1P581**Improving efficiency of conformation sampling in multicanonical molecular dynamics simulation**

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The multicanonical molecular dynamics (MD) method has been widely used to sample conformation space of biomolecules. In this method, a multicanonical potential function is used in place of the potential energy function to produce a flat energy distribution. By analogy to the spectrum of white noise, it is often said that the multicanonical method realizes a "random" walk in energy space. However, the simulation is conducted by solving deterministic equations of motion, and therefore the energy trajectory is, of course, not random, but is determined by the nature of the energy surface. The efficiency of the conformation sampling highly depends on the frequency of transitions from high to low energy state. Although the frequency can be optimized by improving the flatness of the energy distribution, it is limited by the nature of the energy surface: if the energy surface has a deep energy minimum state, the MD trajectory stays there for long time, resulting in a decrease in the transition frequency. To solve this problem, we combined the conformational flooding method, which flattens the energy surface with umbrella potentials, with the multicanonical method. We applied this method to a system of a peptide. The umbrella potentials were calculated from free energy profiles plotted against C α RMSDs from representative conformations that form deep free energy wells. As a result, the transition frequency was increased from 48.9 ns⁻¹ to 80.9 ns⁻¹. Our method is therefore useful to improve the efficiency of conformation sampling.

1P583**Efficient search of protein low-energy conformational space with a newly devised Wang-Landau molecular dynamics technique**○Takehiro Nagasima¹, Akira R. Kinjo^{1,2}, Takashi Mitsui³, Ken Nishikawa^{1,2}¹CIB and DDBJ, National Institute of Genetics, ²Dept. of Genetics, The Grad. Univ. for Advanced Studies (SOKENDAI), ³Fujitsu Limited

Multicanonical molecular dynamics (MD) is a powerful technique for sampling conformations on rugged potential surfaces such as protein. However, it is notoriously difficult to estimate the multicanonical temperature effectively. Wang and Landau developed a convenient method for estimating the density of states based on a multicanonical Monte Carlo method. In their method, the density of states is calculated autonomously during a simulation. In this time we develop a set of techniques to effectively apply the Wang-Landau (WL) method to MD simulations. In the multicanonical MD, the estimation of the derivative of the density of states is critical. In order to estimate it accurately, we devise two original improvements. First, the correction for the density of states is made smooth by using the Gaussian distribution obtained by a short canonical simulation. Second, an approximation is applied to the derivative, which is based on the Gaussian distribution and the multiple weighted histogram technique. A test of this method was performed with a miniprotein, Trp-cage, and it is demonstrated that WL MD can sample much larger conformational space in comparison with replica exchange MD.

1P582**Explicit and GB/SA solvents: each with two different force fields in multicanonical conformational sampling of 25-residue polypeptide**○Daisuke Mitomo¹, Yukihisa S Watanabe², Narutoshi Kamiya³, Junichi Higo¹¹Tokyo Univ. of Pharm. and Life Sci., ²JBIRC, ³Med., Kobe Univ.

We compared implicit (generalized born (GB)) and explicit (TIP3P) solvent models by multicanonical molecular dynamics (MD) simulation of an A β (12-36) peptide of Alzheimer's disease. The GB model is well used in MD simulations to save the computational costs. We did this comparison with two different force fields: FF1, which has a propensity of strand formation, and FF2, which does that of helix formation. In FF1, GB model produced more helical conformations than TIP3P model. In FF2, both models produced the same amount of helical conformations. However, the chain flexibility was different between TIP3P and GB models. The models produced significantly different free-energy landscapes.

1P584**Amyloid β -peptides studied by the multicanonical-multioverlap algorithm**

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Amyloid β -peptide (A β) is comprised of 39 to 43 amino-acid residues and has tendency to form amyloid fibrils, which are associated with Alzheimer's disease. In these amyloid fibrils, A β is perceived to have an intermolecular β -sheet structure. Furthermore, A β (29-42), which is comprised of from the residues 29-42 of A β , has an intermolecular antiparallel β -sheet structure in aqueous solution. The multicanonical-multioverlap algorithm has advantages of both the multicanonical algorithm and the multioverlap algorithm [1-3]. Namely, the multicanonical-multioverlap simulations can sample effectively the conformational space including specific configurations. Applying this method to protein systems, therefore, we can obtain effectively the accurate free-energy landscapes of these systems including specific configurations. In this poster, we apply the multicanonical-multioverlap algorithm to A β (29-42) dimer with implicit water. By employing a β -sheet structure of A β (29-42) as a reference conformation in the multicanonical-multioverlap simulations, we study the secondary structures and aggregation properties of A β (29-42). [1] S. G. Itoh and Y. Okamoto, Chem. Phys. Lett. 400, 308 (2004). [2] S. G. Itoh and Y. Okamoto, J. Chem. Phys. 124, 104103 (2006). [3] S. G. Itoh and Y. Okamoto, in preparation.