Iterated Local Search with Partition Crossover for Computational Protein Design

François Beuvin[1], Simon de Givry[2], Thomas Schiex[2], Sébastien Verel[3], and David Simoncini[1]

[1]Université de Toulouse 1 Capitole
[2]INRAE
[3]Université du Littoral Cote D'Opale

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Abstract

Structure-based computational protein design (CPD) refers to the problem of finding a sequence of amino acids which folds into a specific desired protein structure, and possibly fulfills some targeted biochemical properties. Recent studies point out the particularly rugged CPD energy landscape, suggesting that local search optimization methods should be designed and tuned to easily escape local minima attraction basins. In this paper, we analyze the performance and search dynamics of an iterated local search (ILS) algorithm enhanced with partition crossover. Our algorithm, PILS, quickly finds local minima and escapes their basins of attraction by solution perturbation. Additionally, the partition crossover operator exploits the structure of the residue interaction graph in order to efficiently mix solutions and find new unexplored basins. Our results on a benchmark of 30 proteins of various topology and size show that PILS consistently finds lower energy solutions compared to Rosetta fixbb and a classic ILS, and that the corresponding sequences are mostly closer to the native.

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