**Supplementary Information For:** Flexible CDOCKER: Development and application of a pseudo-explicit structure-based docking method within CHARMM

Jessica K. Gagnon, Sean M. Law, Charles L. Brooks III

**Table 1:**

The PDBIDs and CDOCKER results for CCDC/Astex subset. Included are lowest RMSD conformation found and the RMSD for the lowest energy conformation for the two simulated annealing implementations and the MD+Minimization protocols.

*Rigid CDOCKER results*

| | *SA- 1 Grid* | | *SA- 2 Grids* | | *MD+Minimization* | |
|---|---|---|---|---|---|---|
| PDBID | Lowest RMSD | Lowest Energy | Lowest RMSD | Lowest Energy | Lowest RMSD | Lowest Energy |
| 1a28 | 0.2 | 0.3 | 0.4 | 0.4 | 0.2 | 0.2 |
| 1a6w | 1.8 | 2.2 | 1.5 | 2.9 | 1.8 | 2.1 |
| 1abe | 1.2 | 2.9 | 1.7 | 2.6 | 1.1 | 2.9 |
| 1abf | 0.9 | 3.2 | 2.2 | 3.4 | 1.2 | 3.2 |
| 1acj | 0.6 | 0.7 | 0.3 | 0.6 | 0.4 | 0.5 |
| 1acl | 2.3 | 4.2 | 2.3 | 5.5 | 2.5 | 2.7 |
| 1acm | 1.1 | 2.0 | 1.5 | 2.3 | 0.9 | 1.2 |
| 1aco | 0.9 | 3.7 | 1.7 | 2.9 | 0.8 | 1.4 |
| 1aec | 1.4 | 2.5 | 1.4 | 1.4 | 1.6 | 1.6 |
| 1ai5 | 0.6 | 1.1 | 1.0 | 1.3 | 0.6 | 0.6 |
| 1aoe | 1.9 | 2.2 | 1.8 | 1.9 | 1.8 | 2.0 |
| 1aqw | 0.8 | 2.5 | 1.6 | 2.7 | 0.7 | 1.3 |
| 1ase | 1.6 | 3.1 | 1.7 | 2.9 | 1.1 | 3.1 |
| 1azm | 1.6 | 5.8 | 1.7 | 2.0 | 1.6 | 2.0 |
| 1b59 | 0.4 | 5.3 | 0.5 | 6.9 | 0.5 | 5.6 |
| 1b9v | 1.8 | 2.1 | 1.9 | 2.5 | 1.7 | 2.0 |
| 1baf | 1.0 | 6.1 | 1.9 | 4.4 | 1.1 | 2.4 |
| 1bbp | 1.1 | 8.3 | 1.2 | 2.3 | 1.1 | 2.7 |
| 1bgo | 1.8 | 1.8 | 1.6 | 2.1 | 2.0 | 2.1 |
| 1blh | 1.8 | 1.8 | 1.4 | 2.5 | 1.7 | 1.8 |
| 1bmq | 1.6 | 2.3 | 1.6 | 2.0 | 1.9 | 1.9 |
| 1byg | 0.6 | 2.6 | 0.5 | 1.6 | 0.5 | 1.7 |
| 1c12 | 1.6 | 2.3 | 1.8 | 2.5 | 1.7 | 2.3 |
| 1c1e | 0.6 | 4.4 | 0.7 | 0.8 | 0.5 | 0.6 |
| 1c5c | 1.7 | 2.3 | 1.4 | 3.4 | 1.5 | 2.3 |
| 1c5x | 1.2 | 1.3 | 0.5 | 0.9 | 1.2 | 1.3 |
| 1c83 | 0.6 | 0.6 | 1.0 | 1.0 | 0.6 | 0.9 |

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|---|---|---|---|---|---|---|
| 1cbs | 0.9 | 1.1 | 0.8 | 1.1 | 1.0 | 1.1 |
| 1cbx | 0.7 | 1.1 | 0.9 | 1.3 | 0.6 | 1.1 |
| 1cdg | 1.8 | 4.0 | 1.8 | 2.9 | 2.0 | 2.9 |
| 1ckp | 0.6 | 2.9 | 0.6 | 2.9 | 0.6 | 2.9 |
| 1cle | 2.1 | 3.1 | 1.4 | 1.9 | 2.3 | 2.3 |
| 1com | 1.7 | 4.3 | 0.6 | 4.3 | 1.0 | 1.7 |
| 1coy | 0.8 | 0.9 | 0.7 | 1.2 | 0.8 | 0.9 |
| 1cqp | 1.1 | 1.1 | 1.0 | 2.0 | 1.1 | 1.2 |
| 1cvu | 1.1 | 1.7 | 1.2 | 2.3 | 1.1 | 2.3 |
| 1cx2 | 1.5 | 1.8 | 1.5 | 1.8 | 1.5 | 1.7 |
| 1d0l | 1.2 | 1.4 | 1.2 | 1.8 | 1.2 | 3.0 |
| 1d3h | 1.5 | 7.3 | 0.9 | 1.1 | 1.4 | 7.3 |
| 1d4p | 1.1 | 1.6 | 1.3 | 2.2 | 1.1 | 8.5 |
| 1dbb | 1.8 | 5.3 | 1.4 | 5.2 | 1.3 | 4.6 |
| 1dbj | 0.7 | 0.8 | 0.6 | 0.7 | 0.7 | 0.8 |
| 1dd7 | 3.0 | 3.9 | 3.1 | 6.0 | 1.1 | 4.6 |
| 1dg5 | 1.5 | 5.8 | 1.5 | 6.0 | 1.5 | 2.5 |
| 1did | 1.2 | 5.5 | 1.9 | 2.6 | 1.2 | 5.4 |
| 1dmp | 3.4 | 3.4 | 3.5 | 4.9 | 3.5 | 3.9 |
| 1dog | 0.4 | 4.1 | 1.0 | 3.1 | 0.3 | 3.7 |
| 1dr1 | 0.5 | 2.5 | 1.0 | 2.4 | 0.6 | 2.4 |
| 1dwb | 2.0 | 2.2 | 0.9 | 2.1 | 0.6 | 2.2 |
| 1dwc | 0.9 | 1.3 | 2.6 | 5.6 | 1.0 | 1.0 |
| 1dwd | 2.3 | 6.1 | 2.5 | 5.7 | 1.2 | 1.3 |
| 1dy9 | 1.4 | 1.4 | 1.8 | 3.1 | 1.3 | 1.4 |
| 1eap | 2.2 | 4.3 | 2.3 | 3.6 | 2.3 | 3.8 |
| 1ebg | 0.6 | 3.0 | 0.9 | 2.6 | 0.6 | 3.0 |
| 1ei1 | 0.6 | 0.6 | 1.9 | 1.9 | 0.6 | 0.6 |
| 1ejn | 1.8 | 5.5 | 1.7 | 4.1 | 1.6 | 5.7 |
| 1eoc | 1.5 | 1.7 | 1.3 | 2.5 | 1.5 | 1.5 |
| 1epb | 1.1 | 2.8 | 1.1 | 1.8 | 1.1 | 1.2 |
| 1etr | 0.9 | 0.9 | 0.9 | 0.9 | 1.0 | 1.0 |
| 1ets | 3.5 | 4.5 | 3.2 | 4.2 | 3.6 | 4.6 |
| 1f0r | 2.0 | 4.1 | 1.8 | 3.8 | 2.5 | 3.9 |
| 1f0s | 1.4 | 3.9 | 1.8 | 4.2 | 2.4 | 3.9 |
| 1fen | 0.6 | 0.8 | 0.6 | 0.6 | 0.5 | 0.6 |
| 1fgi | 0.6 | 5.7 | 0.5 | 0.6 | 0.7 | 1.1 |
| 1fkg | 1.4 | 2.3 | 1.0 | 1.8 | 1.0 | 2.0 |
| 1fl3 | 0.6 | 1.2 | 0.7 | 0.7 | 0.7 | 0.8 |
| 1flr | 2.3 | 4.5 | 2.3 | 4.5 | 2.3 | 4.5 |
| 1frp | 1.0 | 1.0 | 1.2 | 2.3 | 0.7 | 1.0 |
| 1glp | 0.9 | 0.9 | 1.0 | 3.0 | 1.6 | 1.8 |
| 1glq | 3.1 | 4.8 | 2.7 | 5.4 | 3.0 | 4.5 |

