Universität Bielefeld

CeBiTec
Center for Biotechnology

Center for Biotechnology
Research Groups

Preface

Prof. Dr.-Ing. Gerhard Sagerer

Founded just a little more than 10 years ago, the Center for Biotechnology (CeBiTec) at Bielefeld University has established itself as a major international research institute of exceptional quality. It is a great example for the University's successful tradition of bringing together various scientific fields in order to tackle today's complex problems.

Combining the expertise of researchers from natural sciences, from life sciences and technological areas such as informatics enables the CeBiTec to solve some of the mysteries of life, and to develop solutions to put this newly gained knowledge to practical use for our everyday lives. We witness the emergence of the scientific basis for the development of new pharmaceuticals, for new technology used in environmental protection such as the application of bio fuels, or for new microscope techniques, to name but a few.

The CeBiTec has continuously expanded and developed a clear and well-formed structure to facilitate the interdisciplinary exchange between the fields involved. Currently, 35 research groups from the Faculties of Biology, Chemistry, Physics, and Technology collaborate at the CeBiTec. Of crucial importance for their work are the various technology platforms which provide the researchers with state-of-the-art technical infrastructure and methods. The Genomics and the Bioinformatics platforms deserve special mention here.

The CeBiTec has also expanded physically: In 2009, an extension was added to the original building completed in 2007 to accommodate the growing number of scientists and students working at the CeBiTec. This laboratory building does not only meet the highest demands of modern research, it is also architecturally appealing and has become an integrated part of the Bielefeld campus.

In spite of the tough financial conditions most universities find themselves in these days, Bielefeld University has pursued an uncompromising policy with respect to the recruitment of top academics. The CeBiTec has succeeded in exerting a great appeal to ambitious researchers, and will seek to do so in the future.

At the same time, the CeBiTec plays an important role in the promotion of the next generation of young scientists. CeBiTec's own Graduate Center offers ideal conditions for doctoral students and provides a starting platform for a successful scientific career. Furthermore, scientists at the CeBiTec have developed innovative study programs which attract gifted students from all over the world.

The CeBiTec not only shines in the international world of science. It also realizes high calibre projects with important cooperation partners in many branches of industry, including multinational companies. CeBiTec also advises companies within the Bielefeld area operating in a nanoscience context, for instance.

I am convinced that the CeBiTec will continue to give impetus for developments in the key areas of the natural sciences and biotechnology, and I would like to wish all participating scientists the best of success for their work.

I hope that you will enjoy reading this brochure, which provides an excellent overview of the various research activities taking place at the CeBiTec.

Prof. Dr.-Ing. Gerhard Sagerer
Rektor, Bielefeld University, September 2011

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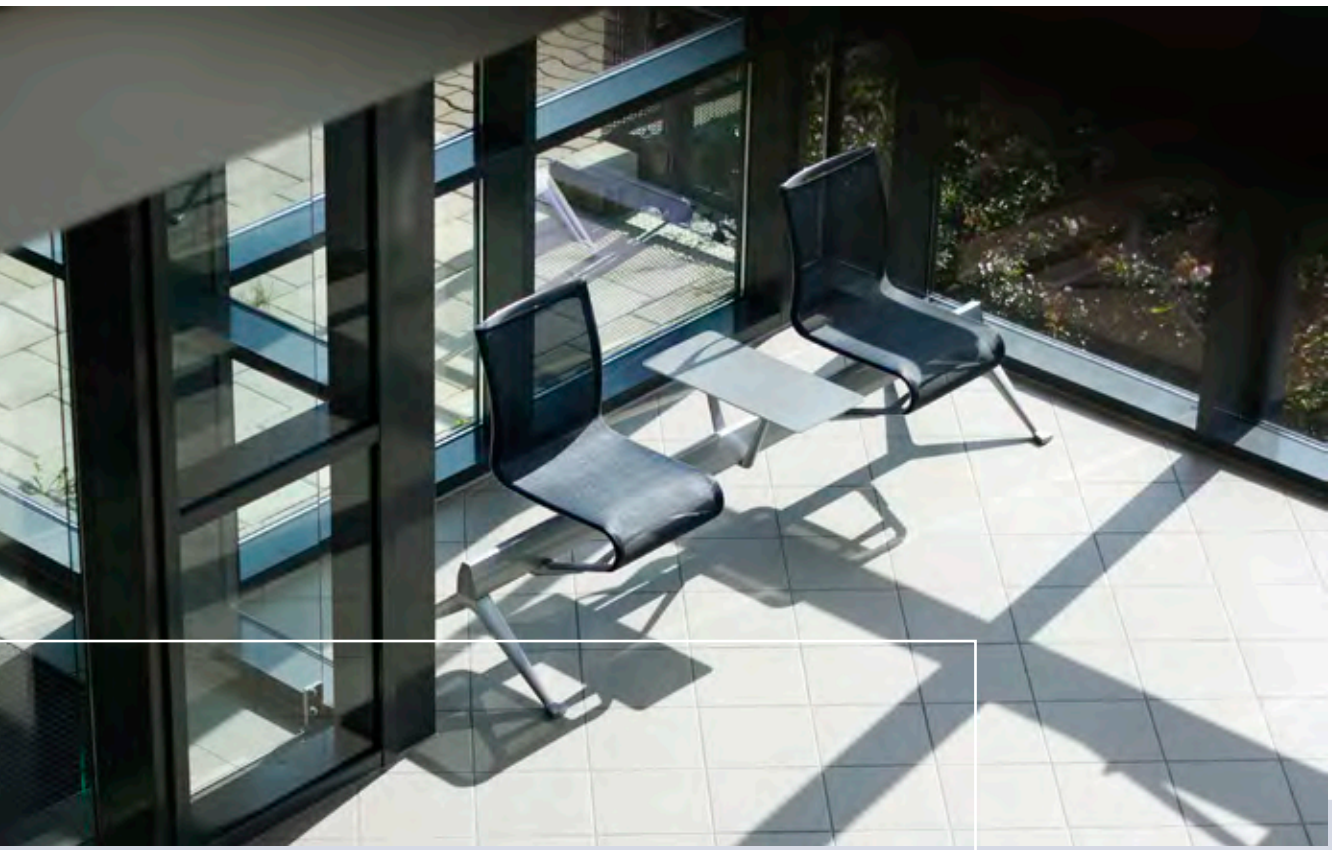

The Center for Biotechnology

A Central Academic Institute of Bielefeld University

Research interests and activities in biotechnology at Bielefeld University are united in the CeBiTec as a faculty spanning central academic institute. Currently 35 research groups cooperate in different research fields while using comprehensive technological infrastructure.

Four Institutes, Technology Platforms and Graduate Programs

The Center for Biotechnology is one of the largest and most prominent central academic institutions at Bielefeld University. The CeBiTec bundles activities and interests of research groups focusing on various aspects of biotechnology within the Faculties of Biology, Chemistry, Physics, and Technology. Its mission is to encourage and to support the development of innovative research crossing discipline boundaries. Since its foundation in 1998 four institutes 'Institute for Bioinformatics – IfB', 'Institute for Genome Research and Systems Biology – IGS', 'Bielefeld Institute for Biophysics and Nanosciences – BINAS', and 'Institute for Biochemistry and Bioengineering – BioChemTech' have been established under the roof of the CeBiTec.
The members of the CeBiTec undertake research projects in a multitude of fields with a main focus on projects in genomics and postgenomics of microorganisms as well as genome research on plants, particularly on *Arabidopsis thaliana*. Research on functional genomics of animal cells and cell culture technology represents a further field of activity. A latter research field concerns solar biofuels and bioenergy production. A fundamental requirement and a key to success for all these research activities are advanced bioinformatics capabilities with a special focus on data management for genome and postgenome research and on the development of efficient algorithms for comparative genomics.
The availability of comprehensive technological infrastructure as being provided by CeBiTec's technology platforms is crucial for a successful scientific work. The 'Technology Platform Genomics' provides the state-of-the-art technical equipment for genomics, transcriptomics, proteomics, and metabolomics. Likewise important as the availability of genome and postgenome methodologies is the management, processing and analysis of the data obtained. The 'Technology Platform Bioinformatics' provides general hardware and software support for all research

Dr. Stefan Weidner

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1996	PhD, Bielefeld University, Germany
1996–2001	Postdoctoral positions, Bielefeld University, Germany
2001–2009	commissioner for the construction of the CeBiTec building
since 2004	Executive Director of the CeBiTec

1999	PhD, University of Bonn, Germany
1999–2005	Group leader, Institute of Biotechnology, Research Center Jülich, Germany
2000	visiting scientist, Imperial Cancer Research Fund, London, UK
since 2005	Professor for Cell Culture Technology, Bielefeld University, Germany
since 2010	Scientific director, CeBiTec

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groups of the CeBiTec within genome and post genome projects. A high-performance compute cluster is available for large scale computations like whole genome annotations or metagenome analysis. Furthermore, a comprehensive software suite to systematically store and analyse all data sets from genomics, transcriptomics, proteomics, and metabolomics has been developed. The activities in bioenergy research will be consolidated in the 'BioEnergieTechnikum' building which will be completed in October 2011. The available equipment and expertise in the fermentation of microorganisms and of animal cell culture are also planned to be combined in a technology platform. Driven by bio- and nano-physicists a platform for a new generation of microscopes especially appropriated for the analysis of biomolecules is currently being planned.
Academic training of graduates is fostered by the Graduate Center offering high-level PhD programs. Initially starting with

The CeBiTec building

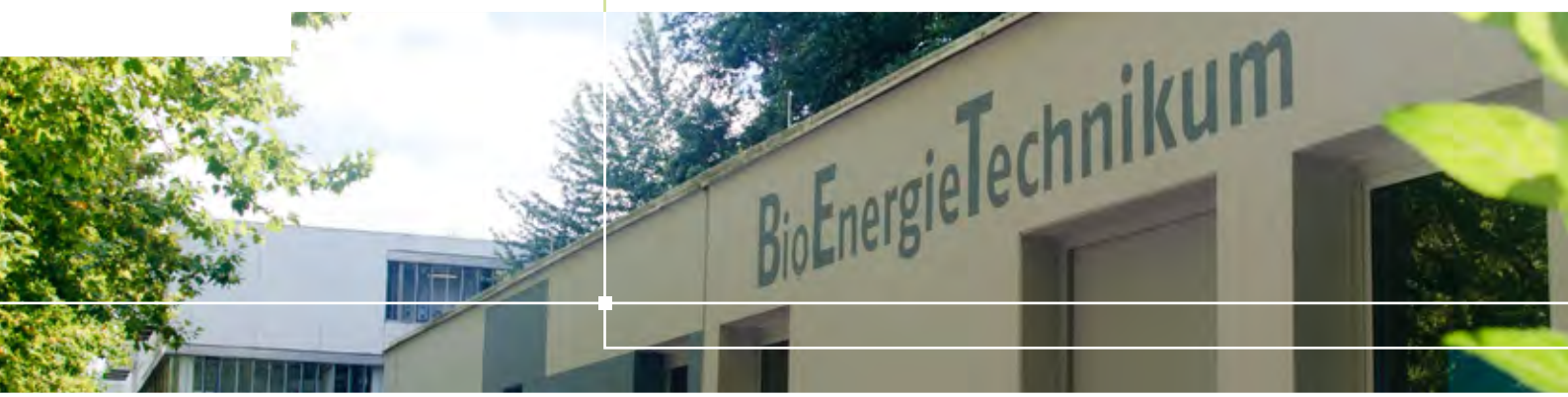
Executive committee of the CeBiTec, May 2011. From left to right: Prof. Dr. A. Gölzhäuser, K. Gorzolka, E. Schulte-Berndt, Dr. A. Goesmann, Prof. Dr. B. Weisshaar, Prof. Dr. O. Kruse, Prof. Dr. R. Giegerich, Prof. Dr. T. Noll (scientific director), Prof. Dr. N. Sewald, S. Konermann, Dr. J. Kalinowski, Prof. Dr. V. F. Wendisch,Dr. S. Weidner (executive director), Prof. Dr. J. Stoye

a program dedicated to bioinformatics and genome research, currently two additional programs are offered. One program is dedicated to industrial biotechnology while the second is an international graduate programme in bioinformatics of signalling networks. To awake pupils' enthusiasm for biotechnology the 'teutolab Biotechnologie' gives upper intermediate pupils (secondary level II) insights into molecular-biological and biotechnological work in practical training. The 'teutolab' is also contributing to the teacher training at the University.

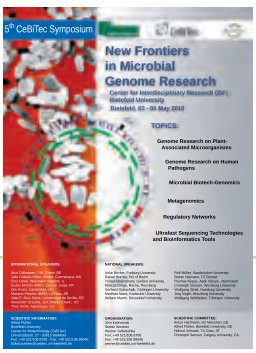
Management of the CeBiTec

With 35 different research groups, the technology platforms and further units the CeBiTec has more than 300 members. This size clearly requires an organizational structure capable of managing not only the day-to-day business, but also the coordination of joint research projects and project applications, as well as setting the future direction. The CeBiTec is headed by Scientific Director Prof. Dr. T. Noll and the Executive Committee composed by representatives of all status groups of the university. The speakers of the four institutes and three further elected members represent the professorate. The groups' research staff, technical staff, and students are also represented in the executive committee by elected members. Dr. S. Weidner is Executive Director of the CeBiTec.

Eight high ranking scientists from industry and academia, all having an excellent expertise in the research areas covered by the CeBiTec, form the CeBiTec Scientific Advisory Board. Prof. Dr. R. Amann (Max-Planck-Institut für Marine Mikrobiologie, Bremen, Germany) is the elected speaker of the board. The Board meets biennially and advises the executive committee in all matters of the CeBiTec, particularly concerning principles of its scientific work and future development.



Posters announcing the six CeBiTec symposia from 2006 to 2011. Every year an up-to-date topic is elucidated and discussed by international invited speakers.



Regular Events and Activities

The CeBiTec organizes various events to foster international contacts and collaborations and exchanges with other scientists. Regularly a colloquium provides a forum for lectures and discussion rounds with project and cooperation partners, and with other invited guest scientists. In summer 2009 a series of Distinguished Lectures was launched, where excellent and outstanding speakers present on current research to members of the CeBiTec and to the public. Furthermore, since 2006 a series of symposia about current research topics is organized annually. Finally, the CeBiTec was successful in launching an European Science Foundation (ESF) research conference series dedicated to 'Industrial Biotechnology' covering three alternating topics 'Microbes and Industrial Biotechnology', 'Microorganisms for Bio-fuel Production from Sunlight', and 'Cell Culture Technologies'. The conferences are accompanied by international summer schools offering young researchers a chance to learn and work with state-of-the-art equipment and technologies offered by CeBiTec's technology platforms. ■

Members of the Scientific Advisory Board of the CeBiTec

Prof. Dr. Rudolf Amann	Max Planck Institute for Marine Microbiology, Bremen, Germany, Director, Head of Department of Molecular Ecology
Dr. Rolf Apweiler	EMBL Outstation – Hinxton, European Bioinformatics Institute, Cambridge, United Kingdom, Head of Sequence Database Group
Prof. Dr. Michael Grunze	Heidelberg-University, Chair of Applied Physical Chemistry
Dr. Ralf Kelle	Evonik Degussa GmbH, Halle/Westf., Vice President R&D Bioproducts
Prof. Dr. Reinhard Krämer	Institute of Biochemistry, University of Cologne, Germany, Executive Director
Dr. Eduard Sailer	Miele & Cie. KG, Gütersloh, Germany, Executive Director
Prof. Dr. Martin Vingron	Max Planck Institute for Molecular Genetics, Berlin, Germany, Director, Head of Computational Molecular Biology Department
Prof. Dr. em. Christian Wandrey	Institute of Biotechnology 2, Forschungszentrum Jülich GmbH, Jülich, Germany

Computational RNA Biology

The universal role of RNA as a regulator of gene expression and metabolism in all kingdoms of life has been recognized just recently. Reaching from the analysis of bacterial immune systems (CRSPR RNA) and metabolite sensing (riboswitches) to post-transcriptional control in eucaryotes by micro-RNAs, the "New RNA World" poses a rich set of bioinformatics challenges.

Previous and Current Research

Our group has long cultivated an interest in the fundamental algorithms for RNA secondary structure prediction. Bioinformatics tools that were born out of this interest in the 1990ies were the visualization tool *RNAmovies* and a heuristic method for riboswitch prediction, *paRNAss*. With the increased recognition of the manifold regulatory functions of RNA, bioinformatics topics related to RNA have begun to dominate the work of our group. Upto 2011, we have produced 14 RNA-related tools, available in open source for download, or for interactive or webservice use via the Bielefeld Bioinformatics Server.
The program *RNAhybrid* (2004) is a widely appreciated tool for the prediction of micro-RNA targets. It combines comparative sequence analysis with the computation of hybridization energy based on thermodynamics, and careful statistics. It allows for, but does depend on heuristic restrictions imposed by many competing programs, such as the much debated "seed-hypothesis" for micro-RNA and mRNA interaction.
Classical RNA secondary structure prediction excludes the so-called pseudoknots for reasons of computational complexity, in spite of their physiological relevance. The programs *pknotsRG* (2004, 2007) and *pKISS* (2010) extend structure prediction to certain types of pseudoknots which occur frequently in functional structures.
The concept of "RNA shape abstraction" was introduced in 2004 and has found a variety of applications. Abstract shapes characterize RNA secondary structure by arrangement of structural components, irrespective of size and sequence content. They help to find significant near-optimal structures (*RNAshapes*, 2004, 2006), which opens a road to comparative structure prediction in the difficult case when structure is more preserved than sequence (*RNAcast*, 2006). Abstract shapes collected in a precomputed index can also significantly speed-up the search of structural RNA family models (*RNAsifter*, 2008). These and other tools are currently used in a DFG project in cooperation with Anke Becker (formerly CeBiTec, now University of Freiburg), where we combine experimental and computational methods in a large scale search for noncoding RNA genes in *S. meliloti* and related Alphaproteobacteria.

Future Projects and Aims

Over the years, our group has worked out the method of "Algebraic Dynamic Programming" (2004), which has been used to great advantage in our own tool development projects. Our recent system "Bellman's GAP" makes this technology available for others, and we seek cooperations and new applications to develop it further. On the theoretical side, a recent review (2011) has shown that there is a lot of unexplored ground with covariance models, designed to describe structural RNA families. Improvement of such models by enhancing them with alternative semantics will constitute a major part of our future work. ■

Life is rich of challenges in the twilight zone of RNA gene evolution, where structure is more conserved than sequence.

Prof. Dr. Robert Giegerich

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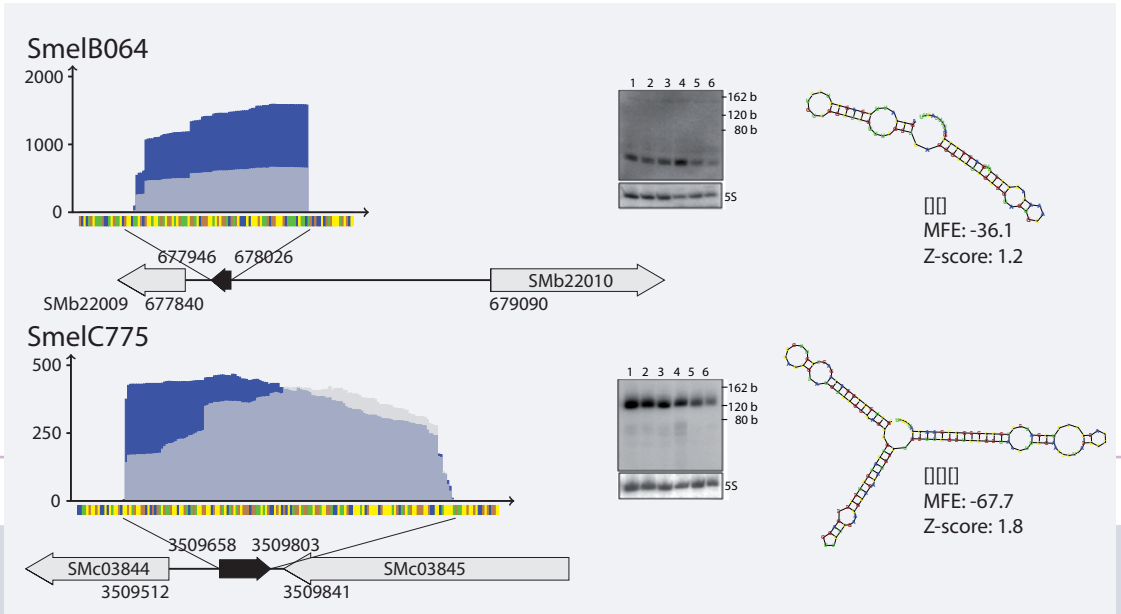
1974	M.Sc. Computer Science, Stanford University
1976	Diploma, Computer Science, TU Munich.
1981	PhD, Computer Science, TU Munich
since 1989	Professor of Practical Informatics, Bielefeld University
since 1993	Building up bioinformatics education and research
2001 – 2007	Speaker of DFG Bioinformatics Center, Bielefeld University

Selected publications

- Rehmsmeier, M., Steffen, P., Höchsmann, M., Giegerich, R.: 2004. *Fast and effective prediction of microRNA/target duplexes*. RNA, 10: 1507-1517
- Giegerich, R., Meyer, C., Steffen, P.: 2004. *A discipline of dynamic programming over sequence data*. Science of Computer Programming, 51(3): 215-263
- Schlüter, J.-P., Reinkensmeier, J., Giegerich, R., Becker, A. *et al.*: 2010. *A genome-wide survey of sRNAs in the symbiotic nitrogen-fixing alpha-proteobacterium* Sinorhizobium meliloti. BMC Genomics, 11(1): 245
- Giegerich, R., Höner zu Siederdissen, C.: 2011. *Semantics and ambiguity of stochastic RNA family models*. IEEE Transactions on Computational Biology and Bioinformatics: 499-516



In search of novel RNA genes: sRNA candidates validated by Northern hybridizations and 5'-RACE. Sequence coverage profile: blue and light grey color denote transcript coverages derived from sample 1 and 2, respectively. Dark grey colored areas represent an overlap of coverages from both samples. y- and x-axis represent coverage and sequence, respectively. Sequence code: blue, A; yellow, C; orange, G; green, U. Grey arrows represent genes flanking or overlapping sRNA genes. Black arrows represent the sRNAs. MFE: minimum free energy within the shape class.

Reconstruction and visualization of Bionetworks

For the implementation of the virtual cell, the fundamental question is how to model and simulate complex biological networks. Our group works on the reconstruction of biological networks based on relevant molecular databases and information systems.

Previous and Current Research

The vision of the implementation of a virtual cell combines bioinformatics and systems biology today. However, we are still a long way from implementing even a simple virtual cell. The first step in reaching this goal is to understand the metabolism which is based on gene-controlled biochemical reactions. Therefore, modeling and simulation of metabolic networks is important. Based on relevant molecular database and information systems, biological data integration is an essential step in constructing biological networks. Our group focuses on tools to create biological networks using data integration and data warehousing methods. For that purpose we develop a software infrastructure for building life science data warehouses using different common relational database management systems. Based on the data from the warehouse infrastructure, we are able to implement project specific (e.g. for cardiovascular disease) and general data warehouse systems (e.g. for metabolic data) to search integrated life science data and simple navigation. In addition, a network editor uses the data from generated biological networks and enriches them with additional information. Using this network editor, different fields of studies are combined such as life-science, database consulting, modeling, visualization and simulation for a semi-automatic reconstruction of complex biological systems. The idea is to extend any molecular data-based network by new targets and interacting elements. Information is visualized in a clear and understandable manner to meet the purposes of underlying research activities. Moreover, our group works on an approach to visualize and analyze inter-cellular and intra-compartmental relationships by correlating pathways with an abstract cell environment in 3D space. The cell can be modeled by using a variety of different eukaryotic and prokaryotic cell component models which are mainly abstractions of electron and light microscopic images. In addition, first approaches of 3D microscopy-based cell component models exist, derived from electron tomographic data.

Future Projects and Aims

In the future, additional databases could be integrated into the systems discussed above. This leads to more comprehensive knowledge in different topics and more complex biological networks as well. It is also planned to integrate text mining approaches and full a text indexing system in the near future. The idea behind the text mining approach is to filter the large

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1990	PhD, Institute of Theoretical Computer Science, University of Bonn
1990 – 1994	Assistant Professor, Institute Applied Computer Science, University of Koblenz-Landau
1995	Habilitation for Applied Computer Science and Bioinformatics at the University of Koblenz-Landau
1995 – 1996	Assistant Professor, Institute of Medical Informatics, IMISE, University Leipzig
1996 – 2001	Professor, Institute of Applied Computer Science, University of Magdeburg
since 2001	Professor, Institute of Bioinformatics and Medical Informatics, Bielefeld University

Selected publications

- Chen, M., Hofestädt, R.: 2006. *A medical bioinformatics approach for metabolic disorders: Biomedical data prediction, modeling, and systematic analysis*. Journal of Biomedical Informatics, 39(2): 147–159
- Töpel, T., Hofestädt, R., Scheible, D., Trefz, F.: 2006. *RAMEDIS, the rare metabolic diseases database*. Applied Bioinformatics, 5(2): 115–118
- Hofestädt, R.: 2007. *Extended Backus-System for the representation and specification of the genome. Journal of Bioinformatics and Computational Biology*, 5(2): 457–466
- Hofestädt, R.: 2009. *DNA-Programming Language of Life*. HBSO, 13:1, 68–72
- Hippe, K., Kormeier, B., Töpel, T., Janowski, S. *et al.*: 2010. *DAWIS-M.D. – A Data Warehouse System for Metabolic Data*. GI Jahrestagung (2): 720–725

amount of data in order to gather the most relevant information. Furthermore, it is planned to automatically integrate PCR and microarray data into a local database. With this feature the user should have the possibility to browse, analyze and store experimental data in a data warehouse. Furthermore, the researcher is able to include experimental data directly into this network model. ■

Reconstruction of the Aliivibrio salmonicida quorum sensing system.

Focusing KIT, the incoming reaction from MPDZ (thick red line) and connections to the alternative locations (thin red lines) are shown, like the Ribosome, Nucleus and Mitochondria.

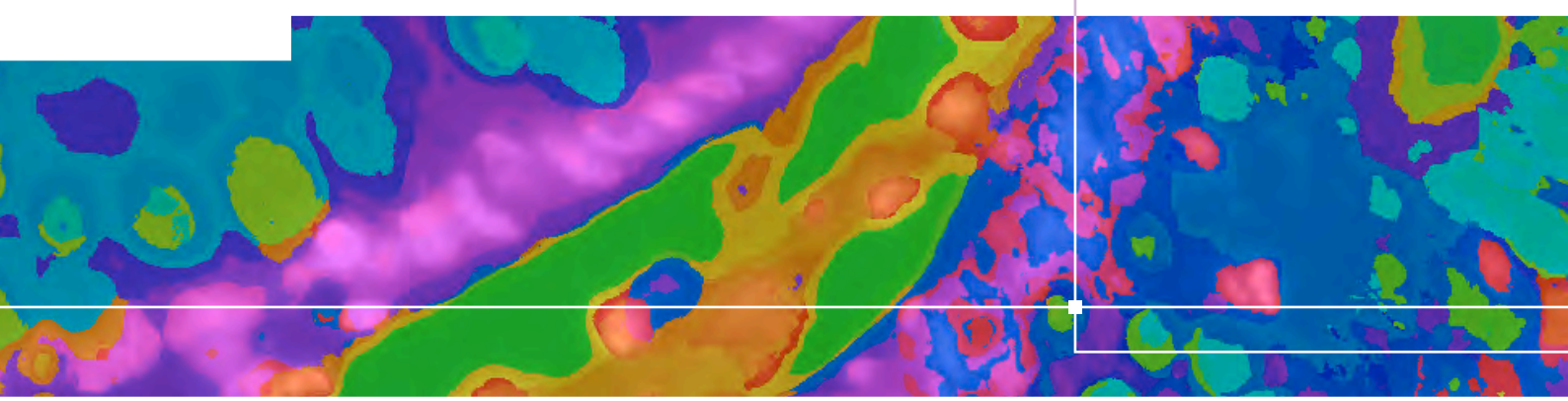
Mining complex biodata

Several technological developments increase the complexity of nowadays collections of biodata almost on a daily basis. The high dimension, the large volume and the non-linear dependencies in the data trigger the demand for new methodologies and tools to enable researchers to find the gold nuggets their mountains of biodata.

Previous and Current Research

The fields of life science and biotechnology are continuously shaped by the ongoing development of new technologies to analyze biological samples. Bioimaging is one example here, since due to its latest advances regarding automation, resolution and dimension, it plays a role of growing importance in life science research. In the last ten years, the Biodata Mining Group gained a lot of experience in the successful development and evaluation of algorithms for the automatic detection and quantification of objects in bioimages and medical images using concepts from the fields of machine learning and neural networks. This approach has shown to have considerable advantages like flexibility and segmentation accuracy. The applications range from automatic tumor detection and classification in MRI of the female breast, via the detection and segmentation of cells in fluorescence micrographs or histopathological slides to the segmentation and quantification of corals in underwater video data. One field of particular interest is the analysis of multivariate bioimages which have been proposed to study molecular networks and interactions. Among these are high-content imaging (HCI), Multi-Epitope-Ligand-Cartography (MELC), Toponome Imaging (TIS), MALDI imaging (MI) or vibrational spectroscopy. The result data of these techniques can be referred to as multivariate images since to each pixel a number of variables is associated. Recently the Biodata Mining Group developed a new technological online platform to enable researchers to analyze such high-dimensional data through the web: BioIMAX (BioImage Management, Analysis and eXploration). The approach combines principles from image processing, unsupervised machine learning, information visualization and new web technology.

In addition the group contributed significantly in other fields of bioinformatics, such as the analysis of new age sequencing data regarding the classification of short sequence reads and the visualization of metagenome data.



How can new computational approaches support biomedical researchers in their attempt to develop mental models for their high dimensional complex data sets?

