Global optimization of Onsager–Machlup action using conformational space annealing

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In computational physics, chemistry, and biology, global searching for reaction pathways is a long-standing challenge. Most available methods perform only local searches due to computational complexity, as a heuristic approach. Here we present a computational approach, Action-CSA, to find multiple diverse reaction pathways connecting fixed initial and final states through global optimization of the Onsager–Machlup action using the conformational space annealing (CSA) method. The computer simulations are reduced into many interatomic potential and force calculations, but key information on their target conformational changes is ultimately retained, so the resulting reaction pathway can be a set of conformations. This protocol provides conceptual insight into how computer simulations can discover conformational changes based on interatomic potential energy and global optimization alone, and it paves the way for a more routine application.