<table>
<thead>
<tr>
<th>Step</th>
<th>Method</th>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Binding pocket</td>
<td>Run ICMPocketFinder, select residues around pocket</td>
<td>1.5 Å radius around pocket.</td>
</tr>
<tr>
<td>- Cytoplasmic residues</td>
<td>Define cytoplasmic domain by selecting Ballouros-Weinstein (BW) residues</td>
<td>BW cytoplasmic residues: 1.48, 2.51, 3.38, 4.51, 5.50, 6.43, 7.45</td>
</tr>
<tr>
<td>Independent replica</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Initialise</td>
<td>GROMACS with explicit waters</td>
<td>FFGMX forcefield, water model SPC, Electrostatics: PME and epsilon_r=1, default pdb2gmx residue charge, BFGS method, 5000 steps. x1 conformation. Use input as reference. 10000 regularisation steps.</td>
</tr>
<tr>
<td>- Minimise cluster</td>
<td>CONCOORD generate conformation</td>
<td></td>
</tr>
<tr>
<td>- Iterative rounds</td>
<td>8 iterative rounds</td>
<td></td>
</tr>
<tr>
<td>- Directory</td>
<td>20 directories</td>
<td></td>
</tr>
<tr>
<td>Sample receptor main chain</td>
<td>CONCOORD generate conformation</td>
<td>x30 conformations. Minimum 200 distance definition for each atom. Fix cytoplasmic residues. Use random seed. x 1.2 Å RMSD. x5 conformations. Sample binding pocket side chains only. 8/10 polar residues. Consider ligand in energy calculations. (Identical to minimisation above) Flexible ligand docking to pre-calculated energy grid. Docking effort: 5. Select best scored conformation. Reline residues 2 Å around ligand.</td>
</tr>
<tr>
<td>Select receptor</td>
<td>Select conformations under a maximum RMSD from the input</td>
<td></td>
</tr>
<tr>
<td>Sample binding pocket side chains</td>
<td>ICONCOORD generate conformations</td>
<td></td>
</tr>
<tr>
<td>Select binding pocket</td>
<td>Select conformations that preserved % of binding pocket polar residues from input</td>
<td></td>
</tr>
<tr>
<td>Rebuild</td>
<td>Add cytoplasm side chains with scoomp</td>
<td></td>
</tr>
<tr>
<td>Minimise</td>
<td>GROMACS with explicit waters</td>
<td></td>
</tr>
<tr>
<td>Dock</td>
<td>ICM docking, binding pocket refinement</td>
<td></td>
</tr>
<tr>
<td>Score</td>
<td>Score docked pose with ICM, receptor with OPUS_PSP</td>
<td></td>
</tr>
<tr>
<td>Scoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Select</td>
<td>Best ICM scored from complexes in this directory</td>
<td></td>
</tr>
<tr>
<td>Final scoring (quantitative and qualitative)</td>
<td>OPUS-ICM rank all complexes and cluster by IFP</td>
<td>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.</td>
</tr>
</tbody>
</table>

References