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| **Quantum mechanical (QM) descriptors (calculated using Gaussian 16)**1 | |
| |  |  | | --- | --- | | Dipole | Total dipole moment of the molecule | | HOMO | Energy of highest occupied molecular orbital in eV | | LUMO | Energy of lowest unoccupied molecular orbital in eV | | MK-C | Electrostatic potential charge of carbon in -CN group using Merz-Singh-Kollman (MK) Scheme | | MK-N | Electrostatic potential charge of nitrogen in -CN group using Merz-Singh-Kollman (MK) Scheme | | NPA-C | Natural charge of carbon in -CN group | | NPA-N | Natural charge of nitrogen in -CN group | | Volume | Total molecular volume | |  |
| **Classical descriptors (calculated using MOE)** | |

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| DCASA | Difference between positive and negative charge-weighted surface area |
| FCASA- | Fractional negative charge-weighted surface area |
| Npr1 | Ratio of the first principal moment of inertia to the third principal moment of inertia |
| Npr2 | Ratio of the second principal moment of inertia to the third principal moment of inertia |
| Vsa\_acc | Sum of VDW surface areas of hydrogen bond acceptors |
| Vsa\_hyd | Sum of VDW surface areas of hydrophobic atoms |
| Vsurf\_A | Amphiphilic moment |
| Vsurf\_G | Surface globularity |
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Details for MOE (Molecular Operating Environment, 2015. Chemical Computing Group, Inc.) can be found at <http://www.cadaster.eu/sites/cadaster.eu/files/challenge/descr.htm>

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| **Dockingdescriptors (calculated using Rosetta)**2 | |
| |  |  | | --- | --- | | fa\_atr | Attractive portion of the Lennard-Jones potential of *interface\_delta* | | fa\_elec | Coulombic electrostatic potential portion of *interface\_delta* | | fa\_rep | Repulsive portion of the Lennard-Jones potential of *interface\_delta* | | fa\_sol | Solvation term of *interface\_delta* | | hbond\_bb\_sc | Hydrogen bonding term between protein backbones and side chains in the interface of ligand (chain X) and the protein | | hbond\_sc | Hydrogen bonding between different side chain at the interface of ligand (chain X) and the protein | | interface\_delta | Interaction energy between the ligand (chain X) and the protein | |  |

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| **Active site descriptors (calculated using ProtDCal 4.0)**3 | |
| |  |  | | --- | --- | | HBd | Number of backbone hydrogen bonds | | W(U) | Number of water molecules close to a residue in an unfolded state | | W(F) | Number of water molecules close to a residue in a folded state | | ΔGc(F) | Folding configurational free energy | | ΔGLJ | Residue-level Lennard-Jones interactions | | ΔGw(F) | Free energy contribution of the entropy of the first shell of water molecules in a folded state | | ΔHf | Heat of formation | | |
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