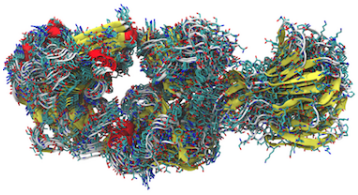

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CpHMD-SBM Simulations to Study the Protein G Stability at Different pHs and Salt Concentrations

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Abstract: In this work, we study the importance of charge-charge interactions in the thermal stability of proteins. pH plays a crucial role in these electrostatic interactions, as well as in the arrangement of ionizable residues in each protein-folding stage. Two coarse-grained models were used to evaluate the effect of pH on the thermal stability of a protein G variant (1PGB-QDD). One of these coarse-grained models, the TKSA, calculates the electrostatic free energy of the protein in the native state via the Tanford-Kirkwood approach for each residue. The other one, CpHMD-SBM, uses a Coulomb screening potential in addition to the structure-based model Cα. Both models simulate the system in constant pH. The comparison between the experimental stability analysis and the computational results obtained by these simple models showed a good agreement. Through the TKSA method, the role of each charged residue in the protein's thermal stability was inferred. Using CpHMD-SBM, it was possible to evaluate salt and pH effects throughout the folding process. Finally, the computational pKa values were calculated by both methods and presented a good level of agreement with the experiments. This study provides, to our knowledge, new information and a comprehensive description of the electrostatic contribution to protein G stability.