



ORIGINAL RESEARCH ARTICLE

## Molecular Docking Analysis of Heavy Metal Interactions with Outer Membrane Porins of *Pseudomonas aeruginosa*: Implications for Environmental Adaptation and Bioremediation

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### ABSTRACT

**Background:** Heavy metal contamination poses a persistent threat to environmental ecosystems, exerting selective pressure on microbial communities and promoting adaptive resistance mechanisms. In Gram-negative bacteria, outer membrane porin protein OprF of *Pseudomonas aeruginosa* play a crucial role in regulating membrane permeability and mediating interactions with environmental stressors.

**Objectives:** This study investigates the molecular interactions between selected heavy metals (Pb, Hg, Cr, Cu, Zn, and Cd) and outer membrane proteins of *Pseudomonas aeruginosa* using molecular docking analysis.

**Methods:** Three-dimensional protein structures were prepared from the Protein Data Bank, and ligand structures were obtained from PubChem. Docking simulations were performed using PyRx software, and interaction patterns were visualized using Discovery Studio.

**Results:** Binding affinity values revealed differential metal–protein interactions, with copper demonstrating the highest binding affinity (−8.3 kcal/mol), followed by zinc (−7.8 kcal/mol), while mercury exhibited the lowest interaction energy (−3.1 kcal/mol). The interactions were stabilized through van der Waals forces and  $\pi$ -related bonding patterns, suggesting potential coordination within porin-associated amino acid residues.

**Conclusion:** The stronger affinity observed for essential trace metals such as copper and zinc may reflect structural compatibility with membrane transport systems, whereas weaker mercury interaction may indicate alternative detoxification pathways. These findings suggest that outer membrane porin protein OprF could contribute to bacterial adaptation in metal-contaminated environments by modulating permeability and influencing metal transport dynamics. This study provides molecular-level insight into heavy metal–porin interactions and highlights the potential relevance of membrane-associated mechanisms in environmental resistance and bioremediation strategies. Experimental validation is recommended to confirm the biological implications of the predicted interactions.

**Keywords:** *Metalloresistance; Docking; Porins; Pseudomonas; Permeability; Bioremediation.*

## 1. INTRODUCTION

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Heavy metal contamination represents one of the most persistent and hazardous forms of environmental pollution worldwide. Metals such as copper (Cu), zinc (Zn), cadmium (Cd), mercury (Hg), chromium (Cr), and lead (Pb) accumulate in aquatic and soil ecosystems as a result of industrial discharge, mining activities, wastewater effluents, and agricultural runoff. Unlike organic pollutants, heavy metals are non-biodegradable and can persist in the environment for extended periods, exerting chronic selective pressure on microbial communities. Continuous exposure to sublethal metal concentrations promotes the evolution of adaptive resistance mechanisms in bacteria, enabling survival in contaminated habitats [1].

Bacterial resistance to heavy metals is mediated through multiple coordinated mechanisms, including active efflux systems, intracellular sequestration, enzymatic detoxification, biofilm formation, and modulation of membrane permeability. In Gram-negative bacteria, the outer membrane acts as a critical protective barrier that regulates the entry and exit of ions and small molecules. Outer membrane proteins (OMPs), particularly porins, form selective channels that control passive diffusion across the membrane. Alterations in porin expression, structure, or regulation can significantly influence cellular susceptibility to toxic compounds, including both antibiotics and metal ions [2].

*Pseudomonas aeruginosa* is an environmentally versatile Gram-negative bacterium widely distributed in soil and aquatic ecosystems. It is recognized for its remarkable intrinsic resistance capacity and its ability to adapt to diverse environmental stresses. Porins such as OprF, OprD, and OprP contribute to selective permeability and nutrient uptake while simultaneously participating in resistance modulation. Environmental stressors, including heavy metals, may influence the structural and functional dynamics of these porins, thereby affecting ion transport and bacterial survival strategies [3].

Recent studies have highlighted the role of outer membrane remodeling in bacterial adaptation to contaminated environments. Changes in porin-mediated permeability may reduce intracellular accumulation of toxic metals while maintaining essential metabolic exchange. Although efflux systems are widely studied in heavy metal resistance, the direct interaction between metal ions and outer membrane proteins remains less explored at the molecular level. Understanding these interactions is essential for clarifying the early stages of metal–bacteria contact and the physicochemical determinants that influence permeability and transport [4].

Computational molecular docking provides a valuable *in silico* approach for predicting the binding affinity and interaction patterns between metal ions and protein targets. By simulating molecular interactions at the atomic level, docking analysis can reveal potential binding sites, energetic stability, and interaction forces involved in metal–protein association. Such insights contribute to understanding how specific metals may interact with porin structures and influence membrane-associated resistance mechanisms [5].