2001 PhD in Computer Science
2002 Juniorprofessor of „Applied Neuroinformatics“
2011 Professor of “Biodata Mining”, Bielefeld University, Germany

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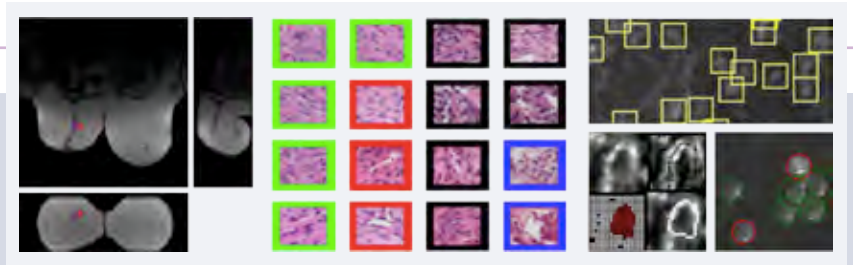
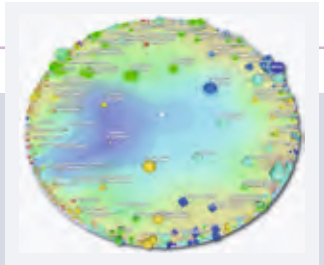
Selected publications

- Nattkemper, T. W., Ritter, H., Schubert, W.: 2001. *A neural classifier enabling high-throughput topological analysis of lymphocytes in tissue sections*, IEEE Transactions on Information Technology in Biomedicine, 5, (2), 138–149
- Martin, C., Solórzano, N. N. D., Ontrup, J., Nattkemper, T. W.: 2008. *Hyperbolic SOM-based clustering of DNA fragment features for taxonomic visualization and classification*, Bioinformatics, Jul 15;24(14): 1568–74
- Diaz, N. N., Goesmann, A., Niehaus, K., Nattkemper, T. W. *et al.*: 2009. *TACOA -Taxonomic classification of environmental genomic fragments using a kernelized nearest neighbor approach*, BMC Bioinformatics, 10: 56
- Albaum, S. P., Hahne, H., Goesmann, A., Nattkemper, T. W. *et al.*: 2011. *A guide through the computational analysis of isotope-labeled mass spectrometry-based quantitative proteomics data: an application study*, Proteome Science, 9: 30
- Langenkämper, D., Khan, M., Rajpoot, N., Nattkemper, T. W. *et al.*: 2011. *Towards protein network analysis using tis imaging and exploratory data analysis*, Workshop on Computational Systems Biology (WCSB), Zürich

Future Projects and Aims

The Biodata Mining Group pursues the goal to build new bridges between complex high volume data and the users. One important future goal is the development of new methodologies to analyze data from different sources (like multimodal data or poly-omics data). As an example one may consider a biomedical scenario, where a group of cancer patients is analyzed using a multitude of techniques leading to a complex data set of clinical data, images, microarrays, histopathology and others. It is our goal to develop integrated approaches to analyze this data make it understandable to the users so they can develop new hypothesis.
In addition, we believe that one important building block of new bridges between data and users is the development of new ways and techniques to visualize biodata and interact with biodata. In the development of these techniques we keep our eyes on the development of the world wide web and the web technology since the ongoing revolutionary development of the web and its influences on our ways to interact with data continuously trigger new ideas and concepts for new biodata mining approaches. ■



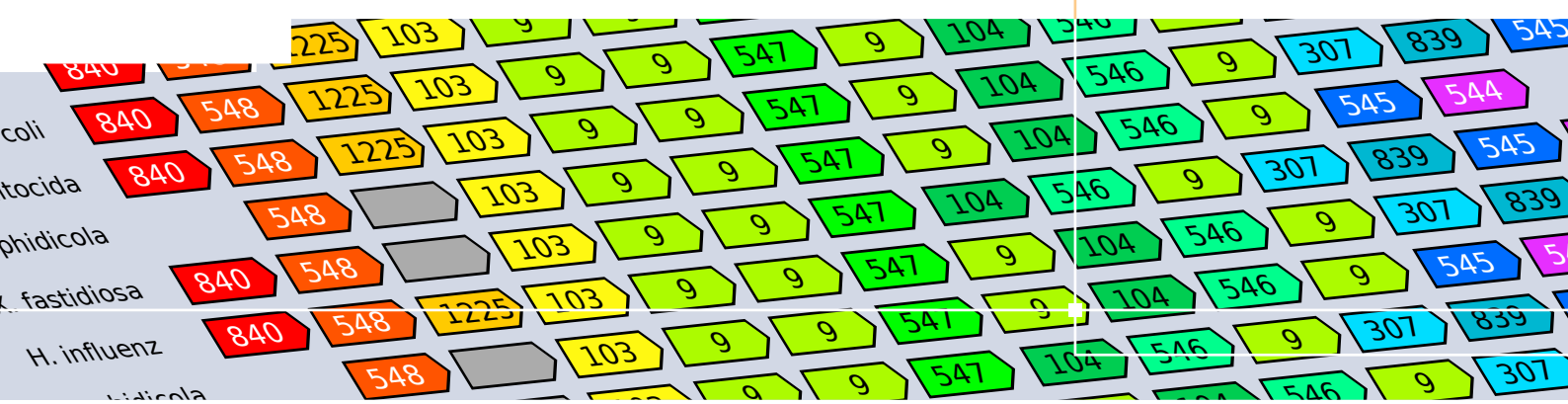


Exploring genome structure and dynamics

Genome informatics aims to fill the gap between genomic data and its biological interpretation by developing efficient and effective computational methods. In our research, we span a broad spectrum from the low level of DNA sequence comparison up to the higher levels of comparative genomics, metagenomics and phylogenetics.

Previous and Current Research

Comparative Genomics is a powerful paradigm for the analysis of genomic data, applied in several contexts, from functional annotation of genes to phylogenomics and comparison of whole genomes. The dramatically increasing amount of available data requires an important research effort in the development of comparative models, biologically sound and mathematically well understood, and of efficient algorithms and software that can handle large data sets.
To achieve these goals, various lines of research are conducted in the Genome Informatics group.
In sequence analysis, we develop index-based analysis methods for large-scale sequence comparison, pattern search, and pattern discovery. A recent research project addresses an important task in whole-genome sequencing. We develop software tools assisting in closing the gaps that remain between the contigs after a standard assembly of shotgun reads. In another, young branch of sequence analysis, metagenomics, we analyze sequencing data obtained from complex environmental samples to characterize their species composition.
In whole-genome comparison, we usually consider genomes at the level of gene orders. Here, one research branch is the study of gene clusters, i.e. sets of genes that are co-localized in several genomes and might thus be functionally related. We develop mathematically sound and biologically reasonable models, and, besides efficient algorithms for their detection, we are interested in the evolution of gene clusters in a phylogenetic context.
We are also working on models and algorithms for genomic rearrangement. The Double-Cut-and-Join (DCJ) operation provides a unifying concept for the well-known rearrangement events such as inversions, translocations, fissions, fusions, and transpositions. This model not only considerably simplifies the



Our research ranges from the low level of DNA sequence up to whole genome analysis. Unifying these into a single model is one of our goals.

Prof. Dr. Jens Stoye

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1997	PhD, Bielefeld University, Germany
1997–1998	Postdoctoral position, UC Davis, U.S.A.
1998–2001	Postdoctoral position, DKFZ Heidelberg, Germany
2001–2002	Group leader, MPI for Molecular Genetics, Berlin, Germany
since 2002	Professor for Genome Informatics, Bielefeld University, Germany

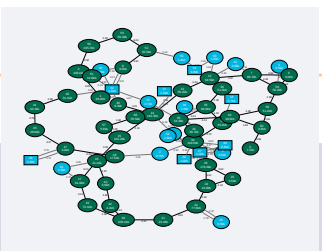
Selected publications

- Kurtz, S. *et al.*: 2001. *REPuter: the Manifold Applications of Repeat Analysis on a Genomic Scale*. Nucleic Acids Res. 29(22): 4633-4642
- Krause, L. *et al.*: 2009. *Phylogenetic Classification of Short Environmental DNA Fragments*. Nucleic Acids Res. 36(7): 2230-2239
- Stoye, J. *et al.*: 2009. *A Unified Approach for Reconstructing Ancient Gene Clusters*. IEEE/ACM Trans. Comput. Biol. Bioinf. 6(3): 387-400
- Bergeron, A. *et al.*: *2010.Rearrangement Models and Single-Cut Operations*. J. Comp. Biol. 17(9): 1213-1225
- Wittkop, T. *et al.*: 2010. *Partitioning Biological Data with Transitivity Clustering*. Nature Methods 7(6): 419-420

formal treatment of the different events. Moreover, the DCJ operation is an important tool with the potential to go even beyond the classical questions, addressing rearrangement problems that involve either gene duplications or missing information about the actual order of genes in a genome.

Future Projects and Aims

Historically, genomic sequence analysis and genome rearrangement studies have been performed at different levels of granularity: While in sequence analysis the DNA bases are the basic entities, in rearrangement studies the order of genes or other unique markers in the evolving genome is studied. Unifying both pictures into one formal model is one of our goals. First, fruitful attempts are considering rearrangements in contig assembly. Also, in a new project, we integrate sequence similarity information into new, more sensible gene cluster models. Moreover, we believe that the mathematical theory of genome rearrangements can be considerably simplified. With our studies of theDCJ operation we have done first steps in this direction, but we believe that much more is possible. ■



Layout graph for the contigs of *Corynebacterium urealyticum* based on matches to six reference genomes.

The Gecko2 user interface (http://bibiserv.techfak.uni-bielefeld.de/gecko/) after a gene cluster search in five different bacteria.

Computational Genomics

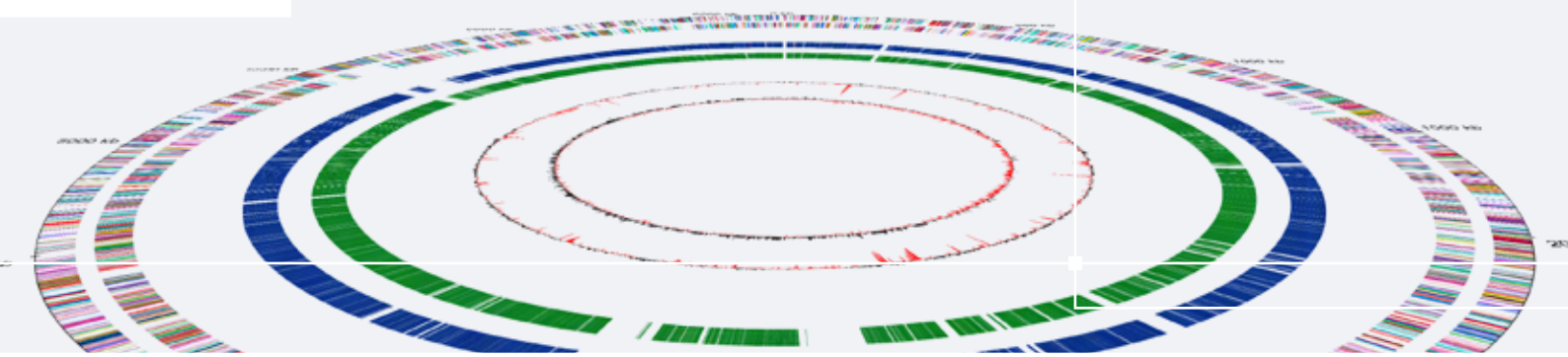
The huge amounts of data acquired from *PolyOmics* technologies can only be handled with intensive bioinformatics support that has to provide an adequate data management, efficient data analysis algorithms, and user-friendly software applications.

Previous and Current Research

Within the junior research group for Computational Genomics we are developing a comprehensive bioinformatics platform for genome and post genome research including software applications for genomics (GenDB, RAPYD, and SAMS) and metagenomics (MetaSAMS), transcriptomics (EMMA), proteomics (QuPE), and metabolomics (MeltDB) as well as comparative genomics (EDGAR). All *omics* applications feature the import of the respective raw data, secure data storage of structured information, and automated high-throughput data analyses.
GenDB and RAPYD support the annotation of complete or draft genome sequences of various microorganisms such as bacteria and yeasts. The GenDB system was successfully used for the automatic and manual annotation of more than 150 microbial genomes. SAMS and MetaSAMS focus on the annotation and evaluation of large sequence sets from ultrafast sequencing reads, for instance EST, cDNA, and metagenome data. EMMA was developed for the evaluation of data obtained from transcriptome studies. Detailed experimental setups and protocols are stored in a separate LIMS component. QuPE provides comprehensive data management and analysis functionality for quantitative proteomics experiments. Based on mass spectrometry data the system guides users intuitively through the process of protein identification by database searches, calculation of abundance ratios from isotopically-labeled proteins, and the statistical evaluation of quantification results. MeltDB facilitates the analysis and annotation of datasets from metabolome experiments. The system covers the process from hyphenated mass spectrometry data to visualization and evaluation of obtained results. EDGAR was developed to accomplish the major tasks in comparative genomics like the identification of orthologous genes in different genomes and the classification of genes as core genes or singletons. Semantic data integration between the different applications is mediated via the BRIDGE layer.

Future Projects and Aims

Forward-looking projects within the computational genomics group focus on the development of bioinformatics analysis



Our goal is the development of novel software systems to identify the meaningful information from the rapidly increasing amount of PolyOmics *data.*

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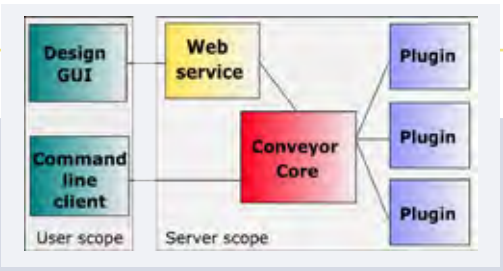
2006 Head of Bioinformatics Resource Facility (BRF) , Bielefeld University
2009 Group leader, Computational Genomics, Bielefeld University

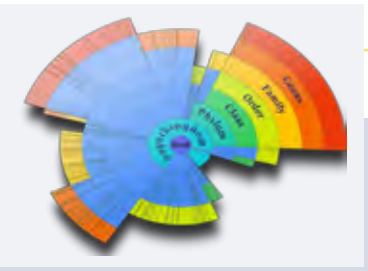
Selected publications

- Blom, J. *et al.*: 2009. *EDGAR: a software framework for the comparative analysis of prokaryotic genomes.* BMC Bioinformatics 10: 154
- Blom, J. *et al.*: 2011. *Exact and complete short read alignment to microbial genomes using GPU programming.* Bioinformatics, 27(10): 1351-58
- Jaenicke, S. *et al.*: 2011. *Comparative and joint analysis of two metagenomic datasets from a biogas fermenter obtained by 454-pyrosequencing.* PLoS ONE 6(1)
- Linke, B. *et al.*: 2011. *Conveyor: a workflow engine for bioinformatic analyses.* Bioinformatics 27(7): 903–11
- Schneider, J. *et al.*: 2011. *RAPYD – rapid annotation platform for yeast data.* J. Biotechnol. 155(1): 118-26

workflows for rapid and parallel data interpretation, which also includes hardware accelerated software implementations. Conveyor is our novel workflow-processing engine to rapidly deploy new bioinformatics data analysis pipelines utilizing either the CeBiTec compute cluster for distributed computing or multi-core servers for local execution. Using a workflow based approach, analyses can be designed using an intuitive graphical designer application. A number of ready-to-use processing steps for bioinformatics analyses already exist with a focus on sequence analysis and sequence annotation. Using the Conveyor2Go tool, an existing workflow can easily be converted into a standalone application.
The program SARUMAN is our first approach based on GPU programming that allows us to boost the performance of complete and exact short read mapping against reference genomes. It needs no server class hardware and can be run on every desktop PC with an installed NVIDIA graphic adapter. As result, various scientific applications can benefit from the parallel computing power provided by current graphics adapters found in many PCs. Results of the read mapping can subsequently be examined and analyzed in depth with our interactive visualization software VAMP.
With these software tools, the basis for efficient, parallel, and data driven processing is established and will be further improved and extended in the future. ■



Architecture of the Conveyor system, showing the main components and component's scopes



Scheme of a phylogenetic classification designed for metagenome data

Computational Metagenomics

Over 99% of the microbial species observed in nature cannot be grown in pure culture making them inaccessible to classical genomic studies. Metagenomics and single cell genomics are two approaches to study the microbial 'dark matter'.

Previous and Current Research

Metagenomics, the direct analysis of DNA from a whole environmental community, represents a strategy for discovering genes with diverse functionality. In the past, the identification of new genes with desired activities has relied primarily on relatively low-throughput function-based screening of environmental DNA clone libraries. Current sequencing technologies can generate more than 600 Gbp of sequence data in a single experiment, allowing sequence-based metagenomic discovery of complete genes or even genomes from environmental samples with moderate microbial species complexity.
The cow rumen metagenome, sequenced at the DOE Joint Genome Institute (JGI), is one of the largest metagenomic datasets from a single sample to date (>500 Gbp). The paucity of enzymes that efficiently deconstruct plant polysaccharides represents a major bottleneck for industrial-scale conversion of cellulosic biomass into biofuels. Cow rumen microbes specialize in degradation of cellulosic plant material and are therefore an promising target for the identification of novel carbohydrate-active genes. Datasets of such a large size require high-throughput computational techniques to cope with the analysis of billions of sequencing reads. In collaboration with the JGI we develop high-throughput gene-centric and de-novo assembly pipelines for metagenomic datasets. In case of the cow rumen dataset, we were able to identify more than 27,000 putative carbohydrate-active genes and assemble 15 uncultured microbial genomes using these pipelines.

A complementary approach to sequencing the DNA of a whole microbial community is single cell genomics. Over 99% of the microbial species observed in nature cannot be grown in pure culture, making it impossible to study them using classical genomic methods. DNA sequencing from single amplified genomes of individual cells is a novel approach in genome research, which allows to study the genomes of uncultured species from diverse environments.
Selective collection techniques such as fluorescence-activated cell sorting (FACS) followed by multiple displacement amplification (MDA) and sequencing can reveal the genomic sequence of isolated single cells. This way, a sample can be enriched for one or several organisms.

Future Projects and Aims

Despite the fact that we managed to assemble a large number of genes and genomes from a complex metagenome as the cow rumen, there is still a need for metagenome-specific assemblers. Current short read assemblers were specifically designed for the assembly of isolate genomes, but metagenome data sets pose a number of challenges on the assembly problem. We are developing new tools and approaches for the metagenomic assembly problem.
For single cell genomics we develop automated bioinformatic pipelines that support each step of the analysis. Tremendous bias in the coverage of the genome, introduced by the amplification technique, pose a challenge for the bioinformatic

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1999–2000	Guest Investigator, The Rockefeller University, New York
2000–2002	Member of Research Practical Computer Science Group
2002–2008	Head of Bielefeld University Bioinformatics Services, Bielefeld University, Germany
2007	PhD, Bielefeld University, Germany
2008–2011	Postdoctoral Fellow, DOE Joint Genome Institute, U.S.A
since 2011	Head of the Bielefeld University Bioinformatics Services and Computational Metagenomics groups, Bielefeld University, Germany

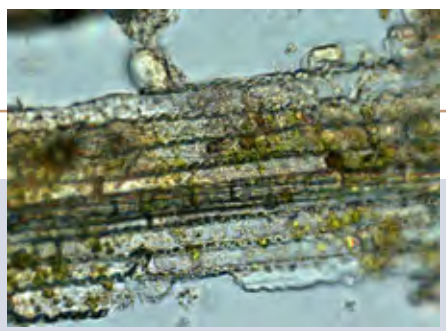
Selected publications

- Gilbert, J. A. *et al.*: 2010. *Meeting report: the terabase metagenomics workshop and the vision of an Earth microbiome project*. Stand Genomic Sci., 3(3):243–8
- Hess, M., Sczyrba, A. *et al.*: 2011. *Metagenomic discovery of biomass-degrading genes and genomes from cow rumen*. Science, 331(6016): 463–7
- Kim, T.W. *et al.*: 2011. *High-throughput in vitro glycoside hydrolase (HIGH) screening for enzyme discovery*. Angew. Chem. Int. Ed. Engl. doi:10.1002/anie.201104685
- Swan, B., Martinez-Garcia, M., Preston, C.M., Sczyrba, A. *et al.*: 2011. *Potential for chemoautolithotrophy among ubiquitous bacteria lineages in the dark ocean*. Science, 333(6047):1296-1300
- Woyke, T., Sczyrba, A. *et al.*: 2011. *Decontamination of MDA Reagents for Single Cell Whole Genome Amplification*. PLoS ONE, to appear

analysis of the resulting sequence data. The raw data has to be pre-processed to achieve good assembly results. At each step, possible sample contamination has to be identified and removed, a difficult task if the target genome is not closely related to any previously sequenced genome. Finally, genome completeness can be estimated using single copy and core gene analyses.

A promising approach for future metagenomic studies is the combination of high-throughput metagenome sequencing and large-scale single cell genomics. Both data sources can be combined into bioinformatic "pan-genome" analyses to gain a better understanding of the phylogenetic composition of microbial communities, their population structure and functionality. ■

Metagenomic sequencing identified 27,755 putative biomass degrading enzymes in the cow rumen microbiome.



Single cell genomics targets sequencing of individual cells: a microbe decomposing a fragment of switchgrass in the cow rumen.

Plant Biochemistry and Physiology

Plant acclimation to stressful environment such as heat, light and toxic compounds is of paramount importance to maintain fitness and high yield. The redox regulatory signaling network of the plant cell senses metabolic disequilibria and orchestrates the in part extremely fast responses at transcriptional and translational levels.

Previous and Current Research

Organisms often encounter rapidly changing or extreme environmental conditions. Such changes challenge plant metabolism and cause redox disequilibria and reactive oxygen (ROS) or reactive nitrogen species formation which may cause cell damage and cell death. Such processes are involved in yield losses in plants and disease development in animals. To counter such imbalances cells operate a redox signalling network. The network senses environmentally induced redox imbalances and initiates compensatory responses either to readjust redox homeostasis or to repair oxidative damage. The network consists of redox input elements, redox transmitters, redox targets and redox sensors. The basic structure and many components of the thiol-disulfide redox regulatory network are conserved among all cells and most cell compartments. The significance of this network is well established for some pathways, but still emergent for additional functions due to the ongoing identification of novel redox targets.

Peroxiredoxins are thiol-dependent redox sensors. They decompose peroxides and thereby undergo major conformational changes between oxidized dimer, reduced dimer, hyperoxidized decamer and higher order aggregate. These conformers have different functions as peroxidase, chaperone and binding partner.

The kinetics of plant responses to the environment at the transcriptional level is dissected. As early as 2 minutes after transfer from low to high light, a whole transcriptional network of specific transcription factors responds with transient upregulation of mRNA levels and control the acclimation of plants. The results show that plants can respond efficiently and on the same time scale as specialized animal cells.

Novel tools are developed to measure protein protein interactions in vivo e.g. by Förster Resonance Energy transfer between two or three interacting proteins (one step or two step FRET) or to elicit single cells with signal-driving stimuli such as local heat with newly deviced thermocapillaries or functionalized nanoparticles (cooperation with Dr. S. Herth and Prof. G. Reiss, Faculty of Physics).

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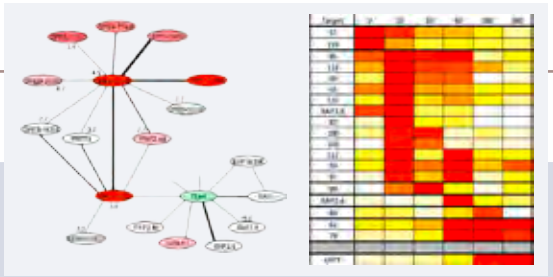
1985 – 1987	Postdoc at Harvard University
1997	Professor Plant Biochemistry and Physiology, Bielefeld University

Selected publications

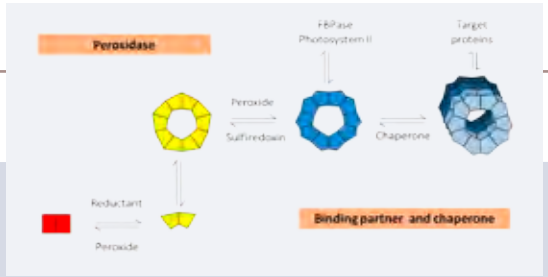
- König, J. *et al.*: 2002. *The plant-specific function of 2-Cys peroxiredoxin-mediated detoxification of peroxides in the redox-hierarchy of photosynthetic electron flux*. Proceedings National Academy of Science USA 99: 5738-5743
- Finkemeier, I. *et al.*: 2005. *The mitochondrial type II peroxiredoxin F is essential for redox homeostasis and root growth of* Arabidopsis thaliana *under stress*. Journal of Biological Chemistry 280: 12168-12180
- Lamkemeyer, P. *et al.*: 2006. *PrxQ of* Arabidopsis thaliana *is attached to the thylakoids and functions in context of photosynthesis*. Plant Journal 45: 968-981
- Romero-Puertas, M. C. *et al.*: 2007. *S-nitrosylation of peroxiredoxin II E promotes peroxynitrite-mediated tyrosine nitration*. Plant Cell 19: 4120-4130
- Dietz, K.-J.: 2011. *Peroxiredoxins in plants and cyanobacteria*. Antioxidants and Redox Signalling: in press

Future Projects and Aims

The redox regulatory network of the cell is a major determinant of cell function and whole organism fitness, but also of disease and pathology. A more complete understanding of the network will enable targeted improvement of acclimation responses. To this end we have to expand our knowledge in both the empirical and theoretical direction: (i) Dissecting the upstream sensors and downstream targets of the transcriptional high light network. (ii) Developing a quantitative model of the redox regulatory network of the chloroplast. (iii) Devlop novel tools to manipulate and measure single cell responses to a varying environment. (iv) Application of the knowledge to crop plants for stress improvement. ■



Transcription factor network controlling high light acclimation and its time dependent response (time in minutes, deep red is maximal expression, white no expression)



Peroxiredoxins as redox sensors adopting different conformational states

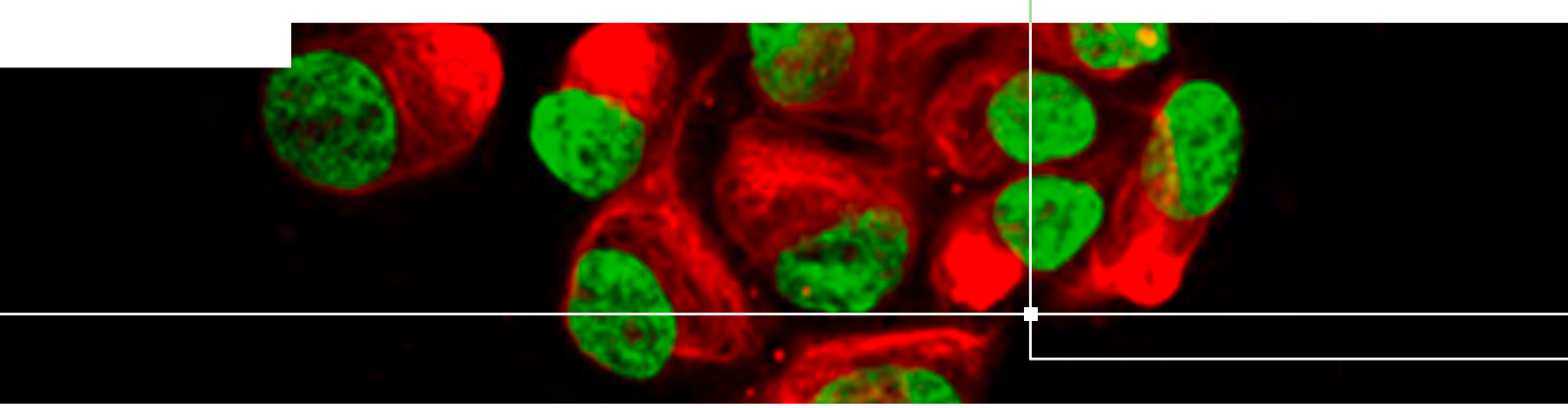
Cell Biology

Understanding molecular mechanisms of stem cell differentiation

Stem cells are the most plastic cells of multicellular organisms. They can produce cells of all germ layers and even whole organisms. Our interest is an understanding of these processes at a molecular level. We are focused on the function of transcription factor NF-kB in regulating multi- or pluripotency and adult neurogenesis.

Previous and Current Research

In current research stem cells play an emerging role both, in basic research and in the development of cellular therapies. Stem cells come in two flavours: embryonic pluripotent stem cells, which can built a whole organism such as a mouse with genetic material from one cell; other stem cell types are adult (tissue) multipotent stem cells. These cells reside within normal adult tissue and have an important role in tissue regeneration. When tissue stem cells have gone wild cancer stem cells could emerge. These are the real tumour initiating cells. In a close cooperation with Prof. Dr. Barbara Kaltschmidt, Molecular Neurobiology, Bielefeld University the role of transcription factor NF-kB in the nervous system is analyzed. NF-kB is a transcription factor regulated by various extracellular stimuli, such as pro-inflammatory cytokines, neurotransmitters and others. We discovered that NF-kB is constitutively active in mature neurons through a continuous activation of NF-kB by the neurotransmitter glutamate. In this line constitutive NF-kB is necessary for normal neuron function. NF-kB functions as a neuroprotective transcription factor, which can protect neurons against various toxic substances such as Alzheimers A-beta peptide. Furthermore activated NF-kB is important for learning and memory. Meanwhile we could identify NF-kB as a crucial factor for neural stem cell proliferation and differentiation. Thus our research interest is now focused on the biology of tissue stem cells. This includes isolation and characterization of novel human stem cells for potential therapies such as Parkinson, Alzheimer and craniofacial injuries.



Nihil tam difficile est, quin querendo investigari possit. (Everything, even the most complicated can be investigated.)

