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Combining docking, scoring and molecular field analyses to probe influenza neuraminidase–ligand interactions

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Abstract

In this project, several docking conditions, scoring functions and corresponding protein-aligned molecular field analysis (CoMFA) models were evaluated for a diverse set of neuraminidase (NA) inhibitors. To this end, a group of inhibitors were docked into the active site of NA. The docked structures were utilized to construct a corresponding protein-aligned CoMFA models by employing probe-based (H+, OH, CH3) energy grids and genetic partial least squares (G/PLS) statistical analysis. A total of 16 different docking configurations were evaluated, of which some succeeded in producing self-consistent and predictive CoMFA models. However, the best model coincided with docking the ionized ligands into the hydrated form of the binding site via PLP1 scoring function ($r^2_{LOO} = 0.735$, r^2_{PRESS} against 24 test compounds = 0.828). The highest-ranking CoMFA models were employed to probe NA–ligand interactions. Further validation by comparison with a co-crystallized ligand–NA crystallographic structure was performed. This combination of docking/scoring/CoMFA modeling provided interesting insights into the binding of different NA inhibitors.

Keywords: Neuraminidase inhibitors; Docking; Scoring; Protein-aligned CoMFA; Multiple binding modes