Universität Konstanz





### Living Research. Chemistry in Konstanz

We do research together. Working in the Department of Chemistry at Konstanz means taking an interdisciplinary approach to science, exchanging ideas and researching within a network. Working together with other teams - within our department, but also crossing the border to colleagues from other disciplines – is the rule in Konstanz, not the exception. It is this philosophy which has helped to shape the special profile of our department. This is reflected particularly in the Konstanz Research School Chemical Biology (KoRS-CB), the DFG Research Group FOR 434, the Collaborative Research Centers 969 and 767, and the Center of Applied Photonics, which is operated conjointly with the Biology and Physics departments.

Our main areas of research range from modern, timely questions from life sciences to hot topics of material sciences. Together with national and international research partners, we work as part of a vibrant network to get to the bottom of the complex interplay of molecules, which determine the lives of each and every organism, and to promote the development of new materials with customized structures and properties.

Our interdisciplinary research enables us not only to enjoy the scientific interactions amongst colleagues, but also to rely on excellently equipped laboratories.

Working in Konstanz means researching in a communicative environment with excellent quality of life and work, and in one of Germany's most attractive regions. We do research together. Would you care to join us? Prof. Dr. Rainer Winter Head of Department

# **Doctorate Level Studies**

The aim of doctorate level studies at Konstanz is to offer postgraduates a structured, research-based framework, and to promote the exchange of scientific knowledge within the faculty as well as on an interdisciplinary level. For this reason, all doctoral students in the Faculty of Chemistry are signed up on structured doctorate courses: the Graduate School Chemistry (GCh) or the Konstanz Research School Chemical Biology (KoRS-CB).

Besides innovative mentoring by the PhD committee, the Graduate School Chemistry also offers doctoral students a qualification course, scientific lecture series and courses from the field of Transferable Skills.

The same is offered by the Konstance Research School Chemical Biology (KoRS-CB), but with an interdisciplinary research focus embracing the Departments of Biology, Chemistry and Computer and Information Science. The aim of this research is to gain an understanding of complex cellular networks, and to discover how physiological processes are controlled on a molecular level and an atomic level. The KoRS-CB is subdivided into five areas of research — Synthetic Chemistry, Cellular Biochemistry, Biomedicine, Biophysics and Bioinformatics & Cheminformatics — and is funded by the German Excellence Initiative.

# University of Konstanz - Towards a Culture of Creativity

Flexible, communicative, strong in research: The University of Konstanz is one of the most successful universities in Germany and is one of the internationally leading younger universities. It was successful in both phases of the German Excellence Initiative. Keenly aware of the fact that innovative ideas can only flourish in an environment marked by communication and interdisciplinary exchange, the university creates optimum conditions for top level research, studying and teaching, offering a high quality of work and life as well as an international character. The University of Konstanz has won awards for its equal opportunities offers and family-friendly structures, and actively supports the careers of young researchers.

Konstanz takes an interdisciplinary approach to research. All departments cooperate in research and teaching. The main focuses of research are on Nanoscience and Material Science, Chemical Biology, Ecology, Cultural Sciences and Decision Sciences.

At the University of Konstanz, teaching is embedded in research.

Students benefit from top-notch research and can make use of the research infrastructure. The University of Konstanz is currently home to some 11,700 students enrolled in around 120 different degree courses in the fields of Mathematics, Sciences, Humanities, Law, Business and Administration.





### **Natural Products Disarming Bacteria**

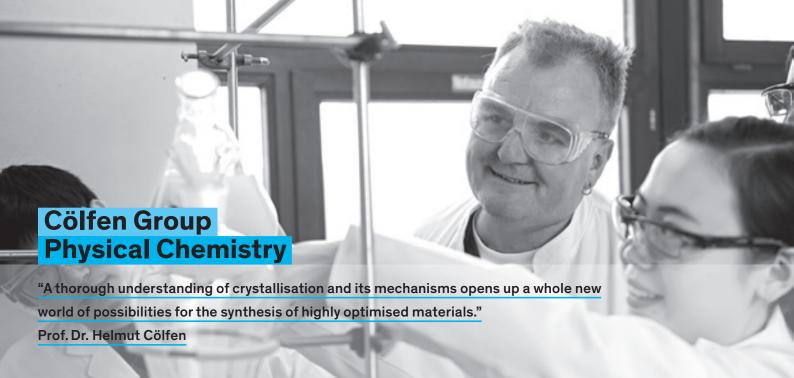
Bacteria are social organisms — at least sometimes. Generally speaking, they don't act as individuals, but coordinate their behaviour at population level. Together, they create biofilms, simultaneously produce toxins or move over surfaces in groups. They communicate with each other via chemical substances — and it's precisely here that Dr. Thomas Böttcher and his team come into play.

