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All-Atom Steered Molecular Dynamics Simulations of Large Proteins in a Small Water Box

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Steered molecular dynamics (SMD) simulations complement force spectroscopy experiments by suggesting which structural changes are associated with force extension data. Typically, steered molecular dynamics simulations of large proteins are done via coarse-grained (CG) models due to the computational expense of simulated SMD stretching of large proteins. In particular, using all-atom systems requires the creation of a very large water box to accommodate a completely extended polypeptide chain. For example, to carry out all-atom SMD simulations of ~500 residue long proteins, one needs a 200 nm-long water box to allow complete extension of the polypeptide backbone. The total system size then exceeds 1.6 million atoms thereby making SMD trajectory calculations, at reasonably slow stretching velocities, impractically lengthy on most computer systems. Here, by performing piece-wise SMD stretching of a large protein in a 10-fold reduced water box, we attempt to analyze whether a stretching simulation conducted under such conditions can replicate force spectroscopy extension data and whether these results agree with simulations utilizing reduced representations of biomolecules. For our system, we find that a SMD simulation in the reduced water box can be completed in a reasonable amount of time and the results given by all-atom SMD differ from those given through a coarse-grained simulation. These results suggest that all-atom SMD can provide an extra layer of detail which may be helpful in interpreting force extension data and designing new experiments.