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|---|---|---|---|---|---|---|
| 1hak | 1.9 | 4.0 | 1.5 | 7.8 | 1.8 | 4.3 |
| 1hdc | 0.8 | 1.2 | 0.8 | 1.2 | 0.8 | 0.9 |
| 1hfc | 2.3 | 3.8 | 2.2 | 3.5 | 1.9 | 3.4 |
| 1hiv | 1.2 | 1.7 | 1.8 | 1.9 | 1.9 | 3.1 |
| 1hpv | 1.0 | 1.2 | 1.1 | 1.4 | 1.0 | 1.1 |
| 1hri | 0.9 | 2.0 | 1.0 | 1.2 | 0.9 | 1.1 |
| 1htf | 1.8 | 1.9 | 1.5 | 7.4 | 1.7 | 3.5 |
| 1hyt | 2.4 | 3.2 | 2.4 | 2.9 | 2.5 | 2.8 |
| 1ibg | 0.7 | 0.8 | 0.6 | 1.5 | 0.7 | 0.7 |
| 1imb | 2.7 | 6.7 | 3.2 | 6.6 | 2.6 | 7.1 |
| 1ivb | 2.0 | 3.5 | 2.4 | 3.3 | 2.0 | 4.5 |
| 1kel | 1.1 | 1.4 | 1.4 | 1.8 | 1.2 | 1.4 |
| 1lah | 0.5 | 1.1 | 1.1 | 2.7 | 0.5 | 1.1 |
| 1lcp | 0.6 | 1.0 | 0.9 | 1.0 | 0.5 | 0.8 |
| 1lic | 1.3 | 3.9 | 1.4 | 2.2 | 1.5 | 2.7 |
| 1lpm | 0.9 | 4.8 | 0.5 | 0.5 | 0.6 | 0.6 |
| 1lst | 1.1 | 1.2 | 1.1 | 2.2 | 1.0 | 2.0 |
| 1mcq | 0.7 | 1.1 | 0.7 | 1.9 | 0.7 | 1.1 |
| 1mdr | 1.3 | 2.5 | 1.5 | 2.6 | 1.3 | 2.5 |
| 1mld | 1.3 | 1.5 | 1.6 | 2.6 | 1.4 | 1.5 |
| 1mrg | 1.2 | 4.8 | 1.0 | 3.4 | 1.2 | 4.8 |
| 1mrk | 1.4 | 1.7 | 1.4 | 1.5 | 1.4 | 1.5 |
| 1mts | 0.9 | 2.1 | 1.1 | 2.1 | 1.1 | 2.0 |
| 1mup | 1.2 | 1.4 | 1.1 | 4.3 | 1.1 | 1.3 |
| 1nco | 1.1 | 3.5 | 1.1 | 2.6 | 1.4 | 3.5 |
| 1ngp | 1.8 | 4.1 | 0.9 | 4.4 | 1.2 | 4.0 |
| 1okl | 1.7 | 2.4 | 1.0 | 3.0 | 1.3 | 2.0 |
| 1pdz | 1.7 | 2.2 | 1.7 | 4.4 | 1.4 | 2.2 |
| 1phd | 1.8 | 3.0 | 2.1 | 7.0 | 1.6 | 3.6 |
| 1phg | 2.1 | 4.9 | 1.3 | 6.4 | 1.9 | 4.9 |
| 1poc | 1.0 | 1.0 | 1.5 | 1.5 | 1.0 | 1.0 |
| 1ppc | 1.6 | 3.1 | 2.3 | 7.5 | 1.2 | 1.2 |
| 1pph | 4.9 | 6.2 | 4.4 | 6.1 | 4.9 | 5.6 |
| 1ptv | 4.3 | 7.3 | 3.9 | 7.2 | 4.3 | 8.6 |
| 1qcf | 1.3 | 1.4 | 0.8 | 0.8 | 1.3 | 1.4 |
| 1qpe | 1.7 | 2.2 | 0.7 | 0.7 | 1.4 | 1.5 |
| 1qpq | 0.7 | 3.0 | 1.1 | 2.4 | 0.7 | 3.0 |
| 1rnt | 0.6 | 0.6 | 0.8 | 1.1 | 0.5 | 0.5 |
| 1rob | 0.9 | 1.1 | 0.7 | 3.3 | 0.9 | 1.1 |
| 1rt2 | 0.6 | 0.6 | 0.6 | 0.7 | 0.5 | 0.6 |
| 1slt | 2.2 | 3.0 | 2.1 | 2.8 | 1.4 | 4.8 |
| 1snc | 1.2 | 5.3 | 2.6 | 5.3 | 0.7 | 1.4 |
| 1srj | 0.9 | 3.6 | 0.9 | 1.2 | 0.9 | 2.8 |

