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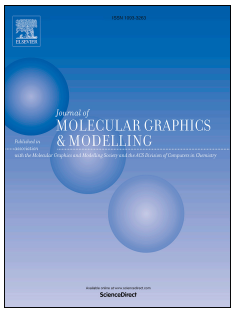

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Ryuhei Harada, Yasuteru Shigeta

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Selection Rules on Initial Structures in Parallel Cascade Selection Molecular Dynamics Affect Conformational Sampling Efficiency

Ryuhei Harada[*,†] and Yasuteru Shigeta[*,†]

[†]*Center for Computational Sciences, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8577, Japan*

Corresponding author: Ryuhei Harada, Yasuteru Shigeta
E-mail: ryuhei@ccs.tsukuba.ac.jp, shigeta@ccs.tsukuba.ac.jp

Abstract

Parallel cascade selection molecular dynamics (PaCS-MD) is a conformational sampling method for generating transition pathways from a given reactant to a product. In PaCS-MD, initial structures relevant to conformational transitions of proteins are selected and resampled by short-time MD simulations. As a general reaction coordinate, a root-mean-square deviation measured from the product (RMSD) is employed to rank the resampled configurations. Quantitatively, *n* initial structures are randomly selected from among the top X % of highly ranked configurations and resampled again. In PaCS-MD, the selection of initial structures and their conformational resampling are repeated as a cycle to promote the essential conformational transitions. Therefore, rules for selecting the initial structures might affect the conformational sampling efficiency. In the present study, to address the conformational sampling efficiency depending on the selection rule, the open-closed transition of di-ubiquitin was reproduced by PaCS-MD based on the resampling from the top X = 0.1, 1.0, 2.0, 5.0, 10.0, 25.0, 30.0, 40.0, and 50.0 % of highly ranked configurations. Judging from broadness of sampled conformational area and required cycles, we conclude that the resampling from the top ~ 2.0 % of highly ranked configurations might be the most efficient for generating a set of transition pathways in PaCS-MD.

Key Words: Molecular dynamics (MD), Conformational transition, Biologically relevant rare event, Parallel cascade molecular dynamics (PaCS-MD), Di-ubiquitin

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