

Fuzzy complexes: ambiguity in protein-protein and protein-DNA interactions is important in transcriptional regulation

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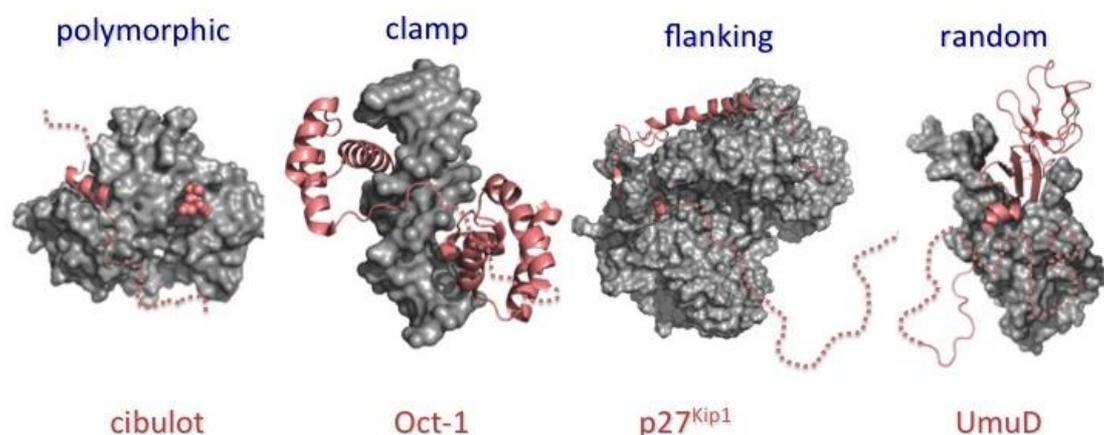
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Intrinsically disordered proteins (IDPs) disobey the classical structure-function paradigm and function as an ensemble of structures. ID proteins are distinguished in regulation of biochemical processes, e.g. control of transcription or gene-expression. Specific molecular recognition via disordered protein regions is described by three models: i) preformed structural elements ii) linear motifs and iii) primary contact sites. The combination of these motifs impart versatility on complexes formed by ID proteins, which will be demonstrated by the p27^{Kip1}/Cdk2/Cyclin complex and the Mediator of RNA polymerase II.

Protein complexes for long were defined by unambiguous, static contacts. Recent results, however, indicate that residues, which do not adopt a well-defined structure even in their bound form, can critically influence selectivity or binding affinity via transient, dynamic interactions. This phenomenon is termed as *fuzziness*. Using various recently characterized examples, formation of fuzzy complexes will be described and the benefits of structural ambiguity in both protein-protein and protein-DNA interactions will be detailed. The dynamic segments can modulate conformational preferences or flexibility of the interface, vary the spacing of the binding motif(s) or serve as a competitive partner. Post-translational modifications and/or additional interactions of structurally heterogeneous regions provide further means to regulate the activity of the complex and expand the functional repertoire of the proteins involved. Genome-wide analysis of tissue-specific alternatively spliced isoforms indicate a connection between fuzzy complexes and context-dependent functioning of proteins.

Topological categories of fuzzy complexes



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