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Dear Editor,

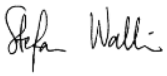
Please find attached our manuscript "Multisequence algorithm for coarse-grained biomolecular simulations: exploring the sequence-structure relationship of proteins" by Adekunle Aina and Stefan Wallin, which we would like to submit for publication in Journal of Chemical Physics.

In this ms, we develop and test an algorithm for biomolecular simulations that allows the thermodynamics of many sequences to be calculated in a single run, which also makes it highly efficient. Quite generally, we believe this ms is timely because of the trememedous current emphasis on biological sequence information driven by advances in sequencing technologies. More specifically, there is a range of areas where our method might be applied, for example, studies of specificity in biomolecular interactions or mechanisms in molecular evolution. As far as we are aware, no previous simulation method has been developed to allow for efficient characterization of equilibrium properties of biomolecular systems across different sequences.

As a test case, we implemented the algorithm in a coarse-grained model for proteins and show that it can provide the folding thermodynamics of over 1,000 sequences with reasonable computational resources. Furthermore, this data allowed us to explore the biophysical properties of proteins, such as structure and native state stability, in the border regions between different folds. Such a systematic exploration of folding behavior of proteins of related sequences has not been carried out before in other than simple lattice models. Our results have potential implications for how new folds arise in evolution, which is not currently well understood.

We believe that the combination of methodological advance and new insights into the phenomenon of protein fold transitions makes our ms of broad interest to researchers in the computational physics, chemical physics and biophysics fields and therefore a good fit for Journal of Chemical Physics.

Sincerely,



Stefan Wallin
Assistant Professor