pH-Replica Exchange molecular Dynamics in proteins using a discrete protonation method

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Protonation controls structure, dynamics and function of many biological molecules and reactions. To enhance the coupling between conformational and protonation sampling, we presented a pH-Replica Exchange Molecular Dynamics (pH-REMD) method. Under a generalized ensemble criteria, conformations are swapped between two neighboring replicas, which are at different pHs. To validate pH-REMD, we applied pH-REMD to a series of model compounds, the uncapped ADFDA pentapeptide, and a hepta-peptide derived from the ovomucoid third domain (OMTKY3). In all studied compounds, the predicted pKa by pH-REMD is very close to Constant pH Molecular dynamics (CpH MD), while pH-REMD has the advantage of more efficient conformational and protonation state samplings, which leads to a considerably faster convergence.