Induced fit docking to tubulin receptors with Glide/Prime

SOP

Contents

I. General information

Project acronym:	NMTrypI	**Date written:**	06/06/2017
GA number:	603240	**Date latest modification:**	21/04/2023
Type of activity:	RD	**Total pages:**	3

II. Objective and field of application

This SOP describes the docking of the trifluralin reference compound and dinitroaniline etherphospholipids **1-9** into *Leishmania* and *Trypanosoma* α-tubulin receptors, using Glide and Prime in Schrödinger Maestro as part of the Induced Fit workflow to allow for receptor side chain reorganization upon ligand binding.

III. Purpose of the SOP

- Binding mode and interaction pattern prediction for dinitroaniline etherphospholipids and their reference compound trifluralin in α-tubulin models while allowing for receptor side chain adaptation to the ligands.
- Ranking of different binding modes of the same ligand as part of different optimized receptor-ligand complexes.
- Rough estimation of binding energies by docking scores and IFDScores.

IV. Equipment and Software

- Schrödinger Induced Fit Docking Protocol, Glide v11.1 and Prime PSP v4.7, 2017, Schrödinger LLC, New York, NY.
- This SOP complies with Schrödinger Release up to v2017-1.

V. Procedure

- Load the prepared tubulin receptors into the workspace. For using the trifluralin-bound reference receptor as the starting point, instead load the corresponding top-ranked docking result.
- Go to *Tasks - Docking - Induced Fit docking*.
- Select ligands to be docked *From File* and pick the prepared trifluralin and/or dinitroaniline etherphospholipid compounds in Maestro file format (.maegz).
- Use the *Standard* protocol.
- Select the centroid in the *'Receptor'* Tab: for Blume site: Ala4; for Consensus site: Thr239; for pironetin site: Leu238; for M-loop: Leu286; for N-loop: Phe49; for interface between M- and N-loop (starting from receptor with two α-tubulins from neighboring protofilaments): Leu286; when starting from complex with trifluralin: centroid of trifluralin in every site. Box size: Auto.
- In the *'Ligands'* Tab: Sample ring conformations with Energy window 2.5 kcal/mol, penalize nonplanar conformation for Amide bonds and Enhance planarity of conjugated pi groups.
- In the *'Glide docking'* Tab: Receptor van der Waals scaling: 0.5, Ligand van der Waals scaling: 0.5 and maximum number of poses: 20.
- In the *'Prime refinement'* Tab: Refine residues within 5 Å of ligand poses, tick: Optimize side chains.

- In the *'Glide redocking'* Tab: Redock into structures within 30.0 kcal/mol of the best structure, and within the top 20 structures overall. Precision: SP.
- Select Number of Glide CPUs and Prime CPUs according to your environment and start the Induced Fit docking workflow.