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Rational Design of Protein Dynamics

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Abstract

*Deciphering structural interrelations and constraints within proteins and their dynamics is key to understand their function and evolution. This is a particularly valid for enzymes, which are singularly complex in terms of function, structure and dynamics. Apprising structural fluctuations on proteins is still challenging due to intrinsic technical limitations of experimental methods, and yet computational techniques can help surmounting these hindrances [DB14, MKH*18]. Rational protein design aims to exploit the structure-function relationships for tailoring different aspects of enzymatic activity. Due to their lesser evolutionary constraints and distance to the catalytic center, recent design efforts have specifically targeted loops – particularly dynamic aperiodic regions flanked by regular secondary structures [BPIGG*13, BSPI*14]. However, loop design approaches still rely more on empirical sampling than on rational design, hinting the need for wider quantitative knowledge about loops flexibility. A particularly challenging task in loop design is transferring a desired property between two proteins by means of loop grafting. A successful loop transplant requires precise geometric overlay of the target structure and meeting dynamical requirements for the engineered property [SPT*19]. To address this problem we are developing a computational framework to compare loops geometry and dynamics on different proteins. Our newly developed strategy will be applicable to a wide range of protein families.*

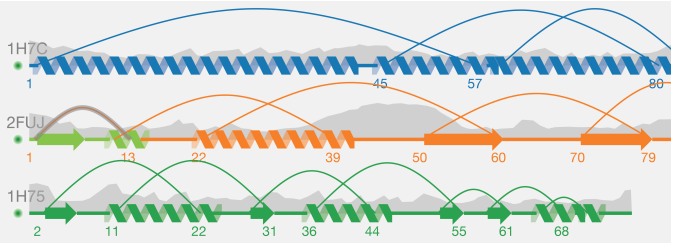

Figure 1: *Comparative visualization of loops distribution, size and position in multiple protein chains can significantly effect the process of understanding the importance of these non-periodic protein structures. In this case, 3 different protein sequences are laid in juxtaposition view for the immediate revelation of similarities and differences between their loops.*

References

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