Supplementary File:

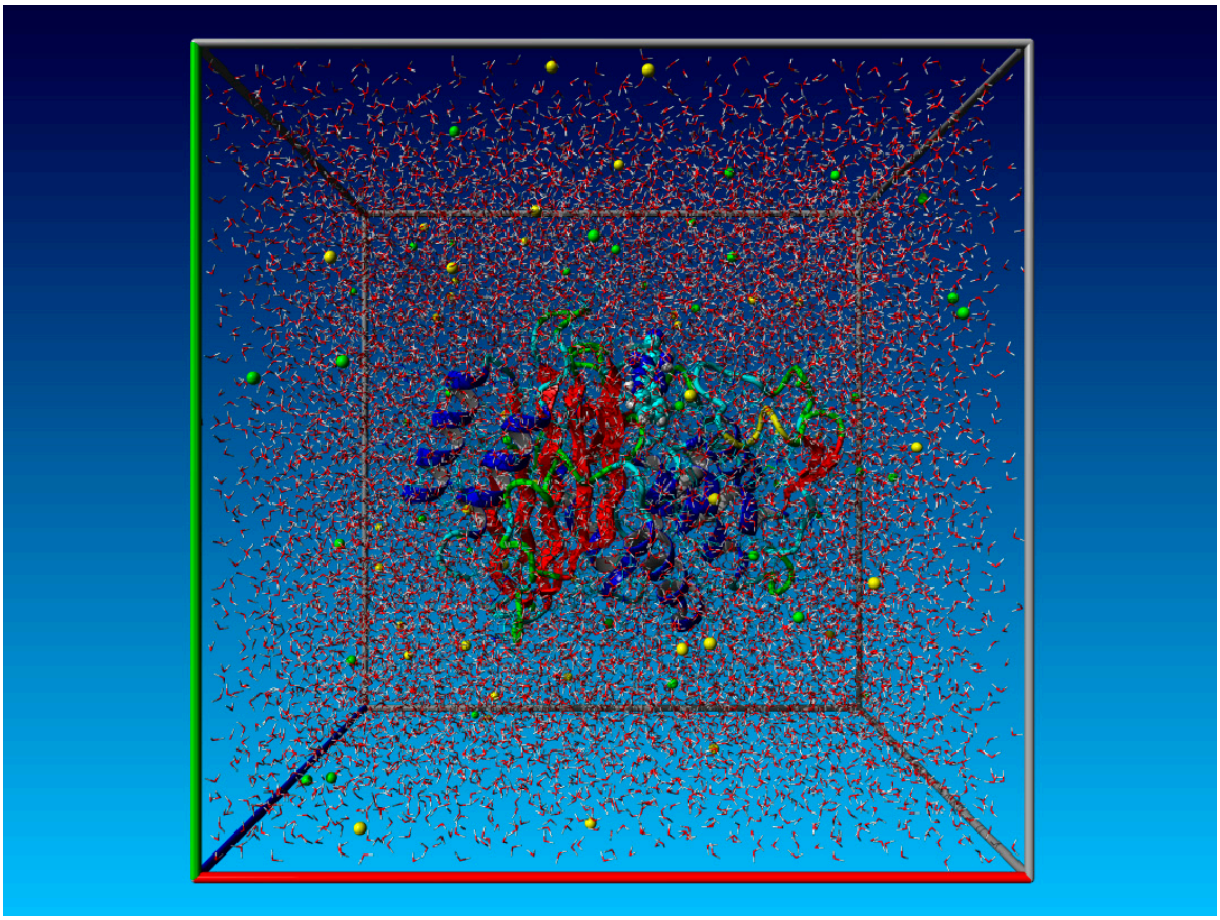

Figure S1: A ray-traced picture of the simulated system.