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|---|---|---|---|---|---|---|
| 1tdb | 1.6 | 1.8 | 1.4 | 3.5 | 1.4 | 2.1 |
| 1tmn | 1.5 | 1.8 | 2.3 | 2.8 | 1.7 | 2.4 |
| 1tng | 0.4 | 0.4 | 4.4 | 4.4 | 0.3 | 0.4 |
| 1tnh | 1.4 | 1.5 | 1.4 | 1.5 | 1.4 | 1.6 |
| 1tni | 1.3 | 3.0 | 1.5 | 2.1 | 1.6 | 1.6 |
| 1tpp | 5.7 | 7.1 | 4.8 | 6.5 | 5.7 | 5.9 |
| 1tyl | 0.8 | 0.8 | 0.6 | 2.1 | 0.9 | 0.9 |
| 1ukz | 0.6 | 6.3 | 0.8 | 4.5 | 0.6 | 0.9 |
| 1ulb | 0.9 | 0.9 | 0.6 | 3.5 | 0.7 | 0.9 |
| 1uvs | 1.8 | 2.2 | 1.7 | 3.9 | 1.5 | 1.7 |
| 1uvt | 3.2 | 3.8 | 3.3 | 3.4 | 3.1 | 3.9 |
| 1vgc | 1.3 | 2.0 | 1.3 | 5.3 | 1.3 | 5.3 |
| 1xid | 1.3 | 2.1 | 1.2 | 2.6 | 1.2 | 1.8 |
| 1xie | 1.6 | 1.9 | 3.9 | 6.5 | 1.5 | 1.9 |
| 1ydr | 0.9 | 4.0 | 0.8 | 3.5 | 0.9 | 0.9 |
| 1yee | 0.9 | 1.0 | 1.1 | 3.2 | 0.9 | 1.1 |
| 25c8 | 1.8 | 2.6 | 1.6 | 1.9 | 1.7 | 2.0 |
| 2aad | 0.8 | 0.9 | 0.5 | 1.0 | 0.8 | 0.8 |
| 2ada | 0.8 | 1.1 | 0.7 | 0.8 | 0.7 | 1.0 |
| 2cht | 1.1 | 3.9 | 1.3 | 4.1 | 1.0 | 3.4 |
| 2cmd | 1.1 | 1.5 | 1.6 | 3.4 | 1.2 | 1.8 |
| 2cpp | 0.3 | 2.7 | 1.5 | 2.8 | 0.3 | 2.6 |
| 2ctc | 2.1 | 2.5 | 2.1 | 2.7 | 1.1 | 1.6 |
| 2fox | 1.4 | 1.4 | 1.1 | 1.3 | 1.2 | 1.6 |
| 2gbp | 0.3 | 0.7 | 0.7 | 3.5 | 0.3 | 0.7 |
| 2h4n | 2.0 | 5.6 | 1.7 | 5.8 | 1.4 | 5.6 |
| 2ifb | 1.0 | 1.3 | 0.9 | 1.6 | 1.0 | 1.5 |
| 2mcp | 1.0 | 3.0 | 4.5 | 4.6 | 0.9 | 1.0 |
| 2pk4 | 1.2 | 2.3 | 1.0 | 2.8 | 1.1 | 2.2 |
| 2r07 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 | 0.7 |
| 2yhx | 0.8 | 2.8 | 1.6 | 5.4 | 1.0 | 1.4 |
| 2ypi | 1.1 | 1.5 | 1.1 | 1.3 | 0.7 | 1.4 |
| 3ert | 0.6 | 1.1 | 1.1 | 1.5 | 0.7 | 1.1 |
| 3gpb | 1.3 | 5.5 | 0.8 | 2.3 | 1.2 | 5.5 |
| 3hvt | 0.9 | 0.9 | 0.8 | 0.8 | 0.9 | 0.9 |
| 4aah | 0.7 | 1.0 | 1.2 | 5.9 | 0.6 | 5.8 |
| 4cox | 0.6 | 0.7 | 0.4 | 0.7 | 0.6 | 0.7 |
| 4cts | 1.8 | 2.1 | 1.7 | 2.1 | 1.3 | 2.2 |
| 4dfr | 2.9 | 4.7 | 1.7 | 5.6 | 2.3 | 3.8 |
| 4est | 2.3 | 2.9 | 2.2 | 3.8 | 2.2 | 3.4 |
| 4fbp | 0.6 | 5.7 | 1.7 | 2.2 | 0.4 | 1.7 |
| 4lbd | 1.0 | 1.0 | 1.0 | 1.2 | 1.0 | 1.0 |
| 4phv | 3.2 | 4.8 | 2.9 | 5.4 | 3.2 | 5.0 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 5abp | 0.8 | 0.8 | 0.8 | 1.4 | 0.8 | 0.8 |
| 5cpp | 2.0 | 3.0 | 1.9 | 2.2 | 2.0 | 3.0 |
| 6rnt | 1.8 | 2.4 | 3.0 | 4.0 | 1.3 | 4.1 |
| 6rsa | 0.8 | 1.1 | 0.9 | 2.1 | 0.8 | 0.8 |
| 7tim | 0.9 | 1.6 | 1.3 | 1.8 | 0.8 | 1.6 |
| **Averages** | 1.4 | 2.7 | 1.5 | 2.9 | 1.3 | 2.4 |

