



# Role of graphene oxide in urease-immobilized biosensor for heavy metals detection: molecular interaction analysis

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## Introduction

The accumulation of toxic heavy metals like Cu<sup>2+</sup>, Cd<sup>2+</sup> and Pb<sup>2+</sup> is a major health risk in ensuring quality and safe access to drinking water besides also threatening many species of aquatic organisms [1]. Due to high toxicity caused by these metal ions there is a conspicuous requirement to quantify them swiftly on site at trace levels. While aiming to tackle heavy metal pollution, this study also hopes to contribute significantly to the UN's Sustainable Development Goals particularly SDG 3 Good Health and Well-Being, SDG 6 Clean Water and Sanitation and SDG 14 Life Below Water [2]. Graphene-based materials are proven for potential source heavy metal toxicological monitoring in recent years [3]. Present blind docking-based investigation [4] reports the candidacy of graphene oxide (GO) for heavy metal biosensing applications.

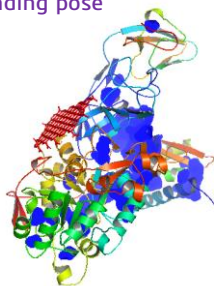
## Computational Methodology

The urease enzyme structure was retrieved from protein data bank (RCSB PDB ID: 1FWJ). The enzyme has been extracted from *Klebsiella aerogenes* bacteria. The structure retrieved was cleaned from water molecules and polar hydrogens were added. Net Kollman charge of -1.0 was added. The 2D GO ligand was obtained from PubChem database (CID: 124202900) and was converted to 3D conformation using Molecular Networks GmbH and Altamira (MN-AM Corina Classic). GO was setup addition of Gasteiger charges and torsional degrees of freedom (TORSDOF) was set to 20. 32 non-polar hydrogens of GO were merged. Urease receptor and GO ligand were prepared using AutoDockTools 1.5.6 (ADT 1.5.6) (Morris et al., 2009). The blind docking was performed using AutoDock Vina software to identify the best interaction pose with the strongest binding affinity. Docking grid size was set to x = 74 Å, y = 70 Å and z = 54 Å with the origin point set at x = 62.719, y = 93.281 and z = 92.033. Blind docking was also performed for direct sensing of urea by GO with docking grid of size x = y = z = 40 Å with origin of x = -0.003, y = 0.041 and z = 0.018.

## Results: Docking Conformations

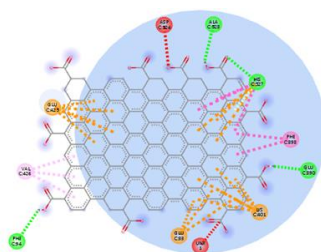
Nine different binding poses and corresponding root mean square deviations were calculated.

Most stable binding pose



| Mode                           | Binding affinity (kcal/mol) | Distance from best mode |                  |
|--------------------------------|-----------------------------|-------------------------|------------------|
|                                |                             | RMSD lower bound        | RMSD upper bound |
| 1 <sup>st</sup> (Most stable)  | -3.6                        | 0.000                   | 0.000            |
| 2 <sup>nd</sup>                | -3.6                        | 18.922                  | 19.704           |
| 3 <sup>rd</sup>                | -3.6                        | 8.294                   | 8.751            |
| 4 <sup>th</sup>                | -3.6                        | 3.554                   | 4.170            |
| 5 <sup>th</sup>                | -3.5                        | 7.814                   | 8.476            |
| 6 <sup>th</sup>                | -3.5                        | 6.024                   | 6.985            |
| 7 <sup>th</sup>                | -3.5                        | 3.627                   | 4.005            |
| 8 <sup>th</sup>                | -3.3                        | 1.812                   | 1.922            |
| 9 <sup>th</sup> (Least stable) | -3.3                        | 2.628                   | 3.032            |

## Indirect Sensing: 2D view of Urease-GO interactions

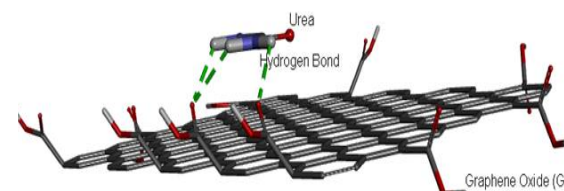


**Interactions**

- Unfavorable Bump
- Conventional Hydrogen Bond
- Unfavorable Acceptor-Acceptor
- Pi-Cation
- Pi-Anion

- Pi-Donor Hydrogen Bond
- Pi-Pi Stacked
- Pi-Pi T-shaped
- Pi-Alkyl

## Direct Sensing: Interactions between Urea and GO



## Conclusion

- In this work molecular docking-based interaction analysis of GO in heavy metals biosensing applications.
- Docking results revealed that GO can be used as an enzyme immobilizer as shown by its strongest binding affinity.
- The binding of urease enzyme with GO is mostly dominated by electrostatic interactions with hydrogen bonding and hydrophobic interactions.
- At this stage of investigation, only the binding between urease and GO is considered. Present in silico study results are promising to conduct further molecular dynamic simulations and in vitro studies.
- Docking results of direct sensing mechanism offers an almost uniform urea-probing sensitivity of the GO layer.

## References

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- [3] Chang, J., Zhou, G., Christensen, E., Heideman, R. and Chen, J., 2014. Graphene-based sensors for detection of heavy metals in water: a review. *Analytical and Bioanalytical Chemistry*, 406(16), pp.3957-3975.
- [4] Morris, G., Huey, R., Lindstrom, W., Sanner, M., Belew, R., Goodsell, D. and Olson, A., 2009. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. *Journal of Computational Chemistry*, 30(16), pp.2785-2791.