Prof. Dr. Christian Kaltschmidt

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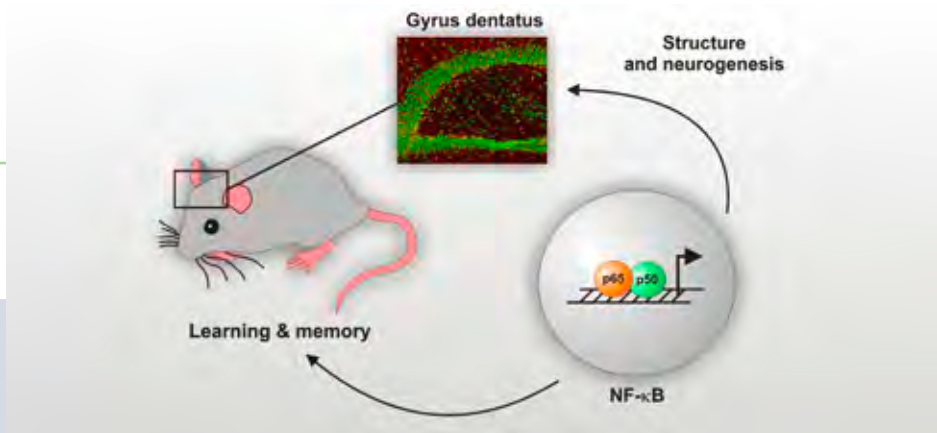
1991	PhD, Gene Center, Max-Planck-Society, Martinsried
1992 – 1996	Postdoc, Gene Center, Martinsried and Freiburg University
1998 – 2000	Heisenberg Stipend of the Deutsche Forschungs-gemeinschaft
2000 – 2007	Professor of Neurobiochemistry, University of Witten/ Herdecke
since 2007	Professor of Cell Biology, Bielefeld University

Selected publications

- Kaltschmidt, B. *et al.*: 1999. *Inhibition of NF-kappaB potentiates amyloid beta-mediated neuronal apoptosis*. Proc. Natl. Acad. Sci. U S A. Aug 3;96(16): 9409–14
- Kaltschmidt, B. *et al.*: 2006. *NF-kappaB regulates spatial memory formation and synaptic plasticity through protein kinase A/CREB signaling*. Mol. Cell. Biol. Apr;26(8): 2936–46
- Kaltschmidt, B., Kaltschmidt, C.: 2009. *NF-kappaB in the nervous system*. Cold Spring Harb Perspect Biol. Sep;1(3): a001271
- Widera, D. *et al.*: 2009. *Adult palatum as a novel source of neural crest-related stem cells*. Stem Cells. Aug;27(8): 1899–910
- Widera, D. *et al.*: 2011. *Schwann Cells Can Be Reprogrammed to Multipotency by Culture*. Stem Cells Dev. Jun 1. [Epub ahead of print]

Future Projects and Aims

Our future aims are a more complete understanding of NF-kB signalling in stem cells of the nervous system. This goal involves the use of sophisticated transgenic models and approaches from systems biology. Furthermore new methods to investigate cells with physical methods are developed in close cooperation with the department of physics. ■



Schematic overview of functions of transcription factor NF-kB in the central nervous system

Chemical Ecology

Most organisms communicate mainly by chemical compounds. Our group is interested in the role of plant metabolites in plant-animal-interactions, how these are modified by environmental conditions and how the organisms feeding on the plants deal with putatively toxic compounds.

Previous and Current Research

Interactions between most organisms are mainly triggered by chemical metabolites. However, our knowledge of key mechanisms and principles in particular interactions is still limited. Generally, natural products of plants deter herbivorous generalists from feeding, whereas they lead specialists to their food. Insects that are able to feed on potentially toxic plants must have evolved adaptations to such metabolites to some extent. They either evolved different detoxification enzymes and/or make use of the toxins by taking them up and storing them in their tissue. The composition of plant metabolites is, however, not at a steady-state but changes constantly due to various endogenous and environmental conditions. Thereby, abiotic factors such as ultraviolet (UV) radiation as well as biotic challenges such as insect herbivory can lead to tremendous changes in local and systemic tissue of the target plant. These changes are partly mediated by phytohormones.

We are interested in the species-specific adaptation of insects feeding on Brassicaceae and Plantaginaceae to their host plant metabolites as well as in plant responses to their environment. Both plant families are well characterized by the presence of glycosides which can be readily degraded to toxic breakdown products. In addition, they contain, of course, a plethora of other compounds, whose chemo-ecological role is only now starting to be revealed. We found that sawfly species of the genus *Athalia* take up the species-specific glycosides for their own defense against predators, and metabolise them by at least two enzymes before excretion. The glycosides of some plant species are in fact induced by herbivory of sawflies. In contrast, these compounds do not respond to increased UV radiation. Other metabolites, such as flavonoids, are highly inducible by UV but little by herbivory.

Next to such targeted analyses of specific compound classes by HPLC and GC-MS, including glycosides, flavonoids and terpenes, we apply up-to-date metabolomics techniques studying overall changes of metabolic fingerprints and how these in turn affect plant antagonists. Therefore, differently treated plant samples, taken from the laboratory as well as the field, are analyzed by LC-ToF-MS and treatment-specific metabolic fingerprints are compared applying bioinformatic tools. Bioassay-guided fractionation is subsequently used to delineate the effects of particular fractions on herbivore feeding. Thereby, we aim to delineate the interactions between plants and herbivores from a chemo-ecological and evolutionary perspective.

This approach enabled us to highlight a surprisingly high overlap in metabolic responses to different signaling hormones (jasmonic acid and salicylic acid). Furthermore, only our metabolic fingerprinting approach could reveal that feeding by specialist and generalist insect species regulates several pathways beyond the phytohormone responses in a highly species-specific way.

Prof. Dr. Caroline Müller

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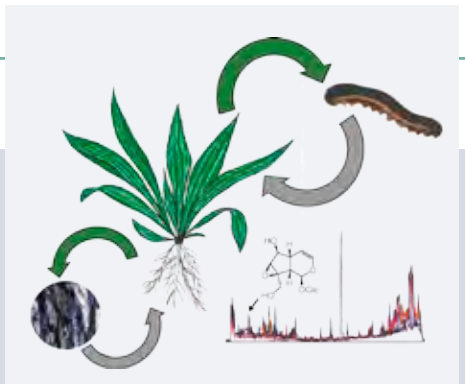
1999–2000	Postdoctoral position, Boyce Thompson Institute, Ithaca, U.S.A.
2000–2003	Postdoctoral position, Leiden University, Leiden, The Netherlands
2003–2007	Group Leader Chemical Ecology, Würzburg University, Germany
since 2007	Professor for Chemical Ecology, Bielefeld University, Germany

Selected publications

- Travers-Martin, N., Müller, C.: 2008. *Matching plant defense syndromes with performance and preference of a specialist herbivore.* Funct. Ecol. 22: 1033-1043
- Kuhlmann, F., Müller, C.: 2009. *Independent responses to ultraviolet radiation and herbivore attack.* J. Exp. Bot. 60: 3467-3475
- Maier, T.S., Kuhn, J., Müller, C.: 2010. *Protocol for field sampling of plants and processing in the lab for environmental metabolic fingerprinting.* Plant Meth. 6: 6
- Kleine, S., Müller, C.: 2011. *Intraspecific plant chemical diversity and its relation to herbivory.* Oecologia 166: 175-186
- Sutter, R., Müller, C.: 2011. *Mining for treatment-specific and general changes in target compounds and metabolic fingerprints in response to herbivory and phytohormones in* Plantago lanceolata. New Phytol.DOI: 10.1111/j.1469-8137.2011.03768.x

Future Projects and Aims

Variation in metabolites can be already intrinsically very high even within a species. Such high variation may be an important pre-adaptation of invasive species as it impedes adaptation abilities of herbivorous insects and other antagonists. We currently extend our research to other plant families and investigate various species that have become invasive in some areas of the world. We aim to understand whether the plasticity of chemical metabolites is involved in the invasion success of these plant species and how herbivores of the native and invasive range respond to such compounds. Furthermore, we continue our research both on induction of plant metabolites due to different challenges, including mycorrhizal fungi, and on plant-mediated indirect interactions between herbivores feeding at different tissue such as roots and shoots. ■



The complex interplay between plants, insect herbivores and mycorrhizal fungi is mediated by plant metabolites, which are analyzed by targeted analyses as well as metabolomics approaches

Proteome and Metabolome Research

Genes, transcripts, proteins and metabolites are the physical building blocks of the cell. The functional relations between these elements form a complex network of interactions that we call life. Our group intends to decode (tiny) parts of such networks to obtain a functional understanding of life processes.

Previous and Current Research

How do plants discriminate between beneficial and pathogenic microbes? To answer this question, the interaction of the legume *Medicago truncatula* with the symbiotic bacterium *Sinorhizobium meliloti* is analysed on a molecular level. The microbe seems able to suppress the plant defence in order to infect its host and thereby provide atmospheric nitrogen. On the other side, plant pathogenic microbes like *Xanthomonas* or the fungus *Aphanomyces* express extracellular proteins that damage the plant's recognition system to facilitate their harmful infection. Plant cell cultures are used to analyse the very early recognition processes involving complex glyco-structures, calcium, GTP-binding proteins and the generation of reactive oxygen species (ROS).
Reconstructing bacterial metabolism based on genome data, and analysing the metabolite flux within bacteria allows the establishment of dynamic models of metabolism that are also relevant for industrial biotechnology.
Food metabolomics and food proteomics are emerging fields in safeguarding sustainable food supply by monitoring quality or optimising production processes. We contribute to this field by analysing the malting process of barley to identify biomarkers for beer brewing. In another project, we can differentiate between wheat from conventional and organic farming by metabolite fingerprinting.
Finally, automated microscopy was developed in collaboration with partners in bioinformatics to generate quantitative data for eukaryotic cells, their compartments, or infecting bacteria, permitting to monitor the behaviour of individual cells. In combination with reporter genes such as the green fluorescent protein (GFP) and smart dyes that give a read out on pH, respiratory activity or the production of ROS, this provides new insights into cellular function.

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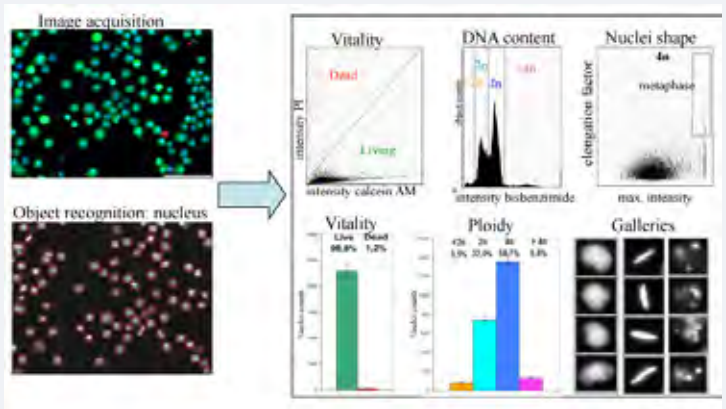
1991 PhD in Genetics, Bielefeld University
1999 Habilitation in Genetics and Cell Biology, Bielefeld University
2005 Head of the Department of Proteome and Metabolome Research, Bielefeld University

Selected publications

- Barsch, A. *et al.*: 2006. *Metabolite profiles of nodulated alfalfa plants indicate that distinct stages of nodule organogenesis are accompanied by global physiological adaptations.* Mol. Plant-Microbe Interact. 19(9): 998–1013
- Tellström, V. *et al.*: 2007. *The lipopolysaccharide of* Sinorhizobium meliloti *suppresses defense-associated gene expression in cell cultures of the host plant* Medicago truncatula. Plant Phys. 143(2): 825–832
- Jensen, N. A. *et al.*: 2009. *Establishment of a high content assay for the identification and characterization of bioactivities in crude bacterial extracts that interfere with the eukaryotic cell cycle.* J. Biotechnology 140(1–2): 124–134
- Liu, P. *et al.*: 2009. *Lipid microdomain polarization is required for NADPH oxidase-dependent ROS signaling in* Picea meyeri *pollen tube tip growth.* Plant J. 60(2): 303–313
- Keck, M. *et al.*: 2011. *Unusual outer membrane lipid composition of the gram-negative, lipopolysaccharide-lacking myxobacterium* Sorangium cellulosum *So ce56.* JBC 286(15):12850–9

Future Projects and Aims

We aim at providing knowledge for biotechnology, screening or biomarker discovery. Thereby we focus on systems biology and plant-microbe interactions. In this field, more quantitative data is required on the levels of the transcriptome, proteome and metabolome in order to establish mathematical models that allow for predictions. Here, we analyse the regulation of the plant NADPH oxidase, the enzyme that generates ROS. As this enzyme is required for plant development, for beneficial and for pathogenic interactions, its activity has to be well balanced. Likewise, by combining metabolic models with gene- and protein-based regulatory networks, global and mechanistic models can be obtained as a foundation for intricate systems biology approaches in industrial biotechnology. Such models can be used to redirect the bacterial metabolism for higher yields or different product qualities. The large-scale production of the biopolymer Xanthan by *Xanthomonas campestris* is our focus in this approach. ■



Automated and quantitative microscopy of living cells in combination with sophisticated bioinformatics determine the DNA content of a single cell and the shape of the nucleus. This can be used to establish screening assays for cytostatic compounds.

Genome Research of Industrial Microorganisms

The rational design of industrial production strains is carried out by applying emerging genome research technologies. In particular, high throughput sequencing, transcriptomics, proteomics and metabolomics in combination with bioinformatics play a crucial role.

Previous and Current Research

The CeBiTec Senior Research Group "Genome Research of Industrial Microorganisms" was started by A. Pühler after his retirement from the Chair of Genetics at the Faculty of Biology, Bielefeld University. Until his retirement, A. Pühler was engaged in the establishment of a nation-wide Research Network for the genome analysis of bacteria playing a role in agriculture, environment and industrial biotechnology. The network, financed by the BMBF, was composed of partners from universities, research institutes and industrial companies with Bielefeld as a center where the emerging technologies of genome sequencing and microarray analyses were established.
With the advent of high throughput sequencing, microbial genome research was accelerated tremendously. In the year 2007 the CeBiTec installed the Genome Sequencer FLX system (Roche) that delivered excellent results from the first day on. The efficiency of this new pyrosequencing technology was demonstrated by the establishment of the *Corynebacterium kroppenstedtii* genome sequence. One run on the GS FLX system resulted in sequence data that could be assembled to a circular chromosome without further experimental work. As a consequence, an additional BMBF grant allowed to continue the sequence analyses of a larger set of bacterial microorganisms involved in agriculture and industrial biotechnology. In the meantime, the genome research work was extended to eukaryotic microorganisms like yeasts and phytopathogenic fungi. The high throughput sequencing work is carried out at the Technology Platform Genomics of the CeBiTec.

Future Projects and Aims

The large amount of data generated with the GS FLX system stimulated research in new scientific fields, such as metagenomics. As a first example, the composition of a microbial community residing in a biogas production plant was analyzed. Currently, this work is continued on the transcriptional level. In addition, the analysis of the metagenome of a microbial community involved in agricultural silage processing was recently started. Both metagenomic projects are of industrial importance and are financially supported by companies. The metagenomic group is headed by Andreas Schlüter.

A further project of special interest concentrates on genome research of the Chinese hamster and derived CHO cells, which play an important role for the production of monoclonal antibodies used in medicine. Genomic DNA of the Chinese hamster as well as of selected CHO cell lines was sequenced. In addition, cDNA libraries derived from mRNA as well as miRNA of selected CHO cell lines are currently sequenced. The genome research

With the development of ultrafast sequencing technologies, genome research has become a rapid and reliable method.

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since 1996	Chief Editor of Journal of Biotechnology
1999–2005	Member of the Science Council in Germany
2004–2010	Speaker of the Executive Board of the CeBiTec, Bielefeld University
since 2008	Senior Research Professor, CeBiTec, Bielefeld University
since 2008	Foreign Secretary of the Union of the German Academies of Sciences and Humanities
since 2009	Member of the BioÖkonomieRat

Prof. Dr. Alfred Pühler

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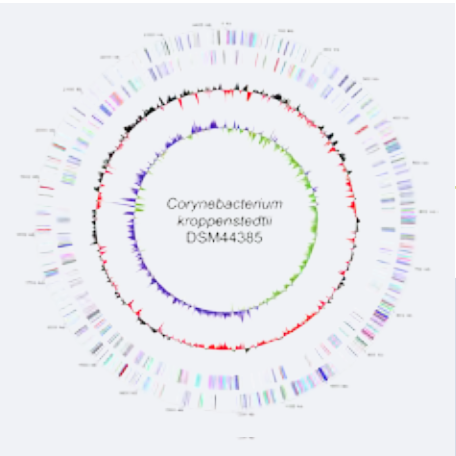
Selected publications

- Capela, D. *et al.*: 2001. *Analysis of the chromosome sequence of the legume symbiont* Sinorhizobium meliloti *strain 1021.* Proc. Natl. Acad. Sci. U S A 98: 9877–9882
- Finan, T. M. *et al.*: 2001. *The complete sequence of the 1,683-kb pSymB megaplasmid from the N_2-fixing endosymbiont* Sinorhizobium meliloti. Proc. Natl. Acad. Sci. U S A 98: 9889–9894
- Galibert, F. *et al.*: 2001. *The composite genome of the legume symbiont* Sinorhizobium meliloti. Science 293: 668–672
- Krause, A. *et al.*: 2006. *Complete genome of the mutualistic, N_2-fixing grass endophyte* Azoarcus sp. *strain BH72.* Nat. Biotechnol. 24: 1385–1391
- Schneiker-Bekel, S. *et al.*: 2006. *Genome sequence of the ubiquitous hydrocarbon-degrading marine bacterium* Alcanivorax borkumensis. Nat. Biotechnol. 24: 997–1004
- Schneiker-Bekel, S. *et al.*: 2007. *Complete genome sequence of the myxobacterium* Sorangium cellulosum. Nat. Biotechnol. 25: 1281–1289

concerning the Chinese hamster and CHO cells is carried out in collaboration with two companies and the University of Natural Resources and Life Sciences in Vienna, Austria. It should be mentioned that the CeBiTec installed Illumina's GAIIx as a prerequisite for this large genome project which produces up to 90 Gb in one sequencing run. The sequencing work of this project is carried out by Karina Brinkrolf. ■

Sunburst view of the bacterial community profile of a production scale biogas plant, based on metagenome sequence data.



Bacterial genome plot of *Corynebacterium kroppenstedtii*

Post-transcriptional regulatory networks

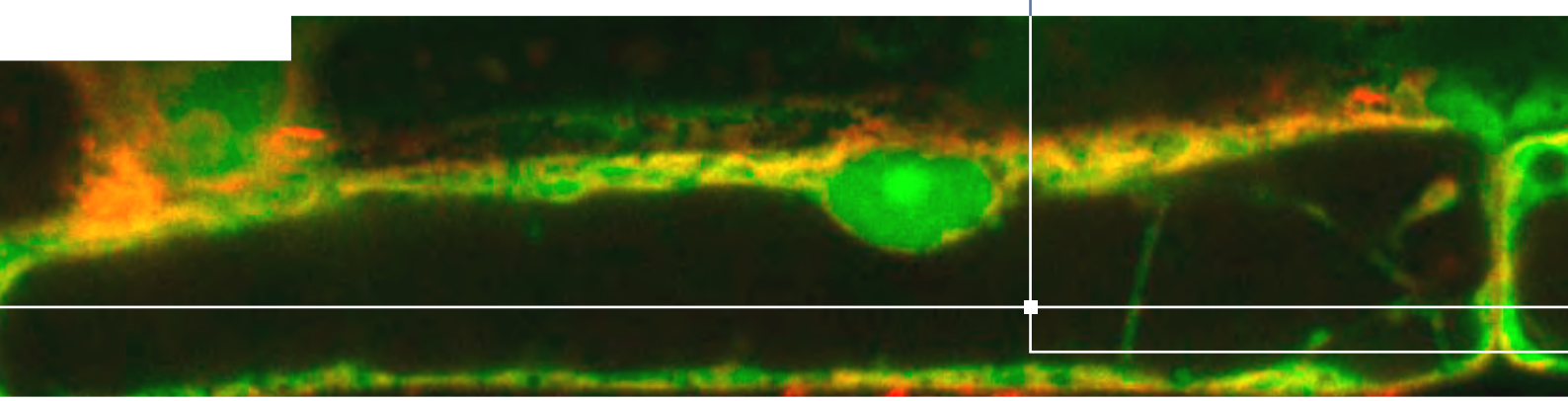
Post-transcriptional control emerges as an important control mechanism in plants. Our research focuses on the molecular underpinnings of RNA-based regulation. We aim at unravelling general principles and molecular players in the model plant *Arabidopsis thaliana*.

Previous and Current Research

We have identified a key posttranscriptional regulator, the RNA-binding protein *At*GRP7 that is located at the intersection between endogenous timing and responses to external cues. *At*GRP7 is involved in signal transduction of the endogenous circadian clock, shaping specific gene expression programs that oscillate with a 24-h period in the course of the day. Further, it contributes to innate immunity against phytopathogenic bacteria.
Upon mutation of a single conserved Arginine within the RNA recognition motif into Glutamine, RNA binding activity and in vivo function are strongly impaired. Notably, this very Arginine is the target of a novel type III effector protein of *Pseudomonas syringae*, suggesting that inactivation of this Arginine interferes with *At*GRP7 binding to target transcripts in vivo and thus subverts *At*GRP7's role in pathogen defence.

Future Projects and Aims

To unveil the regulatory network downstream of the RNA-binding protein, we perform transcript profiling and RNA-seq of plants with altered *At*GRP7 levels.
Furthermore we aim at dissecting a role of *At*GRP7 in regulatory events in the nucleus, e.g. of splicing, and in the cytoplasm, e.g. RNA decay.
To monitor trafficking of the *At*GRP7 protein between the nuclear and cytoplasmic compartment, we have developed a codon optimized reversible photoswitchable fluorescent DRONPA reporter protein, termed DRONPA-s (DRON = "vanish", PA = "photoactivation", s = synthetic).
DRONPA-s shows a higher expression and fluorescence compared to the original DRONPA from Pectinidiae in agroinfiltrated *Nicotiana benthamiana* leaves, and transiently transfected HeLa and Cos-7 cells.



Timing is everything – many biochemical and molecular processes are orchestrated by a complex circadian timekeeping system.

Prof. Dr. Dorothee Staiger

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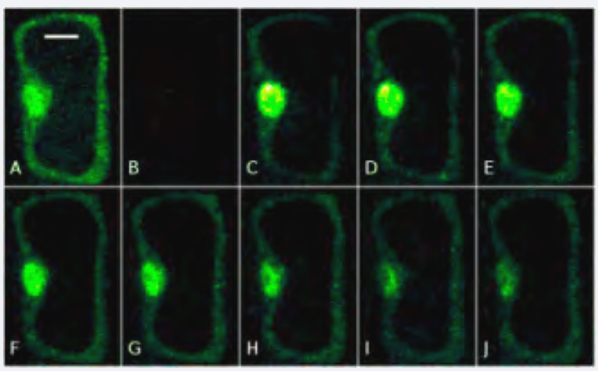
1978–1984	Studies of Biochemistry, University of Tübingen and LMU München, Germany
1985	Diploma, MPI for Biochemistry, München, Germany
1989	PhD, MPI for Plant Breeding Research, Köln, Germany
1990–2002	Research Associate, ETH Zürich, Switzerland
since 2002	Professor for Molecular Cell Physiology, Bielefeld University, Germany

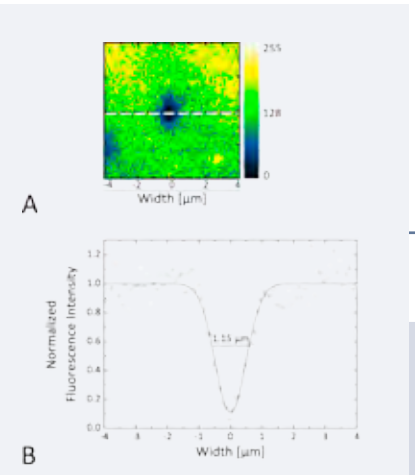
Selected publications

- Fu, Z.Q. *et al.*: 2007. *A type III effector ADP-ribosylates RNA-binding proteins and quells plant innate immunity.* Nature, 447: 284-288
- Schüttpelz, M. *et al.*: 2008. *Changes in conformational dynamics of mRNA upon AtGRP7 binding studied by Fluorescence Correlation Spectroscopy.* J. Am. Chem. Soc., 130: 9507–9513
- Schöning, J.C. *et al.*: 2008. *Reciprocal regulation of glycine-rich RNA-binding proteins via an interlocked feedback loop coupling alternative splicing to nonsense-mediated decay in Arabidopsis.* Nucleic Acids Research, 36: 6977-6987
- Streitner, C. *et al.*: 2010. *Global transcript profiling of transgenic plants constitutively overexpressing the RNA-binding protein AtGRP7.* BMC Plant Biology, 10: 22
- Lummer, M. *et. al.*: 2011. *Reversible photoswitchable DRONPA-s monitors nucleocytoplasmic transport of an RNA-binding protein in transgenic plants.* Traffic, 12:631

Fluorescence recovery after photoswitching and photoactivation experiments are used to dissect nuclear import and export of an *At*GRP7-DRONPA-s fusion protein in transgenic plants. This will provide insights into the function of this protein in regulatory networks in both subcellular compartments. ■



Photoactivation of *At*GRP7-DRONPA-s unveils nuclear export.



Using the Single Photon Confocal Laser scanning Microscope we can selectively photoswitch DRONPA-s in a very small region.

Bioenergetics for Bioenergy

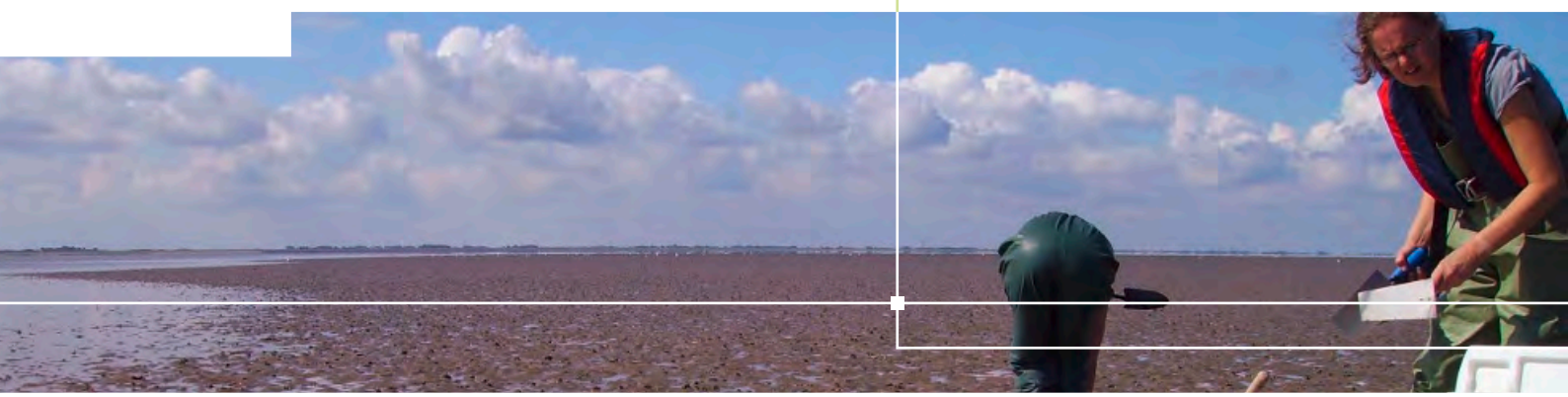
Successful production of renewable energy with microbes depends on the assembly of a suitable microbial community. We investigate how bioenergetic principles can be used to rationally recruit the right microbes for the job and apply this idea to produce methane from algae at high pH.

Previous and Current Research

The biodiversity of microbes in the environment is extremely large and only a tiny fraction of this biodiversity has been described, let alone studied. In theory, microbes may contribute to sustainable energy production in many ways. However, many bottlenecks still need to be overcome.

In our research we apply thermodynamic principles to tap the reservoir of the natural biodiversity in a rational way, independent of textbook knowledge, to recruit the right microbes for the job. In previous research two new microbial processes were discovered that were previously considered to be impossible: anaerobic ammonium oxidation and anaerobic methane oxidation. These processes are being applied in wastewater treatment and lead to substantial energy and cost savings.

A second result of the lack of knowledge about microbes in nature is that the global consequences of human impact (eg fertilization and fossil fuel burning) are difficult to predict. Ongoing research in the context of an ERC starting grant addresses the fate of fertilizer nitrate in tidal sediments. It is currently estimated that fertilization alone is responsible for over 10% of the enhanced greenhouse effect.



To realize bioenergy from microbes, economical principles are more fruitful than ecological approaches.

Prof. Dr. M. Strous

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2000	PhD, Chemical Engineering, Delft University of Technology, The Netherlands
2000 – 2001	Postdoc, University of New South Wales, Sydney, Australia
2002 – 2008	Associate Professor of Geomicrobiology, Radboud University, The Netherlands
since 2009	Professor of Sustainable Energy Production, Bielefeld University, Germany

Selected publications

- Strous, M. *et al.*: 1999. *Missing lithotroph identified as new planctomycete.* Nature 400:446-449
- Raghoebarsing, A.A. *et al.*: 2005. *Methanotrophic symbionts provide carbon for photosynthesis in peat bogs.* Nature 436, 1153-1156
- Strous, M. *et al.*: 2006. *Deciphering the evolution and metabolism of an anammox bacterium from a community genome.* Nature 440: 790-794
- Raghoebarsing, A. *et al.*: 2006. *A microbial consortium couples anaerobic methane oxidation to denitrification.* Nature. 440: 918-21
- Ettwig, K.E. : 2010. *Nitrite-driven anaerobic methane oxidation by oxygenic bacteria.* Nature, 464(7288):543-548

Future Projects and Aims

To produce biofuels in a sustainable way it is necessary to use atmospheric carbon dioxide as the carbon source ("atmospheric carbon capture"). Carbon dioxide is present in the atmosphere at low concentrations and this limits the overall process efficiency. Carbon absorption would be more effective at high pH. Therefore, we investigate the possibility to produce methane from algae at high pH. This has the additional advantage that the carbon dioxide can be recovered from the produced biogas without extra process steps. Methanogenesis is known to occur at high pH in alkaline soda lakes but this potential has not yet been explored for biotechnology. We aim to enrich and characterize methane producing archaea from alkaline soda lakes in laboratory bioreactors.

In addition, we will continue the study of nitrogen cycling microbes from sandy sediments to acquire predictive understanding of the fate of fertilizer nitrate. ■

Bioreactors for cultivating environmental microbes at defined and dynamic conditions

Plant Genetics and Crop Genomics

Structural and functional genomics, next generation sequencing and bioinformatics, classical genetics and molecular biology – these are our tools to investigate plant regulatory networks and to generate knowledge that can be transferred from model systems to agronomically relevant crops.

Previous and Current Research

Plants are essential. They bind carbon and produce oxygen, they preserve soils and water, they serve as food and feed, they provide wood and fibre as well as starch and biofuels – to name just a few aspects of their importance. Deciphering plant genomes and unraveling their functions is key to understand plant development, responses to the environment and to the application of knowledge to crops. The Chair of Genome Research is dedicated to structural and functional genomics in plants. For many of our projects we use the model system *Arabidopsis thaliana*, a small crucifer and one of the first eukaryotes whose genome was fully sequenced back in the year 2000. Gene functions in plants are, however, not accessible by targeted knock out via homologous recombination. Instead, collections of sequence-indexed insertion mutants are used for reverse genetic experimental approaches. With the GABI-Kat project we host the largest population of such T-DNA mutants in Europe and the second worldwide. Scientists can search the project database for lines with insertions in their genes of interest and place orders for relevant lines via the Internet. For about 2,800 *A. thaliana* genes insertion alleles are available from GABI-Kat only. Alleles from the GABI-Kat population make a significant contribution to saturate the *A. thaliana* genome, which contains about 27,000 protein-coding genes, with NULL mutations. In some of our other projects we use these alleles to identify new gene activities and to unravel regulatory networks of transcription factors with a focus on flavonoid biosynthesis control and seed coat development. As a non transgenic tool we have also established the TILLING technology for the detection of point mutations in *A. thaliana* and crop species like rapeseed.

