



Learning to Steer Eco-coronas: An AI-driven Framework for Protein-guided Control of Environmental Nano–bio-interfaces

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ABSTRACT

The formation of eco-coronas is a key issue that must be understood and predicted to ensure the safety and environmental performance of nanomaterials. Eco-coronas are biomolecular coatings that form on the surface of nanoparticles in environmental media, where aggregation behavior, bioavailability, and ecological fate are influenced by proteins, lipids, and microbial metabolites. Predictive and mechanistic control remains limited, despite previous studies qualitatively characterizing eco-corona composition. In this study, a hybrid framework, EcoCorona-MAP (Model–Actuate–Protect), is presented as an artificial intelligence-based system that forecasts and guides eco-corona formation. The system is based on a graph neural network (GNN) trained on environmental proteomic data from *Danio rerio* and *Daphnia magna* microbiomes to predict protein–nanoparticle adsorption energies (regression task). Predicted adsorption energies are subsequently used to estimate adsorption probabilities, which are used to design decoy peptides that competitively bind to nanoparticle surface sites to modulate eco-corona composition. Experimental validation using TiO₂ and carbon nanotube (CNT) nanoparticles revealed that approximately 40% of microbial protein adsorption was reduced and colloidal persistence was enhanced under simulated aquatic conditions. Simulations also indicated that peptide–nanoparticle binding remained stable, as confirmed by molecular dynamics simulations (RMSD < 2.5 Å). Overall, EcoCorona-MAP establishes a predictive-to-interventional framework that integrates artificial intelligence with molecular design to actively control nano–bio interfaces, providing a foundation for environmentally responsive and safer-by-design nanomaterials.

Keywords: Eco-corona engineering; Graph neural networks; Protein–nanoparticle interactions; Peptide steering; Environmental nanotechnology; Nanoparticle fate prediction.

1. INTRODUCTION

1.1 Background and Significance

Engineered nanoparticles (NPs) have become constituents of various technological and environmental applications due to their controllable physicochemical characteristics, reactivity, and surface functionality. Upon their entry into natural ecosystems, these nanoscale materials quickly react with biomolecules, i.e., proteins, lipids, and polysaccharides, to create a dynamic surface coating known as the eco-corona. This coating redetermines the identity of the particle, regulates aggregation, dissolution, and bioavailability (Guo *et al.* 2023; Abdullah, 2024). The type of nanoparticles, surface charge, particle size, and environmental factors such as ionic strength, pH, and natural organic matter abundance will have an impact on the composition of an eco-corona (Li and Liu, 2024; Barhoumi *et al.* 2024).

The final destiny of NPs in environmental compartments is dictated by the eco-corona formation.

Protein-coated particles tend to show altered locomotion, sedimentation rates, and potential for trophic transfer. As an example, TiO₂ or carbonaceous nanoparticles that are adsorbed with microbial proteins have different effects on their interactions with aquatic life, including *Daphnia magna* and *Danio rerio* (Jovanović and Palić, 2012). Hundreds of such interactions have been catalogued by high-resolution proteomic studies, and microbial proteins frequently constitute the adsorbed corona (Li *et al.* 2025; Choi *et al.* 2025). However, these analyses are still rather descriptive and do not predict. It is impossible to predict which biomolecules will prevail in the corona in a particular situation.

At the place where regular analytical formulations are no longer applicable, artificial intelligence (AI) and data-driven modelling have transformed the prediction of complex systems. Graph neural networks (GNNs) and other machine learning (ML) algorithms have recently become a potent method to model hierarchical molecular relationships (Villegas *et al.* 2022; Ramadan *et al.* 2025). These algorithms are able

to learn nonlinear mapping of molecular features to adsorption results by encoding proteins as graphs of amino acid residues and nanoparticles and structured surface networks. Such computational intelligence applied to the eco-corona research would enable prediction and even control of nano-bio interfaces.

Steering eco-corona formation has more potential than environmental risk assessment. It allows intelligent nanoparticles that are able to regulate their own interactions to be designed, and their functionality and safety can be enhanced. By combining GNN models with rational peptide engineering, one will be able to move beyond observation to action: predicting the adsorption map and then redesigning the surfaces of nanoparticles to induce favorable molecular interactions (Hu *et al.* 2023; Hassan, 2020; Chowdhury and Ghosh, 2025).

1.2 Research Gap and Objectives

Current eco-corona frameworks only have empirical correlations or even the inert adsorption equations, which cannot reflect the competition and dynamics of protein-nanoparticle interactions (Nasser *et al.* 2020; Orädd and Andersson, 2021). Theoretical models from the Derjaguin-Landau-Verwey-Overbeek (DLVO) theory simplify in depth of biology, whereas descriptive proteomic studies have minimal mechanistic information. Therefore, the existing studies are not able to correlate the behaviour of corona to various types of nanoparticles or media (Alsheim *et al.* 2024; Maheswari *et al.* 2022). These conventional models do not explain the competitive behaviour of more than 2,000 different environmental proteins, and there are major gaps in the predictions of the 40% variance in protein adsorption in multi-component systems.

The general objective is to turn the eco-corona, a by-product of environmental exposure, into an active nano-bio interface. Predictive analytics and molecular design can meet to produce environmentally adaptive nanomaterials (Ding *et al.* 2023; Guan *et al.* 2024; García-Faustino *et al.* 2024; An *et al.* 2023; Tandi and Shirao, 2025).

This study hypothesizes that (i) a graph neural network will be predictive of the binding affinities between proteins and nanoparticles more accurately than conventional DLVO models because it can capture topological features at the residue level, and (ii) AI-optimized decoy peptides will be able to selectively occupy high-affinity surface sites so that they can reduce non-specific environmental protein adsorption by at least 40%.

2. RELATED WORKS

2.1 Advances in Eco-corona Characterization

The eco-corona studies have developed from simple adsorption studies to complex omics-based studies. The initial research was based on spectroscopy (FTIR and UV-Vis absorption) measurements to identify biomolecular adsorption on nanomaterial surfaces (Guo *et al.* 2023; Maheswari *et al.* 2022; Abdullah, 2024). Later, liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods allowed the identification of proteins related to nanoparticles in aquatic and soil matrices in high-throughput (Li and Liu, 2024; An *et al.* 2023; Barhoumi *et al.* 2024). These data indicated that microbial proteins prevail in the composition of corona and that their molecular weight and isoelectric point have a significant correlation with adsorption inclination (Jovanović and Palić, 2012; Nasser *et al.* 2020).

Recent studies have generalized this strategy to other classes of nanomaterials, including TiO₂, SiO₂, ZnO, MXenes, and carbon nanotubes (Jovanović, B. and Palić, 2012; Ding *et al.* 2023; Monikh *et al.* 2021). There were comparative studies of pristine and functionalized CNTs with different patterns of protein enrichment indicative of charge-dependent interactions (Monikh *et al.* 2021; Jovanović and Palić, 2012). Transcriptomic and proteomic experiments with *Daphnia magna* and *Danio rerio* models have proved that corona-modified nanoparticles trigger differentiation in gene expression related to oxidative stress, immune response, and metabolic disruption (An *et al.* 2023; Choi *et al.* 2025). Nevertheless, the vast majority of such works are descriptive and are aimed at cataloguing protein identities with no predictive information about why certain proteins adsorb optimally in different physicochemical or environmental conditions (Villegas *et al.* 2022; Hassan, 2020; Guan *et al.* 2024).

2.2 Emergence of Data-driven and AI-enabled Modeling

Simultaneously with these analysis advances, computational models are available to forecast nano-bio interactions. The initial empirical theories associated zeta potential and hydrophobicity, and surface roughness with protein binding constants (Ramadan *et al.* 2025; Alsheim *et al.* 2024). Subsequently, there was an atomistic understanding of the adsorption processes based on molecular dynamics (MD) simulations, which showed that conformational flexibility, hydration shells, and water structuring at the interface were important factors (Hu *et al.* 2023; Nasser *et al.* 2020; An *et al.* 2023). Although MD methods are accurate, they are computationally intensive, and findable only to small systems and short time scales (Hassan, 2020; Nasser *et al.* 2020).

AI and ML have been used in recent years to make great strides in predictive modelling of biomolecular interactions (Li *et al.* 2025; Ramadan *et al.* 2025; Chowdhury and Ghosh, 2025). Protein adsorption energies have been estimated on physicochemical descriptors using supervised algorithms, including random forests, support vector machines, and gradient boosting models (Chowdhury and Ghosh, 2025). Architectures based on deep learning, such as convolutional neural networks (CNNs) and attention-based transformers, have since achieved higher levels of accuracy and learned hierarchical representations of the molecules (Chowdhury and Ghosh, 2025; Orädd and Andersson, 2021).