*Flexible CDOCKER results*

| | *SA- 1 Grid* | | *SA- 2 Grids* | | *MD+Minimization* | |
|---|---|---|---|---|---|---|
| PDBID | Lowest RMSD | Lowest Energy | Lowest RMSD | Lowest Energy | Lowest RMSD | Lowest Energy |
| 1a28 | 0.2 | 0.2 | 0.2 | 0.3 | 0.2 | 0.3 |
| 1a6w | 1.8 | 3.0 | 1.8 | 2.8 | 1.7 | 2.2 |
| 1abe | 1.1 | 2.9 | 2.3 | 2.9 | 1.3 | 2.8 |
| 1abf | 0.8 | 3.0 | 3.3 | 10.6 | 1.1 | 3.0 |
| 1acj | 0.4 | 0.7 | 0.6 | 1.2 | 0.3 | 0.4 |
| 1acl | 2.1 | 4.3 | 2.1 | 4.2 | 2.1 | 3.3 |
| 1acm | 1.4 | 2.1 | 3.3 | 10.0 | 0.4 | 2.4 |
| 1aco | 0.4 | 2.9 | 6.2 | 7.2 | 0.6 | 1.1 |
| 1aec | 1.7 | 3.2 | 4.5 | 6.9 | 1.5 | 1.7 |
| 1ai5 | 0.5 | 1.0 | 0.6 | 8.0 | 0.6 | 0.9 |
| 1aoe | 0.9 | 1.7 | 2.6 | 8.0 | 1.7 | 1.8 |
| 1aqw | 1.1 | 2.5 | 1.3 | 6.5 | 0.7 | 2.0 |
| 1ase | 2.4 | 4.9 | 3.1 | 4.7 | 1.4 | 2.7 |
| 1azm | 1.6 | 2.2 | 2.5 | 4.4 | 1.5 | 2.0 |
| 1b59 | 0.4 | 2.7 | 2.9 | 4.0 | 0.4 | 2.2 |
| 1b9v | 1.8 | 1.9 | 2.6 | 8.5 | 1.6 | 1.9 |
| 1baf | 2.3 | 2.5 | 3.9 | 7.3 | 3.3 | 3.9 |
| 1bbp | 1.3 | 8.1 | 2.2 | 3.9 | 1.4 | 1.8 |
| 1bgo | 1.9 | 2.1 | 2.4 | 3.8 | 1.5 | 2.2 |
| 1blh | 1.9 | 1.9 | 3.8 | 4.8 | 1.8 | 2.0 |
| 1bmq | 2.0 | 2.3 | 5.0 | 5.0 | 1.6 | 1.9 |
| 1byg | 0.4 | 1.8 | 0.4 | 0.9 | 0.3 | 0.3 |
| 1c12 | 1.5 | 2.3 | 1.3 | 2.8 | 1.3 | 2.3 |
| 1c1e | 0.3 | 0.3 | 0.4 | 0.4 | 0.3 | 0.4 |
| 1c5c | 1.6 | 4.7 | 2.6 | 5.2 | 1.4 | 3.9 |
| 1c5x | 0.9 | 0.9 | 0.9 | 0.9 | 0.9 | 0.9 |
| 1c83 | 0.6 | 1.0 | 5.5 | 11.1 | 0.8 | 1.0 |
| 1cbs | 0.8 | 1.1 | 1.0 | 3.5 | 1.1 | 1.4 |
| 1cbx | 0.6 | 1.1 | 3.7 | 5.6 | 0.7 | 1.3 |
| 1cdg | 2.0 | 2.0 | 2.0 | 2.5 | 2.0 | 2.6 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1ckp | 0.9 | 1.2 | 3.2 | 5.2 | 0.5 | 1.0 |
| 1cle | 3.6 | 5.1 | 4.2 | 4.7 | 3.0 | 3.1 |
| 1com | 1.6 | 3.9 | 4.8 | 8.3 | 0.9 | 1.9 |
| 1coy | 0.7 | 0.8 | 0.5 | 0.9 | 0.6 | 0.8 |
| 1cqp | 0.7 | 1.0 | 1.1 | 1.6 | 1.0 | 1.5 |
| 1cvu | 0.9 | 1.1 | 1.2 | 1.7 | 1.3 | 1.4 |
| 1cx2 | 1.5 | 1.7 | 1.6 | 1.7 | 1.5 | 1.6 |
| 1d0l | 1.3 | 1.7 | 3.3 | 5.4 | 1.1 | 1.5 |
| 1d3h | 1.5 | 1.9 | 1.3 | 7.6 | 1.5 | 1.9 |
| 1d4p | 1.0 | 1.3 | 1.9 | 7.9 | 1.0 | 1.4 |
| 1dbb | 0.7 | 4.4 | 3.0 | 5.0 | 0.8 | 3.5 |
| 1dbj | 0.4 | 0.8 | 0.9 | 1.3 | 0.4 | 0.5 |
| 1dd7 | 2.3 | 5.1 | 3.8 | 6.3 | 1.8 | 4.0 |
| 1dg5 | 1.4 | 2.9 | 2.5 | 4.6 | 0.7 | 0.9 |
| 1did | 1.0 | 5.7 | 4.9 | 7.7 | 1.0 | 5.7 |
| 1dmp | 3.5 | 5.0 | 3.4 | 4.5 | 3.5 | 4.2 |
| 1dog | 1.6 | 2.2 | 1.9 | 8.4 | 0.2 | 0.3 |
| 1dr1 | 0.4 | 2.4 | 3.6 | 3.6 | 0.3 | 2.3 |
| 1dwb | 0.5 | 0.5 | 0.4 | 2.0 | 0.4 | 0.4 |
| 1dwc | 0.9 | 0.9 | 3.3 | 5.1 | 0.9 | 0.9 |
| 1dwd | 2.2 | 3.7 | 3.6 | 7.5 | 1.3 | 1.9 |
| 1dy9 | 1.6 | 1.6 | 3.5 | 5.6 | 1.4 | 1.5 |
| 1eap | 2.0 | 4.1 | 2.5 | 3.7 | 2.3 | 4.1 |
| 1ebg | 0.5 | 2.0 | 8.7 | 9.9 | 0.4 | 1.6 |
| 1ei1 | 0.4 | 0.5 | 8.2 | 9.7 | 0.5 | 0.5 |
| 1ejn | 1.5 | 7.0 | 1.2 | 4.7 | 1.7 | 3.9 |
| 1eoc | 2.0 | 4.5 | 5.4 | 7.2 | 1.8 | 2.4 |
| 1epb | 1.0 | 1.3 | 0.9 | 1.2 | 1.0 | 1.2 |
| 1etr | 0.7 | 0.7 | 6.1 | 6.8 | 0.8 | 0.9 |
| 1ets | 3.7 | 3.7 | 3.7 | 4.1 | 4.0 | 4.2 |
| 1f0r | 2.2 | 4.6 | 2.2 | 4.0 | 2.4 | 3.3 |
| 1f0s | 2.5 | 4.9 | 1.6 | 3.4 | 1.9 | 5.0 |
| 1fen | 0.6 | 0.7 | 0.5 | 0.6 | 0.6 | 0.7 |
| 1fgi | 0.4 | 0.6 | 2.9 | 4.7 | 0.5 | 0.5 |
| 1fkg | 1.5 | 1.6 | 1.7 | 2.4 | 1.3 | 1.3 |
| 1fl3 | 0.5 | 1.0 | 0.8 | 1.4 | 0.8 | 1.2 |
| 1flr | 2.2 | 4.5 | 2.8 | 4.9 | 2.2 | 4.5 |
| 1frp | 0.4 | 1.1 | 5.8 | 9.8 | 0.4 | 0.5 |
| 1glp | 1.0 | 5.0 | 5.3 | 5.8 | 1.1 | 1.4 |
| 1glq | 2.5 | 6.7 | 5.1 | 6.8 | 2.0 | 2.1 |
| 1hak | 2.2 | 3.8 | 2.3 | 6.2 | 1.9 | 3.7 |
| 1hdc | 0.9 | 1.2 | 0.9 | 1.3 | 0.8 | 1.0 |
| 1hfc | 2.6 | 3.4 | 2.4 | 4.7 | 2.2 | 2.4 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1hiv | 2.2 | 3.5 | 1.3 | 1.3 | 2.5 | 2.5 |
| 1hpv | 1.0 | 1.4 | 1.1 | 1.2 | 1.3 | 1.3 |
| 1hri | 0.9 | 2.5 | 0.8 | 3.8 | 0.7 | 0.9 |
| 1htf | 1.9 | 3.9 | 1.8 | 3.0 | 1.5 | 2.2 |
| 1hyt | 2.5 | 2.8 | 2.4 | 2.9 | 2.4 | 3.2 |
| 1ibg | 0.8 | 1.8 | 1.8 | 2.2 | 0.7 | 0.7 |
| 1imb | 2.8 | 6.5 | 5.4 | 11.8 | 2.6 | 4.2 |
| 1ivb | 1.7 | 3.8 | 2.4 | 4.3 | 1.8 | 1.8 |
| 1kel | 1.0 | 1.3 | 1.8 | 1.8 | 1.4 | 1.4 |
| 1lah | 0.4 | 1.1 | 1.5 | 2.5 | 0.5 | 1.1 |
| 1lcp | 0.8 | 0.9 | 1.2 | 8.2 | 0.6 | 0.9 |
| 1lic | 1.7 | 2.7 | 2.7 | 3.9 | 1.2 | 2.6 |
| 1lpm | 1.9 | 2.4 | 1.6 | 4.2 | 1.2 | 2.3 |
| 1lst | 1.1 | 1.4 | 0.9 | 1.8 | 1.0 | 1.6 |
| 1mcq | 0.7 | 1.7 | 0.7 | 1.2 | 0.7 | 2.5 |
| 1mdr | 1.1 | 3.0 | 2.4 | 4.1 | 1.2 | 2.0 |
| 1mld | 1.5 | 1.7 | 3.6 | 4.1 | 1.4 | 1.8 |
| 1mrg | 1.2 | 2.5 | 5.3 | 10.5 | 1.1 | 1.3 |
| 1mrk | 0.8 | 1.1 | 5.7 | 10.5 | 0.8 | 1.2 |
| 1mts | 0.9 | 1.3 | 1.4 | 2.2 | 1.1 | 1.2 |
| 1mup | 0.9 | 1.4 | 1.2 | 1.5 | 0.9 | 1.2 |
| 1nco | 1.3 | 2.2 | 3.6 | 3.8 | 0.9 | 2.1 |
| 1ngp | 1.1 | 3.6 | 2.9 | 5.0 | 1.0 | 3.7 |
| 1okl | 0.5 | 2.2 | 3.4 | 5.5 | 1.5 | 2.2 |
| 1pdz | 1.4 | 3.7 | 2.7 | 3.2 | 1.4 | 2.0 |
| 1phd | 1.6 | 4.2 | 1.5 | 6.7 | 1.5 | 2.6 |
| 1phg | 2.5 | 4.2 | 2.8 | 6.4 | 2.4 | 2.7 |
| 1poc | 0.8 | 1.0 | 1.3 | 2.1 | 0.9 | 0.9 |
| 1ppc | 2.0 | 3.3 | 3.5 | 7.2 | 1.2 | 2.0 |
| 1pph | 4.9 | 5.6 | 5.2 | 6.1 | 4.8 | 5.7 |
| 1ptv | 4.4 | 8.0 | 4.1 | 9.8 | 4.1 | 8.5 |
| 1qcf | 0.8 | 1.3 | 3.8 | 9.5 | 1.3 | 1.3 |
| 1qpe | 0.7 | 1.2 | 1.7 | 1.7 | 1.1 | 1.3 |
| 1qpq | 1.2 | 1.5 | 2.6 | 12.1 | 0.8 | 1.2 |
| 1rnt | 0.8 | 1.3 | 3.9 | 7.0 | 0.8 | 0.8 |
| 1rob | 0.9 | 0.9 | 4.6 | 8.8 | 0.7 | 1.1 |
| 1rt2 | 0.6 | 0.7 | 0.5 | 0.6 | 0.5 | 1.1 |
| 1slt | 1.3 | 4.7 | 2.1 | 6.3 | 1.0 | 1.8 |
| 1snc | 0.9 | 1.9 | 4.7 | 5.8 | 0.8 | 4.6 |
| 1srj | 0.8 | 1.9 | 3.4 | 3.4 | 0.7 | 1.0 |
| 1tdb | 1.6 | 3.4 | 3.8 | 8.7 | 1.1 | 1.6 |
| 1tmn | 1.8 | 2.1 | 2.4 | 2.7 | 1.4 | 3.0 |
| 1tng | 0.1 | 0.1 | 3.5 | 3.7 | 0.1 | 0.2 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1tnh | 1.4 | 1.8 | 1.3 | 1.6 | 1.4 | 1.7 |
| 1tni | 1.4 | 2.8 | 1.4 | 2.0 | 1.6 | 2.6 |
| 1tpp | 5.6 | 6.0 | 6.3 | 11.2 | 5.5 | 5.8 |
| 1tyl | 0.9 | 1.5 | 1.5 | 3.0 | 0.7 | 0.8 |
| 1ukz | 0.5 | 2.4 | 5.1 | 7.7 | 0.5 | 0.7 |
| 1ulb | 0.5 | 1.3 | 2.7 | 7.8 | 0.4 | 1.3 |
| 1uvs | 1.5 | 1.9 | 3.8 | 6.0 | 1.7 | 2.4 |
| 1uvt | 2.9 | 3.2 | 3.1 | 3.5 | 3.5 | 4.7 |
| 1vgc | 1.1 | 2.0 | 1.1 | 1.5 | 1.1 | 1.5 |
| 1xid | 1.4 | 2.3 | 1.3 | 1.6 | 1.3 | 1.4 |
| 1xie | 1.9 | 4.3 | 8.2 | 12.2 | 1.1 | 2.2 |
| 1ydr | 0.5 | 0.6 | 1.0 | 1.6 | 0.5 | 0.6 |
| 1yee | 1.2 | 1.2 | 2.3 | 3.7 | 1.0 | 1.2 |
| 25c8 | 1.7 | 2.1 | 2.4 | 4.3 | 1.5 | 1.7 |
| 2aad | 0.6 | 0.8 | 3.8 | 6.9 | 0.6 | 0.8 |
| 2ada | 0.4 | 0.5 | 2.9 | 11.1 | 0.5 | 0.5 |
| 2cht | 1.4 | 3.1 | 2.4 | 8.7 | 1.1 | 1.6 |
| 2cmd | 1.3 | 1.8 | 2.8 | 4.1 | 1.3 | 2.1 |
| 2cpp | 0.5 | 2.1 | 1.9 | 5.5 | 0.2 | 0.3 |
| 2ctc | 2.3 | 2.6 | 2.2 | 2.7 | 2.3 | 2.8 |
| 2fox | 1.1 | 1.5 | 6.1 | 7.9 | 0.6 | 1.5 |
| 2gbp | 0.5 | 0.7 | 2.1 | 14.6 | 0.3 | 0.4 |
| 2h4n | 1.6 | 1.7 | 1.8 | 3.9 | 1.6 | 1.8 |
| 2ifb | 1.0 | 1.7 | 1.8 | 2.6 | 1.0 | 1.8 |
| 2mcp | 0.9 | 1.6 | 4.2 | 6.5 | 0.8 | 1.2 |
| 2pk4 | 1.1 | 2.1 | 1.2 | 2.3 | 1.3 | 2.5 |
| 2r07 | 0.6 | 0.9 | 0.6 | 1.3 | 0.6 | 0.8 |
| 2yhx | 0.8 | 2.9 | 1.8 | 6.2 | 0.7 | 0.8 |
| 2ypi | 1.0 | 1.5 | 3.0 | 10.3 | 0.9 | 1.5 |
| 3ert | 1.0 | 1.2 | 0.9 | 1.2 | 0.9 | 1.4 |
| 3gpb | 1.1 | 2.1 | 3.0 | 13.0 | 1.1 | 2.0 |
| 3hvt | 0.5 | 0.7 | 0.4 | 0.8 | 0.7 | 0.9 |
| 4aah | 0.5 | 0.8 | 4.0 | 5.6 | 0.5 | 3.8 |
| 4cox | 0.4 | 0.6 | 0.7 | 0.9 | 0.5 | 0.5 |
| 4cts | 2.1 | 3.7 | 3.9 | 8.2 | 1.5 | 1.6 |
| 4dfr | 2.9 | 8.4 | 3.5 | 5.3 | 2.4 | 3.5 |
| 4est | 2.1 | 2.9 | 2.3 | 2.9 | 2.3 | 3.5 |
| 4fbp | 0.3 | 0.5 | 5.7 | 10.8 | 0.3 | 0.4 |
| 4lbd | 1.0 | 1.0 | 1.0 | 1.1 | 1.0 | 1.0 |
| 4phv | 3.7 | 5.2 | 3.4 | 4.9 | 3.5 | 4.2 |
| 5abp | 0.5 | 0.5 | 2.1 | 11.5 | 0.4 | 0.5 |
| 5cpp | 1.9 | 1.9 | 1.9 | 5.4 | 1.9 | 1.9 |
| 6rnt | 1.5 | 2.1 | 6.7 | 10.8 | 1.0 | 1.1 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 6rsa | 0.4 | 0.8 | 2.6 | 10.1 | 0.4 | 0.9 |
| 7tim | 1.1 | 1.7 | 3.6 | 4.0 | 0.8 | 1.7 |
| **Averages** | 1.3 | 2.4 | 2.8 | 5.2 | 1.3 | 1.9 |

