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Stefan Schiller – understanding and copying complex molecule systems

Proteins, lipids, carbohydrates and nucleic acids are important building blocks of life – however, they need to become macromolecular structures before they are able to fulfil the functions of a cell's daily business. Dr. Stefan Schiller from the Institute for Macromolecular Chemistry at the University of Freiburg became interested in the diversity of molecular possibilities in nature as a student and is now a specialist in bionic chemistry and synthetic nanobiotechnology. Amongst other things, his work involves the construction of complex protein machines that transfer signals, protein networks for use in medicine and drug shuttles that enable the targeted delivery of drugs.

Dr. Stefan Schiller from the University of Freiburg carries out research in the field of bionic chemistry and synthetic nanobiotechnology. (© private)

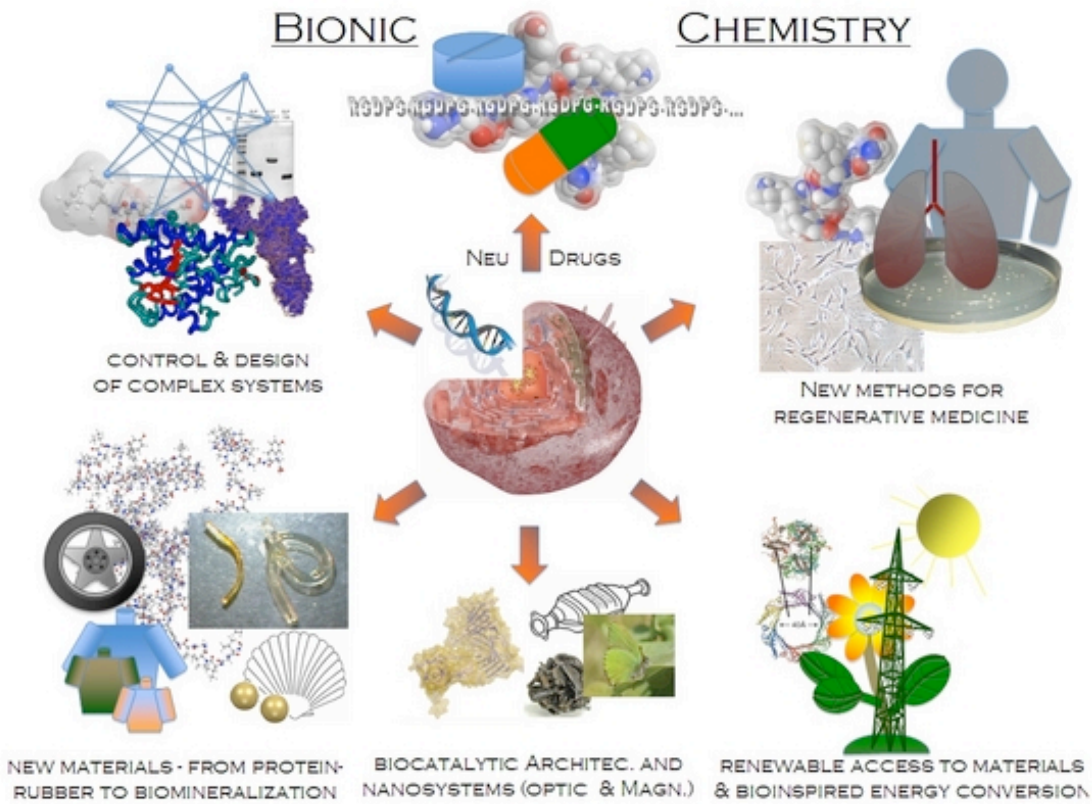
Imagine sitting in the cabin of a crane and assembling building blocks and machines and establishing a production chain work process – but instead of being in a real crane, you're in an imaginary one in the world of molecules and cells. Modern chemists have long been transferring the principle of the polymer sciences to living systems as well as modelling natural principles for use in nanoengineering, a field of research that is nowadays widely known as 'synthetic biology'.

"I have always been interested in complex systems," said Dr. Stefan Schiller from the Institute for Macromolecular Chemistry at the University of Freiburg, Junior Fellow of the Freiburg Institute for Advanced Studies (FRIAS) and member of the Centre for Biological Signalling Studies (BIOSS). Like one of his role models, the Nobel Laureate Hermann Staudinger, Schiller is highly fascinated by the broad range of possibilities arising from combining molecules into higher-level structures. He has learned over the years how to specifically use these possibilities for different applications.

A kit with chemical and biotechnological methods

Artificial multifunctional biomembranes, biomemetic materials for clinical applications or novel energy transducers on solar cell electrodes based on the model of the photosynthesis apparatus of plants – is this possible? Schiller's current interest is based on experiences he had during his studies and a research stay at the University of Massachusetts/Amherst, USA where he learned to construct artificial membrane systems with proteins and lipids and use micromanipulators to form tube-like nanostructures reminiscent of nerve axons.