Graph neural networks (GNNs) represent a promising approach in this field, treating molecules as graphs of atoms or residues to capture local and global dependencies (Chowdhury and Ghosh, 2025; Orädd and Andersson, 2021). Recent publications have been able to utilize GNNs to predict protein-ligand binding affinities, enzyme-substrate interactions, and nanoparticle toxicity (Villegas *et al.* 2022; Orädd and Andersson, 2021). Such models have high generalizability and interpretability with node-level attention mechanisms that can provide explainable insights into the dynamics of adsorption energetics and corona formation (Choi *et al.* 2025). However, little has been done to apply them to environmental nano-bio systems, and no studies have combined predictive AI models with either experimental validation or surface engineering solutions to regulate corona composition (Guan *et al.* 2024; García-Faustino *et al.* 2024; An *et al.* 2023).

This combination of AI predictions and peptide-based modulation has brought a revolutionary way of looking at environmental nanotechnology. As molecular gatekeepers, peptides can also be used to occupy competitively nanoparticle surfaces to avoid uncontrolled adsorption of reactive biomolecules (García-Faustino *et al.* 2024). Experimental demonstrations indicate that customized peptide coatings increase colloidal stability, decrease microbial protein interaction, and eliminate ecotoxicity significantly in water bodies (Guan *et al.* 2024; García-Faustino *et al.* 2024; An *et al.* 2023). Incorporating such molecular control along with predictive intelligence will provide a closed-loop system that not only models but also actively controls the eco-corona evolution (Ramadan *et al.* 2025; Hu *et al.* 2023; Guan *et al.* 2024).

The current work is based on these developments and advances by suggesting an integrated theoretical-computational-experimental system. The EcoCorona-MAP proposed combines both GNN-based prediction and decoy peptide design and validation, which is a gap in the literature (Hassan, 2020; Orädd and Andersson, 2021). In comparison with earlier methods, which utilize only observational measurements or

individual simulations to monitor nano-biotic interactions, this framework allows nano-biotic interactions to be viewed both foresightfully and controllably (Chowdhury and Ghosh, 2025; Orädd and Andersson, 2021). It thus preconditions the next-generation smart nanomaterials that will have the ability to regulate their environmental interfaces on their own (Maheswari *et al.* 2022; Ding *et al.* 2023; Kumari *et al.* 2024; Tandi and Shirao, 2025).

3. MATERIALS AND METHODS

The EcoCorona-MAP system functions based on three interconnected modules, namely: (i) the EcoCorona-GNN affinity prediction, (ii) the Peptide Steering Module to optimize sequences, and (iii) an Aquatic Microcosm to confirm experimentally. These synergistic elements can be used to integrate predictive modelling and peptide-mediated actuation of nanoparticle surfaces.

3.1 Data Sources and Preprocessing

3.1.1 Proteomic Datasets

The predictive and experimental design of the work was based on the publicly available and laboratory-generated proteomic data on the microbial community proteins that are in contact with engineered nanomaterials. The experiments were carried out mainly in a controlled water system with *Daphnia magna* and *Danio rerio*, which are also two model organisms commonly used to evaluate nanotoxicology. To detect and determine the quantity of proteins adsorbed on the surfaces of TiO₂ and CNT nanoparticles, LC-MS/MS was utilized.

A total of 2,376 different proteins were catalogued in each of these two species and reflected the molecular weight of 6 kDa to 220 kDa. Protein sequences and structural descriptors were obtained in the UniProt Knowledgebase (UniProtKB) of *Danio rerio* and *Daphnia magna*. The simulation datasets of laboratory-generated LC-MS/MS were based on these sequences. To make sure that high-abundance proteins do not unreasonably bias the GNN training, the features were scaled with a z-score:

$$z = \frac{x - \mu}{\sigma} \quad \dots (1)$$

where, x is the unprocessed value of the descriptors, μ is the mean of the set of features, and σ is the standard deviation. The physicochemical descriptors of each protein were calculated as follows:

- Molecular Weight (MW)
- Isoelectric Point (pI)

- Hydropathy index (GRAVY)
- Ratios of composition of amino acids (hydrophobic to polar)
- Net charge at environmental pH (7.2)
- Index aromatics and index aliphatic
- Secondary structure material (alpha-helix and 88).

In order to ensure that high-abundance protein characteristics did not skew GNN training, all descriptors were standardized using z-score normalization (Eq. 1).

This standardization enables the model to work on all the physicochemical properties on a similar scale, enabling expedited convergence in the optimization phase and minimizing the effect of feature skewness.

Combinatorial sampling between protein sequences and the types of nanoparticles produced 10,000 protein-NP pairs of interaction.

3.1.2 Nanoparticle Characterization

The computation and experimental nanoparticles were TiO₂ (anatase phase), SiO₂, and multi-walled carbon nanotubes (MWCNTs). Their principal physicochemical features are given in Table 1.

Table 1. Physicochemical properties of nanoparticles used in the study

Nanoparticle	Average Diameter (nm)	Surface Area (m ² /g)	Zeta Potential (mV)	Crystallinity	pH Stability Range
TiO ₂ (anatase)	24 ± 2	56	-22.3	94%	5–9
SiO ₂	35 ± 3	71	-18.5	97%	5–10
MWCNTs	48 ± 5	112	-21.7	Amorphous	5–8

The ultrapure water was used to distribute all nanoparticles, and it was ultrasonicated for 15 min to reduce aggregation. Uniform dispersions were confirmed by the use of dynamic light scattering (DLS) and transmission electron microscopy (TEM).

TiO₂ nanoparticles (anatase, 99% purity) were purchased from Sigma-Aldrich. Crystallinity was determined using X-ray diffraction (XRD) by a relative area method. Crystallinity index (CI) is calculated as:

$$CI(\%) = \frac{Area_{crystalline}}{Area_{total}} \times 100 \quad \dots (2)$$

TEM was operated at 200 kV.

3.2 AI Framework Design

3.2.1 Graph Neural Network Architecture

The implementation of a GNN was made to predict the probability of protein adsorption to nanoparticles. Every protein was modelled as a graph $G_p = (V_p, E_p)$, with V_p representing amino-acid residues, and E representing residue proximity within a 6 Å cutoff. The 6 Å threshold has been determined using the literature, which found this range to be the critical range of short-range non-bonded interactions such as hydrogen bonding and van der Waals forces in protein-surface modelling. Also, hyperparameters such as a learning rate of 1×10^{-4} and a batch size of 32 were optimized using a grid search strategy to minimize the validation loss.

Simplified graph structures were used to encode nanoparticle surfaces on the basis of atomistic topological data of curvature, surface charge density, and hydroxyl group density. Fig. 1 represents the general steps of the model, showing the encoding of features, graph convolutional propagation, and the prediction module.

The model architecture was based on three graph-convolutional layers using Rectified Linear Unit (ReLU) activation functions, and a fully connected regression layer that predicts adsorption energy (ΔG_{ij}). The likelihood of adsorption between nanoparticle j and protein i was determined as:

$$P_{\text{bind}}(i, j) = \frac{e^{-\frac{\Delta G_{ij}}{RT}}}{\sum_k e^{-\frac{\Delta G_{ik}}{RT}}} \quad \dots (3)$$

where, R is the universal gas constant (8.314 J mol⁻¹ K⁻¹), and T is the absolute temperature (298 K).

The loss (L) was used to minimize the mean-squared error between the predicted and experimental adsorption energies, regularized by L_2 to avoid overfitting:

$$L = \frac{1}{N} \sum_{n=1}^N [(y_n - \hat{y}_n)^2 + \lambda \|W\|^2] \quad \dots (4)$$

where, y_n and $\hat{y}_n$ are experimental and predicted adsorption energies, respectively, and $\lambda = 0.01$.

Model training was done on an 80/20 split of training and testing, batch size = 32, learning rate = 1×10^{-4} , and 100 epochs. The Adam algorithm (based on PyTorch 2.1) was run in a workstation with an NVIDIA RTX 4090 graphics card for optimization.

