
A-10**Interaction Energies and Forces of Biomolecules**Jinhyuk Lee^{*2}, Seokmin Shin², Sun-Hee Jung¹¹Structural Biology Center, Korea Institute of Science and Technology (KIST), 39-1 Hawolgok-dong, Seongbook-goo, Seoul, 136-791, Korea,²Dept. of Chemistry, College of Natural Sciences, Seoul National University, Seoul, Korea

We propose a method where interaction energies and force components are calculated separately for each residue of biomolecules. It is found that the correlation factors obtained from the analysis of five types of force terms and one interaction energy term (main chain self-energy) can be used to predict a mutants free energy difference relative to wild type. The correlation factors are determined by comparing the differences in a force or an interaction term between each mutant and wild type against $C_\alpha-C_\alpha$ distance from mutation site to the corresponding residue. We can estimate the free energy difference up to a predictability of 0.998 for the main chain energy term when we use the minimized molecular dynamics (MD) simulation average coordinate of the model system (BPTI). When the minimized X-ray coordinate is used for the analysis, forces due to the total interaction energy of each residue with the rest of the molecule gives a highest predictability of 0.955. As a second method for obtaining correlation factors, we compared the interaction energy and force terms for each mutant against those of wild type. In the case of the total interaction energy term, the second method predicts a mutants free energy difference less accurately (predictability of 0.926) than the first method, when we use minimized MD average coordinate. If the minimized X-ray coordinate is used for the second method, five types of energy terms and one force term give good predictability, up to a value of 0.989 for the electrostatic and total interaction energy terms. We discuss the implications of the two different methods proposed in this study to predict a mutants free energy difference relative to wild type.