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Computational Screening and Design of Next-Generation Gold Nanoparticle-based Chemosensors.

Ligand-coated gold nanoparticles (AuNPs) can serve as advanced nanosensors capable of selectively detecting organic molecules in solution. [1] When combined with NMR-based protocols, analyte signals can be probed directly without the need for secondary reporters or analytical standards. [1] A key aspect of such approach is the formation of self-assembled monolayers surrounding the AuNP core, resulting in transient binding pockets. Through tailoring and rational design of ligands, specificity and binding affinity can be finely tuned. [2] Yet, current methods to assess affinity and selectivity rely on costly and slow experimental assays. In our recent work, we reported a molecular-dynamics (MD) based approach for the design of AuNP-based chemosensors, compatible with NMR-based protocols, for the detection and quantification of 3-methoxytyramine, a prognostic marker of asymptomatic neuroblastoma. [3] Through this approach, the identified lead AuNP was experimentally validated and shown to outperform existing AuNP-based chemosensors, halving the limit-of-detection against previously reported AuNP-based chemosensors. Furthermore, this AuNP was experimentally shown to allow the detection of 3-methoxytyramine from complex mixtures – vital for the clinical application of chemosensors. Building upon that work, we now introduce a rapid and interpretable scoring function for AuNP-analyte binding. [4] Leveraging a dataset of high-quality experimentally determined binding affinities for AuNP-analytes, we trained a scoring function to predict binding affinities based solely on static cheminformatics descriptors (LogP, charge and chemical similarity) with exceptional accuracy (R^2 = 0.85, MAE = 0.45 kcal/mol) when validated against experimental data, enabling the efficient pre-screening of candidate ligands. [4] While we primarily focus on the application of chemosensors design and assessment, in principle, the scoring function can be applied to a variety of areas relying upon AuNP – small molecule binding such as catalysis and targeted drug-delivery to name a few.

[1] Salvia, M. V.; Salassa, G.; Rastrelli, F.; Mancin, F. Turning Supramolecular Receptors into Chemosensors by Nanoparticle-Assisted NMR Chemosensing. J. Am. Chem. Soc. 2015, 137, 11399–11406.

[2] Sun, X.; Riccardi, L.; De Biasi, F.; Rastrelli, F.; De Vivo, M.; Mancin, F. Molecular-Dynamics-Simulation-Directed Rational Design of Nanoreceptors with Targeted Affinity. Angew. Chem. Int. Ed. 2019, 58 (23), 7702–7707.

[3] Franco-Ulloa, S.; Cesari, A.; Zanoni, G.; Riccardi, L.; Wallace, J.; Mascitti, B. B.; Rastrelli, F.; Mancin, F.; De Vivo, M. Rational Design of Gold Nanoparticle-Based Chemosensors for Detection of the Tumor Marker 3-Methoxytyramine. Chem. Sci. 2025, 16, 6282–6289.

[4] Wallace, J.; Riccardi, L.; Mancin, F.; De Vivo, M. A Scoring Function for Monolayer-Protected Gold Nanoparticles Capable of Detecting Small Organic Molecules in Solution. Manuscript in preparation.

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