Strain Problems got you in a Twist? Try StrainRelief: A Quantum-Accurate Tool for Ligand Strain Calculations

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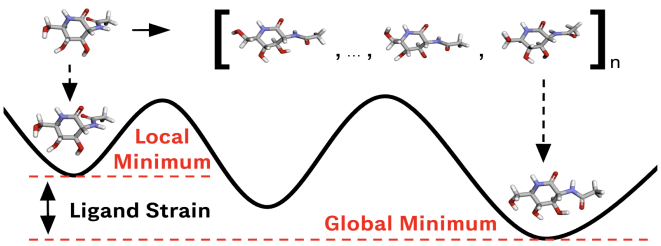

Abstract

Ligand strain energy, the energy difference between the bound and unbound conformations of a ligand, is an important component of structure-based small molecule drug design. A large majority of observed ligands in protein-small molecule co-crystal structures bind in low-strain conformations, making strain energy a useful filter for structure-based drug design. In this work we present a tool for calculating ligand strain with a high accuracy. StrainRelief uses a MACE Neural Network Potential (NNP), trained on a large database of Density Functional Theory (DFT) calculations to estimate ligand strain of neutral molecules with quantum accuracy. We show that