Supplementary text S2:

Global docking result analysis [YASARA log file]

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25 VINA docking runs of the ligand to the receptor yielded the following results,

sorted by binding energy [more positive energies indicate stronger binding, and negative energies mean no binding]

Run |Bind.energy[kcal/mol]|Dissoc. constant [pM]| Contacting receptor residues

----+--------------------+--------------------+----------------------------

001 | 000008.0940 | 00000001166861.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A SER 237 A GLY 238 A GLY 239

002 | 000008.0940 | 00000001166861.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A SER 237 A GLY 238 A GLY 239

003 | 000008.0040 | 00000001358282.8750 | A CYS 69 A SER 70 A ASN 104 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A LYS 234 A GLY 236 A SER 237 A GLY 238 A GLY 239

004 | 000008.0040 | 00000001358282.8750 | A CYS 69 A SER 70 A ASN 104 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A LYS 234 A GLY 236 A SER 237 A GLY 238 A GLY 239

005 | 000007.6640 | 00000002411090.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A ASN 170 A THR 171 A THR 216 A SER 237 A GLY 238 A GLY 239

006 | 000007.6640 | 00000002411090.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A ASN 170 A THR 171 A THR 216 A SER 237 A GLY 238 A GLY 239

007 | 000007.5340 | 00000003002650.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A ASN 170 A THR 171 A SER 237 A GLY 238 A GLY 239

008 | 000007.5340 | 00000003002650.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A ASN 170 A THR 171 A SER 237 A GLY 238 A GLY 239

009 | 000007.4520 | 00000003448351.7500 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A TYR 129 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A THR 216 A SER 237 A GLY 238 A GLY 239

010 | 000007.4520 | 00000003448351.7500 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A TYR 129 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A THR 216 A SER 237 A GLY 238 A GLY 239

011 | 000007.3570 | 00000004048065.2500 | A LEU 155 A GLY 156 A ASP 157 A GLU 158 A THR 159 A ALA 185 A GLN 188 A THR 189 A ARG 191 A ASN 192 A GLY 196 A LYS 197

012 | 000007.3420 | 00000004151859.5000 | A CYS 69 A SER 70 A ASN 104 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A LYS 234 A GLY 236 A SER 237 A GLY 238 A GLY 239

013 | 000007.3100 | 00000004382268.0000 | A CYS 69 A SER 70 A ASN 104 A SER 130 A ASN 132 A PRO 167 A ASN 170 A LYS 234 A THR 235 A GLY 236 A SER 237 A GLY 238 A GLY 239

014 | 000007.2420 | 00000004915227.5000 | A SER 70 A ASN 104 A TYR 105 A TYR 129 A SER 130 A ASN 132 A ASN 170 A THR 215 A THR 216 A LYS 234 A GLY 236 A SER 237

015 | 000007.2060 | 00000005223143.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A GLU 166 A ASN 170 A SER 237 A GLY 238 A GLY 239 A GLY 241 A PRO 268 A LYS 269 A ALA 270 A GLU 271

016 | 000007.2010 | 00000005267408.5000 | A ASP 63 A LEU 155 A GLY 156 A ASP 157 A GLU 158 A THR 159 A SER 182 A ARG 184 A ALA 185 A GLN 188 A THR 189 A ASN 192

017 | 000007.1300 | 00000005938007.0000 | A CYS 69 A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A SER 237 A GLY 238 A GLY 239

018 | 000007.1260 | 00000005978231.5000 | A GLY 43 A ARG 44 A ARG 65 A PHE 66 A PRO 174 A GLY 175 A PRO 177 A THR 180 A THR 264 A GLN 265 A PRO 266

019 | 000007.1050 | 00000006193925.0000 | A SER 70 A ASN 104 A TYR 105 A TYR 129 A SER 130 A ASN 132 A PRO 167 A ASN 170 A THR 216 A LYS 234 A THR 235 A GLY 236 A SER 237 A GLY 238 A GLY 239

020 | 000007.0200 | 00000007149436.0000 | A SER 70 A ASN 104 A TYR 105 A SER 130 A ASN 132 A ASN 170 A THR 215 A THR 216 A ALA 219 A LYS 234 A GLY 236 A SER 237 A ARG 274

021 | 000007.0010 | 00000007382423.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A ASN 170 A SER 237 A GLY 238 A GLY 239 A TYR 240 A GLY 241 A PRO 268 A LYS 269 A ALA 270

022 | 000007.0010 | 00000007382423.5000 | A ASP 63 A GLY 156 A ASP 157 A GLU 158 A THR 159 A PHE 160 A SER 182 A ARG 184 A ALA 185 A GLN 188 A THR 189

