THE UNIVERSITY OF CHICAGO

Departments of Computer Science, Mathematics, Statistics and the Computation Institute

SCIENTIFIC AND STATISTICAL COMPUTING SEMINAR

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Understanding the Role of Sequence Diversity in Protein Structural Symmetry

THURSDAY, January 19, 2017 at 4:30 PM
226 Jones Laboratory, 5747 S. Ellis Avenue

ABSTRACT

β-propeller proteins are a highly evolved family of repeat proteins that can interact with a broad range of binding partners, even though a similar three-dimensional geometry is shared. As for all families of repeat proteins, structural motifs remain consistent between repeating units, in addition to the entire family, but how these motifs may provide a template for evolutionary selection remains unclear. Comparative sequence analysis techniques can be successful in identifying conservation between closely related proteins, but the reasons underlying amino-acid conservation cannot be determined without further experimentation. We overcome this by adapting the dead-end elimination and A* search algorithms for large-scale computational mutagenesis, and demonstrate how the involvement of individual amino acids to overall protein fitness (defined by structural stability and binding interactions) can be deconvolved for a G-protein heterotrimer, and how the β-propeller it contains may have key molecular interactions established. Our computational approach can identify important patterns of interaction for this protein, and provide insight on how associations between and within repeats contribute to overall fitness.

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