Crop genomics is one key to new renewable resources for food, feed, fibre and fuel.

1988	PhD in Genetics, University of Cologne
1989–2003	Postdoc and Group leader at MPI for Plant Breeding Research, Cologne
1994	Visiting scientist at the University of Glasgow
since 2003	Professor for Genome Research, Bielefeld University

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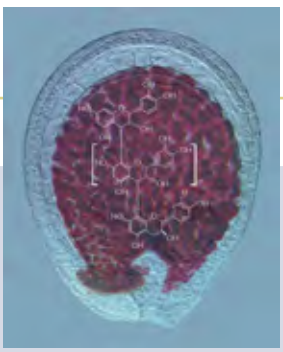
Selected publications

- Li, Y. *et al.*: 2007. *GABI-Kat SimpleSearch: an* Arabidopsis thaliana *T-DNA mutant database with detailed information for confirmed insertions.* Nucleic Acids Research 35: D874–D878
- Uelker, B. *et al.*: 2008. *T-DNA-mediated transfer of* Agrobacterium tumefaciens *chromosomal DNA into plants.* Nature Biotechnology 26: 1015–1017
- Wenke, T. *et al.*: 2009. *An abundant and heavily truncated non-LTR retrotransposon (LINE) family in* Beta vulgaris. Plant Molecular Biology 71: 585–597
- Dubos, C. *et al.*: 2010. *MYB transcription factors in* Arabidopsis. Trends in Plant Sciences 15: 573–581
- Appelhagen, I. *et al.*: 2011. *TRANSPARENT TESTA1 interacts with R2R3-MYB factors and affects early and late steps of flavonoid biosynthesis in the endothelium of seeds.* The Plant Journal 67: 406–419

Future Projects and Aims

In the last few years, tremendous progress was made in the development of new DNA sequencing technologies. We are part of a project to determine the structure and the sequence of the genome of sugar beet, and this project has profited from these technological advances. The rapidly increasing number of available plant genome sequences and the affordability to produce them offers great opportunities for comparative genomics. In cooperation with German grape breeding experts, we will use this approach to understand mechanisms that provide pathogen resistance in grape. We address this by comparing the genomes of resistant and susceptible varieties. RNAseq will be used to compare vegetative and reproductive structures as well as early and late flowering cultivars to identify the genes that control flowering time in grape. We will make use of ChipSeq to determine new transcription factor targets and characterize regulons in flavonoid biosynthesis on a genome wide scale. The ShoreMap approach will be applied to directly characterize mutants by sequencing without mapping and cloning. The ultimate goal of our projects is to transfer knowledge from *A. thaliana* to crop species. ■



Pigment precursors in a young seed

Sugar beet plants in a breeding programme (picture: KWS SAAT AG)

Genetics of Prokaryotes

Systems Biology and Metabolic Engineering of industrially relevant Bacteria

Bacteria can be found in every habitat of Earth. Their metabolic potential is fascinating: origin of atmospheric oxygen, driving biogeochemical cycles, degradation and synthesis of a plethora of compounds. Our group is interested in understanding this potential and in its rational application within the cell factory notion.

Previous and Current Research

We perform research in the field of molecular genetics and applied microbiology. Our aim is to characterize global gene regulation in industrially relevant microorganisms, with a particular focus on the central carbon metabolism and on amino acid biosynthesis, but also with respect to phosphorus and polyphosphate metabolism. Cutting edge methods including DNA microarray analysis and ultrafast sequencing methods are employed. Our work contributes to establishing a systems-level understanding of the bacterial cell with the biotechnologically important *Corynebacterium glutamicum* as an example. Applied research aims at metabolic engineering and rational strain development based on functional genomics results in the form of a genome-based biotechnology. Following synthetic biology approaches, we are developing high-performance strains for the production of amino acids and primary metabolites under the framework of White Biotechnology.

Future Projects and Aims

In fundamental research projects we are characterizing transcriptional regulation and signal transduction with respect to regulation of the central metabolism of *C. glutamicum* on the topological and mechanistic levels which appear to be different from the well-established model bacteria *Escherichia coli* and *Bacillus subtilis*. In a systems biology approach, we are analyzing the energy metabolism of *C. glutamicum*.
The generated knowledge will be applied to optimize *C. glutamicum* as platform organism for White Biotechnology. Along the same line, a flexible feedstock concept for *C. glutamicum* is pursued enabling access to a wide spectrum of carbon and

Our research aims at a systems-level understanding of the bacterial cell and its application within the frame work of the knowledge-based bio-economy.

Prof. Dr. Volker F. Wendisch

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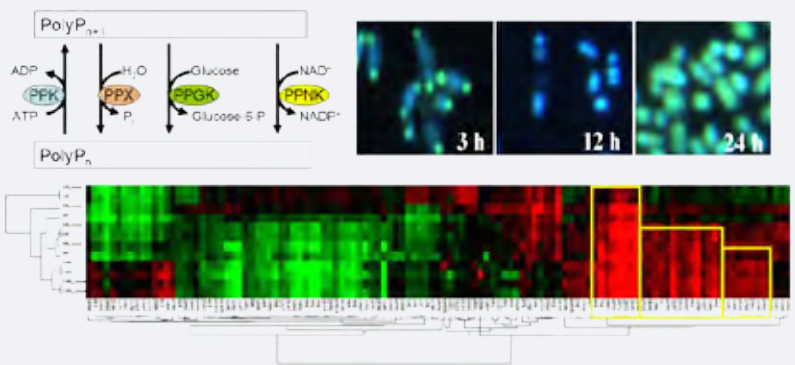
1997	Dr. rer. nat., Düsseldorf University, Germany
1997 – 1999	Postdoctoral researcher, University of California, Berkeley, CA, USA
1999 – 2005	Group leader, Research Center Jülich, Germany
2006 – 2009	Professor for Metabolic Engineering, Münster University, Germany
since 2009	Professor for Genetics of Prokaryotes, Bielefeld University, Germany

Selected publications

- Kato, O., Youn, J. W., Stansen, K. C. *et al.*: 2010. *Quinone-dependent D-lactate dehydrogenase Dld (Cg1027) is essential for growth of* Corynebacterium glutamicum *on D-lactate.* BMC Microbiol. 10: 321
- Schneider, J., Wendisch, V. F.: 2010. *Putrescine production by engineered* Corynebacterium glutamicum. Appl. Microbiol. Biotechnol. 88: 859–68.
- Lindner, S. N., Seibold, G.M., Henrich, A. *et al.* : 2011. *Phosphotransferase system-independent glucose utilization in* Corynebacterium glutamicum *by inositol permeases and glucokinases.* Appl. Environ. Microbiol. 77: 3571-81
- Panhorst, M., Sorger-Herrmann, U., Wendisch, V. F.: 2011. *The pstSCAB operon for phosphate uptake is regulated by the global regulator GlxR in* Corynebacterium glutamicum. J. Biotechnol. 154: 149-55

energy sources including those present in lignocellulosic hydrolysates from agricultural wastes, biorefinery streams or in biodiesel production wastes.
Biocatalysts for new or improved processes in White Biotechnology are being developed by metabolic engineering of *C. glutamicum* and *E. coli*. Typically, the focus is on the production of monomers for subsequent chemical conversions such as putrescine and other diamines or succinate and other diacids.

In a synthetic biology project the metabolic trait of methylotrophy is characterized, modules for bacterial methylotrophy are identified and realized on the genetic level. The generated knowledge will contribute to an increased understanding of bacterial methylotrophy and will facilitate transfer of methylotrophy to biotechnologically relevant bacterial species as a new modular platform for methanol-based production of bulk chemicals. ■



C. glutamicum enzymes form polyphosphate which accumulates in green fluorescent granules when phosphate is abundant (upper part). A complex gene expression response is elicited when phosphate becomes scarce (lower part).

Posttranscriptional regulation of plant gene expression

Fine-tuning of gene expression by microRNAs and nucleo-cytoplasmic partitioning of transcription factors are important regulatory tools. We are interested in how plants use these mechanisms to integrate environmental conditions and development.

Previous and Current Research

MicroRNAs (miRNAs) are a group of small non-coding RNAs that are very important endogenous regulators of the fine-tuning of gene expression. In plants, they act mainly but not exclusively on the post-transcriptional level by target slicing, thereby initiating target mRNA degradation. In cooperation with R. Giegerich, M. Rehmsmeier (Technical Faculty) we predicted many novel mRNA targets for miRNAs of the model plant Arabidopsis thaliana. Currently, we are analyzing the endogenous functions of selected novel miRNA targets. In addition, we use the expression of synthetic miRNAs (smiRNAs) as a very effective means for functional genomics approaches. We modified and optimized the design of smiRNAs to specifically target single mRNAs or multiple related mRNAs and to generate plants that show synthetic down-regulation of specific gene functions.

Nuclear import of proteins into the cell nucleus is known very well. We are interested in plant proteins that are also actively exported from the nucleus. The balance between nuclear import and export rates results in a steady state localization of a given protein that can be influenced and changed. This phenomenon is termed nucleo-cytoplasmic partitioning that is exploited as a regulatory mechanism for signaling pathways in eukaryotic cells. Transport of proteins between the nucleus and the cytoplasm can be monitored in vivo in real time using protein fusions with the photo-activatable GFP combined with two-photon activation and one-photon fluorescence detection (cooperation with D. Anselmetti, K. Tönsing, Faculty of Physics). We are working on specific transcription factors and RNA-binding proteins that show nucleo-cytoplasmic partitioning and examine their functions and the role of protein partitioning for signaling and development in Arabidopsis.

PD Dr. Thomas Merkle

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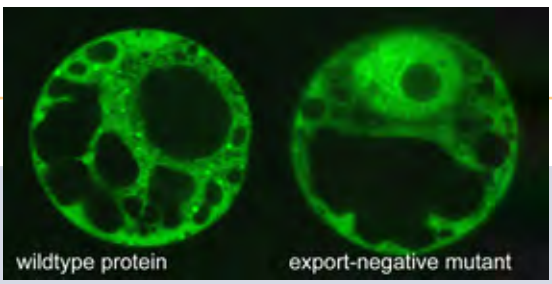
1991	PhD in Biology, University of Freiburg, Germany
1992 – 1996	Postdoctoral Research Fellow, Friedrich Miescher-Institut Basel, Switzerland
2002	Habilitation in Cell Biology, University of Freiburg
2002 – 2003	Lecturer at the University of Kiel, Germany
since 2004	Head of the Junior Research Group "RNA-based Regulation & Nucleo-Cytoplasmic Partitioning", University of Bielefeld, Germany

Selected publications

- Martini, J., Schmied, K., Palmisano, R., Tönsing, K. *et al.*: 2007. *Multifocal two-photon laser scanning microscopy combined with photo-activatable GFP for in vivo monitoring intracellular protein dynamics in real time.* J. Struct. Biol. 158:401–409
- Alves-Jr., L., Niemeier, S., Hauenschild, A., Rehmsmeier, M. *et al.*: 2009. *Comprehensive prediction of novel microRNA targets in* Arabidopsis thaliana. Nucleic Acids Res. 37: 4010–4021
- Merkle, T.: 2010. *Nucleo-cytoplasmic transport of proteins and RNA in plants.* Plant Cell Rep. 30: 153–176
- Niemeier, N., Alves-Jr, L., Merkle, T.: 2010. *Improvement of the design and generation of highly specific plant knockdown lines using primary synthetic microRNAs (pri-smiRNAs).* BMC Res. Notes 3: 59
- Pedersen, D. S., Merkle, T., Marktl, B., Lildballe, D. L. *et al.*: 2010. *Nucleocytoplasmic distribution of the* Arabidopsis *chromatin-associated HMGB2/3 and HMGB4 proteins.* Plant Physiol. 154: 1831–1841

Future Projects and Aims

Using smiRNA technology, simultaneous knockdown of several members of a family of RNA-binding proteins that show nucleo-cytoplasmic partitioning in Arabidopsis produced dwarfed plants that show impaired poly(A) RNA export. We want to further characterize the functions of these RNA-binding proteins by using them as molecular tags in order to isolate RNA-protein complexes and analyze their composition by high-throughput proteomics (cooparation with K. Niehaus, Biological Faculty). This will give insights into poly(A) RNA export and metabolism in plants. ■



Confocal images of protoplasts expressing GFP fusion proteins. The left panel shows the localization of the wildtype protein, the right panel the localization of the corresponding mutated protein that lacks nuclear export activity.

Arabidopsis knockdown mutant seedling (left), generated with smiRNA technology, in comparison with a wildtype seedling of the same age (right)

Medical Microbiology and Genomics

Corynebacteria of the human microflora are increasingly recognized as multidrug-resistant pathogens and associated with (fatal) infections in hospitalized patients. Microbiology and genomics are applied to decipher and interpret corynebacterial genome sequences and to deduce thereof the lifestyle of these emerging pathogens.

Previous and Current Research

The genus *Corynebacterium* was originally delineated in 1896 to accommodate bacteria that showed morphological similarities to the diphtheroid bacillus *Corynebacterium diphtheriae*. Nowadays, it comprises an extremely diverse collection of bacterial species, including the non-pathogenic soil bacterium *Corynebacterium glutamicum* and many new members isolated from human clinical specimens. Previous and current research projects are focused on the systematic reconstruction of the transcriptional regulatory network (TRN) from *C. glutamicum* to improve the industrial production of amino acids and on genome sequencing of corynebacteria from the human microflora to deduce the lifestyle of these microorganisms.
The complete genome sequence of *C. glutamicum* ATCC 13032 was established in 2003 at the CeBiTec and had enormous impact on gene expression profiling during the last decade. Rapid advances in associated bioinformatics approaches enabled new strategies for deciphering the architecture of the TRN of *C. glutamicum*. The TRN is a fundamental biological system controlling the flow of information from the environment toward the gene level and thus to specific cellular functions. It can be conceptualized as the sum total of gene-regulatory interactions in a bacterial cell and reconstructed in form of a directed graph. Our current TRN reconstruction is based on more than 1100 experimentally validated gene-regulatory interactions and revealed a highly connected network that displays a modular and hierarchical structure without feedback regulation at the transcriptional level.
Corynebacteria from the human microflora are increaslingly associated with severe infections in elderly individuals and in immunocompromised patients. Several corynebacteria revealed a remarkable multidrug resistance profile in such a way that only glycopeptide antibiotics remain universally active against these pathogens. The genomes of 27 bacteria from various parts of the phylogenetic tree of the genus *Corynebacterium* were decoded at the CeBiTec, including the multidrug resistant species *Corynebacterium jeikeium* and *Corynebacterium urealyticum*. The genome data revealed that horizontal gene transfer mediated by mobile genetic elements is the main factor contributing to the development of multidrug resistance. Moreover, the interpretation of corynebacterial genome sequences provided comprehensive insights into the gene composition and metabolic capabilities of the respective species and profound information regarding the molecular mechanisms and gene-regulatory networks involved in virulence.

Deciphering the letters of DNA molecules from fatal pathogens is like reading the detective novels of Agatha Christie.

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1996	PhD in Genetics, Bielefeld University, Germany
2006	Head of the Medical Microbiology and Genomics Research Group, Institute of Genome Research and Systems Biology, CeBiTec
2008	Habilitation in Genetics, Bielefeld University

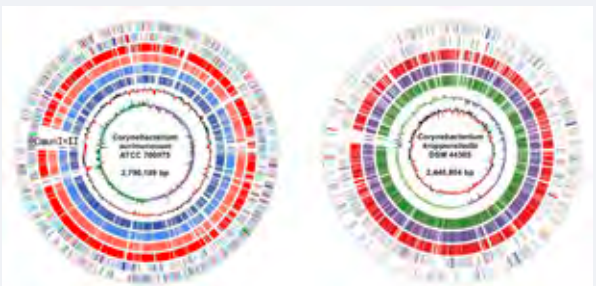
Selected publications

- Ventura, M. *et al.*: 2007. *Genomics of Actinobacteria: tracing the evolutionary history of an ancient phylum*. Microbiol. Mol. Biol. Rev. 71: 495–548
- Soriano, F. and Tauch, A.: 2008. *Microbiological and clinical features of* Corynebacterium urealyticum: *urinary tract stones and genomics as the Rosetta Stone*. Clin. Microbiol. Infect., 14: 632–643
- Schröder, J. and Tauch, A.: 2010. *Transcriptional regulation of gene expression in* Corynebacterium glutamicum: *the role of global, master and local regulators in the modular and hierarchical gene regulatory network*. FEMS Microbiol. Rev., 34: 685–737
- Trost, E. *et al.*: 2010. *Complete genome sequence and lifestyle of black-pigmented* Corynebacterium aurimucosum *ATCC 700975 (formerly* C. nigricans *CN-1) isolated from a vaginal swab of a woman with spontaneous abortion*. BMC Genomics, 11: 91

Future Projects and Aims

The skin bacterium *Corynebacterium jeikeium* is mainly recovered from human axillae and probably plays an important role in human body odor formation due to its lipid-dependent lifestyle. The biotransformation of malodor precursors by lipid-dependent corynebacteria in the human axilla is a well-established route to generate volatile fatty acids that contribute to human body odor. We are currently investigating the molecular basis and the transcriptional regulation of this metabolic route in *Corynebacterium jeikeium* to understand in more detail the formation of human body odor by corynebacteria and to detect targets for the design of new deodorants.

Comparative genomics approaches and pan-genomics are currently applied to learn more about the production of toxins in *Corynebacterium diphtheriae* and *Corynebacterium pseudotuberculosis* strains. In the latter case, the genomic data may help to improve the biotechnological production of phospholipase D that is used as toxoid in vaccination of sheep and goats to effectively control caseous lymphadenitis in these animals. This disease is present in all major sheep and goat production areas of the world and resulted in significant economic losses in wool, milk and meat production. ■



Genetic maps deduced from the complete genome sequences of the clinical isolates *Corynebacterium aurimucosum* ATCC 700975 and *Corynebacterium kroppenstedtii* DSM44385

Genome-based functional analyses in *C. glutamicum*

The soil-inhabiting microorganism *Corynebacterium glutamicum* was discovered in the 1950ies in Japan as a natural producer of L-glutamic acid. Since 1985 our group is engaged in developing cloning systems and later genomics and post-genomics techniques for a systems understanding and its application in biotechnology.

Previous and Current Research

Today *C. glutamicum* is dominant in the global market for the production of various amino acids used in nutrition and health applications. Due to its simple nutritional requirements, fast growth, and its easy handling both in genetic engineering and in fermentation, it is considered today as an ideal basis for the further development to a universal host for production of a large number of different products derived from primary metabolism or as producer of proteins.

The research group is working on *C. glutamicum* for more than 25 years now, starting with the development of tools and techniques for genetic engineering. Major achievements of the group were the initial development of electroporation and conjugal transfer of genetic material from *E. coli* donor strains. In addition, gene-disruption and gene-replacement techniques for *C. glutamicum* and related organisms were introduced by our group in the year 1991. By using these techniques together with gene cloning and functional analyses, initial insights into metabolism and hints for the more rational construction of amino acid producer strains were obtained in the following years. However, the main focus of industrial strain development was still the classical mutation and selection process.

The year 2003 brought a major breakthrough, since two groups working independently published the complete genome sequence of the type strain *C. glutamicum* ATCC 13032. As being one of these (Kalinowski et al. 2003) we were able to bring functional analyses to the next, the genome-wide level. Transcriptomics and proteomics were developed on the basis of the genome sequence and research on gene functions and especially regulation of genetic and metabolic networks in *C. glutamicum* flourished since then. Today, *C. glutamicum* can be considered a model organism for industrial production of metabolites derived from primary metabolism and also for closely related organisms from the Actinobacteria (Wendisch et al., 2006), some of them important pathogens (*C. diphtheriae*, *Mycobacterium tuberculosis*).

The research group is actually working on the following subjects

- genomics of the species *C. glutamicum*, its pan-genome and a minimal genome
- transcriptional regulatory networks including sigma factor networks involved in stress reponse
- advanced transcriptomics including transcriptome sequencing and small RNAs
- proteomics including post-translational modification and the surface-layer protein

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1990	PhD in Genetics, Bielefeld University, Germany
since 1990	Group leader *Corynebacterium glutamicum*, Bielefeld University, Germany
since 2007	Center for Biotechnology (CeBiTec), Bielefeld University, Germany

Selected publications

- Kalinowski, J., *et al.*: 2003. *The complete* Corynebacterium glutamicum *ATCC 13032 genome sequence and its impact on the production of L-aspartate-derived amino acids and vitamins*. J. Biotechnol., 104(1–3): 5–25
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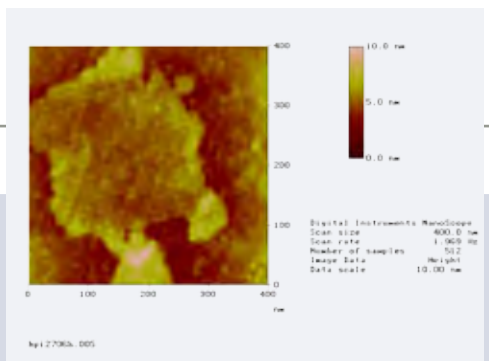
- Nakunst, D., *et al.*: 2007. *The extracytoplasmic function-type sigma factor SigM of* Corynebacterium glutamicum *ATCC 13032 is involved in transcription of disulfide stress-related genes*. J. Bacteriol., 189(13): 4696–707
- Neuweger, H., *et al.*: 2009. *Visualizing post genomics data-sets on customized pathway maps by ProMeTra - aeration-dependent gene expression and metabolism of* Corynebacterium glutamicum *as an example*. BMC Syst. Biol., 3: 82

- metabolic networks and metabolome analysis for amino acid production

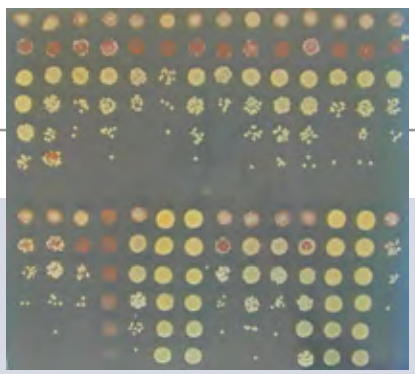
The fast progress in *C. glutamicum* research that we experienced in the "genome age" would not be possible without a large national research network now existing since the 1980ies and with essential contributions by our in-house bioinformatics.

Future Projects and Aims

Our goals for the next years is to advance the knowledge on this organism, its gene functions and regulations for the in-depth understanding of its functional and regulatory systems as well as the application of this knowledge for biotechnological processes. ■



The *C. glutamicum* surface layer protein forms paracrystalline layers visible by atomic-force microscopy.



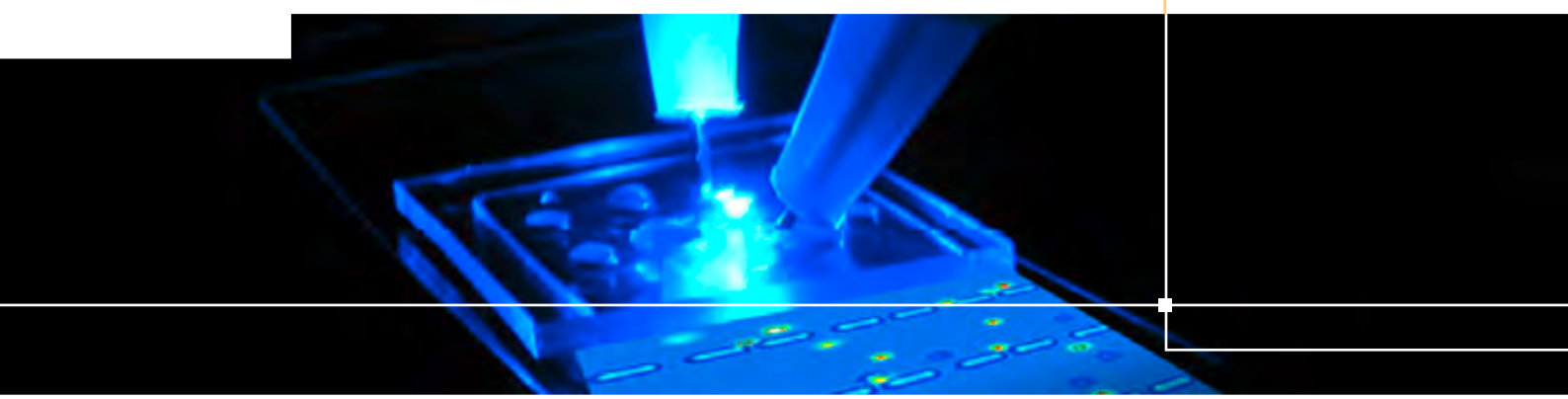
C. glutamicum transposon mutants reacting differentially to selenocysteine.

Single Molecule Biophysics

In bionanoscience, structural and functional properties of biomolecules are being quantitatively investigated in high-resolution experiments at the level of single molecules. This allows fundamental insights into the underlying physical mechanisms as well as to develop novel biomolecular applications thereof.

Previous and Current Research

Specific molecular recognition between and the dynamics of macromolecules are essential for maintaining cellular functions and are driven and maintained by fundamental physical phenomena. Since these are often regulated and controlled at the level of molecular individuals, nanobiological experiments are predestinated to identify and quantify their underlying physical mechanisms. Therefore, cellular functions like cell adhesion and cell organization, transcription regulation and nucleocytoplasmic transport and many others are currently being investigated with single molecule methods like atomic force microscopy (AFM), force spectroscopy, optical tweezers and local non-linear laser scanning methods.
Over the last years, we therefore conducted single molecule binding studies between DNA/RNA and proteins, DNA/enzyme complexes and chemotherapeutic alkaloids for drug screening, proteoglycans, carbohydrates, supramolecular host cavitands and their ligands in an affinity range of 10^{-4} – 10^{-15} M with the sensitivity of single point mutations in a close collaboration with other University research groups in biology and chemistry.
In microfluidics, the migrational dynamics of macromolecules and colloids was investigated in structured microfluidic architectures under thermodynamic non-equilibrium conditions. Non-linear and sometimes unexpected migration phenomena like absolute negative particle mobility and molecular ratcheting could be observed upon using electrophoretic and dielectrophoretic driving and trapping. Based on these effects novel concepts for molecular and particle separation and sorting could be developed.
Analytical binding experiments with single cells were performed with optical tweezers where single, specific interaction forces between a membrane bound receptor on a living B-cell (BCR) could be measured, opening new and fascinating possibilities for future functional probing of living single cells.



Think small – todays´ single molecule experiments let us revisit the concepts of mechanics and fluidics for novel and ultrasensitive biomolecular device applications.

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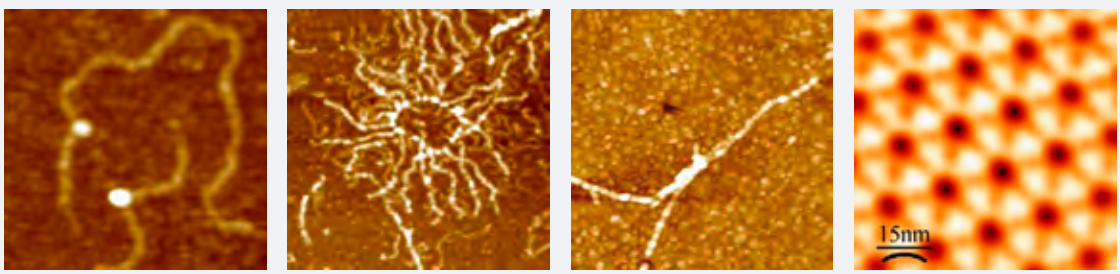
1990	PhD in Experimental Physics, University of Basel
1990–1991	Post-doctoral associate at the IBM Research Laboratory in Rüschlikon
1994–2000	Research fellow (Ciba-Geigy & Novartis)
1998	Habilitation in Experimental Physics, Basel University
since 2000	Full professor at Bielefeld University and Chair of Experimental Biophysics
since 2005	Member of the North Rhine-Westphalian Academy of Sciences and Arts, Düsseldorf
since 2007	Speaker of SFB 613 at Bielefeld University

Selected publications

- R. Eckel *et al.*: 2005. *Supramolecular Chemistry at the Single Molecule Level*. Angewandte Chemie (Intl. Edition), 44: 484-488
- A. Ros *et al.*: 2005. *Brownian Motion: Absolute Negative Particle Mobility*. Nature, 436: 928
- A. Fuhrmann *et al.*: 2009. *Quantitative Single Molecule Interaction Analysis of Glycine-Rich RNA-Binding Proteins*. Biophysical Journal, 96: 5030-5039
- J. Regtmeier et al. *et al.*: 2010. *Dielectrophoretic Trapping and Polarizability of DNA: The Role of Spatial Conformation*. Analytical Chemistry, 82: 7141-7149
- A. Spiering *et al.*: 2011. *Nanopore Translocation Dynamics of a Single DNA-Bound Protein*. NANO Letters, 11, 2978-2982

Future Projects and Aims

In the future, we will bring together the methodological fields of force spectroscopy, optical tweezers, and nanofluidics, in order to investigate cellular translocation dynamics in artificial systems like solid-state nanopores as well as in natural membrane-bound channels and transporters. These experiments will allow closer inspection of phenomena like nucleocytoplasmic transport, exo- and endocytosis, as well as viral infection. ■



AFM-images of DNA-protein complex (left), adhesion proteoglycan macromolecule (middle left), Alzheimer beta-amyloid fibril (middle right) and paracrystalline bacterial surface layer (right).

Supramolecular Systems and Surfaces

Carbon Nano Membranes (CNMs) are similar to plastic foils, but only 1 nanometer thick. CNMs are made by radiation induced cross-linking of surface bound organic molecules. CNMs can be chemically and biologically functionalized as well as transformed into graphene, thus providing a 2D-platform for applications.