"We investigate how microorganisms communicate via chemical substances, how they mutually affect each other's behaviour, and how they defend themselves against other organisms," Thomas Böttcher explains. "In particular, we're interested in substances that

allow us to manipulate the communication and population behaviour of bacteria. This enables us to intervene in infection processes in a highly targeted manner, for example by stopping bacteria from attacking us."

In particular, Thomas Böttcher is interested in natural products that can manipulate and control the behaviour of bacteria. His team searches systematically for such natural products, elucidates their chemical structure and investigates their potential for treating infectious diseases.

- chemistry.uni.kn/boettcher





### Cement à la Sea Urchins

Sea urchin spicules are actually made of lime. Nothing more, and nothing less. But thanks to their special mesocrystal structure, they're very hard to break. Prof. Dr. Helmut Cölfen investigated this nanoscopic structure, transferred his insights to cement – and turned a biomineral structure into a break-proof high-tech building material.

"Our research concentrates on crystallisation – from nucleation to factors that influence crystal growth. The main focuses are on non-classical crystallisation, biomineralisation and nanostructured organic-inorganic hybrid systems," explains Cölfen, describing his team's research. "We also develop detectors and methods for high

resolution polymer and particle analysis such as analytical ultracentrifugation and field flow fractionation."

Break-proof cement is only the start. "A thorough understanding of the processes behind crystallisation will make possible the synthesis of highly optimised crystalline materials in a wide range of fields, from new energy storage devices to bone implants and self-healing teeth," predicts Cölfen. Not without reason is he listed by Thomson Reuters and the Times Higher Education Index amongst the world's top 100 chemists with the highest citation impact scores between 2000 and 2010. — chemistry.uni.kn/coelfen



"Our vision is precision measurement of the structure and dynamics of bio-macromolecules right where they are at work – inside a living cell."

PD Dr. Malte Drescher



### **Elegant Spin Labeling for Magnetic Resonance Experiments**

It's probably the most elegant solution for site-directed spin labeling ever: During the natural biosynthesis of a protein, magnetic markers are added directly to the cell in form of modified amino acids. The structure of the protein in the living cell can now be ascertained by obtaining distance constraints in the nanometer range, by means of electron spin resonance spectroscopy.

The development of intracellular electron spin resonance spectroscopy is a good example of the research work done by Malte

Drescher's team. It develops and applies special spectroscopic methods for investigating the structure and dynamics of macromolecules in complex environments to adress timely questions in biophysics and material science.

"The overall aim is to elucidate the structure and dynamics of macromolecules right where they are at work, inside the cell or the nanoparticle, for example," explains PD Dr. Malte Drescher, whose work is funded by the German Research Foundation's Heisenberg programme.





### **Nucleation Precursors**

Minerals and crystals are benchmarks for hard and brittle substances. In the early stages of crystallisation, however, there can be liquid-like mineral precursors which have been largely ignored in nucleation research until recently. Classic theories fail to describe many aspects and experimental observations during the onset of crystal formation. Dr. Denis Gebauer focuses his research precisely on these initial stages. His quantitative findings have added an alternative viewpoint to the textbook opinions that have existed for hundred years, thus fundamentally changing basic approaches taken in nucleation research.

"We work on the physical-chemical characterization of the molecular mechanisms underlying the precipitation of (bio)minerals from aqueous solutions," explains Gebauer, briefly sketching the research work done by his team. What are the basic precursors of crystals in aqueous solutions? What processes lead from these precursors and intermediate phases to the formation of crystals? How can these processes be controlled and directed? "The target of our research is to develop a new and inherently consistent theory for nucleation, which accounts for all experimental observations," Gebauer explains.



"We develop simpler and more precise gene switches: they don't need transcription factors, because they're part of the protein-coding RNA." Prof. Dr. Jörg Hartig



### An Unusual Perspective on Nucleic Acids

When it comes to Lego, strangely-shaped blocks are often the most interesting. They enable you to think up whole new constructions and formerly impossible functions and designs suddenly become possible. It's the same with nature's molecular building blocks. Nucleic acids can also adopt unusual structures and functions with special characteristics, including the four strand quadruplex structures that frequently occur in nature.

