Intrinsic Disorder in Transcription Factors

Intrinsic Disorder in Transcription Factors

Liu, Jiangang (Al)

Name: Thesisl_Jiangang_ ...
Size: 816.6Kb
Format: PDF

View/Open

Permanent Link: http://hdl.handle.net/1805/324
Date: 2005-08
Keywords: disorder ; transcription

Abstract:

Reported evidence suggested that high abundance of intrinsic disorder in eukaryotic genomes in comparison to bacteria and archaea may reflect the greater need for disorder-associated signaling and transcriptional regulation in nucleated cells. The major advantage of intrinsically disordered proteins or disordered regions is their inherent plasticity for molecular recognition, and this advantage promotes disordered proteins or disordered regions in binding their targets with high specificity and low affinity and with numerous partners. Although several well-characterized examples of intrinsically disordered proteins in transcriptional regulation have been reported and the biological functions associated with their corresponding structural properties have been examined, so far no specific systematic analysis of intrinsically disordered proteins has been reported. To test for a generalized prevalence of intrinsic disorder in transcriptional regulation, we first used the Predictor Of Natural Disorder Regions (PONDR VL-XT) to systematically analyze the intrinsic disorder in three Transcription Factor (TF) datasets (TFSPTRENR25, TFSPNR25, TFNR25) and two control sets (PDBs25 and RandomACNR25). PONDR VL-XT predicts regions of ≥30 consecutive disordered residues for 94.13%, 85.19%, 82.63%, 54.51%, and 18.64% of the proteins from TFNR25, TFSPNR25, TFSPTRENR25, RandomACNR25, and PDBs25, respectively, indicating significant abundance of intrinsic disorder in TFs as compared to the two control sets. We then used Cumulative Distribution Function (CDF) and charge-hydropathy plots to further confirm this propensity for intrinsic disorder in TFs. The amino acid compositions results showed that the three TF datasets differed significantly 5 from the two control sets. All three TF datasets were substantially depleted in order-promoting residues such as W, F, I, Y, and V, and significantly enriched in disorder-promoting residues such as Q, S, and P. H and C were highly over-represented in TF datasets because nearly a half of TFs contain several zinc-fingers and the most popular type of zinc-finger is C2H2. High occurrence of proline and glutamine in these TF datasets suggests that these residues might contribute to conformational flexibility needed during the process of binding by co-activators or repressors during transcriptional activation or repression. The data for disorder predictions on TF domains showed that the AT-hooks and basic regions of DNA Binding Domains (DBDs) were highly

disordered (the overall disorder scores are 99% and 96% respectively). The C2H2 zinc-fingers were predicted to be highly ordered; however, the longer the zinc finger linkers, the higher the predicted magnitude of disorder. Overall, the degree of disorder in TF activation regions was much higher than that in DBDs. Our studies also confirmed that the degree of disorder was significantly higher in eukaryotic TFs than in prokaryotic TFs, and the results reflected the fact that the eukaryotes have well-developed elaborated gene transcription mechanism, and such a system is in great need of TF flexibility. Taken together, our data suggests that intrinsically disordered TFs or partially unstructured regions in TFs play key roles in transcriptional regulation, where folding coupled to binding is a common mechanism.

Description:

Submitted to the faculty of the Indiana University School of Informatics Graduate School in partial fulfillment of the requirements for the degree Master of Sciences in Bioinformatics, August 2005

This item appears in the following Collection(s)

- Informatics Graduate Theses and PhD Dissertations (/handle/1805/303)
- Informatics School Theses and Dissertations (/handle/1805/954)

 Show Statistical Information (#)

My Account

- Login
- Register

Statistics

- Most Popular Items
- Statistics by Country
- Most Popular Authors