Protein dynamics and functions using enhanced MD simulations

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Molecular dynamics (MD) simulations of proteins and other biomolecules are essential tools in molecular and cellular biology. Atomistic MD simulations are useful to investigate protein conformational fluctuations and dynamics related to their molecular functions, while their time-scales available using the current computers are limited to 10-100 microseconds. We therefore developed enhanced conformational sampling methods in MD simulations of biomacromolecules and applied them to understand protein dynamics and functions. In particular, generalized Replica Exchange with Solute Tempering (gREST) [J. Chem. Phys. (2018) 149, 072304], which was extended from REST2 [J. Phys. Chem. B (2011) 115, 9431-9438; JCTC (2011) 7, 231-237; JCC (2011) 32, 1228-1234], is useful to simulate conformational dynamics of large multi-domain proteins [eLife (2022) 11, e75720]. The two-dimensional replica-exchange method, gREST/REUS, is applicable to protein-ligand binding effectively, allowing many binding/unbinding processes and conformational fluctuations of proteins and ligands [PNAS (2019) 116, 18404-18409]. In the talk, we discuss methodological differences between our simulation methods and conventional ones and introduce recent biological applications using our simulation methods.