**Table 2:**

Details of temperatures and molecular dynamics steps for each of the simulated annealing protocols.

| **Protocol** | | **Phase 1** | **Phase 2** | **Phase 3** | **Phase4** |
|---|---|---|---|---|---|
| *SA- 1 Grid* | Temps | 300 ➔ 700 | 700 | 700 ➔ 300 | 300 ➔ 50 |
| | Steps | 2,250 | 10,500 | 5,250 | 2,250 |
| *SA- 2Grids** | Temps | 300 ➔ 700 | 700 ➔ 300 | 500 ➔ 300 | 400 ➔ 300 |
| | Steps | 2,250 | 10,500 | 5,250 | 2,250 |

*Wu, G. S.; Robertson, D. H.; Brooks, C. L. III; Vieth, M. *J. Comput. Chem.* **2003**, *24*, 1549.

**Table 3:**

Results for HIV Reverse Transcriptase cross-docking trial, totaling 173 unique protein-ligand complexes. The MD+Minimization protocol was the only one used in this trial as it was the most successful docking protocol in the redocking trials. Reported are the lowest RMSD structure sampled and the lowest energy RMSD conformation.

| | | *Rigid CDOCKER* | | *Flexible CDOCKER* | |
|---|---|---|---|---|---|
| **Receptor PDBID** | **Ligand PDBID** | **Lowest RMSD** | **Lowest Energy** | **Lowest RMSD** | **Lowest Energy** |
| 1c1b | 1c1c | 0.9 | 6.0 | 1.0 | 1.6 |
| 1c1b | 1ep4 | 1.7 | 7.2 | 1.5 | 5.5 |
| 1c1b | 1rth | 0.9 | 6.2 | 0.9 | 6.2 |
| 1c1b | 1vru | 1.1 | 2.2 | 0.9 | 5.6 |
| 1c1b | 2be2 | 1.3 | 1.8 | 1.4 | 1.5 |
| 1c1b | 2rf2 | 2.6 | 3.4 | 2.6 | 2.9 |
| 1c1b | 2rki | 1.9 | 2.2 | 1.9 | 5.7 |
| 1c1b | 3dlg | 1.2 | 1.3 | 2.4 | 8.9 |
| 1c1b | 3dol | 2.5 | 10.8 | 3.8 | 10.6 |
| 1c1b | 3dya | 2.9 | 3.0 | 2.9 | 3.7 |
| 1c1c | 1c1b | 0.8 | 2.0 | 0.8 | 2.1 |
| 1c1c | 1ep4 | 2.0 | 7.0 | 1.7 | 6.1 |
| 1c1c | 1rt2 | 0.7 | 0.7 | 0.8 | 1.6 |
| 1c1c | 1rth | 1.2 | 14.6 | 1.1 | 6.3 |
| 1c1c | 1vru | 1.5 | 5.2 | 1.5 | 5.5 |