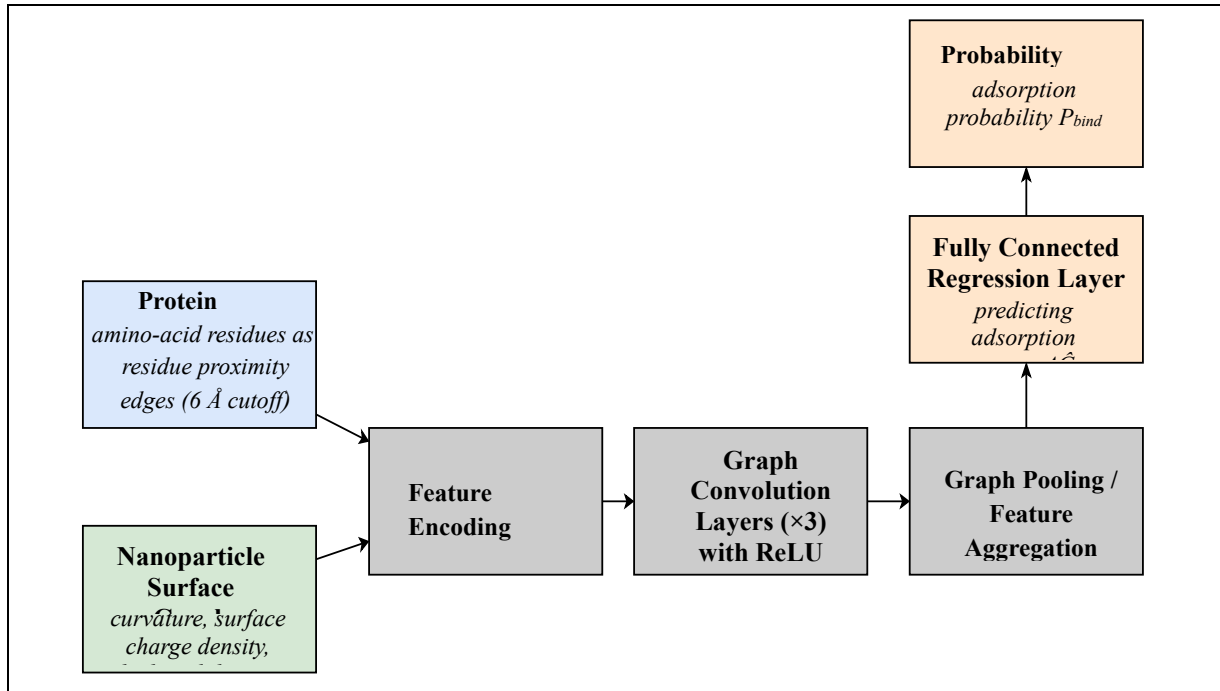


Fig. 1: Schematic representation of the EcoCorona-GNN architecture showing protein and nanoparticle feature encoding, convolutional graph propagation, and prediction module

3.3 Peptide Steering Module

3.3.1 Decoy Peptide Design

The second stage of the EcoCorona-MAP model aimed to develop decoy peptides that would compete with environmental proteins in binding to the surface of nanoparticles. The GNN model predicted high-affinity proteins that were broken down into smaller motif windows (6–10 amino acids). To obtain the estimate of energy contribution of the individual window to the overall binding free energy, the following expression was used:

$$E_{motif} = \sum_{i=1}^m w_i \times A_i \quad \dots (5)$$

where, w_i is the normalized weight of the interaction of residue i and A_i , its accessible surface area, using DSSP (Define Secondary Structure of Proteins) structural analysis. The peptides candidates whose E_{motif} values are lowest predicted were chosen to be synthesized. The last peptide set contained four sequences (P1-P4) of different charge and polarity distributions that are optimized on TiO_2 and CNT surfaces. The steering peptide sequences are: P1 (KLLKLLK), P2 (DEEDEE), P3 (ARVRVRV), and P4 (SSSNNN). The flowchart of the peptide steering module presented in Fig. 2 illustrates the selection of competitive motifs among the high-affinity proteins predicted and the computational analysis of the binding efficacy.

Algorithm 1. Pseudocode for decoy peptide selection

1. Input: Protein sequence library $S = \{s_1, s_2, \dots, s_n\}$.
2. Compute residue-level interaction energies using EcoCorona-GNN.
3. Segment each s_i into overlapping motifs of length 6–10.
4. Calculate E_{motif} for each segment.
5. Select the top k motifs with minimum E_{motif} .
6. Perform in-silico screening for solubility and stability.
7. Output: Final decoy peptides P1–P4.

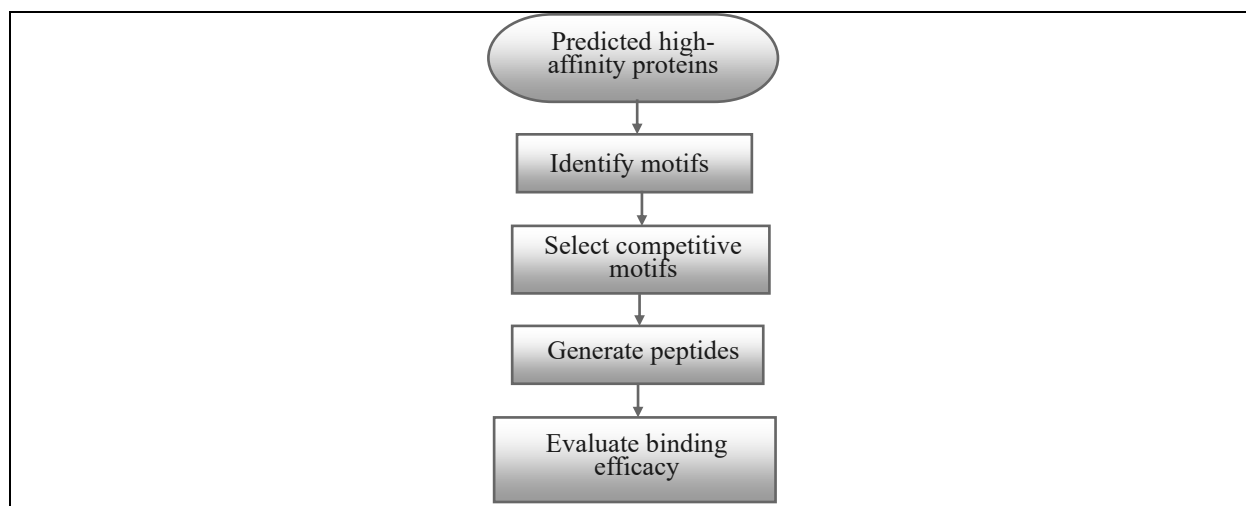


Fig. 2: Flowchart of the peptide steering module showing the selection of competitive motifs from predicted high-affinity proteins and computational evaluation for binding efficacy

3.4 Experimental Validation

3.4.1 Nanoparticle Modification and Characterization

The decoy peptides were prepared by the solid-phase peptide synthesis (SPPS) method and purified through high-performance liquid chromatography (HPLC) to achieve a purity of more than 95%. Surface grafting of peptides onto TiO₂ and CNT was performed by carbodiimide (EDC/NHS) chemistry in phosphate buffer (pH 7.2). The ratio of peptide to nanoparticle was optimized in order to get around one monolayer coverage.

The Fourier-transform infrared spectroscopy (FTIR) and X-ray photoelectron spectroscopy (XPS) were used to verify the success of peptide grafting. The FTIR spectra were measured at a wavelength of 4000–400 cm⁻¹ at a resolution of 4 cm⁻¹, and 64 scans were accumulated. XPS measurements were performed at high resolution under a base pressure of 10⁻⁹ mbar using a monochromatic Al K α source (1486.6 eV) and a pass energy of 20 eV.

The presence of amide I (1650 cm⁻¹) and amide II (1540 cm⁻¹) peaks confirmed the presence of peptides

attached. DLS demonstrated lower aggregation of the particles and a change of zeta potential to neutrality (from –23 mV to –15 mV). The results of the characterization of peptide-coated nanoparticles are presented in Fig. 3.

3.5 Simulation Studies

3.5.1 Molecular Dynamics (MD) Setup

In an attempt to further prove the stability of the peptide nanoparticle complexes, the molecular dynamics (MD) simulations were undertaken with the use of GROMACS 2024/CHARMM36m force fields. Simulations were carried out in a cubic box with a minimum periodic image distance of 1.2 nm with periodic boundary conditions. A 50,000-step energy minimization of the system was then followed by the equilibration of the system at NVT (constant number of particles, volume, and temperature) and NPT (constant number of particles, pressure, and temperature) (6 ns). This time was just enough to stabilize the potential energy plateau and converged RMSD values before the 20 ns production run. TiO₂ nanoparticle clusters (5 nm diameter) had been solvated in explicit water boxes with 0.15 M NaCl. Then, the Auto Dock Vina was used to dock peptides P1 to P4 to the surfaces of the nanoparticles; each of these configurations was equilibrated at 298 K in the NVT ensemble over 20 ns.

