A Systematic Study of Flexibility in Protein Structures and its Implications in Protein Structure Prediction

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Despite some level of overall similarity, proteins sharing the same fold usually display a significant structure variation that prohibits effective use of more distantly related proteins in detailed structure prediction, such as done in comparative modeling.

New generation of proteins structure alignments allow describing and classifying differences in structures between related proteins. The broad survey of structure variations within fold groups performed using FATCAT and POSA algorithms shows that proteins sharing a common fold display strong regularities in how their structure changes in response to mutations and/or substrate or inhibitor binding. Most of the structural variation within any given fold can be described by a small number of parameters, usually a position of a pivot point(s) and an angle(s) of rotation around it.

The results of this survey have important implications for comparative modeling and structural genomics. Flexible templates, rearranged according to the rules independently discovered for a given fold can be used for more accurate comparative modeling. At the same time, relatively small number of structures can be used to characterize structural divergence of large protein families. Specific examples for both applications are discussed.

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