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Use of HPC resources for to find new drugs against biofilm formation

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With the increase in microbial resistance to therapeutics, there is a higher demand for finding new pathways or molecular targets to treat bacterial infections. The Pseudomonas quinolone system (PQS) is a part of the quorum sensing (QS) communication system of *Pseudomonas aeruginosa*, which controls the production of biofilms and several other virulence factors. Inhibiting quorum sensing does not kill the bacteria but decreases its virulence and prevents biofilm formation.
Using a combination of in silico methods such as protein-ligand docking, structured-based virtual screening of large virtual databases of chemical entities, extensive molecular dynamics simulations and accurate free energy calculations, new drugs with potential activity toward two specific targets of the PQS system (PqsD and PqsR) were identified. After developing and validating the docking and virtual screening protocol, 221,146 molecules were screened against both targets. Subsequently, the top 25 candidates were selected for MD simulations and free energy calculations to validate the predictions and estimate binding free energies[1], [2]. We demonstrate that a multi-level computational approach can identify strong candidates for QS inhibition and provide solid structural information on the protein-ligand interactions. Moreover, using HPC resources provides the computational power necessary for processing vast amounts of data at unprecedented speeds, significantly reducing simulation times.

[1] T. F. Vieira, R. P. Magalhães, N. M. F. S. A. Cerqueira, M. Simões, and S. F. Sousa, "Targeting Pseudomonas aeruginosa MvfR in the battle against biofilm formation: a multi-level computational approach,"Mol Syst Des Eng, vol. 7, no. 10, pp. 1294–1306, 2022, doi: 10.1039/D2ME00088A.
[2] D. Lapaillerie et al., "In Silico, In Vitro and In Cellulo Models for Monitoring SARS-CoV-2 Spike/Human ACE2 Complex, Viral Entry and Cell Fusion,"Viruses, vol. 13, no. 3, p. 365, Feb. 2021, doi: 10.3390/v13030365.

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