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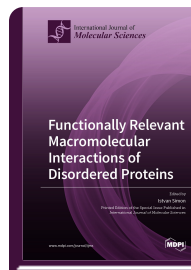
## Functionally Relevant Macromolecular Interactions of Disordered Proteins

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ISBN 978-3-03936-521-0 (Hardback)

ISBN 978-3-03936-522-7 (PDF)



Disordered proteins are relatively recent newcomers in protein science. They were first described in detail by Wright and Dyson, in their *J. Mol. Biol.* paper in 1999. First, it was generally thought for more than a decade that disordered proteins or disordered parts of proteins have different amino acid compositions than folded proteins, and various prediction methods were developed based on this principle. These methods were suitable for distinguishing between the disordered (unstructured) and structured proteins known at that time. In addition, they could predict the site where a folded protein binds to the disordered part of a protein, shaping the latter into a well-defined 3D structure. Recently, however, evidence has emerged for a new type of disordered protein family whose members can undergo coupled folding and binding without the involvement of any folded proteins. Instead, they interact with each other, stabilizing their structure via “mutual synergistic folding” and, surprisingly, they exhibit the same residue composition as the folded protein. Increasingly more examples have been found where disordered proteins interact with non-protein macromolecules, adding to the already large variety of protein–protein interactions. There is also a very new phenomenon when proteins are involved in phase separation, which can represent a weak but functionally important macromolecular interaction. These phenomena are presented and discussed in the chapters of this book.



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