023 | 000006.9650 | 00000007844898.0000 | A ALA 79 A LYS 82 A LYS 83 A SER 86 A GLU 87 A VAL 142 A SER 147 A VAL 148 A PHE 151

024 | 000006.9500 | 00000008046045.0000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A THR 216 A ALA 218 A THR 235 A ARG 274

025 | 000006.7510 | 00000011257744.0000 | A ASP 63 A GLY 156 A ASP 157 A GLU 158 A THR 159 A SER 182 A ARG 184 A ALA 185 A GLN 188 A THR 189 A ASN 192

After clustering the 25 runs, the following 9 distinct complex conformations were found:

Clu |Bind.energy[kcal/mol]|Dissoc. constant [pM]| Contacting receptor residues

----+--------------------+--------------------+----------------------------

001 | 000008.0940 | 00000001166861.5000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A SER 237 A GLY 238 A GLY 239

002 | 000008.0040 | 00000001358282.8750 | A CYS 69 A SER 70 A ASN 104 A SER 130 A ASN 132 A PRO 167 A THR 168 A ASN 170 A THR 171 A LYS 234 A GLY 236 A SER 237 A GLY 238 A GLY 239

003 | 000007.3570 | 00000004048065.2500 | A LEU 155 A GLY 156 A ASP 157 A GLU 158 A THR 159 A ALA 185 A GLN 188 A THR 189 A ARG 191 A ASN 192 A GLY 196 A LYS 197

004 | 000007.2420 | 00000004915227.5000 | A SER 70 A ASN 104 A TYR 105 A TYR 129 A SER 130 A ASN 132 A ASN 170 A THR 215 A THR 216 A LYS 234 A GLY 236 A SER 237

005 | 000007.2010 | 00000005267408.5000 | A ASP 63 A LEU 155 A GLY 156 A ASP 157 A GLU 158 A THR 159 A SER 182 A ARG 184 A ALA 185 A GLN 188 A THR 189 A ASN 192

006 | 000007.1260 | 00000005978231.5000 | A GLY 43 A ARG 44 A ARG 65 A PHE 66 A PRO 174 A GLY 175 A PRO 177 A THR 180 A THR 264 A GLN 265 A PRO 266

007 | 000006.9650 | 00000007844898.0000 | A ALA 79 A LYS 82 A LYS 83 A SER 86 A GLU 87 A VAL 142 A SER 147 A VAL 148 A PHE 151

008 | 000006.9500 | 00000008046045.0000 | A SER 70 A LYS 73 A ASN 104 A TYR 105 A SER 130 A ASN 132 A THR 216 A ALA 218 A THR 235 A ARG 274

009 | 000006.7510 | 00000011257744.0000 | A ASP 63 A GLY 156 A ASP 157 A GLU 158 A THR 159 A SER 182 A ARG 184 A ALA 185 A GLN 188 A THR 189 A ASN 192

While the table above lists the best binding energy in each cluster, it is sometimes

helpful to also look at the energy spread [average and standard deviation], the

dissociation constant has been recalculated from the average binding energy:

Clu |Members|Bind.energy spread [kcal/mol]|Dissoc. constant [pM]