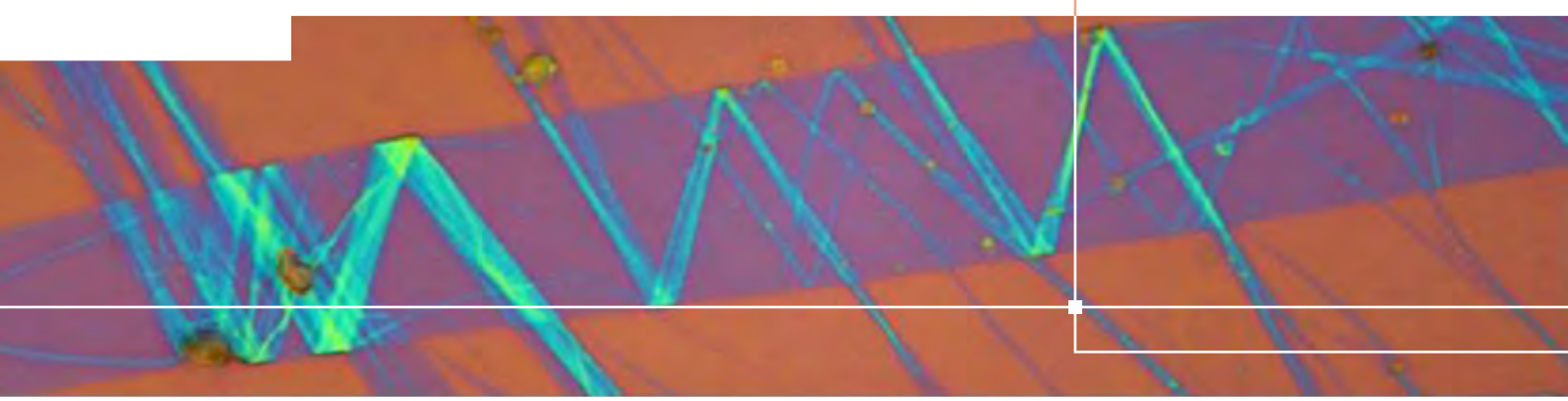
Previous and Current Research

The starting point of CNM fabrication is a self-assembled monolayer (SAM) of aromatic molecules which are linked to a surface via a functional group. When the so-assembled molecules are exposed to radiation, one obtains a 1 nm thick mechanically stable film of cross-linked carbon. This way, membranes with areas of up to 10 cm2 have been built. The Gölzhäuser group is working with partners in Europe, the US and Japan on the characterization of these materials for electrical, optical and mechanical purposes, and towards applications of CNMs into new products.

CNM forms in three steps. Lead compounds are bi- or terphenyls, which adsorb on a surface via a functional group. The SAMs are bombarded with electrons or extreme ultraviolet photons. This breaks intramolecular bonds and adjacent molecules form cross-links. Patterned exposures can be produced by either a shadow mask or a scanning beam. A special method – developed in Bielefeld – allows CNMs to be transferred from one surface onto another, including materials and objects on which otherwise no SAMs form, such as grids for transmission electron microscopy. The transfer technique also allows the integration of CNMs into silicon chips or micro-structured surfaces.

Future Projects and Aims

CNMs have significant potential for technological applications. CNM based products include support membranes for electron microscopy of nanometer scale objects, where the support structure is often thicker than the actual nano-object, which results in a poor image quality. The CNMs, however, are thinner than most nano-objects, which improves the image contrast significantly. In addition to the thickness, the chemical functionalities of the two sides of the CNM can be tailored by the choice of suitable molecules. By selecting the irradiation parameters, the degree of cross-linking and thus the elasticity of



Molecular nanotechnology deals with the fabrication, manipulation and application of functional objects with nanometer dimensions.

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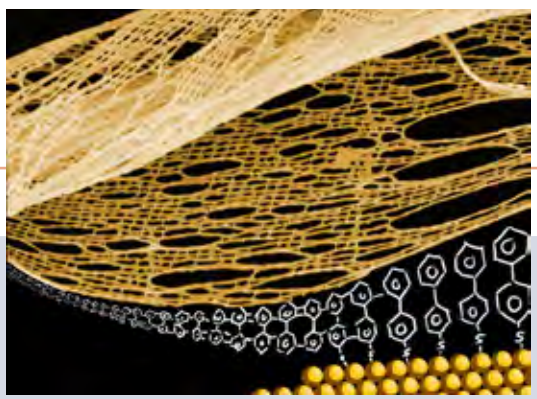
1993	Dr. rer. nat. University of Heidelberg.
1994–1996	Feodor Lynen Fellow, University of Illinois at Urbana-Champaign
2001	Habilitation, University of Heidelberg.
2003	Professor of Physical Chemistry, University of Marburg.
since 2003	Professor of Physics, University of Bielefeld.
since 2007	Speaker of the Bielefeld Institute for Biophysics and Nanoscience (BINAS).

Selected publications

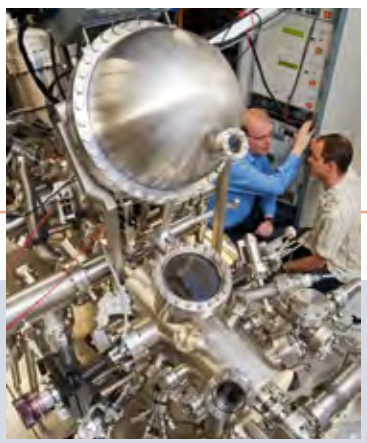
- Turchanin, A., Beyer, A., Nottbohm, C., Zhang, X. *et al.*: 2009. *1 nm thin carbon nano-sheets with tunable conductivity and stiffness*, AdvMat 21, 1233
- Schnietz, M., Turchanin, A., Nottbohm, C. T., Beyer, A. *et al.*: 2009. *Chemically functionalized carbon nanosieves with 1 nm thickness*, Small 23, 2561
- Amin, I., Steenackers, M., Zhang, N., Beyer, A. *et al.*: 2010. *Polymer Carpets*, Small 6, 1623
- Nottbohm, C., Turchanin, A., Beyer, A., Stosch, R. *et al.*: 2011. *Mechanically stacked ultrathin layered materials with tunable optical, chemical and electrical properties*, Small 7, 874
- Turchanin, A., Weber, D., Büenfeld, M., Kisielowski, C. *et al.*: 2011. *Conversion of SAMs into Nanocrystalline Graphene: Structure and Electric Transport*, ACS Nano 5, 3896

the CNM can be tuned. Changes in the elasticity of CNMs can be used for bioanalytics: if a protein binds to a CNM surface, this results in a change of the CNMs resonance frequency.

A discovery of great technical potential is that heating in vacuum (pyrolysis) leads to structural phase transitions that convert the polymeric CNM into a single layer of graphite, i.e. graphene, opening a variety of applications in electronics. CNMs can be perforated and used as filters for materials separation. An elegant way to perforate CNM is the projection of a two-dimensional interference pattern of coherent ultraviolet light onto the SAM, producing a "sieve" with a thickness of 1 nm and holes with adjustable diameters. In summary, CNMs are a new class of materials with interesting properties that lead to innovative products in many fields. ■



Self-assembled monolayers on gold surfaces can be converted in 1 nm thick perforated layers, which can then be detached as self-supporting nanosieves.



X-ray photoelectron spectrometer for quantitative chemical analysis of surfaces and CNMs.

fs/as Moclecular Dynamics

Pump-probe techniques by use of XUV-High Harmonics of ultrashort laser pulses allow the study of electronic and structural dynamics in molecular adsorbates on solid surfaces as well as of photo induced processes and of the photoemission process itself resolved in time on the natural femtosecond or even attosecond scale.

Previous and Current Research

The research interests have been developed from basic research in molecular and surface physics, such as angle- and spin resolved photoemission spectroscopy, circular dichroism on chiral molecules and molecule-surface interaction toward applications in nanotechnology, nanobiotechnology and thin film photovoltaics. One spin-off of the techniques used hereby was the successful development of aperiodic nanometer multi-layer x-ray mirrors which became the basis of application and use of attosecond short laser radiation pulses to resolve the photoelectron emission process on the natural time scale. By means of pump probe techniques with use of laser based high harmonic radiation the atomic photoionization with rare gas atoms, the condensed matter photoemission of a tungsten surface, the photoinduced reconfiguration cycle in a molecular adsorbate layer on a Silicon substrate as well as the Insulator to Metal Phase Transition of VO_2 with its interplay between electronic correlations and coherent structural dynamics have been experimentally studied time resolved on the femtosecond and/or even attosecond natural scale.

Future Projects and Aims

It is the aim of future research to use the attosecond radiation pulses to study the dynamics of electron transport mechanisms through molecular adsorbates, photoswitching processes and reconfiguration cycles in on surfaces adsorbed molecules in time resolved ESCA. The photoemission process itself when studied with an attosecond resolution will allow to distinish coherent and incoherent processes and to analyze dephasing mechanisms in the dynamical development of molecular systems. ■

1980	Visiting lecturer at Imperial College London, U.K.
1981	Award ("Physikpreis") of the German Physical Society
1981 – 1984	Head of a research group (C3) at the Fritz-Haber-Institute of the Max Planck Society, Berlin
since 1984	Professor and head of the chair of Molecular and Surface Physics at the Physics Faculty of Bielefeld University
2000	Visiting professor at Technical University Vienna
2000	Member of the European Academy of Sciences and Arts
2009	DrSc. h.c. by Slovak Academy of Sciences

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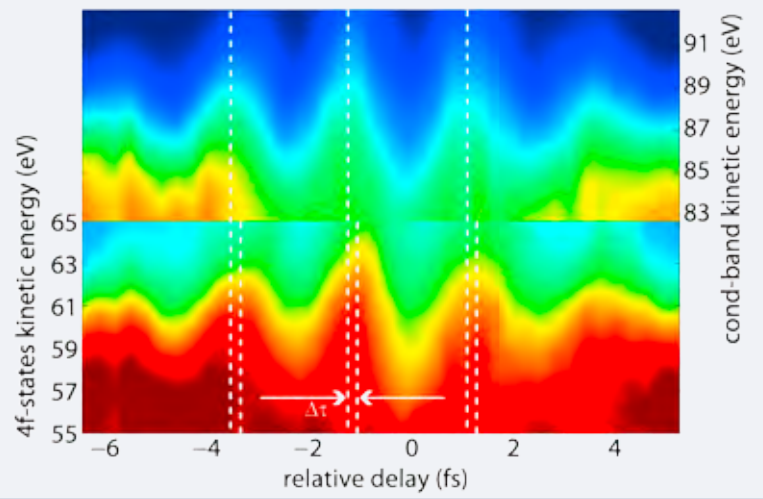
Selected publications

- Hentschel M., et al., 2001. Atto-second metrology. Nature 414, 509-513
- Drescher M., et al., 2002. Time-resolved atomic inner-shell spectroscopy. Nature 419, 803-807
- Kienberger R., et al., 2004. Atomic transient recorder. Nature 427, 817-821
- Cavalieri A. L., et al., 2007, Attosecond spectroscopy in condensed matter. Nature 449, 1029-1032
- Dachraoui H. et al., 2011. Photoinduced reconfiguration cycle in a molecular adsorbate layer studied by femtosecond inner-shell photoelectron spectroscopy. Phys. Rev. Lett. 106, 107401



Attosecond resolved streaking signal of photoelectron emission from W(110) surface: the photoelectrons kinetic energies in the presence of a phase stabilized fs-IR pulse. The photoemitted electrons from the 4f states leave the solid surface 110 attoseconds later than those from the conduction band (Nature 449, 1029 (2007)).

Physics of Nanostructures

Magnetic nanoparticles enables fundamental research and applications in varies physical and medical fields. Due to their magnetic moment controlled motion in microfluidic devices, detection of magnetically labeled biomolecules or reconfiguration of nanoparticular matter can be studied.

Previous and Current Research

During the last decade, magnetoresistive biosensors have been introduced as a new detection method for molecular recognition reactions based on a combination of magnetic markers and XMR-sensors. Besides GMR-sensors also Tunneling Magnetoresistance- (TMR) sensors have been identified of great potential. In cooperation with three chemical groups at Bielefeld, Prof. P. Jutzi, Prof. N. Mitzel and Prof. J. Mattay we have addressed the challenges so as to develop such combined tools for single molecule detection. From a chemical point of view one key issue is to stabilize the magnetic core of magnetic nanoparticles by appropriate organic ligands so as to define their size distribution and simultaneously to preserve their magnetic property by preventing them from oxidation. Moreover, functionalization of these ligand tail groups has been demonstrated so that biomolecules could be marked by magnetic nanoparticles. Furthermore, the physical design of XMR-sensors was successful and a new detection strategy was realized by which magnetically labeled biomolecules could dynamically be detected while passing by XMR-sensors in microfluidic devices. This approach is based on a so called magnetic on-off ratchet allowing the transport of biomolecules attached to magnetic beads by switching magnetostatically between two states. The first state is the on-state, where beads move to a minimum of a magnetostatic potential. The second state is the off-state, where beads diffuse freely. Due to the asymmetry of the potential net flux of beads can be generated. The advantage of this transport mechanism is a simultaneous bead separation by inertia. The mean free path of biomolecules labeled with magnetic beads is much shorter than the one for beads without biomolecules. Integrating TMR-sensor arrays into the magnetic on-off ratchet gave rise to the idea of a magnetoresistive microscope. In the off-state the biomolecules (A) attached to magnetic beads can freely move driven by Brownian motion about the positions of potential minima. The exact location of the center of one biomolecule (A) can hence be calculate from the fraction of magnetic stray field interaction with all sensors involved. Functionalizing the sensors with another biomolecule (B) the dynamic interactions between both molecules A and B can then be monitored.

Future Projects and Aims

Recently, we were able to synthesize different Cobalt nanoparticles in form of disks, spheres and cubes, see picture. Utilizing

Magnetic nanoparticles as reconfigurable matter will definitely revolutionize the future of magnetoresistive sensors.

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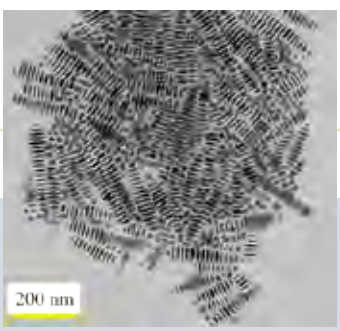
1989	PhD in Physics at Georg-August-University Göttingen, Germany
1990 – 1997	at UC Berkeley, USA and at Leibniz Institute for Solid State and Materials Research Dresden, Germany
2001	Habilitation in Experimental Physics, Bielefeld University, Germany
2005 – 2007	Institute of Nanotechnology of the Forschungszentrum Karlsruhe, Germany
since 2007	Professor of Physics of Nanostructures, Bielefeld University, Germany

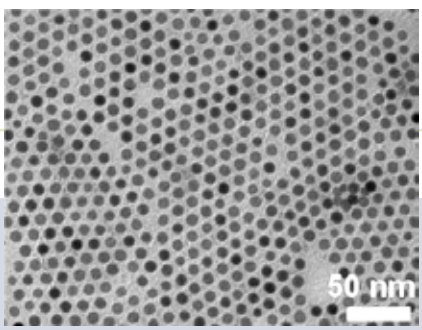
Selected publications

- Berkowitz, A. E. *et al.*: 1992. *Giant Magnetoresistance in Heterogeneous Cu-Co Alloys*. Phys. Rev. Lett. 68: 3745–3748
- Hütten, A. *et al.*: 2004. *New Magnetic Nanoparticles for Biotechnology*. J. Biotechnol. 112: 47–63
- Kämmerer, S. *et al.*: 2004. *Co2MnSi Heusler alloy as magnetic electrodes in magnetic tunnel junctions*. Appl. Phys. Lett. 85: 79–81
- Auge, A. *et al.*: 2009. *Magnetic ratchet for biotechnological applications*. Appl. Phys. Lett. 94: 18: 183507
- Weddemann, A. *et al.*: 2010. *Review and outlook: from single nanoparticles to self-assembled monolayers and granular GMR sensors*. Beilstein J. Nanotechnol. 1: 75–93

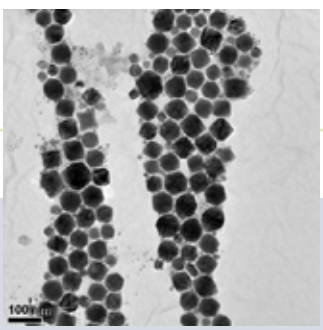
rotational magnetic field these nanoparticles can be reconfigured in chains, patches or huge monolayers in solution and will remain in these shapes on a substrate after drying out the solvent. The dipolar magnetic interaction between these nanoparticles alone will lead to nanoparticular type of GMR- and TMR-sensors which can simply be printed. Thus, magnetic nanoparticles as reconfigurable matter will definitely revolutionize the future of magnetoresistive sensors. ■



Co-discs



Co-spheres



Co-tubes

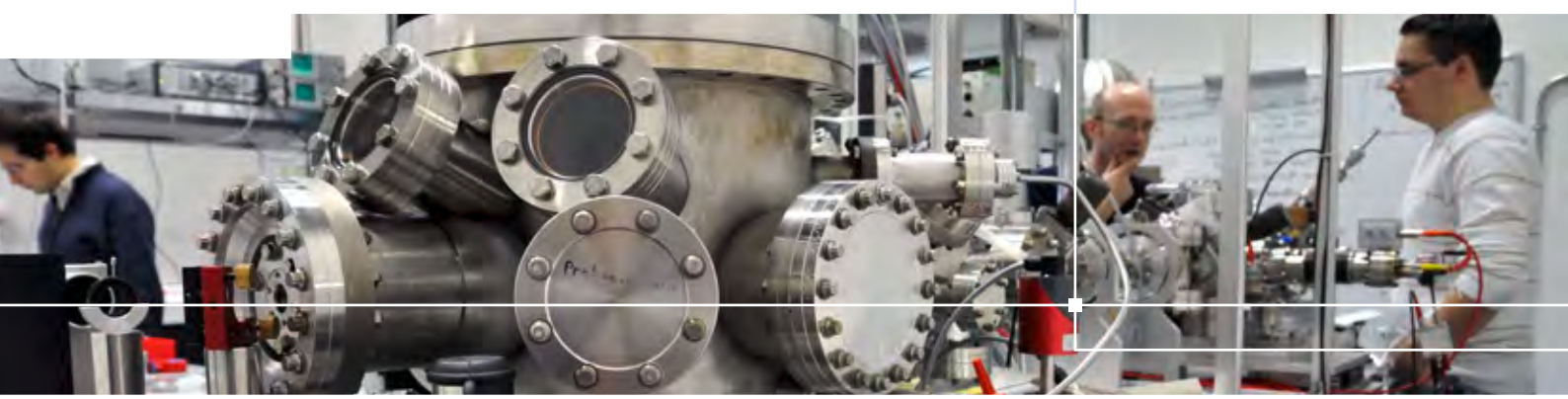
Magnetic Cobalt nanoparticles as potential magnetic India inks

Ultrafast Dynamics on the Nanoscale

Femtosecond laser technology opens new realms for monitoring and controlling ultrafast processes. As main objective we focus on nanoscale phenomena, such as ultrafast electronic transport at interfaces, photoinduced molecular dynamics, ultrafast nanooptics and coherent control of these systems.

Previous and Current Research

Recent developments in laser technology provide means to investigate ultrafast phenomena directly in the time-domain even with sub-femtosecond time resolution. During the last decade we have used ultrafast laser spectroscopy to study electron dynamics at interfaces in particular emphasizing electron dynamics in supported metal nanoparticles and photoinduced ultrafast transport phenomena. The ultrafast electron dynamics at nanostructured surfaces is uncovered by time-resolved laser spectroscopy combined with surface physics techniques like photoemission spectroscopy or scanning tunneling microscopy.
Photocurrent spectroscopy reveals transport and relaxation dynamics in metal-insulator-metal junctions far from equilibrium. At present, we extend the latter experiments on photoinduced charge transfer towards metal-molecule-metal junctions. Using properly anchored molecules, the photocurrent is dominated by the intramolecular charge transport. Time-resolved photocurrent spectroscopy then provides information on excited electron transfer through the molecule. Even more fascinating is the prospect to use the electric field of the laser pulse to control the photocurrent through the molecular junction.
An additional area of research is ultrafast nanooptics. The combination of ultrafast laser spectroscopy, i.e. the illumination using broadband coherent light sources and near-field optics, has recently opened a new realm for nonlinear optics on the nanoscale. For example, local field enhancement and the detection of nonlinear optical signals improve the lateral resolution in SNOM, second-harmonic microscopy and photoelectron emission microscopy. We have shown that adaptive pulse shaping provides means to control simultaneously the spatial and temporal evolution of the optical near-field distribution. Thus, adaptive optics allows manipulating and steering



Prof. Dr. Walter Pfeiffer

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1989, 1993	Diploma and PhD in Physics at the University of Konstanz, Germany
1993–1994	Postdoctoral researcher at the University of Konstanz, Germany
1994–2006	Research assistant at the University of Würzburg, Germany
2000	Habilitation in Physics at the University of Würzburg, Germany
since 2006	Professor for Experimental Physics at Bielefeld University, Germany

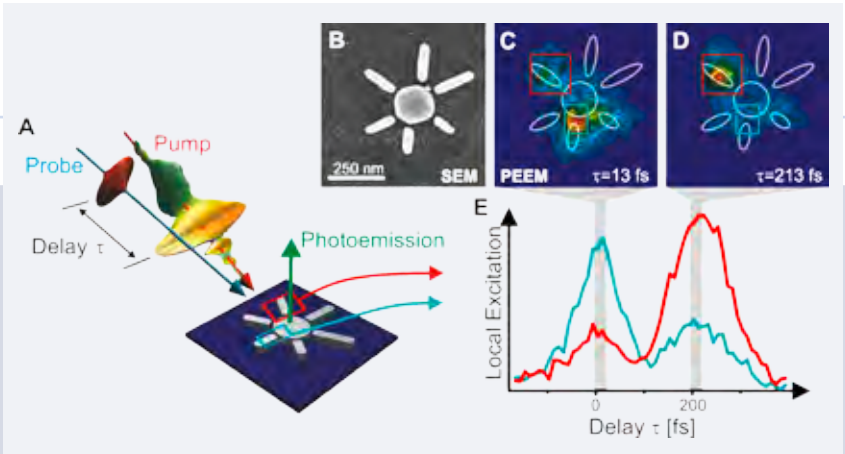
Selected publications

- Brixner, T. *et al.*: 2005. *Nanoscopic ultrafast space-time-resolved spectroscopy.* Phys. Rev. Lett., 95: 093901
- Aeschlimann, M. *et al.*: 2007. *Adaptive subwavelength control of nano-optical fields.* Nature 446:301
- Pfeiffer, W. *et al.*: 2010. *Simultaneous spatial and temporal control of nanooptical fields.* book chapter in: Dynamics at Solid State Surfaces and Interfaces, Wiley-VCH: 555
- Aeschlimann, M. *et al.*: 2010. *Spatiotemporal control of nanooptical excitations.* P. Natl. Acad. Sci. USA, 107:5329
- Dachraoui, H. *et al.*: 2011. *Photoinduced reconfiguration cycle in a molecular adsorbate layer studied by femtosecond inner-shell photoelectron spectroscopy.* Phys. Rev. Lett., 106: 107401

the optical excitation in complex nanostructures, such as for example supramolecular aggregates, or ensembles of qubits.

Future Projects and Aims

The future projects will be dedicated to coherent control of electron dynamics at interfaces and in nanostructures. After its demonstration, coherent control of molecular motion or chemical reactions using shaped ultrashort laser pulses has evolved into an active field of research. In contrast, the control of electronic motion is still rather limited because of the fast dephasing and short relaxation times of electronic excitations. Carrier envelope phase stabilized few femtosecond laser pulses and attosecond laser pulses now provide sufficient temporal resolution to study and control electron motion and, thus, open a new field for research and applications. ■



A Spatiotemporal excitation control using photoelectron emission microscopy (PEEM). **B** Scanning electron microscopy of Ag nanostructure. **C,D** Excitationpattern for different delay. **E** Nanoscale excitation switching between two areas.

Nanotechnology for biotechnical applications

Nanotechnology has become a key issue for progress in biotechnology. Manipulating molecules is, e.g., of large interest for analyzing their properties and for using them to construct functionality. Moreover, devices based on nanostructures become increasingly important for mimicking biological processes such as brain operation.

Previous and Current Research

Neural network devices

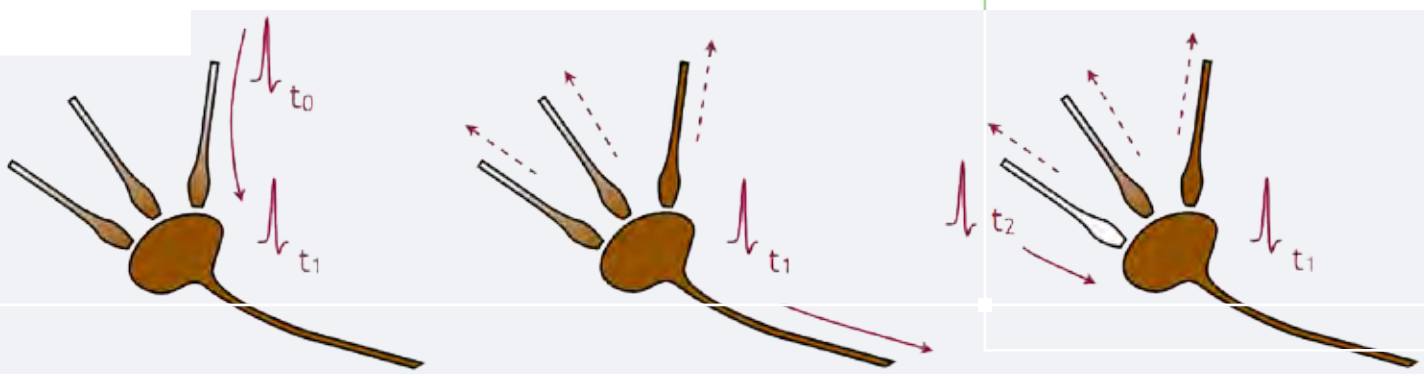
Artificial neural networks are systems that permit computers to function in a manner analogous to that of the human brain. Instead of manipulation of "0"s and "1"s, they create weighted connections (synapses) between switching elements (neurons). This allows for data to be read and stored in ways that resemble human learning and memory.

We found a simultaneous occurrence of synaptic and neuron-like behavior in nanoscopic tunneling elements which consist of two ferromagnetic metallic electrodes separated by an ultrathin insulator (MgO). By applying current pulses with appropriate intensity and duration, the resistance of the elements shows a memristive behavior which enables mimicking synaptic and neuronic functionalities. These devices represent the simplest implementation of neuromorphic hardware available to date.

Since in a neural network synapses outnumber neurons by orders of magnitude, synapses and neurons would be represented by different elements. However, since both could be etched from the same wafer, memristive MTJs may become very attractive for mass fabrication of artificial neural networks. A comparison of the Excitatory Postsynaptic Potential (EPSP) in Long Term Potentiation (LTP) recorded from a hippocampal synapse (reproduced from Bilss et al., 1993. Nature, 361: 31) and the typical change of the conductivity of a memristive tunnel junction induced by 16 train voltage pulses with 500mV demonstrates this similarity. The conductivity represents the strength of the artificial synapse.

Molecule manipulation

DNA-based single-molecule studies, nanoelectronics and nanocargos require a precise placement of DNA in an orientation-defined manner. Until now, there is a lack of



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1989	PhD in Physics, Regensburg University
1992	Post Doc, IBM T.J Watson Research Center, Yorktown Heights
1993	Head of the Thin Film Department, IFW Dresden
1997	Professor for Experimental Physics, Bielefeld University

Selected publications

- Krzysteczko, P. *et al.*: 2009. *Current induced resistance change of magnetic tunnel junctions with ultra-thin MgO tunnel barriers.* J. Magnet. Magnet. Mater. 321: 144
- Krzysteczko, P., Reiss, G., Thomas, A.: 2009. *Memristive switching of MgO based magnetic tunnel junctions.* Appl. Phys. Lett. 95: 112508
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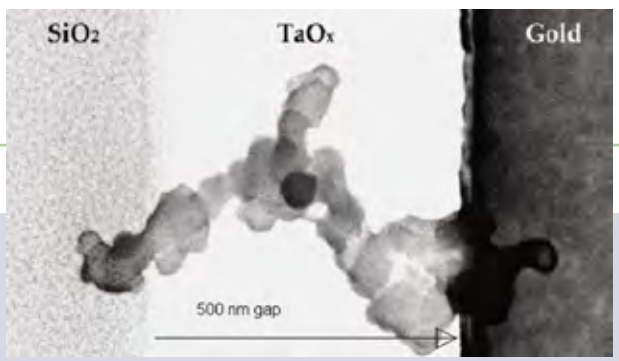
- Venkatesh, A. G., Herth, S., Becker, A., Reiss, G.: 2011. *Orientation-defined alignement and immobilization of DNA between specific surfaces.* Nanotechnology 22: 145301

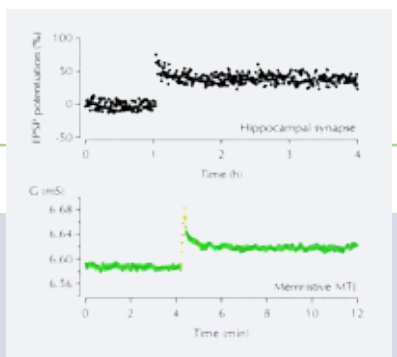
orientation-defined alignment and immobilization of DNA over distances smaller than several micrometers. We tried to realize a defined immobilization by designing bifunctionalized DNA. The DNA is then put on a microchip with two different electrodes separated by a gap. An electric ac field then aligns the DNA and those strands oriented with the functionalized ends towards the specific binding partner are immobilized. In the example shown at the bottom right, DNA was functionalized on one end with thiol and the other with (3-aminopropyl) triethoxysilane. With this method, we succeeded in defined orientation of pUC19 DNA. Alignement was done with an electric ac field of 2V (p-p) at a frequency of 1 MHz.

Future Projects and Aims

In future projects, the group first will integrate memristive tunnel junctions in first working logic circuits. The aim of this work is to emulate learning with memristive devices.
We second aim for using nanoelectronic components such as miniaturized thermocouples, coils and sensors to tackle signal creation and transmission on a single cell level. ■



SEM image of metalized pUC19 DNA aligned between Gold and Silicon-dioxide at an electric ac field of 2V (p-p) at a frequency of 1 MHz



Comparison between the long term potentiation (LTP) of a hippocampal synapse with the according conductivity step of a memristive tunnel junction

Molecular Medicine

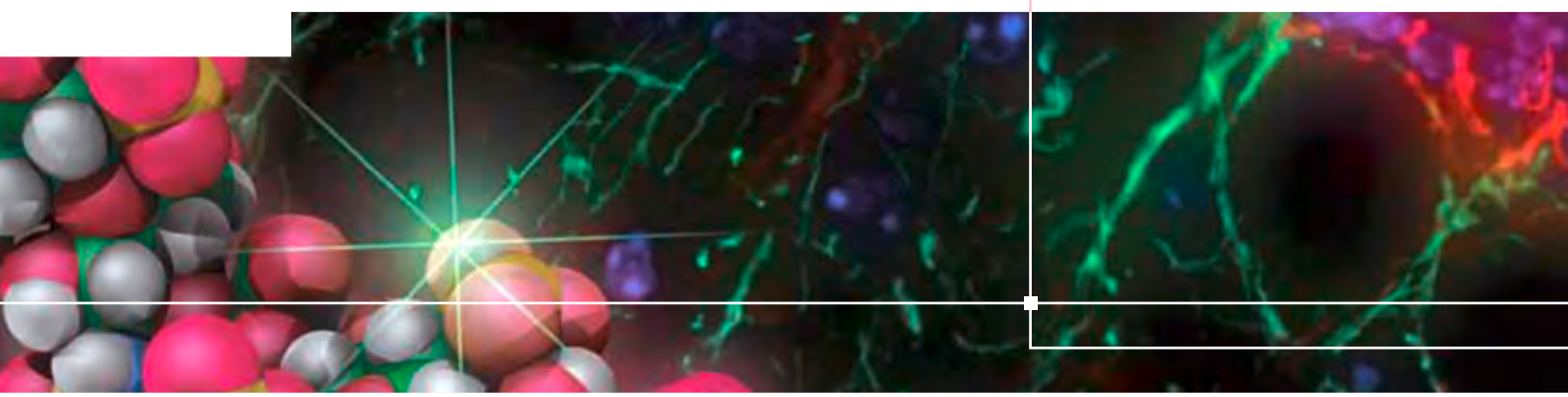
Multi-faceted functions of sulfatases in health and disease

By cleaving endogenous sulfate esters, human sulfatase enzymes are key players in metabolism and signal transduction. Their genetic deficiency leads to severe disorders. To study the molecular basis of these disorders we use knockout mouse models and recombinant sulfatases for enzyme replacement therapy.

