**The multidimensional problem of protein-protein interactions**

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In the last decade, newly developed experimental methods made it possible to highlight that macromolecules in the cell milieu physically interact to support physiology. This shifted the problem of protein-protein interaction from a microscopic, electron-density scale to a mesoscopic one. Further, nowadays evidence increases that proteins in the nucleus and in the cytoplasm can aggregate in membraneless organelles for different physiological reasons. In this scenario, it is urgent to face the problem of biomolecule functional annotation with efficient computational methods, suited to extract knowledge from reliable data and transfer information across different domains of investigation. Here, we revise the present state-of-the-art of our knowledge of protein-protein interaction and computational methods that differently implement it.