| | | | | | |
|---|---|---|---|---|---|
| 1c1c | 2be2 | 1.0 | 2.2 | 1.0 | 1.3 |
| 1c1c | 2rf2 | 2.2 | 6.3 | 2.1 | 6.1 |
| 1c1c | 2rki | 1.8 | 2.5 | 1.7 | 7.8 |
| 1ep4 | 1c1b | 0.9 | 1.3 | 1.4 | 2.8 |
| 1ep4 | 1rt2 | 1.3 | 2.0 | 1.4 | 5.1 |
| 1ep4 | 1rth | 1.2 | 12.4 | 1.7 | 4.6 |
| 1ep4 | 1vru | 1.6 | 5.1 | 2.1 | 4.9 |
| 1ep4 | 2be2 | 1.5 | 1.6 | 1.3 | 2.0 |
| 1ep4 | 2rf2 | 3.2 | 5.8 | 3.3 | 5.8 |
| 1ep4 | 2rki | 2.8 | 5.0 | 3.0 | 5.7 |
| 1ikw | 1c1b | 4.1 | 5.7 | 4.3 | 7.2 |
| 1ikw | 1c1c | 4.2 | 5.9 | 4.7 | 7.0 |
| 1ikw | 1ep4 | 3.7 | 6.6 | 3.9 | 6.5 |
| 1ikw | 1vru | 4.9 | 5.5 | 4.8 | 6.5 |
| 1ikw | 2be2 | 7.1 | 10.4 | 6.7 | 10.8 |
| 1ikw | 2rf2 | 4.4 | 7.3 | 4.4 | 6.7 |
| 1ikw | 2rki | 5.2 | 8.8 | 5.2 | 8.8 |
| 1ikw | 3dol | 7.9 | 10.0 | 7.9 | 10.6 |
| 1rt2 | 1ep4 | 2.2 | 13.6 | 2.1 | 2.8 |
| 1rt2 | 1rth | 1.5 | 14.9 | 4.2 | 14.7 |
| 1rt2 | 1vru | 1.8 | 14.9 | 1.6 | 5.1 |
| 1rt2 | 2be2 | 1.4 | 13.1 | 1.3 | 2.4 |
| 1rt2 | 2rf2 | 2.1 | 15.4 | 2.1 | 2.2 |
| 1rt2 | 2rki | 1.7 | 13.2 | 1.8 | 2.8 |
| 1rt2 | 3dlg | 1.0 | 12.8 | 0.8 | 1.6 |
| 1rth | 1c1b | 0.9 | 4.1 | 0.9 | 2.1 |
| 1rth | 1c1c | 1.3 | 5.4 | 1.2 | 1.7 |
| 1rth | 1rt2 | 2.4 | 7.8 | 2.8 | 7.3 |
| 1rth | 1vru | 1.3 | 4.6 | 0.8 | 5.3 |
| 1rth | 2be2 | 3.1 | 6.6 | 2.6 | 6.3 |
| 1rth | 2rki | 2.8 | 7.7 | 2.8 | 7.9 |
| 1s1t | 1c1b | 0.8 | 1.2 | 1.1 | 1.5 |
| 1s1t | 1c1c | 1.0 | 6.2 | 1.1 | 5.5 |
| 1s1t | 1rt2 | 2.6 | 7.8 | 2.5 | 7.0 |
| 1s1t | 1rth | 1.0 | 13.8 | 1.1 | 6.1 |
| 1s1t | 1vru | 1.2 | 2.3 | 0.9 | 5.2 |
| 1s1t | 2be2 | 2.3 | 6.3 | 2.2 | 6.8 |
| 1s1t | 2rf2 | 1.7 | 1.9 | 1.4 | 4.7 |
| 1s1t | 2rki | 1.7 | 7.6 | 2.4 | 7.4 |
| 1s1t | 3dlg | 3.8 | 11.4 | 4.4 | 8.5 |
| 1vrt | 1c1b | 1.0 | 5.1 | 1.0 | 5.8 |
| 1vrt | 1c1c | 1.1 | 3.2 | 1.1 | 2.9 |
| 1vrt | 1rt2 | 2.7 | 7.3 | 3.0 | 7.3 |

| | | | | | |
|---|---|---|---|---|---|
| 1vrt | 1rth | 0.7 | 14.5 | 0.6 | 6.1 |
| 1vrt | 2be2 | 2.6 | 6.5 | 2.4 | 6.5 |
| 1vrt | 2rf2 | 1.2 | 4.5 | 1.5 | 4.5 |
| 1vrt | 2rki | 2.5 | 8.2 | 2.8 | 6.2 |
| 1vru | 1c1b | 1.0 | 5.0 | 1.0 | 1.9 |
| 1vru | 1c1c | 1.2 | 3.1 | 1.2 | 5.0 |
| 1vru | 1rt2 | 3.3 | 7.9 | 2.9 | 7.1 |
| 1vru | 1rth | 0.8 | 13.0 | 0.7 | 1.3 |
| 1vru | 2be2 | 3.2 | 6.3 | 2.9 | 6.5 |
| 1vru | 2rf2 | 1.5 | 4.5 | 1.4 | 5.8 |
| 2be2 | 1c1b | 1.3 | 1.4 | 1.2 | 5.0 |
| 2be2 | 1c1c | 1.2 | 1.2 | 1.2 | 1.4 |
| 2be2 | 1rt2 | 1.2 | 13.1 | 1.1 | 1.6 |
| 2be2 | 1rth | 1.9 | 13.4 | 2.3 | 5.9 |
| 2be2 | 2rf2 | 2.2 | 5.8 | 2.3 | 6.8 |
| 2hnd | 1c1b | 1.3 | 5.7 | 1.3 | 1.3 |
| 2hnd | 1c1c | 1.3 | 5.5 | 1.1 | 5.5 |
| 2hnd | 1rth | 1.3 | 13.9 | 0.8 | 1.7 |
| 2hnd | 2rf2 | 1.0 | 4.4 | 1.0 | 4.5 |
| 2hny | 1c1b | 1.3 | 5.8 | 1.2 | 5.5 |
| 2hny | 1c1c | 1.2 | 3.3 | 1.2 | 3.1 |
| 2hny | 1rth | 1.2 | 4.4 | 1.0 | 1.3 |
| 2hny | 2rf2 | 0.9 | 4.3 | 0.9 | 4.5 |
| 2hny | 3dlg | 4.6 | 9.5 | 4.8 | 7.8 |
| 2hny | 3dol | 6.9 | 11.4 | 6.5 | 11.2 |
| 2ops | 1c1c | 1.3 | 5.4 | 1.1 | 1.6 |
| 2ops | 1rt2 | 2.2 | 6.2 | 2.7 | 6.3 |
| 2ops | 1rth | 1.1 | 14.3 | 0.7 | 6.0 |
| 2ops | 2be2 | 2.7 | 6.5 | 3.1 | 6.8 |
| 2ops | 2rf2 | 1.6 | 4.6 | 1.5 | 4.5 |
| 2ops | 3dlg | 3.9 | 8.5 | 4.1 | 9.4 |
| 2rf2 | 1c1b | 1.5 | 13.9 | 1.3 | 5.4 |
| 2rf2 | 1c1c | 1.1 | 5.5 | 1.3 | 5.5 |
| 2rf2 | 1ep4 | 3.4 | 9.3 | 3.2 | 7.3 |
| 2rf2 | 1rt2 | 2.8 | 7.6 | 3.0 | 7.9 |
| 2rf2 | 1rth | 1.4 | 16.0 | 1.6 | 6.0 |
| 2rf2 | 1vru | 1.8 | 1.8 | 1.6 | 5.0 |
| 2rf2 | 2be2 | 3.8 | 13.7 | 3.5 | 7.2 |
| 2rf2 | 2rki | 2.7 | 14.9 | 2.6 | 4.2 |
| 2rf2 | 3dlg | 4.2 | 13.1 | 4.3 | 10.2 |
| 2rf2 | 3dol | 6.9 | 13.7 | 6.2 | 12.3 |
| 2rf2 | 3dya | 3.6 | 14.2 | 3.6 | 7.1 |
| 2rki | 1c1b | 1.6 | 12.2 | 1.6 | 2.5 |

