Step	Method	Parameters
● Preparation		
○ Binding pocket	Run ICMPocketFinder, select residues around pocket	1.5 Å radius around pocket.
○ Cytoplasmic residues	Define cytoplasmic domain by selecting Ballosteros-Weinstein (BW) residues	BW cytoplasmic residues: 1.48, 2.51, 3.38, 4.51, 5.50, 6.43, 7.45
● Independent replica		80 replicas
○ Initialise		
■ Minimise	GROMACS with explicit waters	FFGMX forcefield, water model SPC, Electrostatics: PME and epsilon_r=1, default pdb2gmx residue charge, BFGS method, 5000 steps.
■ Starting structure	CONCOORD generate conformation	x1 conformation. Use input as reference. 10000 regularisation steps.
○ Iterative rounds		8 iterative rounds
■ Directory		20 directories
● Sample receptor main chain	CONCOORD generate conformations	x30 conformations. Minimum 200 distance definition for each atom. Fix cytoplasmic residues. Use random seed.
● Select receptor	Select conformations under a maximum RMSD from the input	< 1.2 Å RMSD.
● Sample binding pocket side chains	tCONCOORD generate conformations	x5 conformations. Sample binding pocket side chains only.
● Select binding pocket	Select conformations that conserved % of binding pocket polar residues from input	8/10 polar residues.
● Rebuild	Add cytoplasm side chains with scoomp	Consider ligand in energy calculations
● Minimise	GROMACS with explicit waters	(Identical to minimisation above)
● Dock	ICM docking, binding pocket refinement	Flexible ligand docking to pre-calculated energy grid. Docking effort: 5. Select best scored conformation. Refine residues 2 Å around ligand.
● Score	Score docked pose with ICM, receptor with OPUS_PSP	
■ Scoring		
● Select	Best ICM scored from complexes in this directory	
● Final scoring (quantitative and qualitative)	OPUS-ICM rank all complexes and cluster by IFP	Up to 1,920,000 complexes generated and up to 640 LDM complexes ranked by OPUS-ICM. The top 25 LDM complexes are clustered by IFP. Analyse best scoring LDM complex from each cluster at cutoff ~0.7 Jaccard distance.

References

1. Kabsch W, Sander C. Dictionary of protein secondary structure: pattern recognition of hydrogen-bonded and geometrical features. Biopolymers. 1983;22: 2577–2637.
2. Jorgensen WL, Tirado-Rives J. The OPLS [optimized potentials for liquid simulations] potential functions for proteins, energy minimizations for crystals of cyclic peptides and crambin. J Am Chem Soc. 1988;110: 1657–1666.