

High-throughput prediction of protein-protein, protein-RNA and protein-DNA interactions mediated by disordered regions

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Abstract

Intrinsically disordered proteins (IDPs) and intrinsic disordered regions (IDRs) in proteins lack stable three-dimensional (3D) structure under physiological conditions in vitro. They are common in nature, with eukaryotic proteins having on average about 20% of disordered residues. IDPs and IDRs play important functional roles including transcriptional regulation, translation, and signal transduction, to name just a few, and are enriched in multiple cellular compartments including nucleus, ribosome, and cytoplasm. Since experimental annotations of intrinsic disorder lag behind the rapidly accumulating number of known protein chains, dozens of computational methods were developed for the prediction of IDRs/IDPs from protein sequences [*Cell Res* 2009, 19:929-49; *Brief Bioinform* 2010, 11:225-43; *Curr Protein Pept Sci* 2012; 13:6-18]. These predictors focus on generic intrinsic disorder, without providing insights into its function. Only a few recent studies addressed prediction of disorder mediated protein-protein/peptide interactions [*PLoS Comput Biol* 2009, 5:e1000376; *Bioinformatics* 2012, 28:i75-83].

We report on our current progress to develop models for computational prediction of the protein-protein, protein-DNA, and protein-RNA binding that is mediated by IDPs/IDRs. Our models complement the outputs generated by the predictors of these interactions for the structured proteins and facilitate high-throughput annotation of these functions; our predictions take less than 1 second for a single chain using a modern desktop computer. We comparatively assess predictive quality of our models, their runtime, and provide insights into these disorder driven functions in eukaryotic organisms.