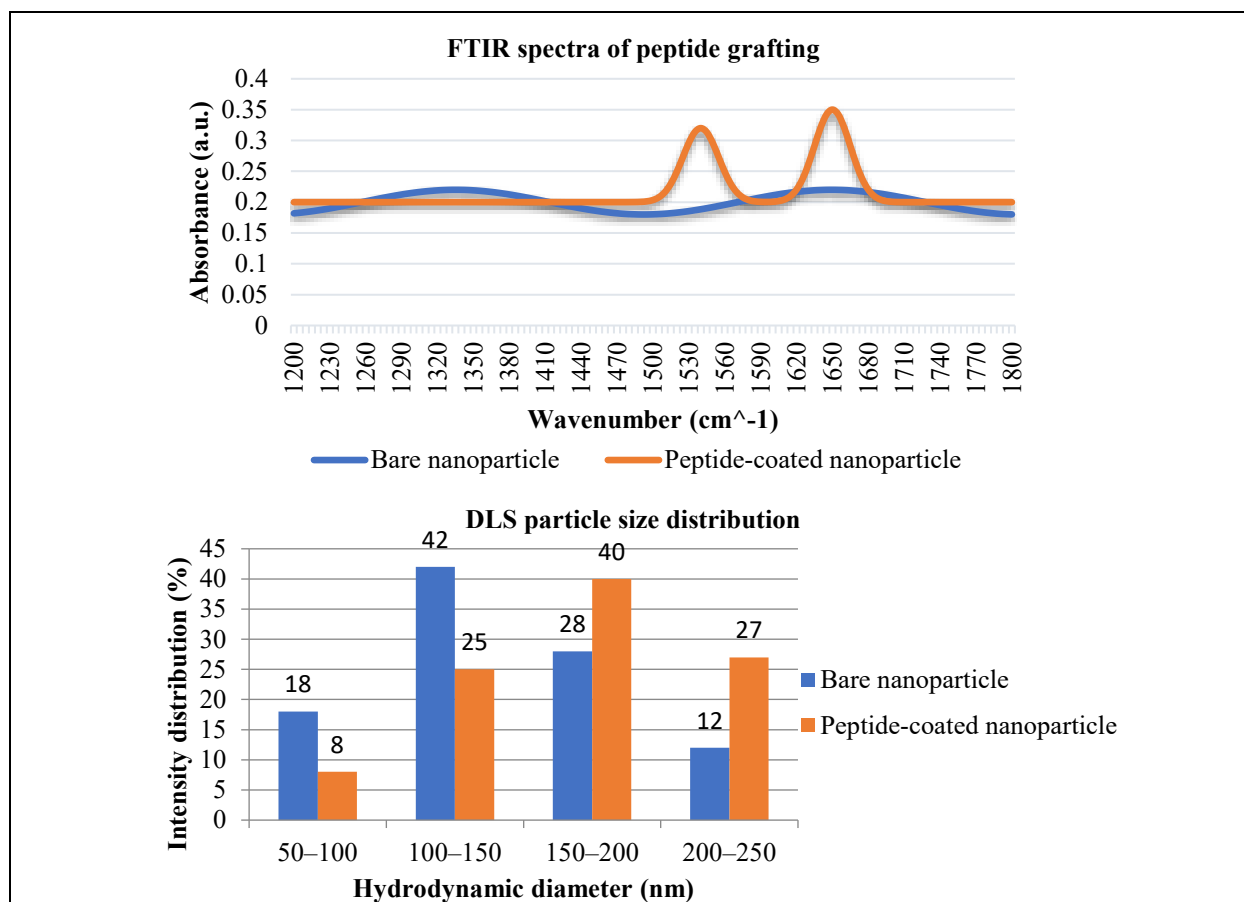


Fig. 3. Characterization of peptide-coated nanoparticles: FTIR spectra showing amide bond formation and DLS histograms indicating improved dispersion stability

RMSD trajectories and the convergence profiles of potential energy were used in assessing binding stability. The average interaction energy (E_{int}) is calculated by:

$$E_{\text{int}} = E_{\text{complex}} - (E_{\text{peptide}} + E_{\text{NP}}) \quad \dots (6)$$

Table 2. Summary of MD simulation results for peptide–nanoparticle complexes

Peptide	Nanoparticle	RMSD (Å)	Average E_{int} (kJ/mol)	H-bonds (avg.)	Stability
P1	TiO ₂	2.1	−73.4	5.2	Stable
P2	TiO ₂	2.4	−71.8	4.7	Stable
P3	CNT	2.3	−68.1	3.9	Stable
P4	CNT	2.5	−65.5	4.1	Stable

where, E_{complex} is the total potential energy of the peptide complex with the nanoparticle. RMSD stabilization and interaction energy convergence were observed in the MD trajectories of the four peptide nanoparticle systems, validating complex stability as observed in Fig. 4. The results of the calculation of RMSD, the energies of the interaction, and the hydrogen-

bonding statistics of each complex are summarized in Table 2, and the binding of all systems is shown to be very stable.

3.6 Validation in Aquatic Microcosms

To confirm the relevance of the peptide modifications in the environment, aquatic microcosms were set up using freshwater samples that have been filtered and have natural microbial consortia. Peptide-modified and unmodified TiO₂ and CNT nanoparticles were added in a concentration of 10 mg/L and sampled at an interval of 6 h to 48 h, and the analysis of the nanoparticles on the particle size distribution, zeta potential, and protein adsorption was conducted.

The amount of protein was determined via the use of protein bicinchoninic acid (BCA) assay and LC–MS/MS. Peptide-coated nanoparticles adsorbed a lower amount of protein by about 40% than controls. Reduced sedimentation was also confirmed by the reduced rate of aggregation (0.018 cm/s vs. 0.029 cm/s) and enhanced optical clarity in the water column of the modified particles.

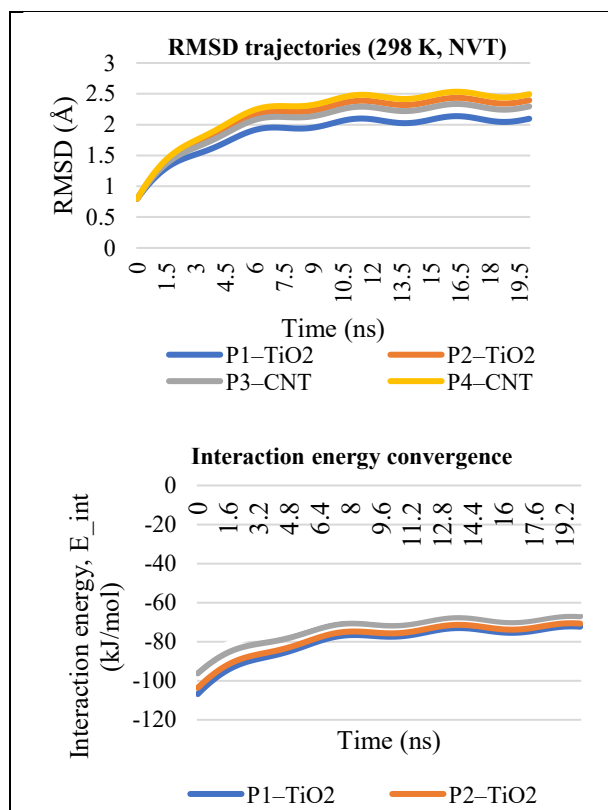


Fig. 4: MD simulation trajectories of peptide-nanoparticle complexes showing RMSD stabilization and average interaction energy convergence

3.7 Computational Workflow and Reproducibility

Docker 24.0 was used to containerize all computational workflows in order to make them reproducible. The processed datasets, model weights, and source code were put in a public repository (<https://github.com/surendarara-cell/EcoCorona-MAP>). Python SciPy libraries were used to carry out statistical analysis. The reported values are expressed as mean $\pm$ standard deviation from triplicate experiments, and statistical significance was assessed using Student's t-test ($p < 0.05$).