Prof. Dr. Jörg Hartig's team researches such unusual structures and characteristics of nucleic acids, particularly catalytically active RNA

(ribozymes) and four stranded nucleic acids. "The biological function of DNA and RNA quadruplex structures ranges from controlling gene expression to controlling the diversification of genetic information. We characterise the formation, characteristics and biological function of this four stranded DNA and RNA," explains Jörg Hartig. "Building on these unusual nucleic acids, we then engineer artificial, RNA-based gene switches which make it possible to re-program natural biological systems." Amongst other things, his team has succeeded in developing an RNA-based gene switch which is able to control oncolytic viruses.

– chemistry.uni.kn/hartig



"Many diseases are caused by misfolded proteins. Hence a molecular understanding of the protein folding process is of fundamental interest to science and crucial for the development of medications."

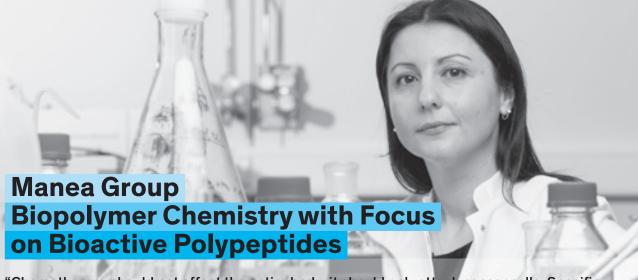
Prof. Dr. Karin Hauser



### Protein Folding in Real-Time

The Hauser group tracks the molecular processes of protein folding in real-time, by observing the dynamics of single amino acids. To elucidate the structure, function and reaction mechanisms of biomolecules in general, they design and use new spectroscopic methods. The team particularly focuses on the development of infrared spectroscopic techniques with a high time resolution, facilitating the analysis of molecular mechanisms on a time scale of nanoseconds. Molecular probes provide an improved spatial resolution of the structural dynamics.

"Gaining a molecular understanding of the protein folding process is of fundamental scientific interest, because many diseases are caused by the misfolding of proteins. Our studies provide an important basis for the pharmaceutical-medical development of drugs," explains Prof. Dr. Karin Hauser. Her team also focuses on charge transfer processes in proteins, photokinetics and protein membrane inter-actions. The investigated molecular systems range from small model peptides to large membrane proteins.



"Chemotherapy should not affect the entire body; it should only attack cancer cells. Specific delivery of chemotherapeutic agents to cancer cells – this is the task of our bioconjugates."

Dr. Marilena Manea



### **Tumor Targeting with Peptides**

Chemotherapy needs to become more targeted and without side effects. Rather than affecting the entire body, the drugs used in "Targeted Chemotherapy" should only affect cancer cells. The idea is to combine chemotherapeutic agents with a carrier molecule, which only binds to certain receptors that are highly expressed on the surface of cancer cells.

With the aid of peptides, Dr. Marilena Manea investigates this approach: "One of our main research areas is focused on the development of cytotoxic bioconjugates consisting of chemotherapeutic agents and peptides," Manea explains. Her research deals with

bioactive polypeptides – their synthesis, structural analysis and mechanism of action – for potential biomedical applications. Successfully: For instance, a combination of the GnRH-III peptide ("gonadotropin-releasing hormone") with the anticancer drug Daunorubicin has proven to be effective in decreasing the tumor growth in colon carcinoma bearing mice, without causing side effects. "Our current work focuses on bioconjugates containing more than one cytostatic agent. We call this 'Combination Targeted Chemotherapy'." The Manea Group also develops bioanalytical methods for identifying and characterising potential protein biomarkers, e.g. to diagnose Alzheimer's disease. - chemistry.uni.kn/manea



"We develop new, chemistry-based approaches for studying complex biological systems that defy state-of-the-art approaches. In particular, we're interested in important biomolecules such as nucleotides, oligonucleotides and proteins." Prof. Dr. Andreas Marx

