Julie Mitchell, University of Wisconsin – Madison, Madison, WI, USA
Omar Demerdash, University of Wisconsin – Madison, Madison, WI, USA
Xiao-lei Zhu, University of Wisconsin – Madison, Madison, WI USA
Michael Daily, University of Wisconsin – Madison, Madison, WI, USA

Knowledge-Based Structural Approaches for Predicting Hot Spots of Protein Binding and Allostery

Using information derived from protein structures, it is possible to predict amino acid positions where mutations will have a deleterious effect on protein binding or allosteric communication. The KFC2 model captures 80% of alanine scanning mutagenesis hot spots, which result in a binding energy increase of at least 2 kcal/mol. A unique feature of the model is a local plasticity feature that suggests whether a change in sequence can be accommodated through local sidechain rearrangements. A different plasticity measure, known as local structural entropy, is a dominant feature in our AlloSIND model for allosteric hot spots that lie between the effector and active sites of allosteric proteins. One possible interpretation is that rigidity of internal protein secondary structure prevents an allosteric protein from absorbing the impact of effector binding locally, resulting in longer range conformation effects.