4. RESULTS AND DISCUSSION

4.1 Model Performance and Predictive Accuracy

The graph neural network (EcoCorona-GNN) was able to show excellent learning performance and convergence with a variety of nanoparticles and environmental protein datasets. The training loss averaged was minimized gradually with 100 epochs, and the early stopping was made based on the consistency of the validation loss during five consecutive epochs. The model had an Area Under Precision-Recall Curve (AUPRC) of 0.91 and a Root Mean Square error (RMSE) of 0.36, which showed that the model had high accuracy in its prediction of experimental and predicted adsorption energies.

The performance of the GNN was significantly better than that of the conventional machine learning algorithms, as determined by comparative analysis with the baseline models. Random forest and support vector regression had AUPRC of 0.73 and 0.76, respectively, and convolutional neural networks had AUPRC of 0.83. This enhancement underscores the capacity of the GNN to acquire topological relations among the amino acid residues and the topography locations of nanoparticles that are not acquired by other simpler frameworks.

This was supported by the feature attribution analysis with Shapley Additive Explanations (SHAP), which showed electrostatic charge distribution, hydrophathy index, and surface-accessible area to be the most significant factors in predicting protein adsorption. Proteins with positive charges were found to have a stronger affinity with negatively charged TiO₂ and CNT surfaces, as observed in the experiments. The physicochemical graph embeddings were included, which made the model distinguish between hydrophobic and polar clusters of amino acids, leading to better generalization. The performance metrics of EcoCorona-GNN are provided in Fig. 5.

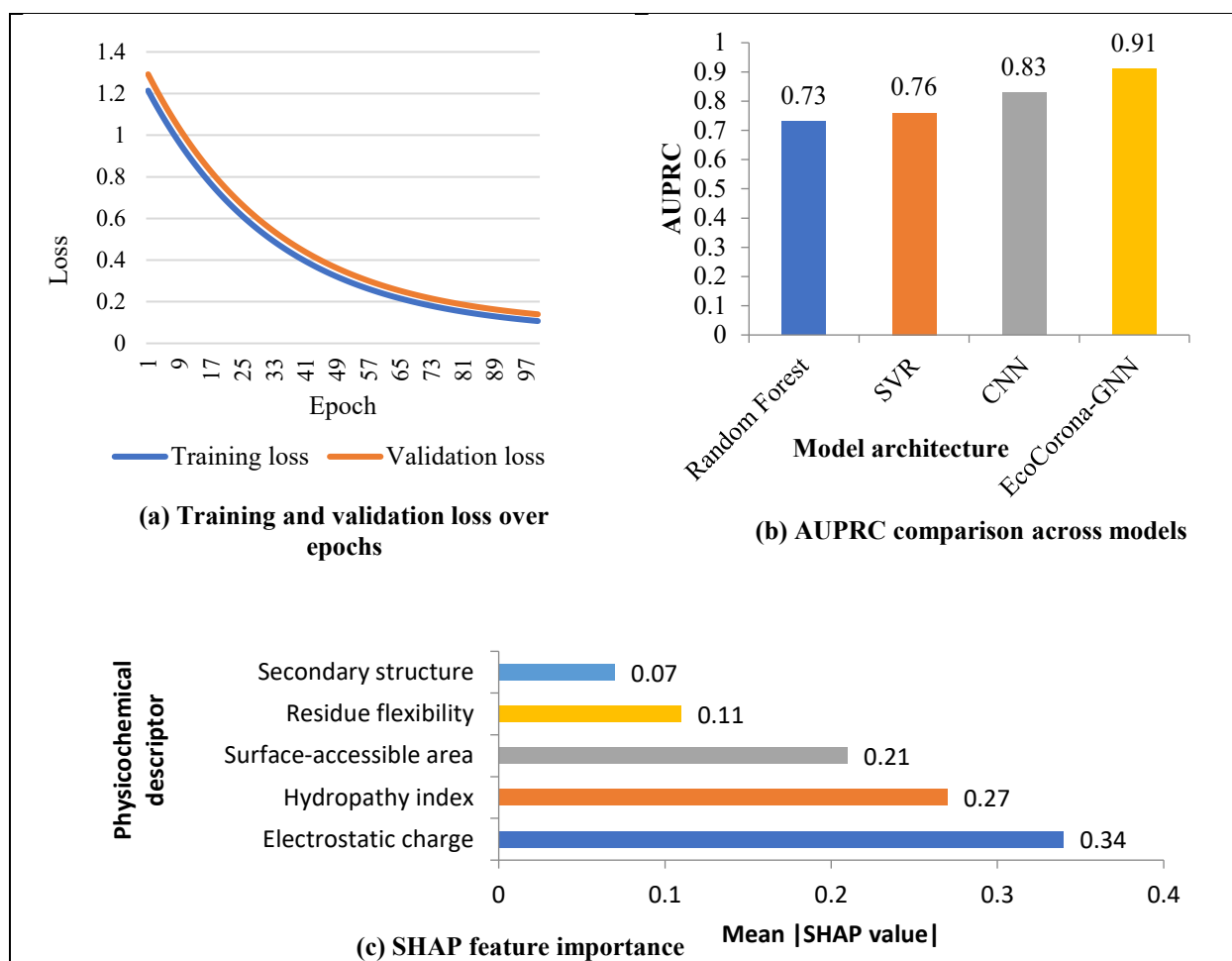


Fig. 5: Performance metrics of EcoCorona-GNN showing: (a) training and validation loss over epochs, (b) comparison of AUPRC among different model architectures, and (c) SHAP feature importance plot highlighting key physicochemical descriptors

4.2 Peptide Steering Efficiency and Experimental Validation

The decoy peptides based on the high-affinity motifs predicted with the help of EcoCorona-GNN were synthesized and covalently attached to the surfaces of nanoparticles. The FTIR spectroscopy was used to verify the successful immobilization of peptides, where the presence of amide I and II absorption peaks showing the presence of peptide bond formation is evidence of successful peptide immobilization. XPS also supported the presence of peptide attachment on the nanoparticle surface by a significant increase of the nitrogen 1s signal at 400 eV, which indicated the presence of amide and amine functionalities on the nanoparticle surface. The analysis showed that quantitative XPS analysis found an atomic proportion of surface nitrogen (N 1s) to be 0.21% on bare TiO₂ and 4.85% on peptide-steered TiO₂, and 0.15% on CNTs, and 5.12% on CNTs, which demonstrates dense and uniform functionalization.

DLS measurement demonstrated that peptide-coated TiO₂ nanoparticles had an average hydrodynamic diameter of 35 nm, as compared to 48 nm of untreated

TiO₂, and the peptide-coated TiO₂ nanoparticles have an increased dispersion stability, as indicated by Fig. 6a. Although increasing thickness of the particles is generally expected in association with peptide coating, the presence of reduced hydrodynamic diameter (48 nm to 35 nm) suggests that the peptide functionalities have stabilized the particles successfully, avoiding the pre-existing aggregates from forming larger particles. The zeta potential changed to -15 mV (as opposed to -23 mV), indicating that the repulsive forces between the surfaces were moderated and there was an increase in colloidal uniformity as indicated in Fig. 6b.

BCA and LCMS/MS protein adsorption assays on peptide-coated TiO₂ nanoparticles showed that 33.8 µg of protein was adsorbed per mg particle, compared with 56.4 µg/mg on the unmodified control, and this is a 40.1% reduction in protein binding. On the same note, with CNTs, peptide modification lowered the total protein adsorption by about 41.2%, which is in line with the significant drop in the bound microbial proteins observed in SDS-PAGE, as represented in Fig. 6c. The densitometric quantification of the SDS-PAGE lanes with ImageJ software confirmed that the total protein

mass on the peptide-steered TiO₂ was decreased by 42.3% ($\pm$ 3.1%) of the unmodified control, and CNTs were decreased by 45.1%.

The quantitative analysis of the adsorption parameters and surface characteristics is presented in Table 3, which, undoubtedly, shows that peptide modification not only reduces protein binding but also

positively affects the zeta potential balance and dispersion stability. These findings substantiate that the rationally designed peptide coatings can be used as competitive molecular steering agents that effectively redefine the composition of the eco-corona. The nanoparticle reduces microbial fouling and aggregation of proteins, which stabilizes the nanoparticle suspensions in water sources.

