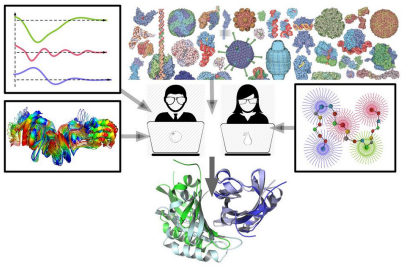

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Integrative methods to study flexible multi-domain enzymes: an experimental approach

Integrative modeling is a powerful tool to study the structure-function relationship in multi-domain flexible systems. Here we will describe the combination of modelling, solution scattering data and flexible fitting as well as biochemical and biophysical analyses that have been used to define the quaternary structure of DDX21, a human DEAD-box helicase with RNA G-quadruplex resolving activity. We discovered that DDX21 is dimeric and propose a model for DDX21 function which suggests that an intact dimerization interface is essential to maintaining dsRNA unwinding and G-quadruplex remodelling activities. We will also discuss the problems that we encounter and questions that remain unsolved.

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