Development of New Algorithms for Molecular Dynamics Simulation and Its Application to Biomolecular Systems

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1. Temperature and Pressure Dependence of Alanine Dipeptide Studied by Multibaric-Multithermal Molecular Dynamics Simulations[1)]

We applied the multibaric-multithermal (MUBATH) molecular dynamics (MD) algorithm to an alanine dipeptide in explicit water (Figure 1). The MUBATH MD simulation covered a wide range of conformational space and sampled the states of P_{II}, C_5, α_R, α_P, α_L, and C_7^{ax}. On the other hand, the conventional isobaric-isothermal simulation was trapped in local-minimum free-energy states and sampled only a few of them. Temperature and pressure dependences of the population of these states were investigated by the MUBATH MD simulations as shown in Figure 2. Such temperature and pressure dependences by molecular simulations were calculated for the first time. We calculated the partial molar enthalpy difference ΔH and partial molar volume difference ΔV among these states by the MUBATH simulation using the AMBER parm99 and AMBER parm96 force fields and two sets of initial conditions as listed in Tables 1 and 2. We compared these results with those from Raman spectroscopy experiments. The Raman spectroscopy data of ΔH for the C_5 state against the P_{II} state agreed with both MUBATH data with the AMBER parm96 and parm99 force fields. The partial molar enthalpy difference ΔH for the α_R state and the partial molar volume difference ΔV for the C_5 state by the Raman spectroscopy agreed with those for the AMBER parm96 force field. On the other hand, ΔV for the α_R state by the Raman spectroscopy was consistent with our AMBER-parm99 force-field result. All the experimental results fall in between those of simulations using AMBER parm96 and parm99 force fields, suggesting that the ideal force field parameter lie between those of AMBER parm96 and parm99.

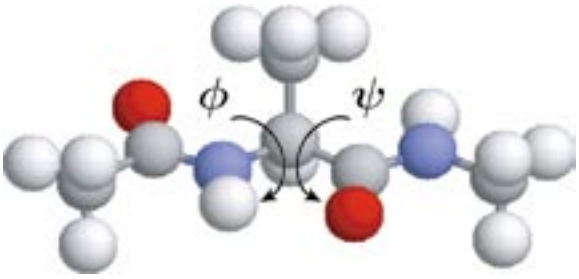

Figure 1. The initial conformations of alanine dipeptide for the MD simulation.

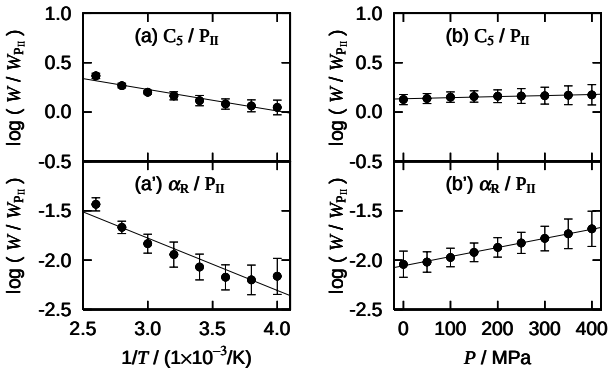

Figure 2. The population ratios of (a) the C_5 state and (a') the α_R state against the P_{II} state as functions of the inverse of temperature $1/T$ at constant pressure of P = 0.1 MPa. The population ratios of (b) the C_5 state and (b') the α_R state against the P_{II} state as functions of pressure P at constant temperature of T = 298 K.

Table 1. Differences ΔH/(kJ/mol) in partial molar enthalpy of the C_5, and α_R states from that of the P_{II} state calculated by the MUBATH MD simulations. Raman experimental data are also listed.

State	AMBER 96	AMBER 99	Raman exp.
C_5	1.8±0.5	3.6±2.2	2.5±0.3
α_R	4.4±1.1	–1.5±2.0	4.4±1.5

Table 2. Differences ΔV/(cm^3/mol) in partial molar volume of the C_5, and α_R states from that of the P_{II} state calculated by the MUBATH MD simulations. Raman experimental data are also listed.

State	AMBER 96	AMBER 99	Raman exp.
C_5	–0.3±0.7	1.5±0.9	0.1±0.3
α_R	–2.3±1.3	1.8±0.8	1.1±0.2

2. Partial Multicanonical Algorithm for Molecular Dynamics and Monte Carlo Simulations[2)]

Partial multicanonical algorithm is proposed for molecular dynamics and Monte Carlo simulations. The partial multicanonical simulation samples a wide range of a part of the potential energy terms which is necessary to sample the conformational space widely, whereas a wide range of total potential energy is sampled in the multicanonical algorithm. Thus, one can concentrate the effort to determine the weight factor only on the important energy terms in the partial multicanonical simulation. The partial multicanonical, multicanonical, and canonical molecular dynamics algorithms were applied to an alanine dipeptide in explicit water solvent. The canonical simulation sampled the states of P_{II}, C_5, α_R, and α_P. The multicanonical simulation covered the α_L state as well as these states. The partial multicanonical simulation also sampled the C_7^{ax} state in addition to the states which were sampled by the multicanonical simulation as shown in Figure 3. In the partial multicanonical simulation, furthermore, backbone dihedral angles ϕ and ψ rotated more frequently than in the multicanonical and canonical simulations. These results mean that the partial multicanonical algorithm has higher sampling efficiency than the multicanonical and canonical algorithms.

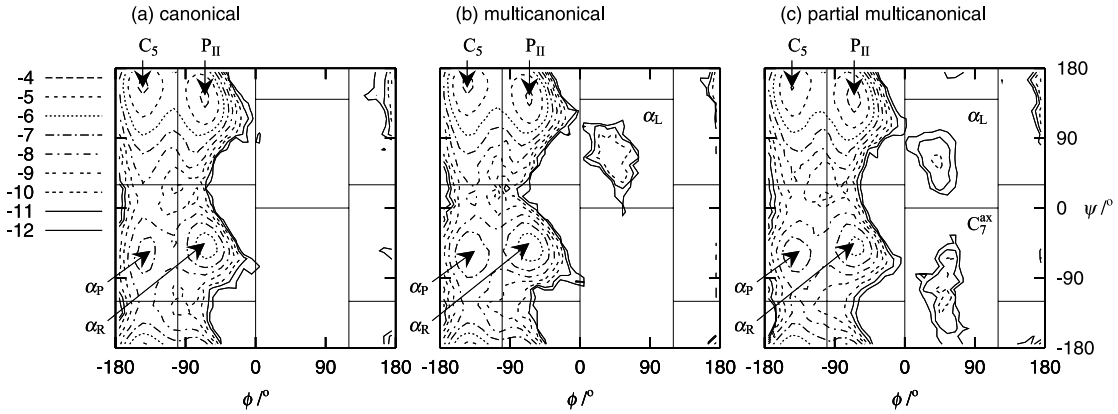

Figure 3. Contour maps of the logarithms of the probability distributions $\log P_{NVT}(\phi,\psi)$ of the backbone dihedral angles ϕ and ψ at T = 300 K obtained (a) by the canonical MD simulation, (b) by the reweighting techniques from the results of the multicanonical MD simulation, and (c) by the reweighting techniques from the results of the partial multicanonical MD simulation.

References

1) H. Okumura and Y. Okamoto, *J. Phys. Chem. B* **112**, 12038–12049 (2008).

2) H. Okumura, *J. Chem. Phys.* **129**, 124116 (9 pages) (2008).