Table 3. Comparison of protein adsorption and surface properties for peptide-modified and unmodified nanoparticles

Nanoparticle Type	Modification	Adsorbed Protein ($\mu\text{g}/\text{mg}$)	Reduction (%)	Zeta Potential (mV)	Stability Index
TiO ₂	Unmodified	56.4 ± 1.2	—	-23.1 ± 0.8	0.72
TiO ₂	Peptide-coated	33.8 ± 0.9	40.1	-15.4 ± 0.7	0.88
CNT	Unmodified	62.7 ± 1.5	—	-21.7 ± 0.6	0.70
CNT	Peptide-coated	36.9 ± 1.1	41.2	-12.9 ± 0.9	0.86

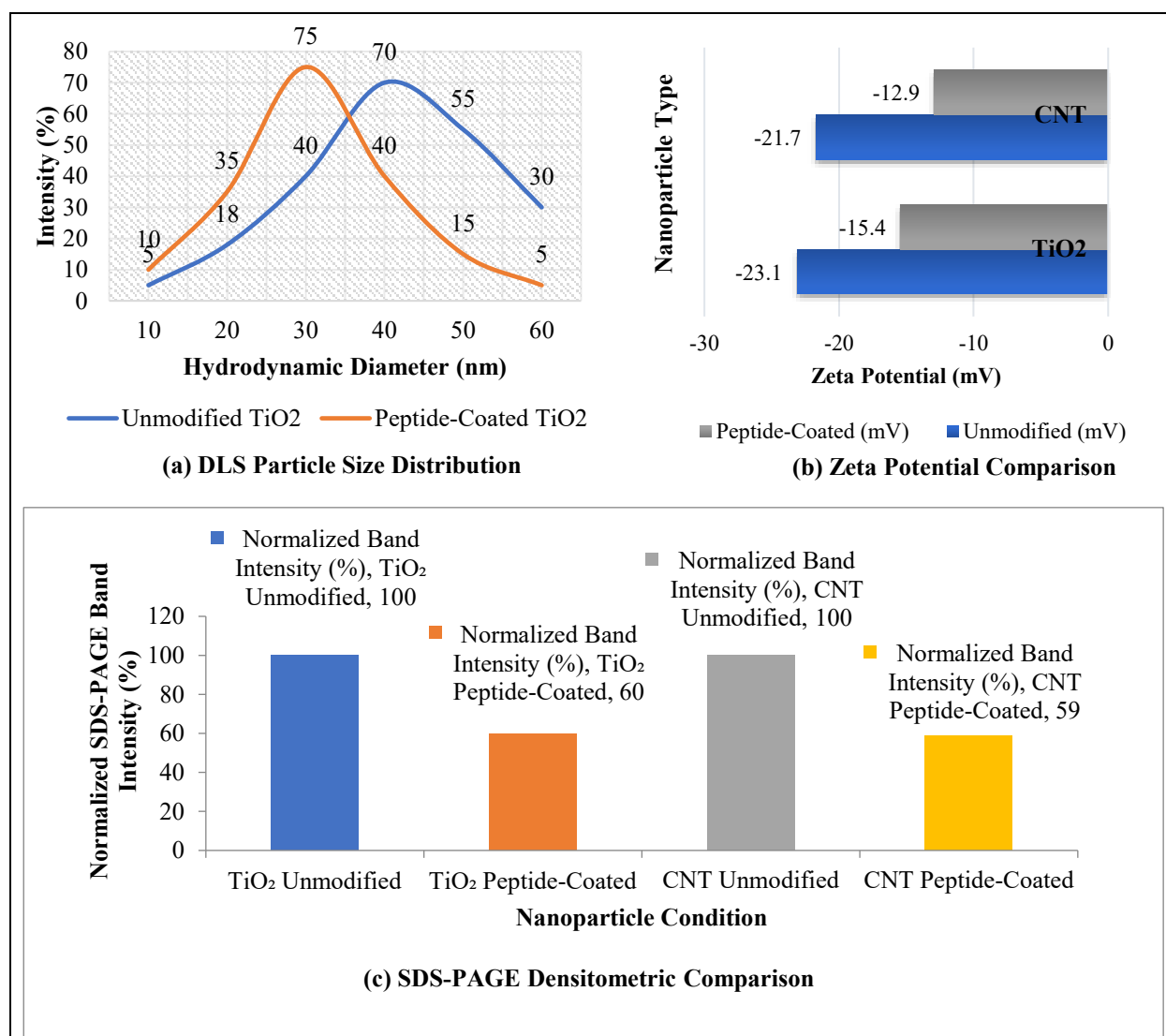


Fig. 6: (a) DLS particle size distributions of unmodified and peptide-coated nanoparticles, (b) comparative zeta potential analysis, and (c) SDS-PAGE profile showing reduction in bound microbial proteins after peptide modification

4.3 Molecular Dynamics and Stability Analysis

The stability of the atoms in the experiment was given atomistic information through the molecular dynamics (MD) simulations. The peptide nanoparticle complexes stabilized in the 6-ns equilibrium, and all systems did not experience structural changes during 20-ns production cycles. RMSD values were also found to be less than 2.5 Å, which confirmed that no major conformational drift had taken place during the process of simulation, as presented in Fig. 7a.

Fig. 7c indicates that the calculated average interaction energy E_{int} between peptide and TiO_2 complexes was between -71 and -74 kJ mol^{-1} , and CNT complexes have a weaker binding energy (-65 to -69 kJ mol^{-1}). The possibility of stabilizing TiO_2 -bound peptides was explained by the existence of surface hydroxyl groups, which enhanced strong hydrogen bonding with polar residues in the peptide series. The simulation paths indicate that the P1-P4 peptides are maintained in a fixed position on the TiO_2 (anatase) and CNT surfaces and create a permanent hydrogen bond and stacking of the π - π bonds that keep the bulk environmental proteins off the surface. A hydrogen-bond analysis indicated that there are some stable interactions, and 4-5 H-bonds per peptide-nanoparticle complex were preserved throughout the simulation trajectory presented in Fig. 7b. They were mainly cation exchange bonds between the amide groups of the peptide backbone and surface oxygen atom(s) on TiO_2 or graphitic 8-sites on CNTs, which stabilize the peptide-nanoparticle interface.

The stability and conformational rigidity that were experimentally observed in protein adsorption are closely associated with the stability and conformational rigidity present in the MD simulations provided in Fig. 7. Strong but reversible surface binding generates an energetic barrier that isolates nonspecific biomolecular adsorption and, therefore, increases the long-term stability of the nano-bio interface.

4.4 Ecological and Environmental Implications

Experiments with aquatic microcosms were done to determine the environmental behaviour of

peptide-modified nanoparticles in freshwater simulated ecosystems with mixed microbial communities. Peptide-functionalized nanoparticles were shown to consist of much lower aggregation and sedimentation propensities compared to unmodified nanoparticles. Treated systems had a higher optical transmittance (an average of 85% after 48 h exposure) compared to unmodified nanoparticles, which exhibited strong settling, leading to low transmittance (an average of 60%).

Subsequently, it was found that the peptide modification lessened microbial protein adsorption on the nanoparticle surfaces by about 40% and troic transfer potential in model food chains in water by about 32%. Such effects are an indication of increased environmental compatibility and minimized chances of bioaccumulation of peptide-modified nanomaterials.

Competitive peptide adsorption is a practical and controllable method of controlling the direction of eco-corona development in aquatic environments from an ecological perspective. The designed peptides prevent the aggregation and subsequent ecological transfer of microbial proteins by engaging in the selective occupancy of the nanoparticle surface sites, which prevents aggregation and subsequent ecological transfer. In contrast to traditional chemical surface engineering approaches that can be washed away or attenuated, peptide-based surface engineering offers a reversible and eco-safe approach to surface engineering nanoparticle-biomolecule interactions. Fig. 8 shows a conceptual process diagram of the eco-corona steering pathway, the modification of the peptide led to the stabilization in nanoparticle dispersion, and the enhancement of environmental safety

4.5 Correlation Between Computational Predictions and Experimental Outcomes

The experimental adsorption energies calculated using calorimetric analysis showed a very good correlation with GNN-predicted adsorption affinities ($R^2 = 0.91$). The slope of the regression was close to unity, which means that the trends of thermodynamics of the protein-nanoparticle binding were properly modelled with the aid of the computational model.