Previous and Current Research

Heparan sulfate (HS) represents a remarkable substrate of sulfatases – essential for vertebrate life and instigator of many disease pathologies. HS is a dynamically sulfated cell surface sugar polymer playing versatile roles in mediating cell signaling and other events, which make it one of the most complex information carriers in the cell. The sulfation 'codes' are developmental stage and cell type specific and mediate binding to growth factors, morphogens, cytokines, chemokines, matrix ligands and cell surface molecules. HS thus acts as a multifunctional signal integration module orchestrating a number of important signaling pathways. Two cell surface sulfatases, Sulf1 and Sulf2, remove specific sulfate groups thereby regulating HS-dependent signaling. Sulf knockout mice show severe phenotypes. Expression data indicate that the Sulfs and the HS biosynthetic enzymes are cooperatively networked allowing dynamic control of the 'heparanome'. The underlying mechanism however, remains enigmatic, as encoding templates are unknown.

In addition, a total reprogramming of the system occurs continuously upon HS turnover in the lysosome. Here HS catabolism involves a battery of specific sulfatases, which we study at the level of biogenesis and sorting, protein structure, enzymatic features, substrate structural requirements and (patho-)physiological (dys-)function in the living (knockout) mouse. Genetic sulfatase deficiencies cause severe lysosomal storage disorders in human. So far for two of these deficiencies treatment by infusion of the corresponding sulfatase is possible (enzyme replacement therapy).



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1990	PhD in Biochemistry, Forschungszentrum Jülich/University of Düsseldorf
1991	Visiting Scientist, Università di Bari (Italy)
1992	Research Associate and Habilitation Fellow (DFG), University of Göttingen
2000	Habilitation in Biochemistry, University of Göttingen, Faculty of Medicine
2004	Professor of Biochemistry at Bielefeld University

Selected publications

- Dierks, T. *et al.*: 2003. *Multiple Sulfatase Deficiency is caused by mutations in the gene encoding the human Cα-formylglycine generating enzyme.* Cell 113: 435–444
- Dierks, T. *et al.*: 2005. *Molecular basis for multiple sulfatase deficiency and catalytic mechanism for formylglycine generation of the human formylglycine generating enzyme.* Cell 121: 541–552
- Frese, M. A., Schulz, S., Dierks, T.: 2008. *Arylsulfatase G – a novel lysosomal sulfatase.* J. Biol. Chem. 283: 11388–11395
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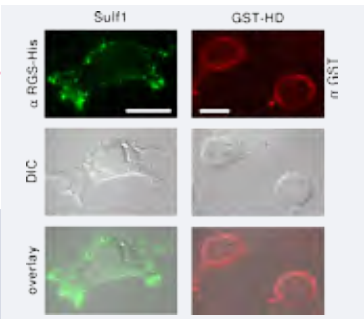
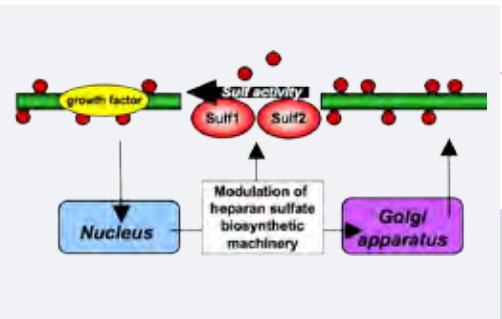
- Kalus, I. *et al.*: 2009. *Differential involvement of the extracellular 6-O-endosulfatases Sulf1 and Sulf2 in brain development and neuronal and behavioral plasticity.* J. Cell. Mol. Med. 13: 4505–4521

Future Projects and Aims

We aim at understanding the role of HS and its modulation by the Sulfs in various developmental processes. These projects involve the genetic manipulation, global characterization and analysis of Sulf-modulated pathways in the mouse and derived cells. Molecular interactions with HS are characterized by various methods. This should allow extension and theoretical modeling of HS-dependent and Sulf-modulated signaling networks. In addition, we generated knockout mice for sulfatases discovered only recently. Here our research aims at identifying their physiological substrates and the corresponding human patients using biomarkers detected in the mouse model. ■



The hydrophilic domain (HD) directs cell surface localization of endogenous Sulf1 (green) as well as exogenous glutathione-S-transferase/HD fusion protein (GST-HD, red) via interaction with heparan sulfate (HS).



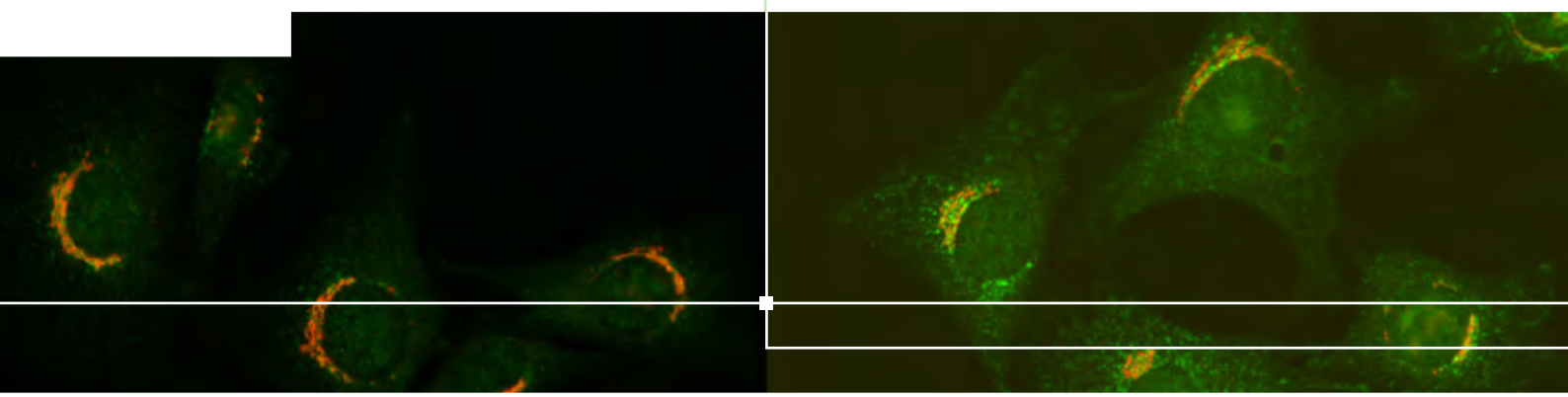
Simplified feedback model with potential interactions between HS desulfation through Sulf activity on the cell surface, cellular signal transduction and expression of HS biosynthetic genes.

Molecular mechanism of endosomal membrane traffic

Survival of eucaryotic cells depends on a highly organized and regulated transport between different membranes. Transport requires the formation and fusion of membrane vesicles. Our aim is a better understanding of transport processes between the cell surface and the interior of the cell.

Previous and Current Research

From yeast to man eukaryotic cells are characterized by specialized compartments, which are enclosed by membranes. Proteins and lipids have to travel between these compartments. For this purpose, membrane vesicles are formed from the donor compartment. It has to be ensured that all necessary components are included. Vesicle and target membrane fuse with each other after identification of the correct target. Several families of evolutionary conserved proteins are required for all of these steps. Endocytosis is the uptake of substances from the extracellular medium and parts of the plasma membrane. In mammalian cells this process is required to supply the cell with nutrients and to remove proteins from the cell surface, which is very important for the regulation of signal transduction. These endocytosed proteins reach endosomes and can be either recycled back to the plasma membrane or transported to lysosomes for degradation. Our main focus are SNARE proteins which are the central components of the membrane fusion machinery. Four different SNARE motifs from vesicle and target membrane form SNARE complexes, which pull both membranes together and fuse them. A specific membrane transport step involves a specific combination of SNAREs. Mammals express about forty different SNAREs while the unicellular baker's yeast *Saccharomyces cerevisiae* encodes 24 SNAREs. As model systems we use baker's yeast as well as mice deficient for certain SNAREs and cells derived from these mice. We found that three SNAREs of the late endosomal SNARE complex are sorted into budding vesicles by binding to an ENTH domain protein in both yeast and mammals. These ENTH proteins participate in the formation of vesicles by interaction with the coat protein clathrin. We generated mice deficient for the trans Golgi network and early endosomal SNARE vti1a or the late endosomal SNARE vti1b. These mice survive with minor defects indicating that vti1a and vti1b can replace each other. In the absence of both vti1a and vti1b mice die at birth with major defects in the nervous system. The



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1992	PhD in Biochemistry, Freie Universität Berlin
1994–1998	Postdoc, University of Oregon, Eugene, USA
1998–2004	Junior group leader, Georg-August Universität, Göttingen
since 2005	Professor for Biochemistry, Bielefeld University

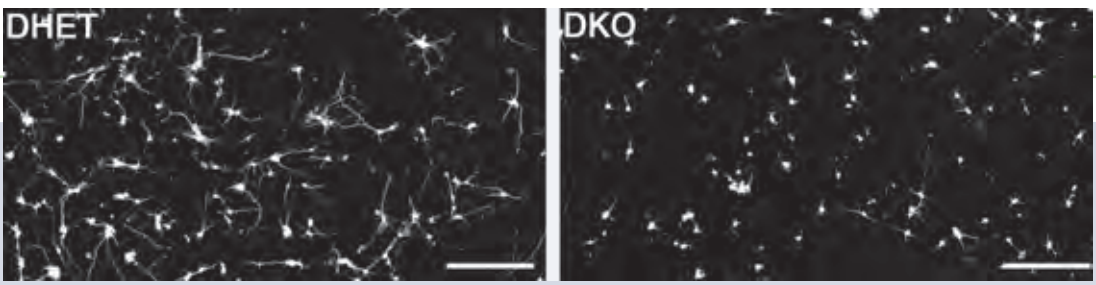
Selected publications

- Chidambaram, S., Zimmermann, J., Fischer von Mollard, G.: 2008. *ENTH domain proteins are cargo adaptors for multiple SNARE proteins at the TGN/endosome*. J. Cell Sci. 121, 329–338
- Dressel, R. *et al.*: 2010. *The exocytosis of lytic granules is impaired in Vti1b or Vamp8-deficient CTL leading to a reduced cytotoxic activity following antigen-specific activation*. J. Immunol. 185, 1005–1014
- Zimmermann, J., Chidambaram, S., Fischer von Mollard, G.: 2010. *Dissecting Ent3p: The ENTH domain binds different SNAREs via distinct amino acid residues while the C-terminus is sufficient for retrograde transport from endosomes*. Biochem. J. 431, 123–134
- Kunwar, A. J. *et al.*: 2011. *Lack of the endosomal SNAREs vti1a and vti1b led to significant impairments in neuronal development*. Proc. Natl. Acad. Sci. USA 108, 2575–2580
- Wang, J. *et al.*: 2011. *ENTH domains bind on opposite sides of two SNAREs*. Proc. Natl. Acad. Sci. USA 108, 12277–12282

number of neurons is reduced in several peripheral ganglia and major axon tracts are missing, reduced in size or misrouted.

Future Projects and Aims

Yeast cells were more sensitive to the loss of the endosomal SNARE Vti1p than mammalian cells to the absence of both evolutionary related proteins vti1a and vti1b. We want to understand the basis of this higher flexibility in mammalian cells and identify SNAREs which are responsible for this compensation. However, neurons were more sensitive to the loss of vti1a and vti1b. They contain a number of highly specialized membrane trafficking pathways, some with very high turnover rates. For example neurons form long axons using highly dynamic growth cones, which sense the environment. Neurons send signals by exocytosis of synaptic vesicles, which have to be recycled via endosomes. By studying defects in vti1a and vti1b deficient neurons we want to elucidate the role of specialized endosomal pathways in neurons. ■



Cultured hippocampal neurons without vti1a and vti1b (DKO) stained for ßIII tubulin compared to controls (DHET). bars: 250 µm

Biorefinery Concepts

High-value products from algae, residues converted to biogas

Using biotechnology to guide mankind into a green future leads to biorefinery concepts. In the framework of biotechnology such a biorefinery could be based on algae for providing valuable substances and the residue of the biomass may be converted to biogas.

Previous and Current Research

Considerable efforts are being undertaken in order to provide mankind on the basis of renewable raw materials. These strategies imply that one part of the biomass may be exploited to obtain substances for use in many fields of application – from high value pharmaceutically active ingredients to biofuels and biogas. However, in order to be able to use renewable raw materials economically for producing bulk materials which, today are mainly based on mineral oil, science and engineering has to develop the appropriate technology. One way out of this actual economic constraints would be to couple the production of high value products with that of commodities. This includes the development of closed processes with internal recycling of materials and energy.

Besides the recycling of microbial biomass, mainly biorefinery concepts based on algae biomass are pursued. Growing algae may have considerable advantages over cultivating plants in the future, when cheap cultivation systems for improved algae might become available. In the meantime, uses in the framework of biorefineries have to be envisaged. The primary goal is to use *Euglena gracilis*, a eukaryotic protist that grows photoautotrophically as well as heterotrophically as a source of high-value products. Due to this feature it represents an interesting microorganism since it can grow by collecting solar radiation for fixing carbon dioxide as well as by utilising residual C-sources from diverse industries. High-value products from *E. gracilis* are α-tocopherol (vitamin E) and paramylon, a β-1,3-glucan which is of interest for a variety of uses. A major challenge with *E. gracilis* as a producing organism is its unfavourable growth caracteristics especially under phototrophic conditions. Nevertheless, the biomass concentrations obtained for phototrophic growth compare well with those of other algae. In consequence, the main emphasis has been given so far to medium optimization combined with reactor development for photoautotrophic cultivation of fragile

Our objective in the development of biorefineries is guided by the challenge to optimise the utilisation of renewable raw materials.

1976	PhD at the Institute of Technical Chemistry at the Technical University Hannover, Germany
1977 – 1990	Assistant, lecturer, and scientific adjunct at the Institute of Chemical Engineering, Swiss Federal Institute of Technology Lausanne (EPFL), Switzerland
since 1990	Professor for Fermentation Engineering at the Faculty of Technology, Bielefeld University, Germany

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Selected publications

- Risse, J. M. *et al.*: 2001. *Recycling of biomass resulting from fermentation processes with* Bacillus licheniformis. Chem. Eng. Technol. 24 (Eng. Life Sci. 1): 141–145
- Blaesen, M. *et al.*: 2006. *Sustainable production: recycling of bacterial biomass resulting from a fermentation process with* Klebsiella planticola. Chem. Biochem. Eng. Q. 20(3): 263–268
- Blaesen, M. *et al.*: 2007. *Recycling of bacterial biomass in a process of L-threonine production by means of a recombinant strain of* Escherichia coli. J. Biotechnol. 132(4): 431–437
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- Santek, B. *et al.*: 2010. *Production of paramylon, a β-1,3-glucan, by heterotrophic cultivation of* Euglena gracilis *on potato liquor*. Eng. Life Sci. 10(2): 165–170

microorganisms. In parallel, reactors for biogas production have been developed and operated successfully for converting residual materials obtained after extraction of the biomass – in order to close the biorefinery scheme.

Future Projects and Aims

Since mass production of *Euglena gracilis* as well as a number of other algae has been achieved, the whole process of extraction of α-tocopherol, paramylon, and a number of additional products can be studied in detail. This also enables to assess the utilisation of residues of extracted biomass for the generation of biogas. In both topics – phototrophic cultivation and biogas generation – process and bioreactor development will be in the focus of studies. Detailed caracterisation of the processes are rendered possible by specialised analytical tools. In addition, the CeBiTec is going to have a dedicated biogas laboratory for general studies at its disposal. ■

Two-stage continuously operated biogas reactor

Mass production of algae in a photobioreactor with central illumination

Enzyme Catalysis in Organic Synthesis

Our interdisciplinary research activities at the interface between biology and organic chemistry focus on the application of enzymes as catalysts in synthetic reactions. A particular goal is the development of synthetic processes fulfilling the criteria of high efficiency, sustainability and scalability.

Previous and Current Research

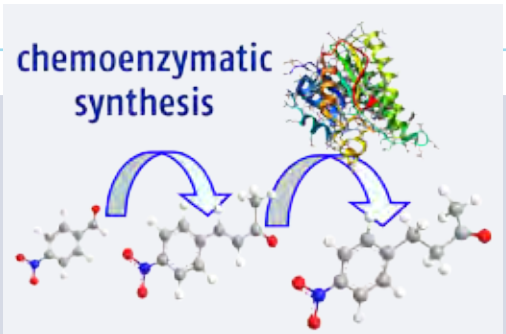
Applied enzyme catalysis (biocatalysis), also nowadays known as "white biotechnology" is considered to be one of the key technology areas of the 21th century. In spite of the potential and importance of enzymes as catalysts in organic chemistry, however, the number of efficient industrially applied processes is still limited in comparison to „classic" chemical or chemocatalytic syntheses. At first, this might surprise when considering the obvious advantages of biocatalysis such as high enantio-, diastereo-, regio-, and chemo-selectivity, the use of water as a reaction medium, and the potential to realize environmentally friendly processes. On the other hand, however, the use of enzymes in organic synthesis is still often limited, e.g., by the incompatibility of enzymes with organic solvents, narrow substrate range and the typical separation of biocatalytic reactions from „classic chemical" types of reactions. Overcoming these limitations represents a major challenge in biocatalysis in order to fully benefit from the tremendous catalytic potential of enzymes and to develop efficient, environmentally friendly *and* technically feasible organic synthetic reactions.
In the research area of bioprocess development Gröger and his teams (in industry until 2006, at the University of Erlangen-Nürnberg from 2006 to 2011 and at Bielefeld University since 2011) developed successfully many new biocatalytic processes. Within these interdisciplinary projects jointly with collaboration partners several processes running on industrial scale have been realized. A representative highlight is the developed asymmetric biocatalytic reduction and reductive amination technology based on the use of recombinant whole cell catalysts. Both types of processes run at high substrate loading of typically >100 g/L and give the desired products with >99% ee. Recently, jointly with collaboration partners new biocatalytic processes have been developed based on the use of enoate reductases (for C= C-reduction), P450-monooxygenases (for hydroxylation) and L-threonine aldolases (for aldol reactions). A further research highlight is the successful development of various chemoenzymatic one-pot multi-step processes in water by combining "classic" chemical reactions, metal-catalyzed reactions and organocatalytic reactions, respectively, with enzymatic transformations. The desired products are formed in an efficient fashion and with excellent enantioselectivity, underlining that such types of combinations of the two "worlds of catalysis", chemocatalysis and biocatalysis, are possible. Such combinations enable advantageous synthetic processes, thus avoiding solvent-intensive and waste-generating work-up steps. Furthermore, we could successfully apply biocatalysts in the enantioselective (multi-step) synthesis of pharmaceutically relevant molecules such as non-natural α-amino acids, β-amino acid derivatives and specific chiral alcohols.

Biocatalysis will play a key role in the future development of sustainable production processes for industrial chemicals and pharmaceuticals.

1994–1997	Doctoral thesis at the University of Oldenburg
1997–1998	Post-doc researcher at the University of Tokyo
1998–2001	Head of laboratory at the research department "Chemische Forschung" of SKW Trostberg AG
2001–2003	Project Manager at the Project House Biotechnology of Degussa AG
2004–2006	Senior Project Manager at the Service Center Biocatalysis of Degussa AG
2006–2011	Associate Professor of Organic Chemistry at the University of Erlangen-Nürnberg
since 2011	Full Professor of Organic Chemistry at Bielefeld University

Future Projects and Aims

Among major current challenges are the development of efficient biocatalytic oxidation and C-C bond forming processes as well as the development of novel chemoenzymatic one-pot processes in water by, e.g., combining three or more synthetic steps. In addition, a further focus is on novel retrosynthetic approaches towards pharmaceutically relevant molecules based on the use of enzymatic key steps. ■



Principle of a chemoenzymatic two-step one-pot process in aqueous media

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Selected publications

- Gröger, H., Chamouleau, F., Orologas, N., Rollmann, C. *et al.*: 2006. *Enantioselective Reduction of Ketones with "Designer Cells" at High Substrate Concentrations: Highly Efficient Access to Functionalized Optically Active Alcohols*. Angew. Chem., 118: 5806–5809; Angew. Chem. Int. Ed., 45: 5677–5681
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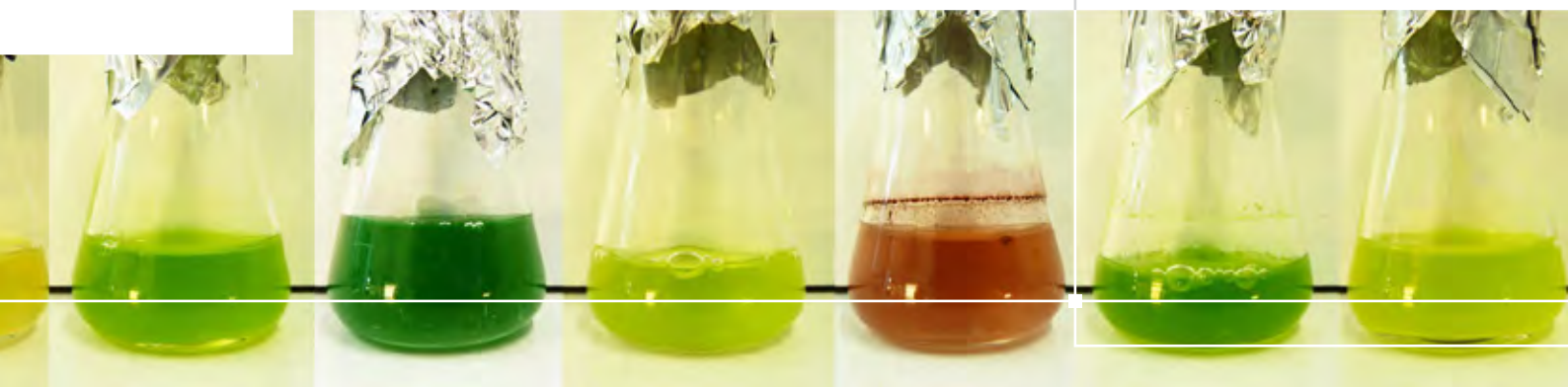
Microalgae for biotechnology and bioenergy applications

The molecular biology and biotechnology research programs with microalgae aim to explore the potential of these unicellular phototrophic organisms as green cell factories to efficiently convert sun light energy into biomass, bioenergy and high value products.

Previous and Current Research

Microalgae are plant-like phototrophic organisms, increasing ly emerging as natural catalysts for solar energy conversion into biomass and biofuels, for bio-degradation approaches and for the production of pharmaceutical products. In current molecular biology and biotechnology research, these unicellular organisms are playing a substantial role to elucidate the impact of photosynthetic CO_2 fixation and sun light energy transition and its complex cellular regulation as a fun damental basis for targeted process optimization.
Our research focus at the CeBiTec is on understanding elementary regulatory aspects of sun-to-biomass conversion via photosynthesis in microalgae and identifying, characterizing and optimizing potential bottlenecks such as light harvesting. In a parallel research stream we characterize and systematically improve direct and indirect solar energy conversion into gaseous and liquid biofuels using advanced molecular biology tools. This is of particular relevance, since the development of clean fuels is of vital importance to human and environmental health and global prosperity, more than almost any single issue facing mankind today. Bioenergy production is currently not competitive to fossil fuels without subsidization, because production costs are still too high and the technology still is in its infancy. Today bioenergy concepts with microalgae can only be commercially viable in multi-stage biorefineries in which microalgae are preliminary used as green single cell production factories before the residual algal biomass can be converted into ready-to-use fuels like biodiesel or biomethane. A number of potential products from microalgae have been identified so far, such as hydrogen, sulfated polysaccharides, lipids and fatty acids, pigments or other bioactive molecules. The integration of such products into biorefineries are continuously being tested in our group at the CeBiTec.



It is our goal to use phototrophic microalgae for the efficient conversion of sun light energy, CO_2 and nutrients into biomass, bioenergy and high value products.

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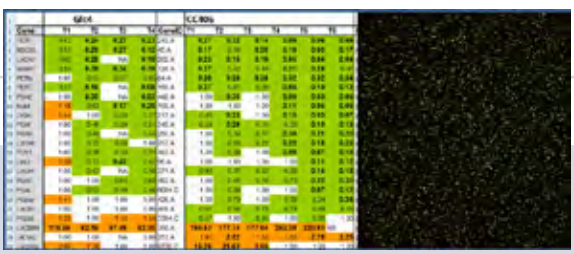
1994 – 1997	Postdoctoral position, Imperial College London, U.K.
1997 – 2005	Group Leader for Algae Molecular Biology, Bielefeld University
2006	Head of Life Sciences of the European Science Foundation (ESF), Strasbourg
2007	Australien Research Council Fellow, University of Queensland, Australia
2007 – 2009	Head of AlgaeBioTech Group, Bielefeld University
since 2009	Professor for Algae Biotechnology & Bioenergy, Bielefeld University

Selected publications

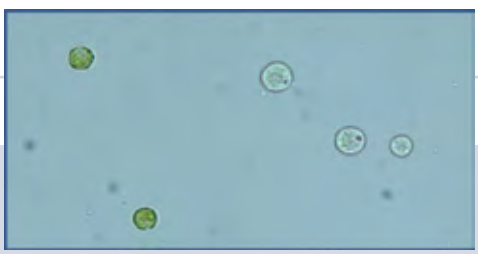
- Doebbe A., *et al.*: 2010. *The interplay of proton, electron and metabolite supply for photosynthetic H_2 production in* C. reinhardtii. J. Biol. Chem. 285 (39): 30247–30260
- Kruse, O. and Hankamer, B.: 2010. *Microalgal hydrogen production*. Curr. Opin. Biotechnol. 21: 238–243
- Mussgnug, J. H. *et al.*: 2010. *Microalgae as substrates for fermentative biogas production in a combined biorefinery concept*. J. Biotechnol. 150 (1): 51–56
- Stephens, E., *et al.*: 2010. *An Economic and Technical Evaluation of Microalgal Biofuels*. Nature Biotechnol. 28(2): 4–6
- Blifernez, O. *et al.*: 2011. *Protein arginine methylation modulates light-harvesting antenna translation in* Chlamydomonas reinhardtii. The Plant J. 65: 119–130

Future Projects and Aims

Our main research goal is to identify new algae strains with better production performance in systematic forward genetics screens and to directly construct high efficiency strains by genetic engineering in reverse genetic approaches using the unicellular microalga *Chlamydomonas reinhardtii*. The basis for these projects is the CeBiTec technology platform with its –omics technologies and bioinformatics support which we use for our Systems Biology strategies in order to elucidate the regulatory network of light harvesting, and to establish metabolic flow models of algal biofuel production pathways. ■



A new *C. reinhardtii* AGILENT© 4x44k micro-array based on 15.000 predicted gene models and its application on differential transcriptome analysis of a high H_2 producer (Glc4) and a wild type (CC406) to identify bottlenecks of H_2 production.



Light microscopic image of *C. reinhardtii* wild type cells (left; dark green) and of an engineered cell line with a reduced light harvesting antenna complex (right, light green).

Supramolecular Photochemistry

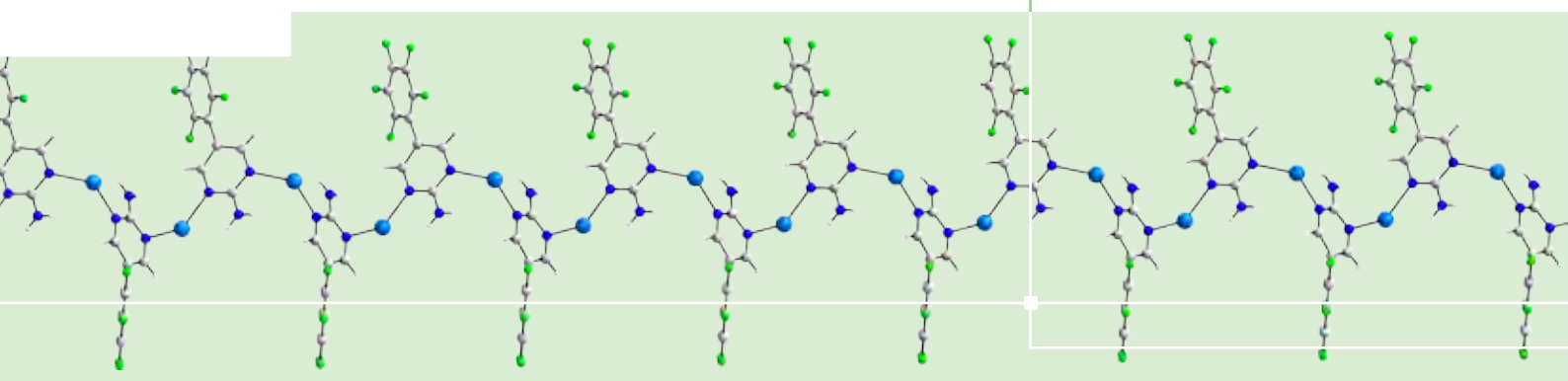
The "chemistry beyond the molecule" has opened the view to understand, design and use assemblies of molecules. We are especially interested in supramolecular photochemistry, which is at the crossroads of chemistry, physics and biology and at the interface between matter and light.

Previous and Current Research

Our research program covers aspects of small organic molecules, higher noncovalent aggregates at the nanoscale, and large entities at the mesoscopic scale. We are especially interested in evaluating the factors which determine the reactivity of molecules and which control their self association to higher aggregates such as molecular capsules, self assembled monolayers, and new materials for electronic applications.

