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Review

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Fuzzy complexes: specific binding without complete folding

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Abstract

Specific molecular recognition is assumed to require a well-defined set of contacts and devoid of conformational and interaction ambiguities. Growing experimental evidence demonstrates however, that structural multiplicity or dynamic disorder can be retained in protein complexes, termed as fuzziness. Fuzzy regions establish alternative contacts between specific partners usually via transient interactions. Nature often tailors the dynamic properties of these segments via post-translational modifications or alternative splicing to fine-tune affinity. Most experimentally characterized fuzzy complexes are involved in regulation of gene-expression, signal transduction and cell-cycle regulation. Fuzziness is also characteristic to viral protein complexes, cytoskeleton structure, and surprisingly in a few metabolic enzymes. A plausible role of fuzzy complexes in increasing half-life of intrinsically disordered proteins is also discussed.