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The Role of Dynamics in the Disease Development of Human Ferritin AVISHEK KUMAR, TYLER GLEMBO, BANU OZKAN, Arizona State University — After analyzing different protein families, we observed the alteration of dynamics through allostery leads to functional changes, suggesting that disease-associated mutations impair allosteric regulations, causing loss of function. In this study, we analyzed the dynamics of the wild-type light chain subunit of human ferritin protein along with the neutral and disease forms. We performed replica exchange molecular dynamics of wild-type and mutants to obtain dynamics; then, we computed the dynamic flexibility index (DFI) of each position for the wild-type and mutants. DFI quantifies the resilience of a position to a perturbation providing a flexibility/rigidity measurement for a given position. The DFI analysis reveals that neutral variants and the wild-type exhibit similar flexibility profiles in which critical positions act as hinges in controlling the overall motion. Disease mutations alter the conformational dynamics, making hinges more loose, thus impairing the allosterically regulated dynamics.

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