| | | | | | |
|---|---|---|---|---|---|
| 2rki | 1c1c | 1.6 | 5.7 | 1.3 | 5.5 |
| 2rki | 1ep4 | 2.4 | 10.9 | 2.3 | 7.5 |
| 2rki | 1rt2 | 1.5 | 13.3 | 1.2 | 1.6 |
| 2rki | 1rth | 2.3 | 13.7 | 2.6 | 6.0 |
| 2rki | 1vru | 2.1 | 6.6 | 3.1 | 4.3 |
| 2rki | 2be2 | 1.7 | 12.2 | 2.0 | 2.1 |
| 2rki | 2rf2 | 1.5 | 12.8 | 1.2 | 4.7 |
| 2rki | 3dlg | 1.5 | 4.8 | 1.5 | 1.5 |
| 2rki | 3dol | 2.5 | 10.8 | 2.3 | 2.3 |
| 2rki | 3dya | 1.6 | 11.6 | 1.5 | 8.7 |
| 2zd1 | 1c1b | 1.5 | 2.7 | 1.5 | 1.6 |
| 2zd1 | 1c1c | 1.8 | 6.7 | 1.9 | 6.6 |
| 2zd1 | 1ep4 | 3.3 | 6.8 | 3.3 | 6.4 |
| 2zd1 | 1rt2 | 3.0 | 7.7 | 3.0 | 7.9 |
| 2zd1 | 1rth | 1.1 | 5.4 | 0.9 | 6.2 |
| 2zd1 | 1vru | 1.6 | 2.3 | 1.8 | 2.4 |
| 2zd1 | 2be2 | 3.1 | 7.6 | 2.4 | 6.0 |
| 2zd1 | 2rf2 | 2.5 | 5.0 | 2.4 | 5.1 |
| 2zd1 | 2rki | 3.0 | 8.2 | 3.0 | 8.1 |
| 2zd1 | 3dlg | 4.6 | 9.8 | 4.3 | 9.2 |
| 2zd1 | 3dol | 6.5 | 11.7 | 6.6 | 11.4 |
| 2zd1 | 3dya | 3.4 | 6.7 | 3.4 | 6.5 |
| 3bgr | 1c1b | 1.4 | 3.1 | 1.4 | 6.1 |
| 3bgr | 1c1c | 1.9 | 7.0 | 1.9 | 6.7 |
| 3bgr | 1ep4 | 2.8 | 8.7 | 2.8 | 6.2 |
| 3bgr | 1rt2 | 2.5 | 9.0 | 3.0 | 7.8 |
| 3bgr | 1rth | 1.1 | 6.1 | 1.0 | 1.5 |
| 3bgr | 1vru | 1.5 | 3.3 | 1.7 | 4.0 |
| 3bgr | 2be2 | 2.2 | 5.6 | 2.0 | 5.6 |
| 3bgr | 2rf2 | 3.0 | 5.2 | 2.9 | 5.1 |
| 3bgr | 2rki | 2.8 | 10.3 | 3.1 | 8.2 |
| 3bgr | 3dol | 6.5 | 13.0 | 6.2 | 9.4 |
| 3bgr | 3dya | 2.3 | 6.4 | 2.9 | 6.4 |
| 3dle | 1c1b | 1.2 | 14.3 | 1.3 | 6.0 |
| 3dle | 1c1c | 1.5 | 6.0 | 1.3 | 4.8 |
| 3dle | 1ep4 | 2.3 | 13.2 | 2.2 | 2.7 |
| 3dle | 1rt2 | 0.7 | 12.4 | 0.5 | 0.8 |
| 3dle | 1rth | 3.7 | 14.6 | 4.8 | 5.0 |
| 3dle | 1vru | 3.2 | 5.3 | 3.8 | 5.2 |
| 3dle | 2be2 | 1.4 | 1.7 | 1.3 | 2.5 |
| 3dle | 2rf2 | 2.3 | 5.0 | 2.7 | 7.4 |
| 3dle | 2rki | 2.4 | 15.4 | 2.0 | 2.8 |
| 3dle | 3dol | 1.1 | 4.4 | 1.7 | 2.2 |

| | | | | | |
|---|---|---|---|---|---|
| 3dle | 3dya | 2.5 | 11.9 | 2.4 | 2.5 |
| 3dlg | 1c1b | 1.3 | 13.9 | 1.7 | 5.2 |
| 3dlg | 1c1c | 1.2 | 14.6 | 1.6 | 6.3 |
| 3dlg | 1ep4 | 2.2 | 13.7 | 2.1 | 5.6 |
| 3dlg | 1rt2 | 1.0 | 13.4 | 1.0 | 2.1 |
| 3dlg | 1rth | 1.9 | 12.4 | 6.0 | 12.5 |
| 3dlg | 1vru | 2.7 | 14.8 | 3.5 | 4.5 |
| 3dlg | 2be2 | 1.2 | 1.5 | 1.0 | 1.5 |
| 3dlg | 2rf2 | 2.3 | 5.0 | 3.7 | 5.6 |
| 3dlg | 2rki | 2.2 | 11.9 | 2.2 | 6.8 |
| 3dlg | 3dol | 1.4 | 2.4 | 1.7 | 2.5 |
| 3dlg | 3dya | 2.5 | 3.6 | 2.3 | 2.5 |
| 3dol | 1c1b | 4.7 | 13.5 | 2.6 | 2.6 |
| 3dol | 1c1c | 4.4 | 5.5 | 4.8 | 5.7 |
| 3dol | 1ep4 | 3.0 | 12.8 | 4.0 | 8.4 |
| 3dol | 1rt2 | 1.9 | 11.8 | 2.2 | 2.6 |
| 3dol | 1vru | 5.4 | 15.8 | 4.8 | 6.8 |
| 3dol | 2be2 | 2.4 | 2.4 | 2.3 | 2.9 |
| 3dol | 2rki | 3.4 | 13.3 | 3.2 | 4.3 |
| 3dol | 3dlg | 1.6 | 2.7 | 1.4 | 1.4 |
| 3dol | 3dya | 3.2 | 4.1 | 1.5 | 1.5 |
| 3dya | 1c1b | 2.3 | 2.5 | 2.2 | 2.2 |
| 3dya | 1c1c | 2.1 | 6.6 | 1.9 | 6.5 |
| 3dya | 1ep4 | 2.1 | 3.0 | 2.0 | 2.8 |
| 3dya | 1rt2 | 2.3 | 2.9 | 2.1 | 2.4 |
| 3dya | 1rth | 3.0 | 13.6 | 3.2 | 6.7 |
| 3dya | 1vru | 3.3 | 6.0 | 3.9 | 5.8 |
| 3dya | 2be2 | 1.3 | 2.3 | 1.4 | 2.3 |
| 3dya | 2rf2 | 1.9 | 2.7 | 1.9 | 6.4 |
| 3dya | 2rki | 2.2 | 2.7 | 2.0 | 2.3 |
| **Averages** | | 2.3 | 7.7 | 2.3 | 5.2 |

**Table 4:**

HIV Reverse transcriptase cross-docking results with comparison to results as published by Rizzo et al.

| | | %Found | %Scored |
|---|---|---|---|
| **131 Unique Complexes** | Flexible CDOCKER | 47.3 | 19.1 |
| | Rigid CDOCKER | 48.1 | 10.7 |
| **61 Overlap Complexes** | Flexible CDOCKER | 63.9 | 24.6 |
| | Rigid CDOCKER | 65.6 | 14.8 |
| | DOCK 6* | - | 66.7 |
| **70 Complexes** | Flexible CDOCKER | 32.9 | 14.3 |
| **"Non-viable Pairings"** | Rigid CDOCKER | 32.9 | 7.1 |

* Allen, W. J.; Balius, T. E.; Mukherjee, S.; Brozell, S. R.; Moustakas, D. T.; Lang, P. T.; Case, D. A.; Kuntz, I. D.; Rizzo, R. C. *J. Comput. Chem.* 2015, *36*, 1132.