Light belongs to the simplest "reagents" to control the reactivity of molecules and the affinity of receptors. In one of our projects we aim at the design of photoswitchable host-guest systems derived from calixarenes. Molecular capsules which may be used for transport of active substances e.g. through membranes will be studied to complement our activities focussed on the synthesis of photoswitchable ion channels. In addition, anthracene modified calixarenes immobilized on surfaces display rather robust binding properties and they might serve as model for various future applications using self-assembled monolayers. There, locally structured functional surfaces (e.g. arrays) can be prepared by UV writing and erasing procedures to recognize and bind molecules.

Fluorescence imaging has become an essential tool in biological and biomedical sciences for imaging of living cells and tissues. To overcome the spatial resolution of ca. 200 nm (Abbe's law) several attempts are currently investigated, e.g. in STED microscopy. In another approach we use optical switches for fluorescence imaging. For example, a dyad composed of a photochromic and a fluorescent dye unit is able to modulate the fluorescence emission. Fluorescence photoswitching of such molecules at the single-molecule level has opened possibilities to develop ultra-high-density optical memories and super-high-resolution fluorescence imaging. This concept was recently



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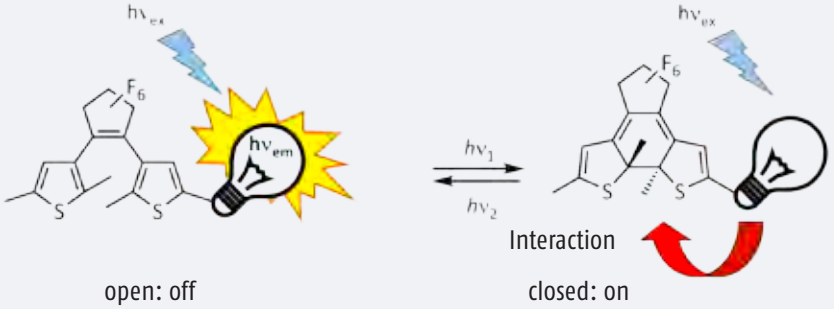
1978	PhD at RWTH Aachen
1979–1980	Postdoctoral research at Columbia University, New York, NY, USA
1984	Habilitation at RWTH Aachen
1985–1989	Professor RWTH Aachen
1989–1995	Professor Münster
1995–1998	Professor Kiel
since 1998	Professor at Bielefeld University

Selected publications

- Schäfer, C. *et al.*: 2007. *Single Molecular Affinity Switch*. J. Am. Chem. Soc., 129: 1488–1489
- Schröder, T. *et al.*: 2010. *Single-Molecule Force Spectroscopy of a supramolecular heterodimeric capsule*. Phys. Chem. Chem. Phys., 12: 10981–10987
- Stoll, I. *et al.*: 2010. *2-Aminopyrimidine-silver(I) based hybrid organic polymers. Self assembly and phase transitions of a novel class of electronic material*. Chem. Mater., 22: 4749–4755
- Seefeldt, B. *et al.*: 2011. *Kinetic studies on vis light switchable photochromic fluorophores based on diarylethenes*. Photochem. Photobiol. Sci., DOI:10.1039/C1PP05051F
- Siewertsen, R. *et al.*: 2011. *Tuning of switching properties and excited-state dynamics of fulgides by structural modications*. Phys. Chem. Chem. Phys., 13: 3800–3808

been successfully applied to the synthesis of new water-soluble photoswitchable fluorescent SiO_2-nanoparticles.

Organic semiconductors are important materials for various applications due to their low cost fabrication processes and the possibility to fine-tune desired functions by chemical modifcation of their building blocks. Recently, we synthesized a novel class of organic electronic material by self-assembly of 2-aminopyrimidines and silver(I)salts. The optical properties could be tuned by changing the silver counterion or by the reversible solvent extrusion and interchange. Furthermore, the electrical conductivity of the material was proven for a thin crystalline film. In future, we aim to investigate these materials in electronic devices to determine fundamental optoelectrical data of this type of compounds. ■



Photoswitchable fluorescence: the photoswitch allows FRET from the electronically excited fluorescence dye only in its closed form.

Cell Culture Technology

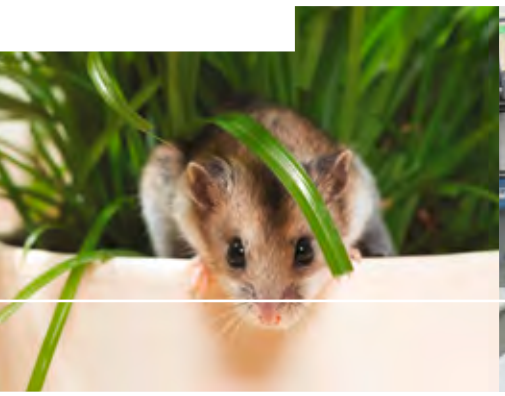
Functional genomics for rational bioprocess development with mammalian cell lines

Mammalian cell lines are the most important biological system for the production of therapeutic and diagnostic proteins with complex post-translational modifications. But their intrinsic cellular complexity confronts us with many challenges in the development of efficient bioprocesses.

Previous and Current Research

Despite all progress the development of fermentation processes with mammalian cells is to a large extend still based on empirical knowledge and historical experience. This is mainly due to missing qualitative and especially quantitative data and understanding of intracellular mechanisms under bioprocess conditions. Concomitantly there is an increasing economical and social interest in efficient processes for the production of biopharmaceuticals to ensure the supply of the public with modern, highly efficient and safe therapeutic and diagnostic proteins. In microbial research the combination of classical biotechnological methods with functional genomics and bioinformatics has led to substantial progress in the rational development of high performance production strains and optimized fermentation processes. Due to the much higher complexity of mammalian cells these technologies have not been applied in cell culture technology, although the potential of these methods has been shown in an increasing number of scientific publications.

In this context we are working on the development and optimization of functional genomics techniques and their application in bioprocess and cell line development. This includes the sequencing of CHO cDNA (jointly with the University of Natural Resources and Life Sciences, Vienna) and the development of a proprietary CHO microarray, as well as the generation of a CHO proteom 2D-master gel and data base for the differential analysis of process parameters on the cellular proteom. We have successfully used this approach to identify the reasons for the increase in cell-specific productivity in substrate limited perfusion culture. For intracellular metabolomics several methods have been developed for a rapid and gentle quenching of the cellular metabolism based on microstructure heat exchanger or on filtration. Rapid quenching is necessary to conserve the



Modern cell culture technology requires the integration of functional genomics and bioinformatics with cell biology, molecular biology and biochemical engineering.

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1999–2005	Group leader, Institute of Biotechnology, Research Center Jülich, Germany
2000	visiting scientist, Imperial Cancer Research Fund, London, UK
since 2005	Professor for Cell Culture Technology, Bielefeld University, Germany
since 2010	Scientific director, CeBiTec

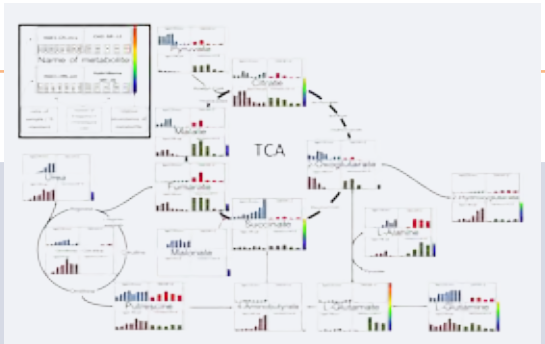
Selected publications

- Link, T., Backstrom, M., Graham, R., Essers, R. *et al.*: 2004. *Bioprocess development for a recombinant Mucin-1 fusion protein expressed by CHO cells in protein-free medium*. J. Biotechnol., 110: 51–62
- Bohnenkamp, H., Coleman, J., Burchell, J., Taylor-Papadimitriou, J. *et al.*: 2004. *Breast carcinoma cell lysate-pulsed dendritic cells cross-prime MUC1 specific cytotoxic T-cells identified by peptide-MHC-class-I tetramers.* Cellular Immunology, 231: 112
- Krämer, O., Klausing, S., Noll, T.: 2010. *Methods in mammalian cell line engineering: from random mutagenesis to sequence specific approaches.* Appl. Microbiol. Biotechnol. 88: 425–436
- Volmer, M., Northoff, S., Scholz, S., Thüte, T. *et al.*: 2011. *Fast Filtration for Metabolome Sampling of Suspended Animal Cells*, Biotechnology Letters. 33(3): 495–502

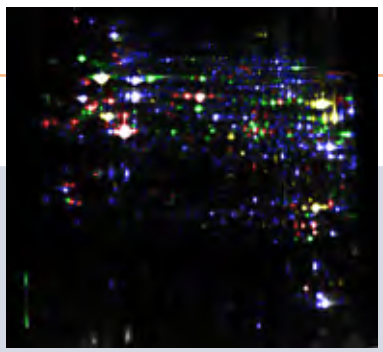
intracellular metabolic situation of cells in bioprocesses until analysis. This has been used to investigate the influence of process conditions on the central metabolism and on the glycosylation machinery of production cell lines.

Future Projects and Aims

Our previous and current research provided us with the necessary tools to get a deep insight into pharmaceutical production processes on a cellular and molecular level, making it possible to identify targets for rational process optimization and cellular engineering. Our main focus will be on posttranslational modifications to unravel the reasons for macro- and microheterogeneity in protein glycosylation which should pave the way for more efficient processes resulting in more homogeneous products. Further targets are on inhibiting apoptosis to enhance maximum cell density and prolong cultivation time and on the increase in cell specific productivity. First successful attempts have been undertaken using a stable siRNA approach by lentiviral transduction of production cell lines. ■



Intracellular metabolite concentration in a bioreactor cultivation of a production cell line



Differential 2D-gel comparing the cell proteom of two bioreactor conditions

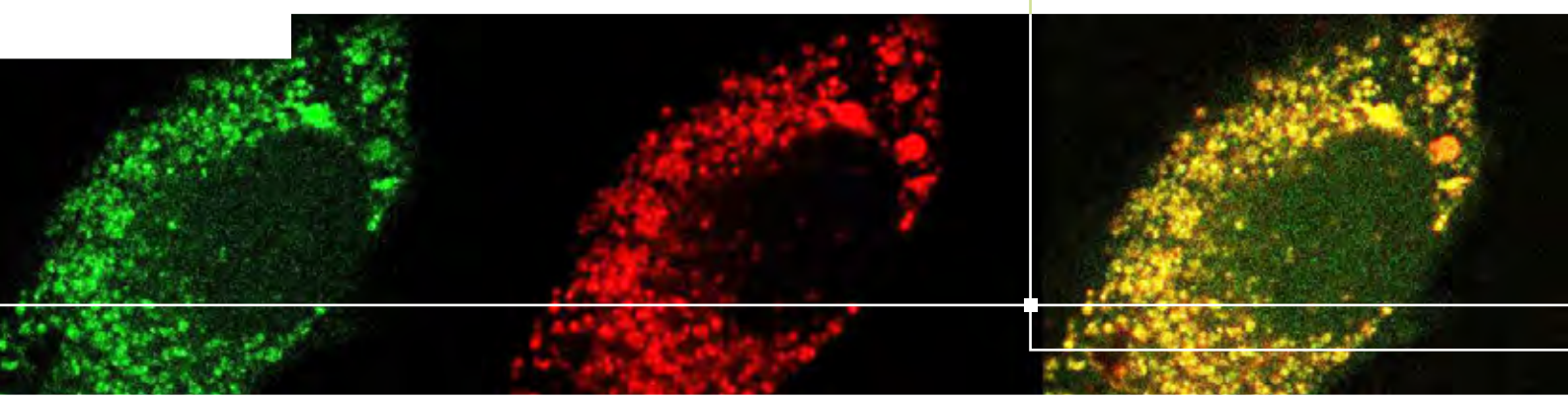
Molecular Tools for the Life Sciences

The vast amount of data originating from the different genome initiatives in the context of systems biology requires more and more emphasis to be placed on the elucidation of dynamic processes present in the living cell on the functional level. Synthetic tailor-made probes have been proven to facilitate this analysis.

Systematic analysis of the proteins expressed by a cell at a certain time and under certain condition with designed molecules (Functional Proteomics) is of eminent importance. Moreover, Chemical Genomics is a powerful strategy to evaluate the influence of synthetic small molecules (e.g. drug candidates) on biological systems.

Previous and Current Research

Either an enrichment step or selective tagging with reporter groups (e.g. fluorescent labels, radioactive tags, or biotin) can be utilized for the generation of proteome subsets. As separation of protein mixtures by 2D-PAGE usually involves denaturing conditions, only such protein families could until now be tagged where irreversibly binding ligands (suicide inhibitors) were known. Irreversibly binding ligands are not available for the vast majority of proteins. We developed novel engineered chemical probes for the creation of proteome subsets of such protein families, comprising a (semi-)specific, reversibly binding protein ligand (inhibitor) linked to a reporter group and a reactive group (photoaffinity label). Small-molecule kinase inhibitors, metalloprotease inhibitors, sulfatase inhibitors, and integrin ligands, respectively, have been chemically modified to allow for family-wise



Prof. Dr. Norbert Sewald

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1991	PhD, TU München, Germany
1991 – 1992	Postdoctoral Fellow with Prof. Sir J.E. Baldwin, Dyson Perrins Laboratory, Oxford University, UK
1998	Habilitation, Universität Leipzig, Germany
since 1999	Full Professor of Organic and Bioorganic Chemistry (Chemical Biology) Bielefeld University, Germany

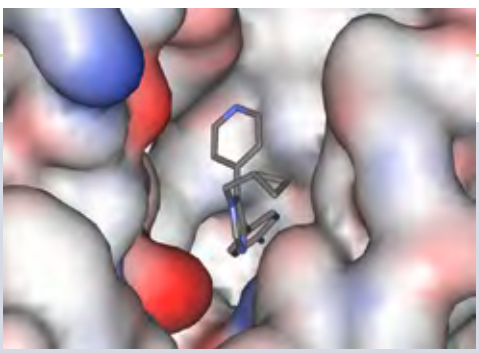
Selected publications

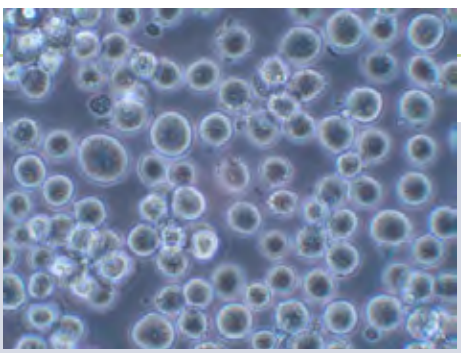
- Hagenstein, M.C. *et al.*: 2003. *Affinity-based tagging of protein families with reversible inhibitors: A concept for functional proteomics*. Angew. Chem. Int. Ed. 42: 5635–5638
- Hagenstein, M.C., Sewald, N.: 2006. *Chemical tools for activity-based proteomics*. J. Biotechnol. 124: 56–73
- Collet, M. *et al.*: 2007. *Molecular tools for metalloprotease subproteome generation*. J. Biotechnol., 129: 316–328
- Lenger, J. *et al.*: 2011. *Evaluation of sulfatase-directed quinone methide traps for proteomics*. Bioorg. Med. Chem., 2011, doi: 10.1016/j.bmc.2011.04.044
- Lenger, J. *et al.*: 2011. *Labeling and enrichment of* Arabidopsis thaliana *matrix metalloproteases using an active-site directed, marimastat-based photoreactive probe*. Bioorg. Med. Chem., 2011, doi: 10.1016/j.bmc.2011.06.068

- protein enrichment using magnetic beads or affinity chromatography
- covalent tagging with a fluorophor or biotin using photoaffinity labelling.

Future Projects and Aims

The current projects aim at the development of novel molecular tools tailored to the elucidation of biochemical relationships. In the focus of the investigations are protein-protein and protein-drug interactions. The novel tools will not only be suitable for the detection of binding partners and protein classes in eukaryotic systems, but also in the evaluation of interactions in prokaryotes, including complex microbial systems. ■



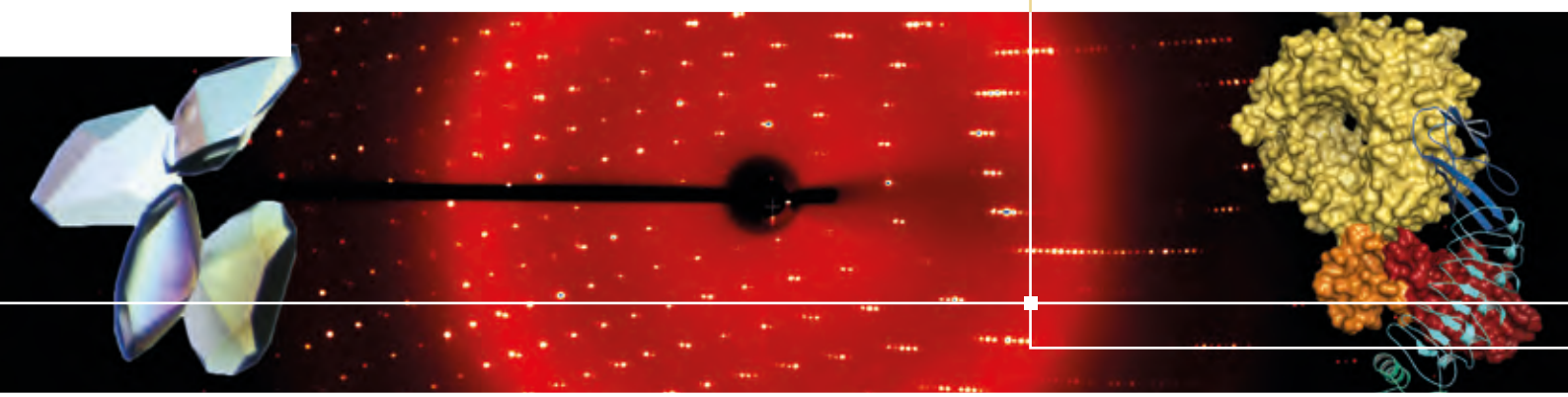


Structural Biochemistry

X-ray crystallography is the method of choice to determine the three dimensional structure of biological macromolecules and their complexes. We investigate structural aspects of how bacterial virulence factors influence host cell signaling during an infection.

Previous and Current Research

The receptor tyrosine kinase Met transduces the signals of hepatocyte growth factor and regulates cell growth and cell motility during embryonic development. In the adult, Met activation contributes to wound-healing and tissue regeneration. Inappropriate activation of Met promotes cancer metastasis. Therefore, the development of protein-based therapeutics that target Met is an attractive goal. Met antagonists could be used in treatment of cancer, while Met agonists could be useful to prevent or remedy tissue damage.
In order to rationally develop such protein therapeutics, it is desirable to understand the molecular mechanism of ligand induced Met activation. Three dimensional structures obtained by X-ray crystallography invaluably contribute to such an understanding. However, the physiological Met ligand is an unusually complex multi-domain growth factor and complexes of hepatocyte growth factor and Met have so far mostly proven recalcitrant to crystallization and structure determination.
In recent years we have therefore studied the mechanism by which a simpler molecule, the bacterial protein InlB, activates Met. Met is targeted by the pathogen *Listeria monocytogenes* during an infection. Like many other pathogens *L. monocytogenes* subverts host cell function by using dedicated virulence factors that specifically interact with eukaryotic target molecules. The *Listeria* invasion protein InlB binds to and activates Met, thereby facilitating uptake of the facultative intracellular bacteria into host cells. Using X-ray crystallography in combination with biochemical and cell biological methods, we could develop a mechanistic model of ligand mediated Met dimeriza-



Understanding the way in which pathogens influence their eukaryotic host often teaches us exciting lessons in basic cell biology.

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2002	PhD, Max-Planck-Institute for Medical Research, Heidelberg
2002–2007	Postdoctoral position, Helmholtz Centre for Infection Research, Braunschweig
since 2007	Juniorprofessor, Bielefeld University

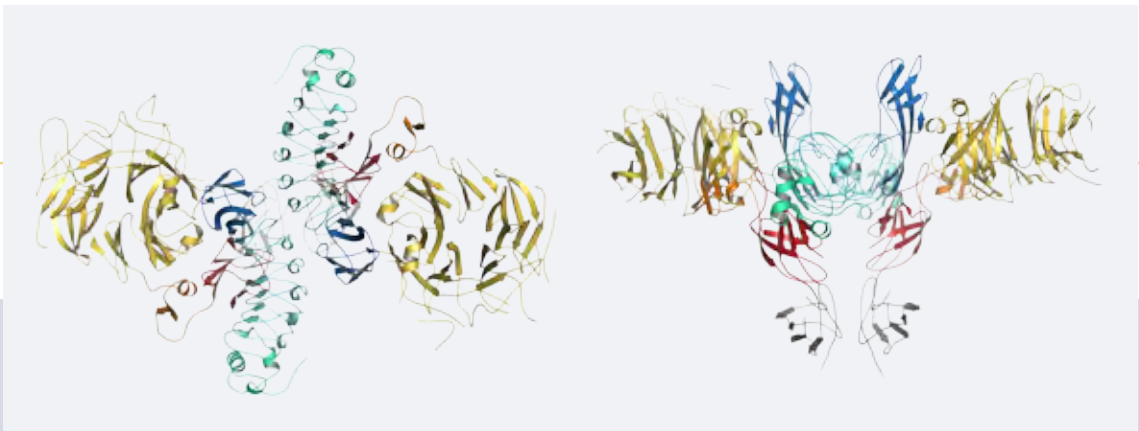
Selected publications

- Niemann, H. H. *et al.*: 2007. *Structure of the human receptor tyrosine kinase Met in complex with the Listeria invasion protein InlB*. Cell, 130: 235–246
- Ferraris, D. M. *et al.*: 2010. *Ligand-Mediated Dimerization of the Met Receptor Tyrosine Kinase by the Bacterial Invasion Protein InlB*. J. Mol. Biol., 395: 522–532
- Ebbes, M. *et al.*: 2011. *Fold and function of the InlB B-repeat*. J. Biol. Chem., 286: 15496-15506

tion that provides a structural explanation for receptor activation upon binding of InlB.

Future Projects and Aims

Several co-receptors modulate the activation of the Met receptor by its physiological ligand hepatocyte growth factor and by the bacterial protein InlB. In the future, we want to study the structural basis of co-receptor binding by the ligands, the role of co-receptors in signal transduction across the membrane, and the associated intracellular signaling networks that determine the cellular response. We will also continue our efforts to translate basic science into potential applications. Based on InlB as a scaffold, we will try to engineer potent Met activators and inhibitors that may become useful e.g. for tissue engineering. ■



Crystal structure the dimeric InlB/Met complex. InlB is shown in blue and green, Met is shown in yellow, orange, red and gray. Dimerization is mediated by a contact on the convex side of the ligand InlB. Left: top view. Right: side view.

Protease diagnostics

Proteases regulate important physiological processes. To learn more about the individual role and redundancy of these enzymes in a complex physiological context, probes based on tailored synthetic inhibitors that selectively bind their target protease are versatile tools for this task.

Previous and Current Research

Based on the data of the human genome project, today it is known that the human body is equipped with approximately 600 proteases that contribute to the regulation of important physiological processes. Our knowledge, however, of many key proteases is still limited.
In this context, our research is focused on the development of novel diagnostic tools for proteolytic activity based on synthetic protease inhibitors as recognition devices. For the different application areas including fluorescence microscopic imaging, affinity blotting, and flow cytometry, these inhibitors are functionalized with the appropriate reporter groups. We apply for the design of these inhibitors peptidic and peptidomimetic concepts coupled with structure-based approaches. Additionally, natural products with protease-inhibiting properties play as lead structures also an important role.
We have selected as targets for our studies amongst the papain-like cysteine proteases the human cysteine cathepsins and amongst the trypsin-like serine proteases the mast cell-specific human tryptases. To develop affinity probes for cysteine cathepsins, the thiol-reactive group (2S,3S)-oxirane-2,3-dicarboxylic acid represents a privileged platform. By functionalizing both carboxylic acid groups with peptide sequences it is possible to address simultaneously S and S′ sites along the entire active-site cleft. Following this strategy we have designed and synthesized a probe for the dipeptidyl carboxypeptidase activity of cathepsin B that allowed for identification of novel physiological functions of this enzyme (cooperation partners: Dr. P. Henkart, NIH Bethesda, USA, and Prof. K. Brix, Jacobs University, Bremen, Germany). Furthermore, based on the unique tetrameric architecture of β-tryptase, we have designed a dibasic inhibitor that addresses simultaneously two S1 binding pockets of neighboring subunits of the tetramer. We utilized an immobilized version of our bivalent inhibitor to develop an affinity chromatographic procedure that allowed for the discovery of so far unknown hetero-tetrameric tryptases (cooperation partner: Prof. C. P. Sommerhoff, Department of Clinical Chemistry and Clinical Biochemistry, Clinic of the LMU, Munich, Germany).

Future Projects and Aims

Given the fact that selectivity for an individual cysteine cathepsin cannot always be achieved solely with interactions along

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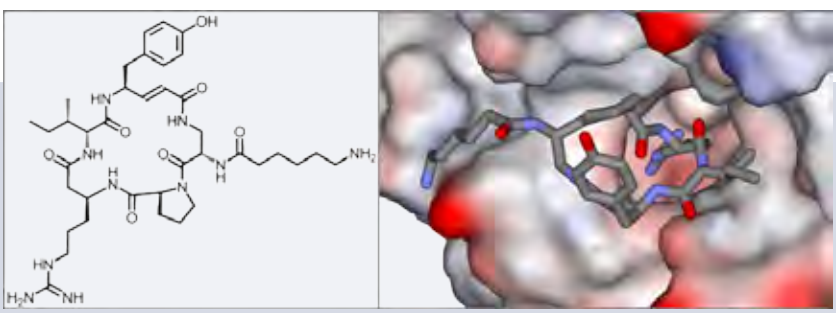
1998	PhD in Organic Chemistry, TU Munich, Germany
1998–2005	Postdoctoral Fellow and Research Associate at the MPI of Biochemistry, Martinsried, Germany
2006	Habilitation in Organic Chemistry at Bielefeld University, Germany
since 2006	Group leader and 'Privatdozent' at Bielefeld University, Germany
since 2007	Heisenberg Fellow at Bielefeld University, Germany

Selected publications

- Schaschke, N. *et al.*: 2000. *Epoxysuccinyl peptide-derived affinity labels for cathepsin B*. FEBS Lett. 482: 91–96
- Balaji, K. N. *et al.*: 2002. *Surface cathepsin B protects cytotoxic lymphocytes from self-destruction after degranulation*. J. Exp. Med. 196: 493–503
- Schaschke, N. *et al.*: 2005. *Affinity chromatography of tryptases: design, synthesis and characterization of a novel matrix-bound bivalent Inhibitor*. ChemBioChem. 6: 95–103
- Schaschke, N. *et al.*: 2008. *Inhibition of cathepsin L by epoxysuccinly peptides addressing simultaneously active-site and remote-site regions*. ChemBioChem. 9: 1721–1724
- Schaschke, N. and Sommerhoff, C. P.: 2010. *Upgrading a natural product: inhibition of human β-tryptase by cyclotheonamide analogues*. ChemMedChem. 5: 367–370

the active-site cleft, we are currently extending our platform approach. Thus, with attached peptide sequences we want to address in addition to interactions within the active-site cleft also defined areas on the surface of the protease (remote-sites). Using cathepsin L and its zymogene as a first model system, we could demonstrate that information provided by the prodomain can be exploited as guide to identify such remote-sites. Furthermore, to develop novel strategies for β-tryptase diagnostics, we are also interested in canonically binding inhibitors for the probe design. In this context, we want to take advantage from the feature that β-tryptase has an extended substrate specificity. Using the natural product cyclotheonamide E4 as lead structure, we could show that it is possible to exploit this preference of β-tryptase for basic residues in P3 position for the design of potent and selective β-tryptase inhibitors. ■



Cyclotheonamide E4-based β-tryptase inhibitor. Chemical structure and proposed binding mode.

Dynamics and Function of Sensory Light Receptors

Sensory blue light receptors regulate central processes in plants and animals. Our research focuses on the primary mechanisms of signal generation in these sensors. The sequence of photochemical events and secondary structural changes in the proteins are studied by infrared spectroscopy.

Previous and Current Research

Blue light is one of the major environmental factors governing the growth of plants and the 24 h rhythm of many organisms. Even the magnetic orientation of animals is connected to blue light activation. Although these effects have been studied for more than a century, only now the underlying molecular processes are being revealed. Light perception is achieved by means of sensory photoreceptors, which are proteins incorporating a chromophore as light-sensitive molecule. Most blue-light receptors use derivatives of riboflavin (vitamin B2) as chromophore. The main representatives of flavin-containing receptors are phototropins and cryptochromes.
We are interested in the molecular mechanisms of signal transfer from the chromophore to the surface of the blue light receptor proteins. Information about the light conditions in the environment of the organism somehow needs to be converted from a localized electronic excitation to a movement of structural elements of the protein and to a change in interactions with signaling partners. The reaction principles of blue-light receptors differ from those of all other known photosensory receptors such as the rhodopsin in our eyes.
To track the structural changes taking place in the biomolecules, we are mainly applying a combination of UV/Vis spectroscopy and Fourier transform infrared spectroscopy. This combination allows us to gain a comprehensive overview of chemical processes of the light-absorbing molecule as well as responses by the protein shell. The temporal evolution of the light-driven reactions is followed by highly time-resolved techniques, resolving processes from nanoseconds to minutes.
Many of the investigated receptors have been expressed in our laboratory. We have, for instance, succeeded in establishing an expression of a plant cryptochrome in *E. coli*. This development enabled us to shed light on the primary light-induced processes in the sensory domain of plant cryptochromes. Similar studies were performed on an animal cryptochrome from *Drosophila* and on an algal phototropin in its full length, obtained from collaboration partners.
Further research interests of our group include the photochemistry of small molecules, which are involved in intramolecular electron transfer processes or are used as dyes for super-resolution microscopy of cells and organelles.