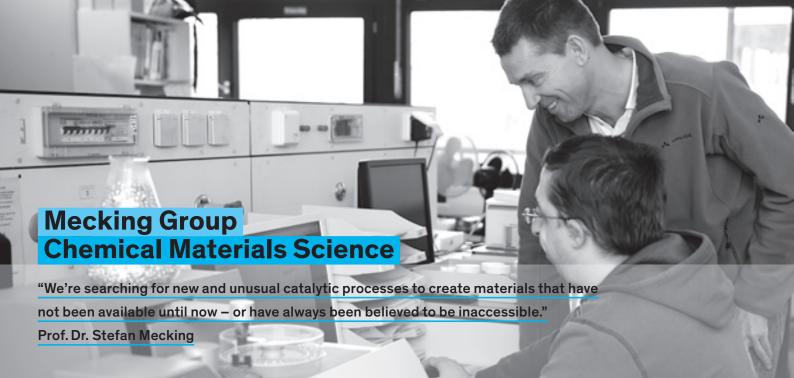


### Tailor-Made Molecules

How do you read a genome? How is the information contained in it transcribed, and how is this regulated? With its research into the chemical biology of DNA replication, the Marx Group has set itself the task of uncovering the mechanisms that determine and control biological processes. "Our research involves the targeted synthesis of biomolecules with a tailor-made profile of characteristics and functions, for example nucleotides, oligonucleotides and proteins. Their application gives us insights into complex biological processes," explains Prof. Dr. Andreas Marx. An important role is played here by DNA polymerases – "genome synthesis machines", which are responsible for duplicating DNA during cell division. Together with his team, Marx develops tailor-made and multi-functional polymerases, which are used amongst other things in simplified mainstream procedures for the early diagnosis of medical conditions.

Andreas Marx' scientific work is shaped by his commitment to transfer theory to practice in industry and clinical diagnostics. Together with other scientists from the University of Konstanz, he founded the company myPOLS Biotec to develop and market DNA polymerases which are optimised for their intended use. For his research on artificial replication systems for epigenic applications, Andreas Marx received the ERC Advanced Grant in 2013.

- chemistry.uni.kn/marx





#### A Dream Reaction Come True

Repeatedly, it's been called a "dream reaction": a functional group from the centre of a molecule is transformed into an ester group at the end of the molecule. In this case, it was vegetable oils and algae oils which were transformed via the "dream reaction" – into a new chemical element, which, on a regenerative basis, opens the door to a whole new range of materials and products. This multi-faceted challenge is one example of the subject areas covered by the Mecking Group.

"Our research deals with the discovery of new and unusual catalytic paths, which open the door to materials which have been inaccessible up to now," Prof. Dr. Stefan Mecking explains. "The aim of our

research is to understand the different processes, some of which are interlocking, of catalytic transformations on a molecular level." This includes the activation of small molecules, without allowing the active centre to be destroyed by functional groups which are also highly reactive, as well as the development of larger defined molecular and supramolecular structures enabled hereby. Special attention is paid to the question of how the properties of a material evolve during its creation. In his research, Stefan Mecking has already found an industrial application, in designing plastics which are less breakable and hence more durable.

- chemistry.uni.kn/mecking



"Focusing on main group elements, in particular on highly polar organometallics containing phosphorus, we specifically investigate molecules containing elements in unusual oxidation states, coordination numbers, coordination geometries or bonding situations."

Prof. Dr. Gerhard Müller



# **Exploring the Extremes of Chemical Bonding by Structural Methods**

With approaches from the fields of inorganic chemistry, structural chemistry and main group organometallics, Prof. Dr. Gerhard Müller investigates molecules in unusual bonding situations. "Such molecules may serve as prototypes to show the extremes of chemical bonding in general," Müller explains. Structural criteria are primarily used to probe the mode of bonding, which provides clues as to their electronic structure.

"These data are augmented by NMR studies in solution and in the solid state which often give a complementary view of structure and bonding," Müller points out.

A special focus lies on highly polar organometallics containing phosphorus. Müller applies anionic phosphines to induce phosphorus coordination to main group elements which are known to be notoriously reluctant to form phosphine complexes. A second field of research is the structural chemistry of biologically active molecules, e.g. amino acids, small peptides and their metal complexes.



"We want to go beyond computer simulations that show us only a single level of resolution. That's why we combine multiple simulation models with each other to produce a meaningful overall picture."

Prof. Dr. Christine Peter



### A Question of Resolution

The computer simulation of chemical or biological processes is a question of resolution. Take the folding and aggregation of proteins, for example: on the one hand, we want to study the processes in atomic resolution, but on the other hand, we don't want to lose sight of the macroscopic process as a whole. Computer simulations in principle allow us to observe individual atoms, but typical computing power is limited to about a million atoms, and a time scale of nanoseconds to microseconds – not enough for many biological or biomaterials systems.

Prof. Dr. Christine Peter develops models for the computer simulation of just such situations — by offering a "coarse grained" perspective, which combines atoms into groups. To achieve this, she links models at different levels of resolution to create one multi-scale simulation model. "This enables us to access complex systems where it is necessary to understand both microscopic properties and macroscopic processes," explains Christine Peter. The computer models are used to examine biological and material science systems, as well as to support the analysis of experimental, e.g. spectroscopic, data.



