Protein binding pocket optimization for virtual high-throughput screening (vHTS) drug discovery

Supporting Information

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Running title: Binding pocket optimization by Monte Carlo

Supplemental 1

Torsional angle sampling input

```
FILE Protein
TITL Protein for torsional angle sampling
TITL Solute molecules move, swap and torsions
HRDW VC32              ! 32-bit vector
SVVC SPCC 13.00     ! Solvent cutoff
SUVC SPGC 13.0       ! MI on the solute
SUUC SPGC 17.0       ! Molec-based MI for intrasolute
PBCN HEXG 99.00  99.00  99.00    !hexagonal PBC
TEMP 998
NSLV 0   ! Only solute
STEP  0.00   00.0   0.55    40.0 10
SVPT TIP3 TIP3         ! Solvent-solvent pot: CHARMM
SUPT CHRM
SETC DIEL 2.0
SLTA  SMPL MMC FILE (N)         !(N) is the number of atoms
PRMF CHRM par_all22_prot_na.inp
!Torsion pot param file
PART UNIF RAND RAND 1.0
!Torsion strategy and frequency
TORD INPT (N)         !Definiton of active torsions where (N) is the number of torsions
…                     !Definitions of cative torsions from mcs file
CNFG RANI ASCI
!SWAP 0.2              !Specify swapping frequency
TRAJ CHRM
RUNS 1000000 100  20000 1000 5000
STOP SLFT
```

Supplemental 2

Pocket size calculation input

```
FILE Protein
PRNT ECHO
HRDW VC32                    ! 32-bit vector
SVVC SPCC 9.05               ! Solvent cutoff
SUVC MIGC 0.0                ! MI on the solute
PBCN RECT 76.0 91.0 91.0   !Rectangular PBC
MOVE RAND                    ! Random selections
TEMP 298
NSLV 000
STEP  0.00   00.0   0.55    40.0  60
! slt, slv stepsize, slt move freq.
SVPT TIP3 TIP3
SUPT CHRM
SAMP METC 0.5
MOLD 1 (N)                   !Where (N) is the number of atoms
PFRD CHRM toppar/par_all36_prot.prm
SLTA  SMPL MMC FILE (N)    !Where (N) is the number of atoms
GCEN CAVB RSIG ALTI
   1.0    2.5      1000.0      250  250  250 1000    1    1   0010000     50000
CNFG READ PDB
PRTG PDB ALLG AGLS  1 0 0.6
STOP
```