**Figure 1:**

The time taken by Flexible CDOCKER to generate 50 conformations for a single docking trial as distributed over the CCDC/Astex clean-set. All complexes took under 10 minutes for Rigid CDOCKER.

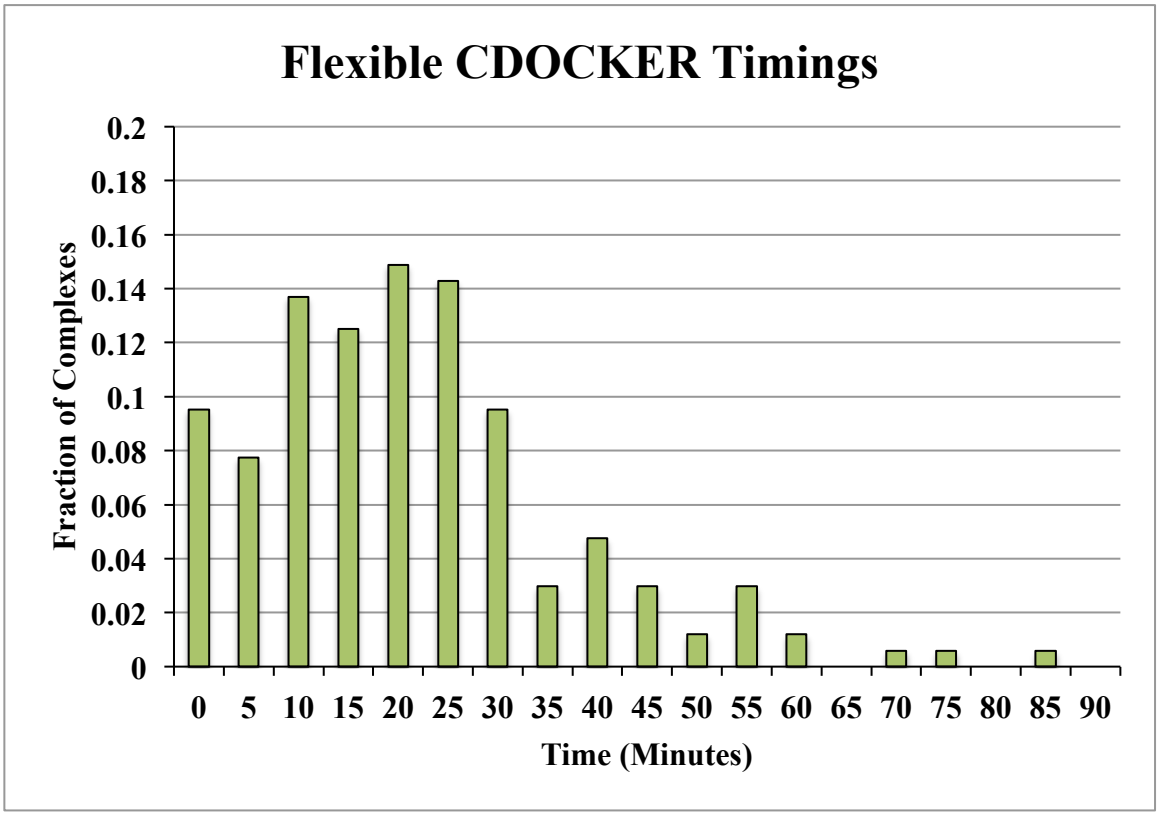

**Figure 2:**

The time taken for a single docking trial scales linearlly with the number of explicit atoms included in the flexible receptor docking.

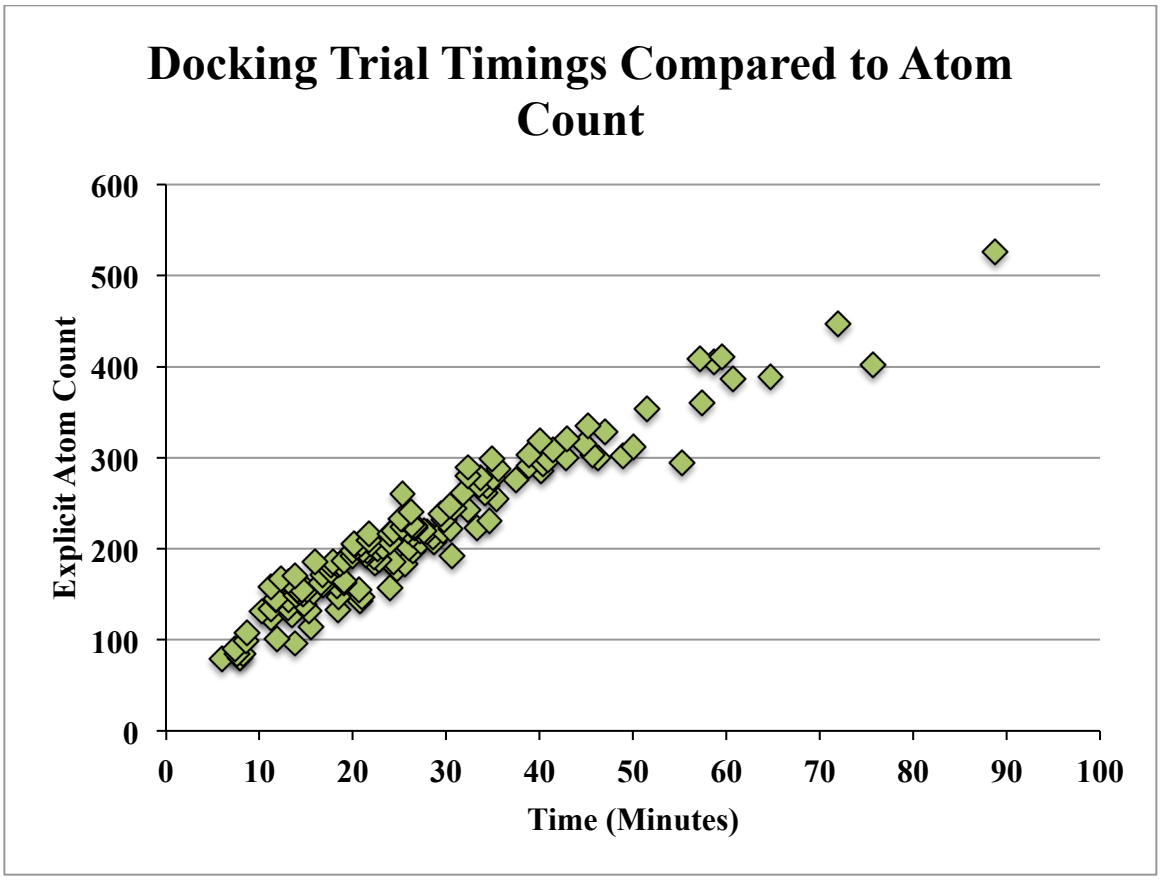

**Figure 3:**

(Supporting information Figure 1 in section "Flexible CDOCKER improves cross-docking accuracy: A case study")

Overlay of the predicted lowest free energy conformation found with Flexible CDOCKER and crystallographic structures of Alpha MMC. The ligand conformation (gray) has an RMSD of 1.42Å from the crystallographic conformation. The tyrosine residue on the protein from the apo structure (green) clashed with ligand causing a dihedral angle shift of this residue in the holo structure (blue). The tyrosine from the predicted conformation (magenta) remains near the apo dihedral angle, suggesting that this small shift is sufficient to achieve a low energy docked conformation.