

Supporting Information

S1. Link to download the MD_antagonist_1 and MD_agonist_1 ensembles for ensemble docking together with the set of agonists, antagonists and decoys for benchmarking of the docking performance:

https://figshare.com/articles/Androgen_receptor_ensemble_docking/6170159

S2. Parameters for Glide_SP docking

[STAGE:LIGPREP]

```
STAGECLASS ligprep.LigPrepStage
INPUTS ORIGINAL_LIGANDS,
OUTPUTS LIGPREP_OUT,
RECOMBINE YES
RETITLE YES
MIXLIGS YES
SKIP_BAD_LIGANDS YES
UNIQUEFIELD NONE
OUTCOMPOUNDFIELD s_vsw_compound_code
USE_EPIK YES
METAL_BINDING NO
PH 7.0
PHT 2.0
NRINGCONFS 10
COMBINEOUTS NO
STEREO_SOURCE geometry
NUM_STEREOISOMERS 32
REGULARIZE NO
```

[STAGE:SAMPLERINGS]

```
STAGECLASS macromodel.SampleRingsStage
INPUTS LIGPREP_OUT,
OUTPUTS SAMPLERINGS_OUT,
OUTCONFS_PER_SEARCH 10
```

[STAGE:POSTLIGPREP]

```
STAGECLASS ligprep.PostLigPrepStage
INPUTS SAMPLERINGS_OUT,
OUTPUTS POSTLIGPREP_OUT,
UNIQUEFIELD s_vsw_compound_code
OUTVARIANTFIELD s_vsw_variant
PRESERVE_NJOBS YES
LIMIT_STEREOISOMERS YES
MAXSTEREO 4
REMOVE_PENALIZED_STATES YES
```

[STAGE:PRE_DOCK_SP_1]

STAGECLASS gencodes.RecombineStage
INPUTS POSTLIGPREP_OUT,
OUTPUTS DOCK_SP_1_INPUT,
NUMOUT njobs
OUTFORMAT maegz
MIN_SUBJOB_STS 300
MAX_SUBJOB_STS 3000
GENCODES NO
UNIQUEFIELD s_vsw_compound_code

[STAGE:DOCK_SP_1]

STAGECLASS glide.DockingStage
INPUTS DOCK_SP_1_INPUT, GRID_1
OUTPUTS SP_OUT_1,
RECOMBINE NO
PRECISION SP
UNIQUEFIELD s_vsw_compound_code
PERCENT_TO_KEEP 100
DOCKING_METHOD confgen
POSES_PER_LIG 1
WRITE_XP_DESC NO
NENHANCED_SAMPLING 1
BEST_BY_TITLE YES
LIG_VSCALE 0.8
LIG_CCUT 0.15
MAXATOMS 300
MAXROTBONDS 50
AMIDE_MODE penal
POSE_OUTTYPE PV
POSTDOCK YES
POSTDOCKSTRAIN YES
COMPRESS_POSES YES
EPIK_PENALTIES NO
FORCEPLANAR YES

S3. Parameters for Induced Fit docking

TAGE GLIDE_DOCKING2
BINDING_SITE ligand A:1
INNERBOX 10.0
OUTERBOX auto
LIGAND_FILE InducedFit__2oz7.mae
LIGANDS_TO_DOCK all
GRIDGEN_RECEP_CCUT 0.25
GRIDGEN_RECEP_VSCALE 0.50
DOCKING_PRECISION SP
DOCKING_LIG_CCUT 0.15
DOCKING_CV_CUTOFF 100.0
DOCKING_LIG_VSCALE 0.50
DOCKING_POSES_PER_LIG 20

DOCKING_RINGCONFCUT 2.5
DOCKING_AMIDE_MODE penal

STAGE COMPILE_RESIDUE_LIST
DISTANCE_CUTOFF 5.0

STAGE PRIME_REFINEMENT
NUMBER_OF_PASSES 1
USE_MEMBRANE no
OPLS_VERSION OPLS3

STAGE SORT_AND_FILTER
POSE_FILTER r_psp_Prime_Energy
POSE_KEEP30.0

STAGE SORT_AND_FILTER
POSE_FILTER r_psp_Prime_Energy
POSE_KEEP20#

STAGE GLIDE_DOCKING2
BINDING_SITE ligand Z:999
INNERBOX 10.0
OUTERBOX auto
LIGAND_FILE InducedFit__2oz7.mae
LIGANDS_TO_DOCK self
GRIDGEN_RECEP_CCUT 0.25
GRIDGEN_RECEP_VSCALE 1.00
DOCKING_PRECISION SP
DOCKING_LIG_CCUT 0.15
DOCKING_CV_CUTOFF 0.0
DOCKING_LIG_VSCALE 0.80
DOCKING_POSES_PER_LIG 1
DOCKING_RINGCONFCUT 2.5
DOCKING_AMIDE_MODE penal

STAGE SCORING
SCORE_NAME r_psp_IFDScore
TERM 1.0,r_i_glide_gscore,0
TERM 0.05,r_psp_Prime_Energy,1
REPORT_FILE report.csv