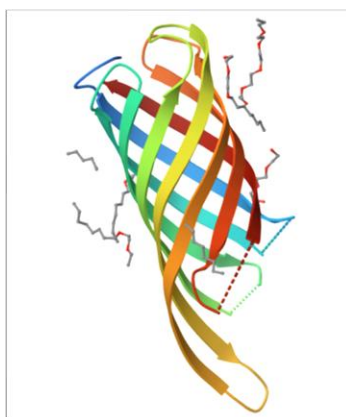
Therefore, the present study aims to investigate the molecular interactions between selected heavy metals (Pb, Hg, Cr, Cu, Zn, and Cd) and outer membrane proteins of *Pseudomonas aeruginosa* using molecular docking analysis. By evaluating binding affinities and interaction patterns, this research seeks to provide mechanistic insight into porin–metal associations, such as copper (Cu), zinc (Zn), cadmium (Cd), mercury (Hg), chromium (Cr), and lead (Pb), and their potential implications for environmental adaptation and bioremediation strategies in metal-contaminated ecosystems.

## 2. MATERIALS AND METHODS

Information on each released gas that was believed to be a pollutant was gathered using an *in silico* method with the help of the Protein Bank Database (PDB) and the PubChem website ([www.pubchem.com](http://www.pubchem.com)). Molecular docking was done using PyRx 2021, and the docked molecules were visualized using Discovery Studio Visualizer 2021 [6]. In order to replicate the virtual binding of emissions and polluting gases with the OMPs receptor, the programs were downloaded from the network using free links [7]. A list of the alleged gases created by contaminated water could be Lead (Pb), Mercury (Hg), Chrome (Cr), Copper (Cu), Zinc (ZN) and Cadmium (Cd).

### 2.1 Getting the OMPs receptor ready

The PDB website was used to retrieve and store all of the information and chemical formula related to the OMPs receptor (<https://www.rcsb.org/>). Only chain A was fully preserved throughout the protein's structural arrangement when the receptor OMPs was initially viewed using the Discovery Studio Visualizer 2021 application. Most water molecules and superfluous residues were removed. For later docking with each ligand and additional aquatic pollutants, the OMPs protein was maintained in its modified configurational structure (Figure 1).



**Figure 1 :** 3D structure of protein OprF (<https://www.rcsb.org/structure/4RLC> )

### 2.2 Getting the tested ligands ready

The SDF formulas for every chemical formula related to water pollutants were obtained via the [pubchem.com](http://pubchem.com) website. To perform virtual binding, the ligand needs to be made in a special fashion that allows it to occupy the receptor's active region. All heavy metal compounds were converted utilizing the PyRx 2021 software's "convert to ligand" option after specific chemical configuration changes were made to interact with the modified OMP receptor in the previous phase.

### 2.3 Docking via software *In silico* instruments

In order to demonstrate the binding sites between the amino acids of the two coupled molecules as well as the bonds that hold them together, the compounds that were produced by docking were all saved and then shown again using Discovery Studio Visualizer 2021.

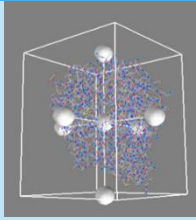
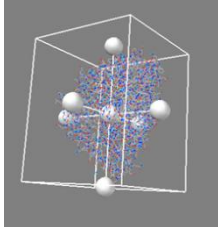
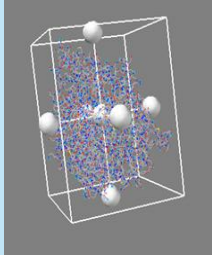
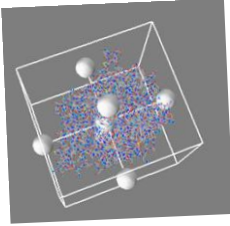
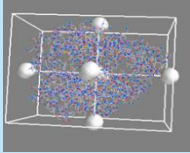
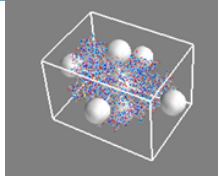
## 3. RESULTS

Molecular docking analysis was conducted to evaluate the interaction between selected heavy metals (Pb, Hg, Cr, Cu, Zn, and Cd) and outer membrane proteins (OMPs) of *Pseudomonas*

*aeruginosa*. Binding affinities were calculated to estimate the relative stability of metal–protein complexes and to predict potential interaction patterns within porin-associated regions.

The configurational parameters applied during docking, including RMSD values and VINA box dimensions for each ligand, are presented in Table 1. These parameters ensured consistent spatial sampling of the receptor binding region and allowed reliable comparison of ligand interaction energies.

**Table (1):** Ligand Configurations in VINA Docking Box of OprF protien with heavy metals

No.	Tested ligand	RSMD lower bond	RSMD upper bond	VINA box dimensions
1	Lead	1.8	2.7	
2	Mercury	1.2	2.8	
3	Chrome	0.013	1.95	
4	Copper	9.7	14.7	
5	Zinc	1.5	2.13	
6	Cadmium	12.6	13.6	

The calculated binding affinities demonstrated clear variation among the tested metals. As shown in Table 2, copper exhibited the strongest predicted interaction with the OMP receptor ( $-8.3$  kcal/mol), followed by zinc ( $-7.8$  kcal/mol) and lead ( $-7.2$  kcal/mol). Cadmium showed moderate binding affinity ( $-4.0$  kcal/mol), while chromium ( $-3.4$  kcal/mol) and mercury ( $-3.1$  kcal/mol) displayed comparatively weaker interactions.