### When 1+1 is more than 2

Skillful architecture – the ingenious interaction of individual components – is what makes a house more than just "bricks and mortar". It's the same in chemistry and material sciences. Applying the principles of architecture to the nanoscale, the Polarz Group searches for cooperative and systematic effects in the field of functional materials. Ideally, the different components of a system should interact in such a way as to produce more than the mere sum of their properties. They should generate new characteristics, which none of the individual components can produce on its own. The hierarchical

structure of complex materials, and hence the precise geometric assembly of functional units interacting with each other, are the key to achieving this goal.

The research work in the team headed by Prof. Dr. Sebastian Polarz concentrates on inorganic, organic and hybrid materials, including the field of semi-conductors and the catalysts for new energy sources. For his research into a new class of surfactant systems with inorganic head groups, Polarz received an ERC Consolidator Grant in 2014.



"Our investigations on biological, biomimetic and artificial nanocomposites give a chance to understand whether basic principles and laws of 'classical' crystallization are also valid for the description of the formation of nanostructured materials and, in particular, of 'mesocrystals'." Dr. Elena Sturm (née Rosseeva)



### Insights in Nanocomposites

The research and development of nanostructured materials is one of the most emerging interdisciplinary areas of materials science. Due to their unique and sophisticated structuring, nanocomposite materials reveal unique physical and chemical properties significantly different from the bulk properties of their components. The most fascinating natural examples of nanocomposites are represented by so-called biominerals, acting as functional materials in living systems.

The Konstanz' researcher Dr. Elena Sturm (née Rosseeva) puts a focus on investigating the basic principles of biomineralization and structure of the apatite-based dental (dental-like) hard tissues of the elements of the feeding apparatus of conodonts (one of the earliest

vertebrates) and cichlid fishes as well as their respective biomimetic materials.

"The basic philosophy driving our research work is to get a deeper insight into the fundamental principles of structuring and formation of nanocomposite materials from biological, biomimetic and artificial systems," Sturm explains. Inspired by this remarkable natural design concept of biological and biomimetic materials, her research also focuses on the synthesis and characterization of "artificial" nanocomposite materials which are formed by a controlled self-assembly of nanoparticles with mutual crystallographic orientation (e.g. mesocrystals).

— chemistry.uni.kn/sturm



"We combine approaches of chemical biology and genomics to gain new insights into epigenetic mechanisms of transcriptional regulation – and to open up new doors in the diagnosis and treatment of cancer."

Dr. Daniel Summerer



### **Expanding the Programmability of DNA Recognition**

An adult human consists of more than 200 different cell types. All these cells essentially contain the same genomes. Their different characteristics are determined by the regulation of gene expression. How the expression of genes is controlled by epigenetic mechanisms, and how this process can be influenced, is Dr. Daniel Summerer's field of research. Using chemical biology approaches, the Summerer Group studies and reengineers protein-nucleic acid complexes with key epigenetic functions, which enables otherwise inaccessible insights into epigenetic regulation processes, and holds potential for diagnostics and therapy.

For example, through the molecular re-design of so-called TALEs

(transcriptionactivator-like effectors), Daniel Summerer succeeded in constructing receptors with an expanded programmability of DNA recognition. These cannot only identify the canonical DNA bases A, T, G and C, but also epigenetically modified DNA bases such as 5-methylcytosine (mC) and 5-hydroxymethylcytosine (hmC) – in userdefined DNA sequences. This opens the door to a completely new and very simple analysis approach for epigenetic DNA modifications. Summerer's method is particularly relevant when it comes to cancer research, as mC and hmC are important biomarkers for cancer tissue. For his research, Summerer has been awarded the Hellmut Bredereck Price of the GDCh in 2015. - chemistry.uni.kn/summerer



"Organometallic  $\pi$ -systems combine redox reactions at low potential with high electron mobilities, intensive absorption bands in the visible spectrum and the near infrared, and high stabilities in paramagnetic states. We exploit the coupling of these functions and strive to develop new applications." Prof. Dr. Rainer Winter



# A Smart Window into Future Applications

The Winter Group focuses primarily on conjugated organometallic  $\pi$ -systems. Through intimate coupling of electrochemical and spectroscopic methods, the team identifies the electronic properties of these systems. One aspect of particular interest in this is the impact of redox reactions on the bonding characteristics and properties of the chemical systems. "We are especially interested in how the direct linking of dyes with redox-active metal units influences their absorption and emission behaviour," explains Prof. Dr. Rainer Winter. These compounds are used, for example, in dye-modified solar cells and in switchable electrochromic windows ("smart windows").