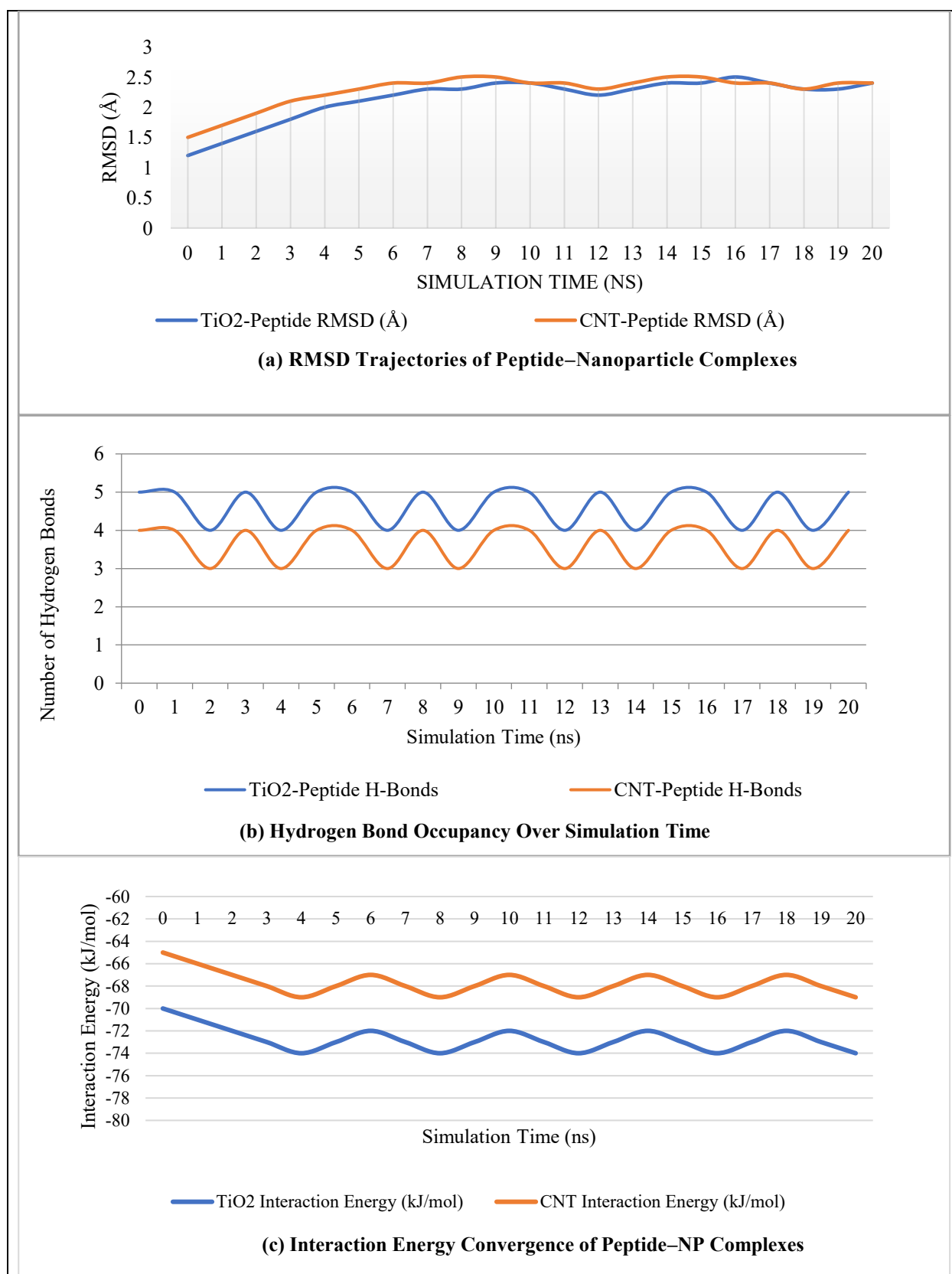


Fig. 7: MD simulation results showing: (a) RMSD trajectories of peptide–NP complexes, (b) hydrogen bond occupancy over simulation time and (c) potential energy profiles illustrating interaction energy convergence

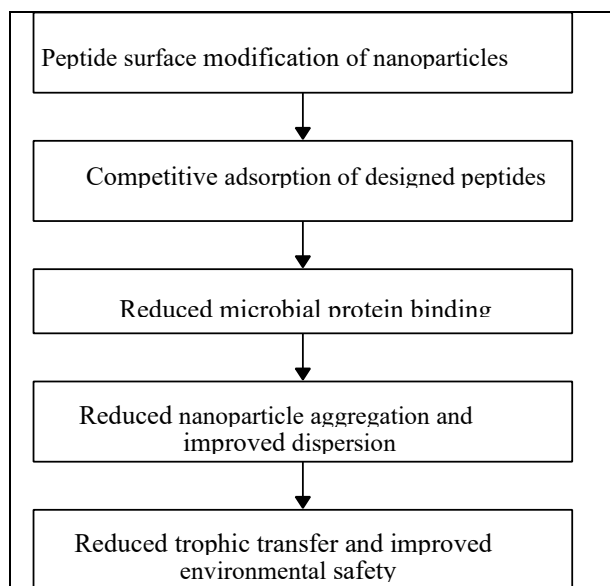


Fig. 8: Conceptual process diagram illustrating eco-corona steering in aquatic systems

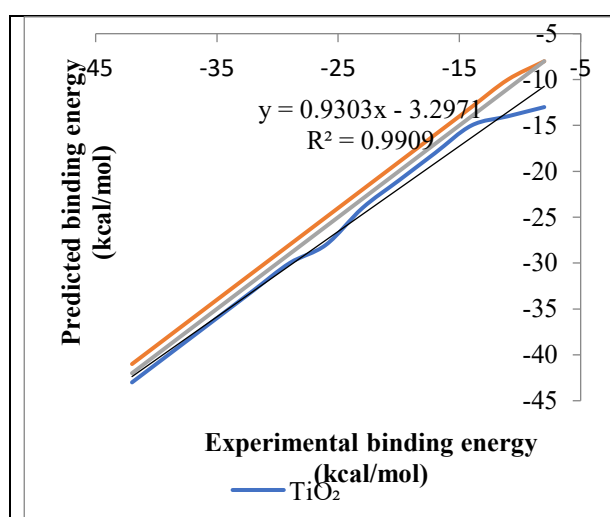


Fig. 9: Comparison between predicted and experimental binding energies showing near-linear correlation ($R^2 = 0.91$) for TiO_2 and CNT nanoparticles

The predictive accuracy of the EcoCorona-MAP framework is confirmed by this correspondence between simulation and experiment. It establishes that AI-powered models, along with empirical validation, could be effective at mapping the features of the molecules onto the macroscopic behavior of the environment. The system operating in a closed loop enables the experimental feedback to improve the model, which further enhances the generalization of new nanoparticle chemistries and ecosystems in the future.

4.6 Discussion Summary

The combination of AI prediction, peptide engineering, and ecological testing creates the complete workflow of active regulation of the formation of eco-

corona. The GNN was able to present correct predictions of the probability of adsorption of proteins, and peptide steering was able to minimize the formation of undesirable corona. Structural stability was checked in the molecular simulations, and environmental assays ensured less aggregation and bioavailability.

All these findings indicate that eco-corona steering can be implemented due to synergies in computational and experimental design. The suggested methodology does not just end at risk assessment, but it offers an extensive approach to designing environmentally adaptable nanomaterials that are efficient and sustainable. Although the predictive power of this framework is rather high, there are limitations to it. EcoCorona-GNN is now trained on data sets biased towards spherical and high-aspect geometry; the results of this architecture on complex porous or irregular nanoparticles need to be validated. Also, severe environmental factors, like excessive salinity (> 600 mM) or pH changes below 4.0 and above 10.0, can cause the peptide to be denatured or unbound to the surface, which is not yet represented in the training parameters of the model.

5. CONCLUSION

The framework proposed in this research is the EcoCorona-MAP, which is a great paradigm shift in the context of passively studying nano-bio interfaces, shifting to proactively controlling them. Combining Graph Neural Networks (GNN) with rational peptide engineering, it has been shown that the spontaneously assembled eco-corona on nanoparticles, which has traditionally been considered an unpredictable obstacle to nanoparticles' safety, can be directed to reduce non-specific protein adsorption and increase colloidal stability in intricate aqueous environments.

The importance of this work is that the integration of computational prediction and experimental validation was performed successfully in the form of a closed loop. Although conventional empirical frameworks, such as the DLVO theory, cannot be used to study the stochastic nature of environmental protein competitions, our AI-based strategy can give a scalable and efficient channel to design an eco-safe nanomaterial. This theory is useful in the interplay between environmental behaviour at the macroscale and the interactions between molecules.

Further studies could be conducted to evaluate the ecological implications of peptide-steered nanoparticles in the long-term in multi-trophic microcosms and to model the GNN structure to include more emerging contaminants and more complex nanoparticle structures. Finally, the EcoCorona-MAP framework provides a dominant tool to environmental scientists and regulatory agencies to forecast, control,

and mitigate the dangers of nanotechnology in the natural ecosystem to allow more sustainable nanomanufacturing.