**Table (2):** Affinity of interactions of heavy metals with the OprF protein

Ligand	Affinity (kcal/ mol)	Chemical bond/s
Lead	-7.2	Pi-Pi Vander Waals Pi-Alkyl
Mercury	-3.1	Vander Waals
Chrome	-3.4	Pi-Alkyl Pi-Sigma
Copper	-8.3	Pi-Pi Vander Waals
Zinc	-7.8	Pi-Pi Vander Waals
Cadmium	-4.0	Vander Waals Pi-Alkyl

#### 4. DISCUSSION

The higher affinity observed for copper and zinc may be attributed to their physicochemical characteristics, including ionic radius, coordination capacity, and electronic configuration, which favor stable interactions with amino acid residues within porin structures. Both copper and zinc are essential trace elements involved in bacterial enzymatic systems, and bacteria possess regulated uptake and homeostasis pathways for these metals. The strong docking affinity may therefore reflect structural compatibility between these ions and metal-coordinating residues located within or near the porin channel [8].

Interaction analysis revealed stabilization primarily through van der Waals forces and  $\pi$ -related interactions ( $\pi$ - $\pi$  stacking,  $\pi$ -alkyl, and  $\pi$ -sigma bonding). These non-covalent interactions suggest potential transient association within the porin lumen rather than irreversible binding. Such interactions could influence channel conformation, permeability dynamics, or ion diffusion rates under metal stress conditions [9].

In contrast, mercury demonstrated the lowest binding affinity. Mercury is a highly toxic, non-essential metal that often exerts cytotoxic effects through thiol-binding and protein denaturation mechanisms in the cytoplasm rather than through stable association with membrane channels. The weaker docking interaction observed in this study may indicate that mercury detoxification in *Pseudomonas aeruginosa* relies more heavily on intracellular enzymatic systems and efflux mechanisms rather than strong porin-mediated interactions [10].

Outer membrane proteins, including porins such as OprF, OprD, and OprP, play a central role in regulating membrane permeability in Gram-negative bacteria [9]. Environmental exposure to heavy metals can induce adaptive responses involving modulation of porin expression or structural remodeling of the outer membrane [11]. Reduced permeability may limit passive diffusion of toxic

ions, while coordinated activation of efflux pumps enhances detoxification efficiency. The differential binding affinities observed in this study suggest that certain metals may interact more favorably with porin-associated residues, potentially influencing transport selectivity and membrane-associated resistance strategies [12].

From an ecological perspective, heavy metal accumulation in aquatic and soil environments exerts persistent selective pressure on microbial communities [13]. The ability of *Pseudomonas aeruginosa* to modulate membrane permeability through OMPs contributes to its survival in contaminated habitats [14]. Stronger predicted interactions with copper and zinc may reflect adaptive compatibility with metals that are both environmentally prevalent and physiologically relevant, whereas weaker interactions with mercury and chromium may indicate reliance on alternative detoxification pathways [15].

These findings support the hypothesis that outer membrane proteins may contribute to early-stage metal–bacteria interactions and influence resistance phenotypes under environmental stress, resulting in huge effect on living organisms in ecosystem [17, 18]. However, it is important to emphasize that molecular docking provides predictive computational insight and does not directly measure transport activity or biological uptake. Experimental validation through gene expression profiling, porin mutagenesis, and metal accumulation assays would be required to confirm the functional relevance of the predicted interactions [19].

Overall, the integration of molecular docking with environmental microbiology provides a mechanistic framework for understanding metal–porin interactions. Such insights may contribute to the development of optimized bacterial systems for bioremediation applications in metal-contaminated ecosystems [20].

## 5. CONCLUSION

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This study investigated the molecular interactions between selected heavy metals and outer membrane proteins of *Pseudomonas aeruginosa* using molecular docking analysis. The results indicated that copper and zinc exhibited stronger binding affinities with the OMP receptor compared with other tested metals, suggesting a higher potential for interaction with porin-associated amino acid residues. These interactions may contribute to bacterial adaptation mechanisms under heavy metal stress by influencing membrane permeability and metal transport processes.

The findings provide molecular-level insights into the possible role of outer membrane proteins in bacterial responses to metal contamination. Furthermore, understanding these interactions may support the development of microbial strategies for environmental bioremediation in heavy-metal-polluted ecosystems. However, further experimental studies are necessary to validate the biological significance of the predicted docking interactions.

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## CONFLICTS OF INTEREST

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The authors declare no conflict of interest.

## AUTHOR CONTRIBUTIONS

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E.A.M. conceptualized the study, performed the molecular docking analysis, and wrote the original manuscript draft. W.D.A. contributed to data interpretation and manuscript revision. S.A.K. assisted in methodology development, literature review, and final editing of the manuscript. All authors reviewed and approved the final version of the manuscript.

## DATA AVAILABILITY STATEMENT

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All generated data are included in the published manuscript. This research received no external funding.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

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Ethics approval was received from the Research and Technology Center of Environment, Water and Renewable Energy, Scientific Research Commission. In addition, the study was conducted in accordance with the Declaration of Helsinki's guiding principles.

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