"We are currently developing particularly efficient polyelectrochromics, emitters and new classes of organometallic single-molecule magnets with uncoupled spins which are ferromagnetically aligned," Rainer Winter explains. "We also have developed methods whereby the charge and spin localization or delocalisation in extended organometallic  $\pi$ -systems featuring one or more identical or different redox-active entities can be determined and quantified." Nationally and internationally, the Winter Group supports other teams with their electrochemical and spectroelectrochemical expertise.



"Modern nanotechnology is a cross-disciplinary field with enormous prospects for the future. The challenge here is to bring different scientific traditions together." Prof. Dr. Alexander Wittemann



### Playing Lego on a Nanolevel

"When you look at our research, imagine a colloidal game of Lego," suggests Prof. Dr. Alexander Wittemann, "where the building blocks are only a few billionths of a metre in size." The Wittemann team uses such nanoscale building blocks to construct complex, but hierarchical organized structures on the mesoscopic up to the macroscopic scale. These enable the scientists on the team to generate new materials with customised properties. "This requires traversing the complete chain, from the synthesis of suitable nanoparticles to the preparation of nanoparticle assemblies, to the review of possible applications for the new superstructures," Alexander Wittemann explains.

The research work done by the Wittemann Group is classified as colloid chemistry, with elements of materials science as well as nanotechnology and mesotechnology.

The aim is to understand more fully the way functional nanoscopic components self-organise into supracolloidal structures. The Wittemann Group's basic research is only a stone's throw away from its field of application. The team has succeeded, amongst other things, with the synthesis of plasmonic particle clusters from gold nanoparticles – which is highly interesting for surface-enhanced spectroscopy.

- chemistry.uni.kn/wittemann



"In nature, carbohydrates do more than just provide energy. They're involved in significant biological recognition processes. Our aim is to gain a better understanding of these processes in order to control them and suppress the development of diseases such as cancer." Prof. Dr. Valentin Wittmann



### Carbohydrates' Recognition

"How can we make carbohydrate structures visible in a living cell?" asks Prof. Dr. Valentin Wittmann. There are genetic methods for marking proteins in cells, but these techniques founder when it comes to carbohydrates. Wittmann developed an elegant method to perform this task: he modifies sugar molecules with unusual functional groups, "feeds" them to cells, and is thus able to mark glycoproteins and glycolipids in the cell and colour them with fluorescent dyes. This opens the door to research on decrypting the biological functions of carbohydrates.

The Wittmann Group is particularly interested in the role of carbohydrates in biological recognition processes, such as the processes involved in cell adhesion. The Group studies multivalent interactions between carbohydrates and proteins. "When a number of ligands and receptors interact simultaneously, it leads to a disproportionately high gain in affinity. We study these processes mechanistically," Wittmann explains. To this purpose, his team develops artificial multivalent ligands which have great potential for inhibiting viruses, bacteria and toxins, as well as potential in the field of diagnosis.



"We want to understand the dynamic processes in tiny systems. The development of more sensitive and selective methods for optical microscopy set the stage for us in this." Prof. Dr. Andreas Zumbusch



# Spectroscopy in a Tiny Space

The Zumbusch Group is irrevocably wedded to four capital letters: CARS – the abbreviation for Coherent anti-Stokes Raman Scattering microscopy. This spectroscopic microscopic procedure opens the door to a highly sensitive and selective analysis of molecules, with a high spatial resolution. Samples do not need to be marked in CARS microscopy, since the procedure exploits the resonances of molecular vibrations to generate contrasts. This procedure, which is now widely used, was largely developed by Prof. Dr. Andreas Zumbusch and his team. But although it is the best known invention produced by the Zumbusch team, it represents only one aspect of their research.

"Our aim is to understand more fully the dynamic processes in the tiniest possible structures," Andreas Zumbusch explains. "To this purpose, we develop and apply new methods for optical microscopy, particularly by using ultra-short laser pulses." Another main focus of research in the team is on the dynamics of organelles, colloids and the reciprocal effects of proteins in biological cells. The microscopy techniques developed by the Zumbusch team also have great potential for applications in medicine. Research is currently underway to see how CARS microscopy can support operations, to distinguish benign from malignant tumor tissue without the need for a biopsy.

- chemistry.uni.kn/zumbusch