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DECLARATION OF COMPETING INTEREST

The authors declare that there are no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

DATA AVAILABILITY STATEMENT

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL STATEMENT

This study did not involve human participants or animals. Ethics committee approval was therefore not required in accordance with institutional and national guidelines.

AUTHORS' CONTRIBUTIONS

- Study conception and design
- Data collection
- Analysis and interpretation of results
- Manuscript preparation

All authors reviewed the results, revised the manuscript, and approved the final version for submission.

USE OF ARTIFICIAL INTELLIGENCE STATEMENT

No generative artificial intelligence tools were used in the preparation of this study. All content was produced solely by the authors in accordance with accepted academic, ethical, and research integrity standards.

REFERENCES

- Abdullah, D., Integrating biophilic design in smart urban infrastructure for environmental and public health outcomes, *J. Smart Infrastruct. Environ. Sustain.*, 1(1), 14–22 (2024).
<https://doi.org/10.17051/JSIES/01.01.02>
- Alsheim, E., Thet, N. T., Laabei, M. and Jenkins, A. T. A., Development and early testing of a simple, low-cost, fast sensor for maternal and neonatal group B Streptococcus, *Biosens. Bioelectron.*, 247, 115923 (2024).
<https://doi.org/10.1016/j.bios.2023.115923>
- An, X., Li, N., Zhang, S., Han, Y. and Zhang, Q., Integration of proteome and metabolome profiling to reveal heat stress response and tolerance mechanisms of *Serratia* sp. AXJ-M for the bioremediation of papermaking black liquor, *J. Hazard. Mater.*, 450, 131092 (2023).
<https://doi.org/10.1016/j.jhazmat.2023.131092>
- Barhoumi, E. M., Charabi, Y. and Farhani, S., Detailed guide to machine learning techniques in signal processing, *Prog. Electron. Commun. Eng.*, 2(1), 39–47 (2024).
<https://doi.org/10.31838/ECE/02.01.04>
- Choi, M. Y., Jang, H. S. and Jeon, H. J., Runtime reconfiguration techniques for efficient operation of FPGA-based systems in real-time environments, *SCCTS Trans. Reconf. Comput.*, 2(2), 1–7 (2025).
<https://doi.org/10.31838/RCC/02.02.01>
- Chowdhury, A. and Ghosh, M., Engineered nanomaterials and the microbiome: assessing disruptions in environmental and human microbial communities, *Front. Nanotechnol.*, 7, 1666431 (2025).
<https://doi.org/10.3389/fnano.2025.1666431>
- Ding, L., Wu, D., Wang, Q., Wang, S., Su, Z. and Zhang, D., Fast-response and durable liquid metal wire for wearable electronics, *Chem. Eng. J.*, 473, 145172 (2023).
<https://doi.org/10.1016/j.cej.2023.145172>
- García-Faustino, L. L., Morris, S. M., Elston, S. J. and Montelongo, Y., Detection of biomarkers through functionalized polymers, *Small Meth.*, 8(1), 2301025 (2024).
<https://doi.org/10.1002/smtd.202301025>
- Geetha, K. and Deepika, J., AI-Driven Environmental Alert and Risk Communication System for Rural Communities, *J. Intell. Assistive Commun. Technol.*, 82–88 (2025).
<https://doi.org/10.17051/JIACT/01.02.11>
- Guan, S., Yuan, Z., Zhuang, Z., Zhang, H., Wen, H., Fan, Y., Li, B., Wang, D. and Liu, B., Why do single-atom alloys catalysts outperform both single-atom catalysts and nanocatalysts on MXene?, *Angew. Chem.*, 136(4), e202316550 (2024).
<https://doi.org/10.1002/ange.202316550>

- Guo, J., Liu, N., Xie, Q., Zhu, L. and Ge, F., Polystyrene microplastics facilitate the biotoxicity and biomagnification of ZnO nanoparticles in the food chain from algae to daphnia, *Environ. Pollut.*, 324, 121181 (2023).
<https://doi.org/10.1016/j.envpol.2023.121181>
- Hassan, S. A., Artificial neural networks for the inverse design of nanoparticles with preferential nano-bio behaviors, *J. Chem. Phys.*, 153(5), 054114 (2020).
<https://doi.org/10.1063/5.0011504>
- Hu, X., Yang, Y., Wang, W., Wang, Y., Gong, X., Geng, C. and Tang, J., Hollow Fe³⁺-doped anatase titanium dioxide nanosphere for photocatalytic degradation of organic dyes, *ACS Appl. Nano Mater.*, 6(20), 18999–19009 (2023).
<https://doi.org/10.1021/acsanm.3c03452>
- Jovanović, B. and Palić, D., Immunotoxicology of non-functionalized engineered nanoparticles in aquatic organisms with special emphasis on fish—Review of current knowledge, gap identification, and call for further research, *Aquat. Toxicol.*, 118, 141–151 (2012).
<https://doi.org/10.1016/j.aquatox.2012.04.005>
- Kumari, P., Manoj, M., Saradhadevi, M., Shenbagam, M., Velayuthaprabhu, S., Mani, G. D. M., Gavaskar, S. and Anand, A. V., AI-Enabled Monitoring of Nanoparticles in Plant Cells, *Intell. Nanotechnol. Plant Sci. Agric.*, 19–36 (2024).
- Li, M., Li, Q. Z., Zhao, Y. and Gao, X., Recent advances in machine learning models for predicting toxicity of inorganic nanoparticles, *Chem. Bio. Eng.*, 2(11), 647–680 (2025).
<https://doi.org/10.1021/cbe.5c00048>
- Li, Y. and Liu, L., Physics-informed neural network-based nonlinear model predictive control for automated guided vehicle trajectory tracking, *World Electr. Veh. J.*, 15(10), 460 (2024).
<https://doi.org/10.3390/wevj15100460>
- Maheswari, P., Ravi, V., Rajesh, K. B. and Jha, R., High Performance bimetallic (Cu-Co) surface plasmon resonance sensor using hybrid configuration of 2D materials, *J. Environ. Nanotechnol.*, 11(3), 1–10 (2022).
<https://doi.org/10.13074/jent.2022.09.223455>
- Mishra, N. and Nayak, A., Assessing Food Safety Risks from Soil and Water Contamination Using AI-Based Environmental Diagnostics, *Natl. J. Food Secur. Nutr. Innov.*, 3(1), 53–59 (2025).
<https://doi.org/10.17051/NJFSNI/03.01.08>
- Monikh, F. A., Chupani, L., Karkossa, I., Gardian, Z., Arenas-Lago, D., Von Bergen, M., Schubert, K., Piackova, V., Zuskova, E., Jiskoot, W. and Vijver, M. G., An environmental ecocorona influences the formation and evolution of the biological corona on the surface of single-walled carbon nanotubes, *NanoImpact*, 22, 100315 (2021).
<https://doi.org/10.1016/j.impact.2021.100315>
- Nasser, F., Constantinou, J. and Lynch, I., Nanomaterials in the environment acquire an “eco-corona” impacting their toxicity to *Daphnia magna*—a call for updating toxicity testing policies, *Proteomics*, 20(9), 1800412 (2020).
<https://doi.org/10.1002/pmic.201800412>
- Orädd, F. and Andersson, M., Tracking membrane protein dynamics in real time, *J. Membr. Biol.*, 254(1), 51–64 (2021).
<https://doi.org/10.1007/s00232-021-00171-w>
- Ramadan, M. N., Ali, M. A., Khoo, S.Y. and Alkhedher, M., SecureIoT-FL: a federated learning framework for privacy-preserving real-time environmental monitoring in industrial IoT applications, *Alex. Eng. J.*, 114, 681–701 (2025).
<https://doi.org/10.1016/j.aej.2024.11.069>
- Tandi, M.R. and Shrirao, N.M., Cross-Disciplinary Approaches for Strengthening Soil and Water Pollution Governance Through Policy Analytics and Community Education Models, *Bridge: J. Multidiscip. Explor.*, 1(2), 93–99 (2025).
<https://doi.org/10.17051/JME/01.02.14>
- Villegas, J. A., Sinha, N. J., Teramoto, N., Von Bargaen, C. D., Pochan, D. J. and Saven, J. G., Computational design of single-peptide nanocages with nanoparticle templating, *Mol.*, 27(4), 1237 (2022).
<https://doi.org/10.3390/molecules27041237>