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The Curious Case of Intrinsically Disordered Proteins

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Proteins are macromolecules that carry out most of the functions in a living cell. These functions are largely attributed to the structure they adopt natively in the cell. Intrinsically Disordered Proteins (IDPs), a unique and important extension of the protein kingdom, challenge the well-established concept of "one protein–one structure–one function"in structural biology. IDPs are highly dynamic proteins that adopt an ensemble of conformations. Found abundantly in nature, some of them perform very important biological functions, and have been implicated in a wide variety of diseases such as cancer, cardiovascular disease and neurodegenerative diseases.

In the absence of a well-defined structure, then, how do IDPs manage to play their biological role? And how do we explain the "one protein–many structures–one to many functions"concept they exhibit? Given their significance in disease, can these ensembles of structures be subjected to rational drug design?

In my talk, I will uncover these questions while highlighting the peculiar biophysical characteristics of IDPs, and the techniques used to study them. I will also elaborate on my research on the druggability of IDPs, in which I use a computational drug-design method that we have developed, coupled with the experimental measurements from Small-Angle X-Ray Scattering, to study the interactions of small drug-like molecules with IDPs.

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