Future Projects and Aims

We will continue with our investigations of the mechanisms of photoreceptors focusing mainly on the cryptochromes, which are found in all organism kingdoms. Cryptochromes are still at

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2004 Helmholtz Young Investigator, Structural Biology, Research Center Jülich

2006 Helmholtz Young Investigator, Bielefeld University and Research Center Jülich

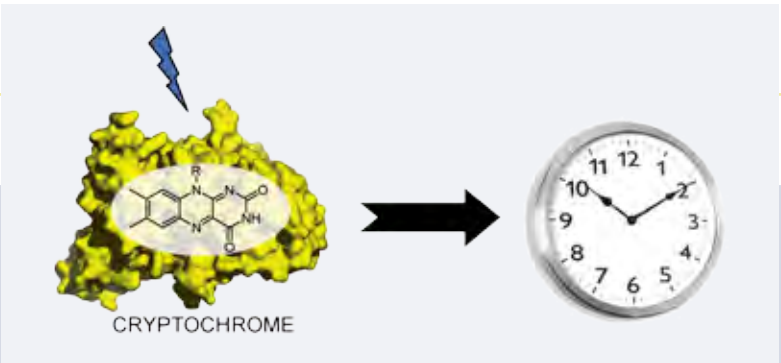
2007 Junior Group Leader, Biophysical Chemistry, Bielefeld University

Selected publications

- Immeln, D. *et al.*: 2007. *Blue light induces radical formation and autophosphorylation in the light-sensitive domain of* Chlamydomonas cryptochrome. J. Biol. Chem. 282: 21720–21728
- Langenbacher, T. *et al.*: 2009. *Microsecond light-induced proton transfer to flavin in the blue light sensor plant cryptochrome*. J. Am. Chem. Soc. 131: 14274–14280
- Pfeifer, A. *et al.*: 2009. *Time-resolved Fourier transform infrared study on photoadduct formation and secondary structural changes within the phototropin LOV domain*. Biophys. J. 96: 1462–1470
- Kottke, T. *et al.*: 2010. *Identification of the product of photoswitching of an oxazine fluorophore using Fourier transform infrared difference spectroscopy*. J. Phys. Chem. Lett. 1: 3156–3159
- Pfeifer, A. *et al.*: 2010. *Blue light induces global and localized conformational changes in the kinase domain of full-length phototropin*. Biochemistry 49: 1024–1032

the beginning of being characterized by biophysical techniques due to manifold problems associated with protein preparation. At the same time, several technical challenges have to be met when dealing with such demanding systems for infrared spectroscopy.

The long-term aim is a thorough understanding of the primary steps of regulation of central biological processes by blue light such as the biological clock or the orientation in the magnetic field. It is expected that the insight into the mechanisms of blue light receptors gives further impulses to the development of sensors or photo-switchable devices. First promising applications as fluorescence markers for cell imaging and as a tool to control cell motility by light have been demonstrated. ■



Cryptochrome regulates plant growth, sets the biological clock in plants and insects, and acts as a magnetosensor.

Bielefeld University Bioinformatics Services

The Bielefeld University Bioinformatics Service (BiBiServ) provides a collection of bioinformatical tools, support services, and eLearning courses for public access over the internet.

Services

The BiBiServ group supports internet based collaborative research in bioinformatics. BiBiServ follows the software as a service (SaaS) model by making tools developed by the different CeBiTec bioinformatic groups available to the community. Currently, more than 50 software tools and various educational media are available online. These include tools from different research areas such as RNA structure prediction and comparison, comparative genomics, phylogeny and primer design.

Usability

All tools published on BiBiServ follow the same design rules to allow non-bioinformatic users easy access. The BiBiServ team supports authors to integrate their tools into the server environment, comply with the usability rules, and design all 'up-to-date' interfaces (i.e. interactive browser based webservices, webservice interfaces, BioMoby services).

Persistence

A problem which is faced by many in the field of bioinformatics is the lack of persistence and usability of bioinformatic resources. The BiBiServ environment imposes certain well-defined technical requirements on all tools to be offered online. The curator team supports developers to meet these requirements. In return, tool developers are rewarded with service persistence: online services for any tool on the BiBiServ will be continued until a better tool for the same purpose becomes available, or its purpose becomes obsolete. At this point the tool will switch to an archived state, but all resources will remain available for download as long as the BiBiServ exists.

Semantic Technologies

One of the major problems in bioinformatics today is the huge and fast growing amount of experimental data that is being produced by techniques such as high-throughput sequencing. Another often underestimated problem for users of web-based/distributed bioinformatical tools is the multitude of formats for the same type of data and missing knowledge about which tool accepts which kind of format for the given data type. The integration of Semantic Web Technologies into BiBiServ (e.g datatype and tool class semantics) will enable the system to infer equivalencies between input/output data types and tools addressing similar or identical problems. This allows for automatic inclusion of previously unavailable input and output formats and the automated suggestion of alternative tools to try for users of BiBiServ. Semantically annotating the tools, data, persons, publications and educational content presented by BiBiServ will make these entities easier to find and better

Service in usability, persistence and semantics of online tools and education in bioinformatics research.

Dr. Alexander Sczyrba

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1998	Diploma, Computer Science in the Natural Sciences, Bielefeld University, Germany
1999–2000	Guest Investigator, The Rockefeller University, New York
2000–2002	Member of Research Practical Computer Science Group
2002–2008	Head of Bielefeld University Bioinformatics Services, Bielefeld University, Germany
2007	PhD, Bielefeld University, Germany
2008–2011	Postdoctoral Fellow, DOE Joint Genome Institute, U.S.A
since 2011	Head of the Bielefeld University Bioinformatics Services and Computational Metagenomics groups, Bielefeld University, Germany

Selected publications

- Seibel, P. N., Schwarzer, K., Krüger, J., Hartmeier, S. *et al.*: 2006. *XML schemas for common bioinformatic data types and their application in workflow systems.* BMC Bioinformatics, 7, Pages: 490
- Hartmeier, S., Krüger, J., Giegerich, R.: 2007. *Webservices and Workflows on the Bielefeld Bioinformatics Server: Practices and Problems.* NETTAB 2007 Proceedings
- Lamprecht, A.-L., Margaria, T., Steffen, B., Sczyrba, A. *et al.*: 2008. *GeneFisher-P: variations of GeneFisher as processes in Bio-jETI.* BMC Bioinformatics, 9 Suppl 4, Pages: S13
- Sczyrba, A., Konermann, S., Giegerich, R.: 2008. *Two interactive Bioinformatics courses at the Bielefeld University Bioinformatics Server.* Briefings in Bioinformatics, Pages:doi: 10.1093/bib/bbm063

integrated within and outside the BiBiServ environment. Ultimately, adding semantical annotations will enable users to perform their scientific work with more confidence about the meanings of their result data.

Distance Education

BiBiServ Media & Distance Education supports teaching in bioinformatics with internet-based courses. The most recent ones are 'The ADP Pages' (interactive pages that allow to study an experiment with classical dynamic programming algorithm), 'Sequence Analysis with Distributed Resources' (a web-based course on sequence analysis using distributed web resources) and 'About Dynamic Programming' (an introduction into the technique of dynamic programming with interactive application examples). ■

BIBIServ: International Top 20, tool usage 2010

country	usage	country	usage
USA	30350	Korea	2865
Germany	11716	Thailand	1835
China	8968	Singapore	1723
France	7745	Australia	1652
Un. Kingdom	4766	Denmark	1409
Japan	4700	Mexico	1387
Canada	3505	Colombia	1162
Spain	3049	Sweden	1126
Taiwan	2956	Israel	1121
Italy	2832	Netherlands	1119

Bioinformatics Resource Facility

The Bioinformatics Resource Facility (BRF) operates a complex and highly specialized hardware and software infrastructure which forms the basis for the academic and scientific activities within CeBiTec.

History

The BRF's origin dates back to 1998 when its predecessor unit was started with two staff members operating a single file and backup system providing service for a dozen workstations and a handful of laboratory computers. During the last decade the hardware infrastructure has been continously expanded so that a growing staff is able to develop and maintain a bioinformatics platform that receives widespread national and international attention.

Profile

One of the BRF's key tasks is the structured acquisition and storage of experimental data and – to the greatest possible extent – the automated processing of that data. It is achieved with the aid of a compute cluster that accesses the required data via high-performance network links on storage and database systems.

Computing Infrastructure

In addition to a flexibly deployable general-purpose compute cluster, the BRF operates several special-purpose computer systems in order to be able to cope with the ever increasing requirements for complex bioinformatics analysis. Among these compute nodes are systems capable of running hardware-accelerated BLAST searches and several GPU systems that are used to perform short-sequence mapping operations.

Global Access

All services provided by the BRF are accessible from almost everywhere in the world by either web interfaces or directly via the Bioinformatics Desktop that is available on thin client terminals. Deploying this technology is possible wherever an Internet connection is available and represents a convenient and cost-effective tool for national and international collaboration that often involves the processing of huge data sets. ■

Dr. Alexander Goesmann

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2004 PhD Bielefeld University, Germany

2006 Head of Bioinformatics Resource Facility (BRF) , Bielefeld University

2009 Group leader, Computational Genomics, Bielefeld University

Selected publications

- Meyer, F., Goesmann, A. *et al.*: 2003. *GenDB – an open source genome annotation system for prokaryote genomes.* Nucleic Acids Research 31(8): 2187 - 2195
- Neuweger, H. *et al.*: 2008. *MeltDB: A software platform for the analysis and integration of metabolomics experiment data.* Bioinformatics 24(23): 2726–32
- Albaum, S. P. *et al.*: 2009. *QuPE – a rich internet application to take a step forward in the analysis of mass spectrometry-based quantitative proteomics experiments.* Bioinformatics 25(23): 3128–34
- Bekel, T. *et al.*: 2009. *The Sequence Analysis and Management System – SAMS-2.0: Data management and sequence analysis adapted to changing requirements from traditional Sanger sequencing to ultrafast sequencing technologies.* J. Biotechnol. 140(1–2): 3–12
- Dondrup, M. *et al.*: 2009. *EMMA 2–A MAGE – compliant system for the collaborative analysis and integration of microarray data.* BMC Bioinformatics (10:50)

Hardware infrastructure & services at a glance

300 general purpose compute nodes (3750 CPU cores)

8 special purpose compute nodes:
- 4 nodes with 12 TimeLogic DeCypher SeqCruncher Cards
- 1 Convey HC-1ex FPGA System
- 3 nodes with 6 NVIDIA Tesla M2070 GPU Cards

approx. 430 TB disk storage, 1290 TB tape storage

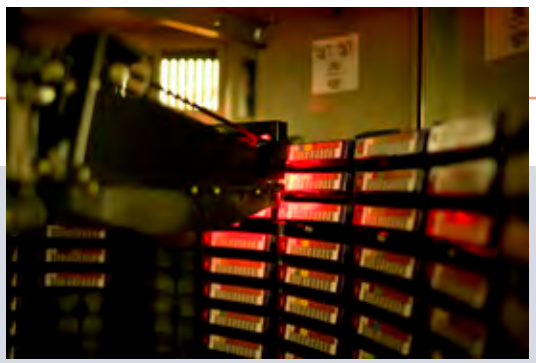
>300 Sun Ray terminals providing the Bioinformatics Desktop

HA database system (4 TB capacity)

support for 17 local research groups with >500 users

providing application access for >1500 external accounts

Training session in the BRF seminar room



Tape library performing an inventory of its tape cartridges

Technology Platform Genomics

Supporting Genome and Post-Genome Research by High-Throughput Technologies

The information flow in a living cell proceeds from DNA (genes) to mRNA (transcripts) to proteins to metabolites. With recent techniques we are able to determine the entirety of these molecules in living systems, called genome, transcriptome, proteome, and metabolome, respectively.

Technologies and Research

The Technology Platform Genomics (TPG) comprises four sections: genomics, transcriptomics, proteomics, and metabolomics, the most important technologies in genome and post-genome research.

Genomics at the TPG mainly comprises genome sequencing. Two of the most recent high-throughput sequencing systems, the Roche Genome Sequencer flx and the Illumina Genome Analyzer GA IIx, are currently installed and running. These sequencing machines have been used to sequence the entire genomes of bacteria and yeasts and are currently applied to even larger genomes as that of plants or the Chinese Hamster and to complex DNA samples like meta-genomes.

Transcriptomics at the TPG cover all techniques used to analyze transcripts, with a focus on mRNA. This includes determination of gene expression by microarrays as well as gene-specific, quantitative approaches by real-time reverse-transcriptase (RT)-PCR. Currently, transcriptomics also applies sequencing of cDNA generated from reverse-transcribed transcriptomes. Although computationally highly demanding, this method provides unprecedented sensitivity and resolution. The transcriptomics techniques are mostly applied to bacteria, many of them of industrial relevance.

Proteomics at the TPG involve gel-based and non-gel-based separation of proteomes as well as identification and quantification of proteins by tryptic fingerprints and MALDI-TOF mass spectrometry (Bruker ultrafleXtreme) or analysis of protein modification by MALDI-TOF MS/MS or by LC-ESI mass spectrometry. Generally, a first step in proteomics is to fractionate the

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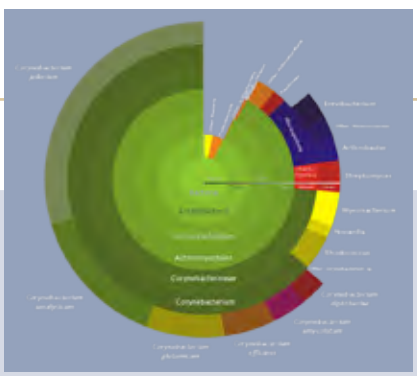
1990	PhD in Genetics, Bielefeld University, Germany
since 2000	Head of Technology Platform Genomics, CeBiTec, Bielefeld University, Germany
since 2004	Member of the Executive Board, CeBiTec, Bielefeld University, Germany

Selected publications

- Wendisch, V. F., Bott, M., Kalinowski, J., Oldiges, M. *et al.*: 2006. *Emerging* Corynebacterium glutamicum *systems biology.* J. Biotechnol. 124(1): 74–92
- Schneiker, S., *et al.:* 2007. *Complete genome sequence of the myxobacterium* Sorangium cellulosum. Nature Biotechnol. 25(11): 1281–1289
- Chao, T. C., Kalinowski, J., Nyalwidhe, J., Hansmeier, N.: 2010. *Comprehensive proteome profiling of the Fe(III)-reducing myxobacterium* Anaeromyxobacter dehalogenans *2CP-C during growth with fumarate and ferric citrate.* Proteomics 10(8): 1673–1684
- Persicke, M., Plassmeier, J., Neuweger, H., Rückert, C. *et al.*: 2010. *Size exclusion chromatography – An improved method to harvest* Corynebacterium glutamicum *cells for the analysis of cytosolic metabolites.* J. Biotechnol. 154(2–3): 171–178

cellular proteomes. In the bacteria analysed, the extracellular proteome can be separated from the outer or the inner membrane proteome, and the cytosolic proteome fraction. In higher organisms as in Chinese Hamster Ovary cells, more subcellular compartments are present and even more proteomic fractions can be generated.

Metabolomics at the TPG embrace metabolic profiling and flux analysis by gas-chromatography (GC) or liquid-chromatography (LC) coupled to mass spectrometry (MS). GC-MS is very sensitive and able to separate hydrophobic molecules. The coupling to mass spectrometry again allows the determination of masses of specific ions and comparison with mass spectral databases helps in identification of a specific substance. The TPG is running three GC or GCxGC mass spectrometers. However, a number of very hydrophilic molecules can not be separated by GC-MS. Therefore, LC-MS is an ideal complement to GC-MS, since it enables the separation of water-soluble molecules. Two LC-MS instruments are available at the TPG, a quadrupole TOF and an ESI ion-trap mass spectrometer. ■



Phylogenetic nearest-neighbour analysis of genes from a newly sequenced bacterial genome.

Microarray printing in a clean room.

CeBiTec Graduate School

Internationally and interdisciplinary post-graduate three year study programs

Currently, three interdisciplinary PhD programs are carried out at the CeBiTec: "Theoretical and applied Bioinformatics and Genome Research", "Research in industrially and biotechnologically relevant areas" and "Analysis of cellular signaling networks".

Characteristics of the CeBiTec post-graduate programs

The first PhD program, the "International NRW Graduate School in Bioinformatics and Genome Research", was endowed in 2001 by grants from the Ministry of Innovation, Science, Research and Technology of the state North Rhine-Westphalia (MIWFT NRW) and from German Research Foundation (DFG). Researchers from distinct faculties collaborate in this program as one faculty to define and supervise three-year PhD projects. Highly-qualified students from the fields of biology, bioinformatics, biochemistry, biotechnology or biomathematics are selected by means of international tendering. The Graduate School combines wet lab molecular biology research with bioinformatics methods for algorithmic data analysis and data management. Highest standards of PhD education are ensured through yearly written progress reports, half-yearly scientific retreats and soft skill trainings. Funds for travelling and publications foster the international visibility of the research work. Members of the Graduate School contribute to research areas such as structural RNA alignments, genome wide synteny studies and comparative assemblies, sequence based gene cluster analyses, biological data partitioning and the integration of metabolic networks into a virtual 3D cell by developing dedicated algorithms and software solutions (see publications). Currently, there are 20 PhD projects ongoing and 57 students have successfully finished their PhD education, three of them today are professors at German or foreign universities.

Expanding the structural components and experiences of the first Graduate School, the "CLIB Graduate Cluster Industrial Biotechnology" was initiated in 2009. Characteristics of the Graduate Cluster are: the joined initiative of the three partner universities HHU Düsseldorf, TU Dortmund, Bielefeld University and the close connection to industry by "CLIB^{2021} Cluster of Industrial Biotechnology" as a partner. More detailed information about the Graduate Cluster is provided in an extra article.



Our aim is to attract outstanding students by inspiring PhD topics and to provide them with exceptional equipment and supervision to achieve brilliant results.

2001	PhD in Genetics, Bielefeld University
2002–2003	Scientist, Sequencing Department Qiagen GmbH, Hilden
2004	Mentor, Intl. Graduate School in Bioinformatics and Genome Research
2008	Managing Director, Intl. Graduate School in Bioinformatics and Genome Research
2010	Leader of the Graduate Center

Dr. Susanne Schneiker-Bekel

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schneike@cebitec.uni-bielefeld.de

Selected publications

- Bremges, A., Schirmer, S., Giegerich, R.: 2010. *Fine-tuning structural RNA alignments in the twilight zone.* BMC Bioinformatics 11: 222
- Husemann, P., Stoye, J.: 2010. *r2cat: synteny plots and comparative assembly.* Bioinformatics 26(4): 570–571
- Sommer, B., Künsemöller, J., Sand, N., Husemann, A. *et al.*: 2010. *CELLmicrocosmos 4.1: An interactive approach to Integrating spatially localized metabolic networks into a virtual 3D cell environment.* In Fred, Ana; Filipe, Joaquim; Gamboa, Hugo (eds.): BIOINFORMATICS 2010 - Proceedings of the 1st International Conference on Bioinformatics (BIOSTEC 2010): 90–95
- Wittkop, T., Emig, D., Lange, S., Rahmann, S. *et al.*: 2010. *Partitioning biological data with transitivity clustering.* Nature Methods 7(6): 419–420
- Wittler, R., Stoye, J.: 2010. *Consistency of Sequence-based Gene Clusters.* Proceedings of RECOMB Comparative Genomics 2010, LNBI 6398: 252–263

In 2010, the "International Graduate Program Cell Signaling Networks", funded by Bielefeld University, was established at the CeBiTec adopting the structural properties and experiences of the previous schools. Six PhD fellowships are provided for three years to foster the understanding of the mechanisms, regulation and functions of cellular signaling networks. Through close interdisciplinary interaction between bioinformaticians and theoretical life scientists on the one hand and experimental biochemists, molecular biologists and geneticists on the other hand, an optimal integration and exploitation of available data and deep level theory formation complementary to on-going experiment driven-projects is aimed at.

Ongoing associations and future perspectives

Actually three PhD programs are administrated by the Graduate Center in close collaboration with the speakers and coordinators (Table 1). Convinced by the success of these interdisciplinary PhD programs the CeBiTec prospects to stabilize the existing programs and to develop additional PhD programs in newly emerging research areas. ■

Structured PhD program	Start	Speaker	Coordinator
International NRW Graduate School in Bioinformatics and Genome Research	2001	Prof. Dr. Robert Giegerich Prof. Dr. Alfred Pühler	Dr. S. Schneiker-Bekel
CLIB Graduate Cluster Industrial Biotechnology	2009	Prof. Dr. Alfred Pühler Prof. Dr. Karsten Niehaus	Dr. Iris Brune
International Graduate Program Bioinformatics of Signaling Networks	2010	Prof. Dr. Karl-Josef Dietz	Dr. Kolja Henckel

CLIB-Graduate Cluster "Industrial Biotechnology"

The CLIB-Graduate Cluster allows a joint education of the scholars from different locations of the Cluster, supervised by three universities and industrial companies, whereupon education of the scholars' also takes place in close agreement with research projects supported by CLIB[2021].

Background and History

In April 2009, the innovative, structured doctorate program CLIB-Graduate Cluster "Industrial Biotechnology" started as a joint initiative of the three universities Heinrich-Heine Universität Düsseldorf, Technische Universität Dortmund and Bielefeld University. The program is embedded into the Cluster Industrial Biotechnology CLIB[2021] and based on the four technology platforms PolyOmics, Expression, Biocatalysis and Downstream processing that are established at the three universities. This structure enables a direct transfer of knowledge between universities and industry and advances the interdisciplinary work of the technology platforms. The NRW Ministry of Innovation, Science, and Research and the three universities provide the considerable amount of 7.2 million Euros including material, travel and additional training expanses. Altogether, scholarships for 84 excellent junior scientists within a tight network between University and Industry are funded.

Education within the CLIB-Graduate Cluster

The CLIB-Graduate Cluster "Industrial Biotechnology" at the Center for Biotechnology (CeBiTec) at the Bielefeld University was initiated by Prof. A. Pühler and Prof. K. Niehaus.
The scientific branch realized at the CeBiTec, PolyOmics, is headed by Dr. J. Kalinowski and includes the development of new technologies for genome and post genome research. Thus the scholars in Bielefeld have the opportunity to perform projects applying modern instruments of genomics, transcriptomics, proteomics, metabolomics, and bioinformatics in the diversified field of genome and post-genome research. Within the years 2009 to 2014 all in all 28 fellows will complete their doctorate at Bielefeld University. In addition to these funded scholars, up to now nine doctoral students that are financed by means of other industrial relevant projects are associated to the program.

Dr. Iris Brune

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manBIE@graduatecluster.net

1996–2002	Studies in biology, Bielefeld University, Germany
2006	PhD in genetics and molecular biology, Bielefeld University, Germany
2006–2008	Post Doctoral Position, Bielefeld University, Germany
2009	Local coordinator CLIB-Graduate Cluster, Bielefeld University, Germany

Selected publications

- Schneider, J. , Blom, J., Jaenicke, S. *et al.*: 2010. *RAPYD – rapid annotation platform for yeast data*. J. Biotechnol., 155(1): 118-26.
- Schneider, J., Vorhölter, F. J., Trost, E. *et al.*: 2010. *CARMEN – Comparative Analysis and in silico Reconstruction of organism-specific Metabolic Networks*. Genet. Mol. Res. 9(3): 1660–72
- Trost, E., Götker, S., Schneider, J., *et al.*: 2010. *Complete genome sequence and lifestyle of black-pigmented* Corynebacterium aurimucosum *ATCC 700975 (formerly C. nigricans CN-1) isolated from a vaginal swab of a woman with spontaneous abortion*. BMC Genomics 11(1): 91
- Trost, E., Ott, L., Schneider, J., *et al.*: 2010. *The complete genome sequence of* Corynebacterium pseudotuberculosis *FRC41 isolated from a 12-year-old girl with necrotizing lymphadenitis reveals insights into gene-regulatory networks contributing to virulence*. BMC Genomics 11(1): 728

During the 3-year program, the doctoral students complete their research project and additionally participate in an individual study program where they further qualify by the collection of (30) credit points. For this purpose they have access to exclusive courses for students of the CLIB-Graduate Cluster, like lab courses at the three Universities and courses in innovation management and patent law organized by the central coordinator. Furthermore, the students have the opportunity to take part in key qualification courses including scientific writing and presentation skills. All courses within the CLIB-Graduate Cluster are given in English. To keep the faculty informed about the project's progress, each student has to write a progress report twice a year and to give oral and poster presentations on the regularly organized retreats. Following the intention to prepare the students also for future positions in industry, the participants of the program get the opportunity of a 3-month practical industrial training e.g. in CLIB[2021] member companies.

A strong ambition exits to establish the program on a long term perspective to further jointly work against the skill shortage. Obviously the competitive advantage of the Graduate Cluster "Industrial Biotechnology" is the industrial orientation and the close link to CLIB[2021] member companies. ■

Experiment, Discover, Analyze

Search for genetic clues in the *teutolab*-biotechnology

It is under this motto that the *teutolab* for biotechnology offers courses for young persons of secondary and trading schools in order to enable insights into biomolecular and biotechnological operations. One goal, amongst others, is the effective promotion of scientific interest to ensure the next generation of young academics.

About us

In 2010, a students lab was founded at the center for biotechnology – the *teutolab*-biotechnology. By means of a visit to the *teutolab* for biotechnology, biotechnological operations can be conveyed to students in a context-sensitive way, whereby the interest in the natural sciences can demonstrably be promoted and maintained. During one-day courses with focus on molecular genetics, students can acquire practical knowledge about restriction analysis, polymerase chain reaction, gel electrophoresis, and electron microscopy.

Basis concept of the *teutolab*-biotechnology

Molecular biology is a compulsive subject in the curriculum of biology, which comprises about a third of the qualification period of secondary school. As part of the standardized Abitur examinations, one of the three areas of examination is molecular biology. However, students often perceive the field of genetic engineering as very abstract because it can only be taught theoretically due to technical means or due to laws concerning genetic engineering. Moreover, even young and well-trained teachers are often not up to date with the scientific research. Therefore, the transfer of knowledge of this important topic should be systematically strengthened. Biology teachers should offer their students the possibility to work practically in the field of biotechnology.

Goals of the *teutolab*-biotechnology

The students lab *teutolab* for biotechnology mainly addresses trading schools and adolescents of secondary schools. The students lab not only conveys professional and practical knowledge, but also the importance of biotechnology to our society.

Learning in laboratory is for natural sciences what light is for plants' growth.

Honorarprof. Dr. Walter Arnold

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warnold@cebitec.uni-bielefeld.de

1988	PhD in Genetics, Bielefeld University, Germany
since 1997	Academic Director
since 2009	'Honorarprofessor'
since 2010	Chairman of the scientific staff council, Bielefeld University
since 2011	Scientific director of *teutolab*-biotechnology, CeBiTec

Selected publications

- Jacq, C., Alt-Mörbe, J., Andre, B., Arnold, W. *et al.*: 1997. *The nucleotide sequence of* Saccharomyces cerevisiae *chromosome IV.* Nature, 387(6632 Suppl), 75–78
- Strauch, E., Hammerl, J. A., Konietzny, A., Schneiker-Bekel, S. *et al.*: 2008. *Bacteriophage 2851 is a prototype phage for dissemination of the Shiga toxin variant gene 2c in* E. coli *O157:H7.* Infection And Immunity, 76(12): 5466–5477
- Tauch, A., Trost, E., Tilker, A., Ludewig, U. *et al.*: 2008. *The lifestyle of* Corynebacterium urealyticum *derived from its complete genome sequence established by pyrosequencing.* J. Biotechnol., 136(1–2), 11–21
- Trost, E., Götker, S., Schneider, J., Schneiker-Bekel, S. *et al.*: 2010. *Complete genome sequence and lifestyle of black-pigmented* Corynebacterium aurimucosum *ATCC 700975 (formerly* C. nigricans *CN-1) isolated from a vaginal swab of a woman with spontaneous abortion.* BMC Genomics, 11:91

In order to measure up to the growing importance of biotechnology, the following steps are taken in the *teutolab* for biotechnology:

- Transfer of current knowledge in science into schools for teachers and students
- Training of teachers in the area of practical work, for example by means of practical trainings or workshops
- Development of new ways of learning, for example for the creation of project courses
- The possibility of borrowing equipment and working material
- Bringing schools into contact with businesses of biotechnology as extracurricular possibilities – with special consideration to occupational orientation
- Advisory service for the establishment of students labs
- Conducting fora, trial lessons, informative lessons to inform students about possible occupational fields
- Supplying platforms for teachers on the internet
- Supporting very talented adolescents, for example by means of a study taster or by visiting a summer camp at the University of Bielefeld. ■

Location

By train

Bielefeld is easy to reach both by car and by train: every hour an intercity train on the route from Cologne/Bonn to Berlin stops at Bielefeld Hbf. Then you take *Stadtbahn Linie 4* towards *Universität* (7 minutes).

By plane

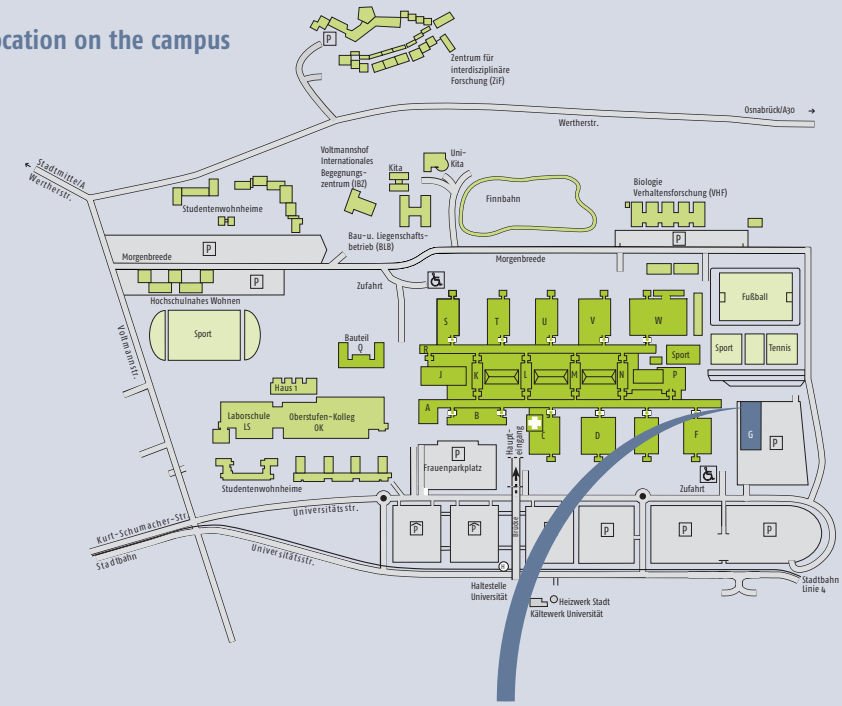
The closest airports to Bielefeld are Paderborn/Lippstadt and Hannover.

By car

You can take the A2 from Dortmund to Hannover, exit at *Bielefeld-Zentrum*, follow the street signs towards the centre (*Zentrum*), and from there the University (*Universität*) is signposted.
The CeBiTec laboratory building is labeled as part G on the plans of the University.

Overview

Location on the campus



Entrance of the CeBiTec building

Impressum

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