

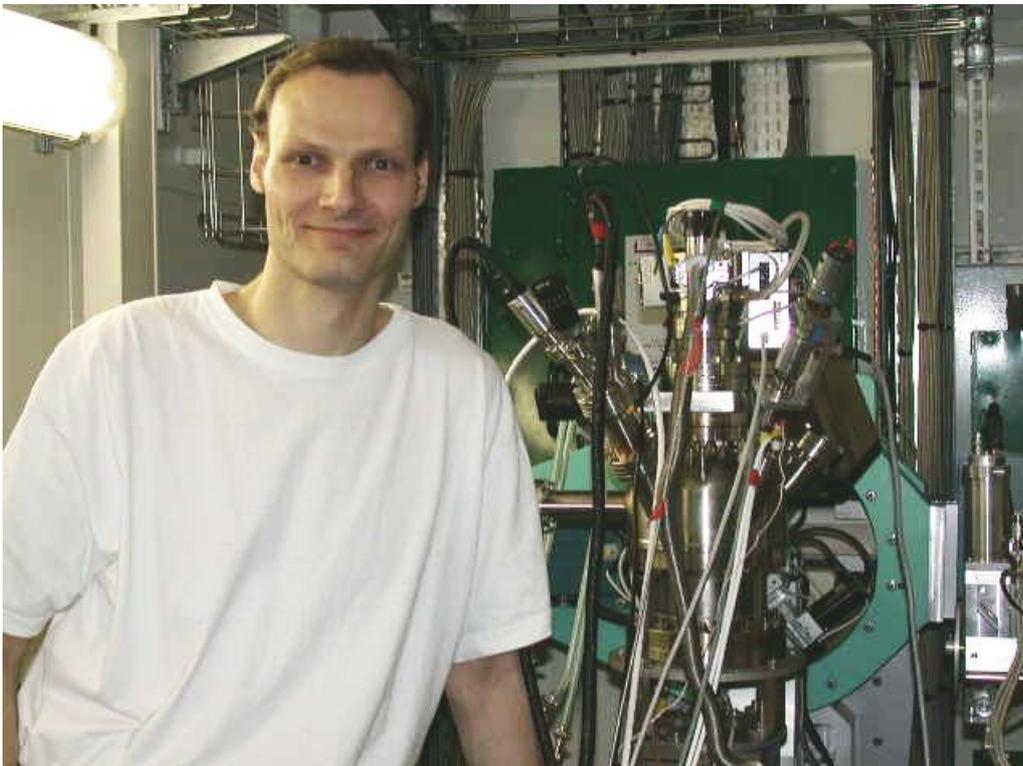
## Healthcare industry BW

### Salt aggregates proteins or dissolves them

**Proteins accomplish many vital tasks in biological systems and organisms. They are not only building blocks of cells, but can also act as signalling substances and chemical tools. In order to understand the processes in cellular tissue and other biological systems, scientists need to know the interactions of proteins with other substances and with water. Researchers from Tübingen have recently discovered some fundamental properties of proteins.**

A group of researchers at the University of Tübingen led by Prof. Frank Schreiber at the Institute of Applied Physics, in cooperation with colleagues from Saarbrücken and Oxford, have shown for the first time that proteins aggregate when certain salts are added. They also found that the proteins dissolved again when more salt was added.

This fundamental finding is an important contribution to a better understanding of the properties of proteins. The research results of the German-British project were pre-published online by the scientific journal *Physical Review Letters* (101, 148101, 2008). The research involved a number of researchers from the University of Tübingen, including Prof. Frank Schreiber, Dr. Fajun Zhang as well as Stefan Zorn from the Institute of Applied Physics and Prof. Oliver Kohlbacher from the Centre of Bioinformatics.



Prof. Dr. Frank Schreiber was appointed professor of biophysical structure research at the Institute of Applied Physics at the University of Tübingen in 2004. (Photo: University of Tübingen)

Protein aggregation is a common feature of many neurodegenerative diseases, and it is believed that the aggregation process plays a central role in the pathogenesis of neurodegenerative diseases such as Alzheimer's disease, prion diseases such as bovine spongiform encephalopathy (BSE) and Creutzfeldt-Jakob disease. In addition, protein crystallisation, i.e., the controlled aggregation of proteins, is also important in the clarification of protein structure, which in turn is a prerequisite for the development of new drugs. The interaction with the water surrounding the proteins, and with the salt ions (positively or

negatively charged particles) contained in the water plays a central role in the structure and function of proteins. A well-known effect is that an increase in the salt concentration in a solution results in the shielding off of the protein's charge. This leads to a reduction in the electrostatic repulsion of the proteins among themselves, which results in their aggregation and precipitation.

The scientists from Tübingen, Saarbrücken and Oxford have now succeeded in showing that under certain conditions adding certain salts with highly-charged ions (for example, yttrium and lanthanum salts) to an aqueous protein solution reverses protein aggregation and the proteins dissolve again. This effect is explained by the fact that negatively charged globular proteins in solution aggregate and become neutral as the multivalent ion concentration is raised above a certain threshold. Further addition of multivalent ions at higher concentrations reverses the aggregation. Above a redissolution threshold, all proteins are redissolved in the solution. This effect was already known in the case of simple colloids, finely distributed substances in a liquid (emulsion paint, for example). However, the researchers' finding was a world first in the case of more complex proteins.

The experiments, which involved optical spectroscopy and small-angle x-ray scattering, were carried out under the leadership of the physicists Dr. Fajun Zhang and Prof. Frank Schreiber. The physicists worked in collaboration with the theoretical scientists from Dr. Andreas Hildebrandt's group at the Saar Centre of Bioinformatics and Prof. Oliver Kohlbacher's group from the Tübingen Centre of Bioinformatics and they succeeded in producing a computer simulation of the charge of proteins in solution. The researchers have prepared a complete phase diagram detailing the amount of salt required for a given amount of proteins to dissolve again. This opens up completely new perspectives for the fundamental understanding of proteins and also for a number of applications in the use of protein systems, for example for the creation of protein crystals that are required to clarify protein structure.

Literature:

F. Zhang, M. W. A. Skoda, R. M. J. Jacobs, S. Zorn, R. A. Martin, C. M. Martin, G. F. Clark, S. Weggler, A. Hildebrandt, O. Kohlbacher, F. Schreiber: Reentrant Condensation of Proteins in Solution Induced by Multivalent Counterions. *Physical Review Letters*, 2008, 101, 148101

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**Press release**

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