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# The Whole Is More Than the Sum of Its Parts

## Physical chemist Thorsten Hugel receives prestigious grant from European Research Council

**Thorsten Hugel**, professor of physical chemistry at the University of Freiburg, has been awarded a Consolidator Grant from the European Research Council (ERC) to develop an approach that applies single molecule methods to improve our understanding of biological machines. In living organisms a multitude of proteins work hand in hand to perform complex cellular tasks. Hugel and his team aim to produce a dynamic picture of this protein interaction in real time. The physical chemist will receive just under 1.9 million euros in funding for his project PROSINT (Multi-protein interaction kinetics by single molecule methods) in the next five years.

Researchers have a considerable knowledge of the interaction between two proteins, even in cases in which this interaction is dynamic, i.e. dominated by temporary and sometimes fast processes. However, most cellular processes involve dynamic interaction between three or more proteins. Standard methods are insufficient for studying these processes. With new fluorescence-based single molecule methods, Hugel and his team aim to study the dynamic interaction between several proteins using the example of the Hsp90 system.

The heat-shock protein Hsp90 is a very common protein in human cells. It is of great significance as it is responsible for regulating many fundamental processes. Among other things, it plays an essential role in the folding of simple amino acid chains to form functioning proteins with a precisely

defined structure. As in the case of many other proteins, Hsp90 does not accomplish this feat on its own but through direct cooperation with numerous other proteins. Another thing Hsp90 has in common with many other proteins is that it uses energy from the cleavage of ATP, the most important energy source in human cells. It is largely unknown how this energy is used in the Hsp90 multi-protein system.

What is known is that Hsp90 does not work in a state of energetic equilibrium. The study of such non-equilibrium systems is still in its infancy, although they are what makes life possible in the first place – equilibrium corresponds to the state of the lowest possible energy and thus to death. In the PROSINT project, the researchers are developing new single molecule methods and forms of data analysis for investigating the physical-chemical processes and the structure of non-equilibrium multi-protein systems in detail.

The goal of the project is to reach a better understanding of the way in which the energy from ATP cleavage is used to fold proteins, to accumulate proteins, or to break down protein aggregates. Moreover, the researchers hope to learn how it is possible that a system consisting of many proteins is more than the sum of its individual parts. Finally, the experiments are also significant for pharmaceutical research, since Hsp90 is regarded as a promising target protein for cancer treatments.

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