----+-------+----------------------------+--------------------

001 | 005 | 000007.4372+-000000.3851 | 00000003535841.6913

002 | 006 | 000007.4427+-000000.3015 | 00000003503367.8404

003 | 001 | 000007.3570+-000000.0000 | 00000004048367.3411

004 | 002 | 000007.1310+-000000.1110 | 00000005928420.4022

005 | 002 | 000007.1010+-000000.1000 | 00000006236330.6297

006 | 001 | 000007.1260+-000000.0000 | 00000005978663.4065

007 | 001 | 000006.9650+-000000.0000 | 00000007845448.8655

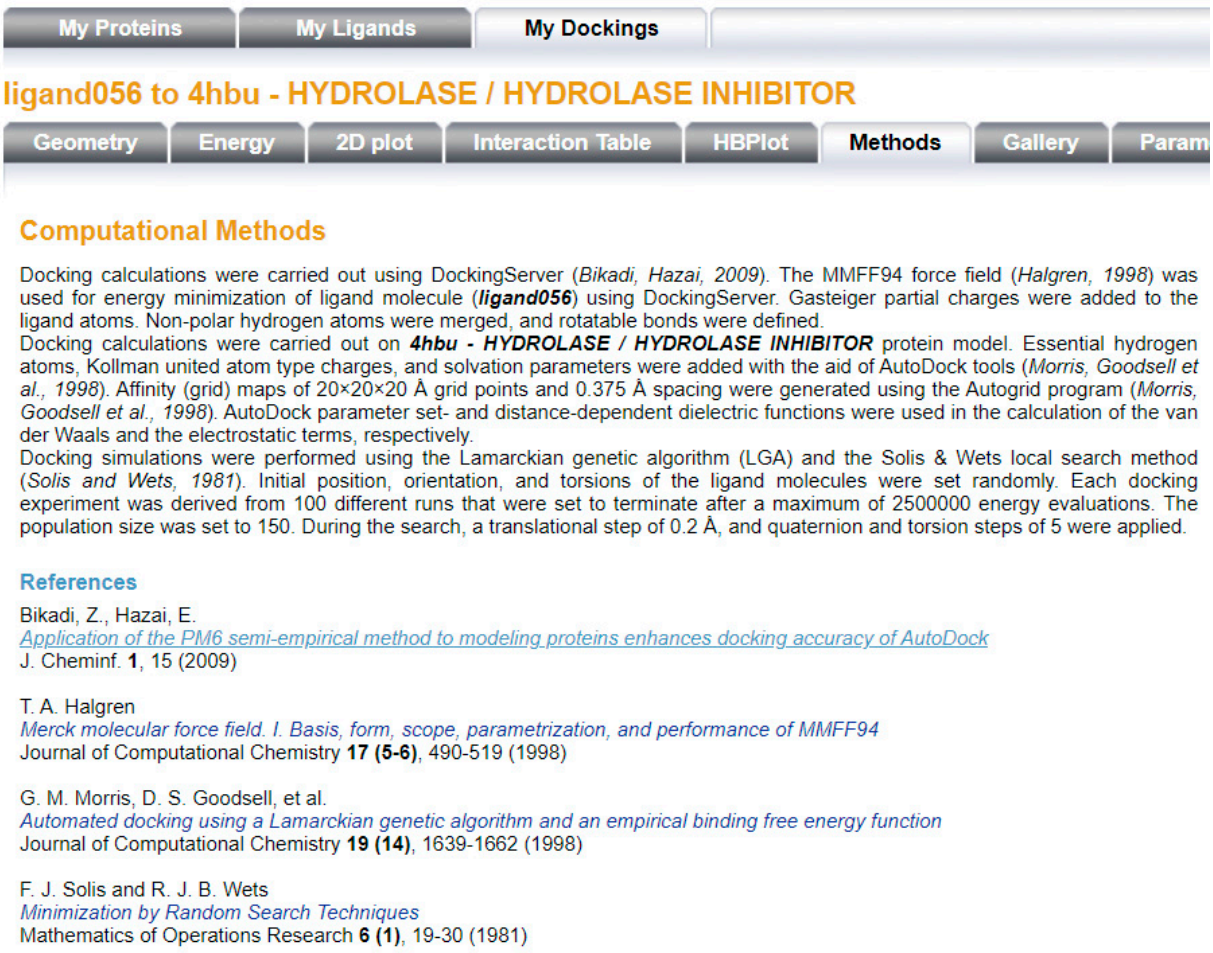
008 | 001 | 000006.9500+-000000.0000 | 00000008046613.2435

009 | 001 | 000006.7510+-000000.0000 | 00000011258514.7405

Point charges and dihedral barriers were obtained from the AMBER03 force field.

Supplementary text S3:

Methodology used by DockingServer:



##Note: The ligand having ID as MCULE-1352214421-0-56 has been referred as ‘ligand056’ for brevity in the screenshot shown above.

Docking Parameters

Advanced Settings

tstep	0.2
qstep	5.0
dstep	5.0
rmstol	2.0
ga_pop_size	150
ga_num_evals	2500000
ga_num_generations	540000
ga_run	100