A Study of Disorder-to-order Transition by Characterizing the Binding Partners using a Statistical Potential

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Introduction: Intrinsically Disordered Proteins or Regions (IDPs/IDRs) participate in crucial biological and pathological processes. The functional advantages of IDPs/IDRs are facilitated by their disorder-to-order transitions, in short peptide regions, called binding-sites through low affinity interaction with receptor partner proteins.

Motivations: Presence of a relevant partner is a prerequisite for induced-binding in peptides. Thus we aim to propose a novel hierarchical approach to identify binding-sites in peptides from sequence only that purposefully utilizes the properties of partner residues that potentially promote the induced-folding. The technique will be useful in assembling potential interactomes.

Contributions: We developed a new binding-inducing region predictor (BIRpredict) in receptor proteins using model stacking. We attempted to verify that properties of partner residues provide supplemental information in predicting binding-sites in peptides. We further computed binding-energy (PSBE) from sequence only to recognize hot-spots.

Table 1: Comparison on binding-inducing residue prediction

<table>
<thead>
<tr>
<th></th>
<th>ACC</th>
<th>PPV</th>
<th>F1</th>
<th>MCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIRpredict</td>
<td>0.603</td>
<td>0.674</td>
<td>0.324</td>
<td>0.361 (0.524)</td>
</tr>
<tr>
<td>SPRINT</td>
<td>0.646</td>
<td>0.694</td>
<td>0.164</td>
<td>0.136 (0.326)</td>
</tr>
</tbody>
</table>

*BCC: on different test datasets, reported in respective articles.

Future Works
- We aim to investigate what are the most influential structural properties of binding-inducing residues of partners that promote induce-folding.
- We are currently tuning the parameters of PBSpredict and benchmarking its performance against existing state-of-the-art predictors.
- With BIRpredict, PBSpredict and PSBE, we aim to accurately identify the hot-spots of peptide-protein interface.