ag_8 interacting with adenine leads to the NH_2 group free has the strongest vibration enhancement phenomenon.

Some cases have a reduced Raman activity coefficient ($EF_{int} < 1$) such as C-H group vibrations in and out of the pyrimidine ring, imidazole ring breathing vibrations, C-N asymmetric vibrations of the pyrimidine ring, N-H wagging vibrations and C-H asymmetric vibrations of the imidazole ring. These vibrations are mainly belong to the ring of adenine, the reason is that when interacting with the Ag $cluster_8$, the structure of the adenine molecule is more stable, the conjugated system π of the two aromatic rings imidazole and pyrimidine is kept more fixed. Besides, the Ag $cluster_8$ has a Raman activity coefficient that is always higher than that of the Ag single atom, which has been studied by the DFT/B3LYP/6-311+G(d,p) method [15].

4. Conclusions and Recommendations

The study calculated the Raman spectrum of adenine and SERS of the Ag_8•A complex with the initial excitation wavelength investigated at different ranges of 325 nm, 442 nm, 532 nm and 198.57 nm with adenine having maximum vibration intensity, similarly

428.02 nm corresponding to the Ag_8•A complex has maximum vibration intensity. Among the excitation wavelengths investigated, the wavelength at 325 nm helps enhance the signal and obtain the most characteristic vibrational spectral peaks, this wavelength has also been set up in spectral analyzers on the market. The research results have identified the characteristic vibrations of adenine, determined the enhancement of the Raman spectrum signal due to Ag_8 created for adenine, the results obtained have a higher activity coefficient than previously published research. These are important results in designing adenine sensors using silver metal clusters especially the Ag $cluster_8$.

Author Contributions: T.L.V.P., H.P.C., T.D.N.T., N.Y.D.T. and Q.D.H.: methodology, formal analysis, investigation, resources, data curation, and writing—original draft preparation; M.P.N.T. and V.H.N.: conceptualization, supervision, writing—review and editing. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by An Giang University, Vietnam National University Ho Chi Minh City.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Acknowledgments: The authors would like to thank the Computational Chemistry Laboratory, University of Science, Vietnam National University Ho Chi Minh City, and the Center for Computational Materials Science, Institute for Materials Research, Tohoku University, Japan (MASAMUNE-IMR, 202312-SCKXX-0504), for providing computational resources used in this study.

Conflicts of Interest: The authors declare no conflicts of interest and the funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Abbreviations

The following abbreviations are used in this manuscript:

SERS	Surface-Enhanced Raman Scattering
DFT	Density Functional Theory
TD-DFT	Time-Dependent Density Functional Theory
IEF-PCM	Integral Equation Formalism Polarizable Continuum Model
EF_{int}	Integrated Enhancement Factor
UV	Ultraviolet
DNA	Deoxyribonucleic Acid
RNA	Ribonucleic Acid
Def2- TZVP	Second generation of definitive Triple-Zeta Valence with Polarization basis set
PBE0	Perdew-Burke-Ernzerhof hybrid functional

References

1. Zhang, W.; Zhang, H.; Li, J.; Zou, X.; Wang, W.; Hu, H.; Iqbal, K.; Zhou, P.; Ye, W. PVP-capped silver nanoparticles for efficient SERS detection of adenine based on the stabilizing and enrichment roles of PVP. *Microchim. Acta* **2024**, *191*, 1.
2. Tzeng, Y.; Lin, B.-Y. Silver SERS Adenine Sensors with a Very Low Detection Limit. *Biosensors* **2020**, *10*, 53.
3. Kundu, J.; Neumann, O.; Janesko, B.G.; Zhang, D.; Lal, S.; Barhoumi, A.; Scuseria, G.E.; Halas, N.J. Adenine- and Adenosine Monophosphate (AMP)–Gold Binding Interactions Studied by Surface-Enhanced Raman and Infrared Spectroscopies. *J. Phys. Chem. C.* **2009**, *113*, 14390–14397.

4. Pagliai, M.; Caporali, S.; Muniz-Miranda, M.; Pratesi, G.; Schettino, V. SERS, XPS, and DFT Study of Adenine Adsorption on Silver and Gold Surfaces. *J. Phys. Chem. Lett.* **2012**, *3*, 242–245.
5. *Gaussian 16, Revision C.01*; Gaussian, Inc.: Wallingford, CT, USA, 2016.
6. Lu, T.; Chen, F. Multiwfn: A multifunctional wavefunction analyzer. *Carbon* **2020**, *165*, 461–467.
7. Ramazanov, R.R.; Nasibullin, R.T.; Sundholm, D.; Kurtén, T.; Valiev, R.R. Nonradiative Deactivation of the Fluorescent Ag_{16}-DNA and Ag_{10}-DNA Emitters: The Role of Water. *J. Phys. Chem. Lett.* **2024**, *15*, 10710–10717.
8. Hu, Z.; Chulhai, D.V.; Jensen, L. Simulating Surface-Enhanced Hyper-Raman Scattering Using Atomistic Electrodynamics-Quantum Mechanical Models. *J. Chem. Theory Comput.* **2016**, *12*, 5968–5978.
9. Scientific, H. Instrument Presentation: Typical Laser Wavelengths Used for Raman Spectroscopy. Available online: https://www.horiba.com/usa/scientific/technologies/raman-imaging-and-spectroscopy/raman-spectrometer-presentation/ (accessed on).
10. Renishaw, P. inVia Qontor Confocal Raman Microscope [Product Brochure]. Renishaw plc. Available online: https://www.renishaw.com/en/38037.aspx?srsltid=AfmBOopSS0dL5iVrgOdO4t1Lv51kKxN7RrEM65ZNIN2gpcN0DY2Of-8Q (accessed on).
11. Nergui, N.; Chen, M.-J.; Wang, J.-K.; Wang, Y.-L.; Hsing, C.-R.; Wei, C.-M.; Takahashi, K. Dependence of Adenine Raman Spectrum on Excitation Laser Wavelength: Comparison between Experiment and Theoretical Simulations. *J. Phys. Chem. A* **2016**, *120*, 8114–8122.
12. Burova, T.G.; Ermolenkov, V.V.; Ten, G.N.; Shcherbakov, R.S.; Baranov, V.I.; Lednev, I.K. Raman Spectroscopic Study of the Tautomeric Composition of Adenine in Water. *J. Phys. Chem. A* **2011**, *115*, 10600–10609.
13. Giese, B.; McNaughton, D. Surface-Enhanced Raman Spectroscopic and Density Functional Theory Study of Adenine Adsorption to Silver Surfaces. *J. Phys. Chem. B* **2002**, *106*, 101–112.
14. Gao, D.; Yang, X.; Teng, P.; Kong, D.; Liu, Z.; Yang, J.; Luo, M.; Li, Z.; Wen, X.; Yuan, L.; et al. On-line SERS detection of adenine in DNA based on the optofluidic in-fiber integrated GO/PDDA/Ag NPs. *Sens. Actuators B Chem.* **2021**, *332*, 129517.
15. Huang, R.; Zhao, L.-B.; Wu, D.-Y.; Tian, Z.-Q. Tautomerization, Solvent Effect and Binding Interaction on Vibrational Spectra of Adenine—Ag+ Complexes on Silver Surfaces: A DFT Study. *J. Phys. Chem. C* **2011**, *115*, 13739–13750.