

A Linear Programming Approach for the Protein Morphing Problem

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Many important phenomena in molecular biology involve conformational changes of proteins. For quantitative understanding of these phenomena, it is imperative to know the free-energy changes associated with the conformational changes. Conformational free energy is also an essential notion in predicting protein structures from their sequences, as conformational free-energy differences provide the relative stability of different protein structures.

This work addresses the computation of conformational free-energy differences using morphing, i.e., transformation of a source conformation into a target conformation. To enhance the morphing procedure, we employ permutations of atoms; we transform atom n in the source conformation into atom $\phi(n)$ in the target conformation rather than directly transforming atom n into atom n . As shorter morphing paths reduce the cost of the free-energy computation, we seek to find the permutation ϕ that minimizes the root-mean-square distance traveled by the atoms.

Instead of performing this combinatorial search in the space of permutations, we relax the search onto the space of bi-stochastic matrices and solve the relaxed problem by linear programming. Using Birkhoff's theorem, we show that the solution of the relaxed problem is indeed identical to the solution of the original problem. We demonstrate that the use of such optimal permutations significantly improves the efficiency of the free-energy computation.

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