Schiller, who was born in Wiesbaden in 1971, returned to Germany after being in the States and did his degree thesis at the University of Mainz where he specialised in organic chemistry, biochemistry and macromolecular chemistry. He learned to synthesise so-called glycolipids such as those found on the surface of cancer cells, which are important targets for the immune system. He went on to do his doctoral thesis at the Max Planck Institute for Polymer Research in Mainz. His doctoral work, which he finished in 2003, focused on the synthesis of complex structures from lipids with the goal of imitating biological membranes. "Back then, there was no membrane system available with the typical biological properties, i.e. the right mixture of stability and fluidity, which is one of the key prerequisites for the anchoring of membrane receptors."

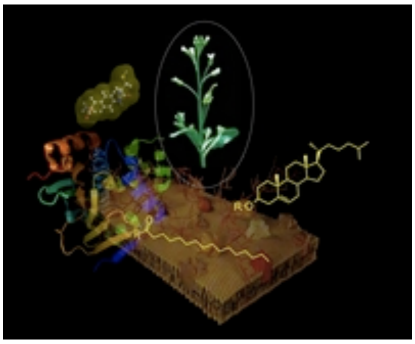


Potential fields of application of bionic chemistry. (© Dr. Stefan Schiller)

After his doctoral thesis and his first steps towards biomimetic syntheses, Schiller was the proud owner of a kit of chemical and biotechnological methods that enabled him to handle the chemical building blocks of life like an engineer. The only thing he still lacked was experience with proteins, which is why he decided to spend some of his postdoctoral period at the Scripps Research Institute in La Jolla in California, USA. His supervisor, Prof. Dr. Pete Schultz, had developed a system that made it possible to specifically introduce amino acids that were different from the 20 natural ones in proteins. Such modifications are necessary in order to enable researchers to specifically alter the function of proteins. "For example, unnatural protein building blocks affect the function of an enzyme or alter the binding properties of a cellular structural element. Schiller succeeded in optimising the method to a degree that enabled him to attach new unnatural amino acids to specific locations in a protein. Equipped with this know-how, Schiller returned to Germany in 2008 to become Junior Fellow at the Freiburg-based FRIAS.

Deciphering the lipid code? Copying photosynthesis?

"Our major field of research is a mix of bionic chemistry and synthetic biotechnology," said Schiller emphasising that his team is specifically interested in obtaining a detailed understanding of natural molecular building blocks, combining them into complex/supramolecular systems, controlling and modifying them in such a way that their new functions enable them to be applied in biological signalling research, biomedicine and biomaterials research. One such application is a project in which Schiller and his cooperation partners from the field of developmental biology are working on the modification of certain signalling molecules with the aim of altering cellular developmental processes. Another of Schiller's projects has recently received a considerable financial injection from the University of Freiburg's Innovation Fund and from the Research Seed Capital (RiSC) programme run by the Baden-Württemberg Ministry of Education, Research and the Arts. This provided the basis for further funding of the idea as part of the DFG- (German Research Foundation) funded 1623 programme entitled "Chemoselective reactions for the synthesis and application of functional proteins".



Deciphering the lipid code: lipids that are attached to proteins have important functions in cells, including the anchoring of proteins in the cell membrane or in the membrane of other organelles, which is crucial for the control of the spatial and temporal distribution of enzymes and signalling molecules. (© Dr. Stefan Schiller)

This particular project focuses on the role of lipid components that are bound to cellular proteins. Lipids are important for many protein functions; for example, they mediate the binding of proteins to membranes inside cells, which makes them indispensable for the spatial and temporal distribution of proteins. In a way, they help conduct cellular processes. "The lipid code needs to be deciphered before it can be applied to cellular protein chemistry," said Schiller highlighting his team's plans for the next few years.

Two more examples show that Schiller's team is both interested in and dealing with a broad range of different topics. Schiller and his colleagues are currently experimenting with doughnut-like protein polymer structures that they attach to the surface of solar cell electrodes. The centre of the doughnuts can be equipped with different metal nanoparticles and used to convert sunlight into electricity, just like the reactive centres of the photosynthesis machines in plants. They provide excellent prospects for solar technology.

Using a patented biotechnological procedure based on a plasmid, Schiller and his team are also able to construct structures from modified components of the protein elastin, which normally occurs in the skin. The researchers thus create novel polymers that can be used in all areas of the material sciences and in the field of biomedicine. These polymers can be produced in E. coli, which is a lot cheaper than chemical procedures and can also be easily scaled up. In summary, a lot of construction work is going on in Freiburg, albeit that most of the constructions are only visible under the microscope.

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A contribution from:

Further information:
Dr. Stefan Schiller
Freiburg Institute for Advanced Studies (FRIAS)
University of Freiburg
Tel.: +49 (0)761/ 203 - 97 405
E-mail: stefan.schiller(at)frias.uni-freiburg.de

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