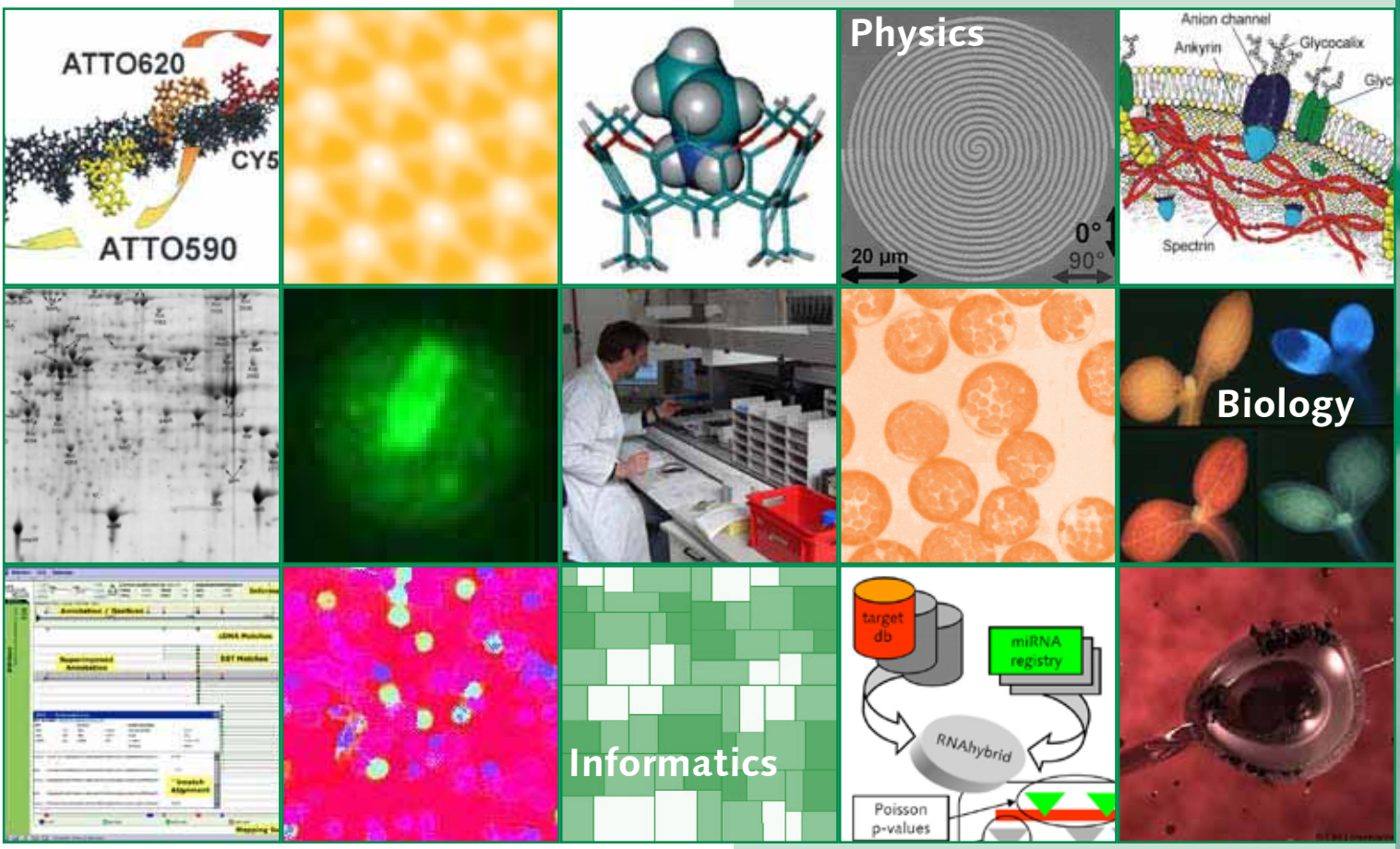
CeBiTec

The Center for Biotechnology
at Bielefeld University

from molecules to living systems …



Preface

The outstanding characteristic of Bielefeld University ever since it was first established has been its interdisciplinary nature. The Center for Interdisciplinary Research was founded as the 'germ cell' in 1968, only one year after the founding of the university. It was the model for 'Centers for Advanced Study' all over Europe and has made a decisive contribution to establishing the university's international reputation.

The Center for Biotechnology (CeBiTec) is in the best sense the continuation of the Bielefeld tradition of interdisciplinarity in an area of research of particular significance for the future. In recent years, the traditional separation between the various life sciences has been eliminated for all practical purposes. A research area of this complexity demands a broad range of competencies: biologists, physicists, chemists, even mathematicians and computer scientists now work closely together in this fascinating field. The Bielefeld University recognized this tendency very early and established a Faculty of Technology with the two departments Computer Science and Biotechnology at the beginning of the 1990s. This type of structure combining such fields was at the time extremely unusual; but it has proven to be completely correct and innovative in view of the enormous amounts of data obtained in genome research and biotechnology.

In the course of the great generation transition among the scientists which took place at the university in this decade, it has consistently aimed its appointment policies in the direction of strengthening its interdisciplinary focus. This has also been of benefit to the departments which have been merged in institutes for bioinformatics, genome research as well as biophysics and nanosciences under the umbrella of the CeBiTec for several years. The excellent research which goes on here has been highly recognized internationally as well as domestically. Bielefeld scientists play an important role in numerous research networks, such as the Competence Network Genome Research on Bacteria relevant for Agriculture, Environment and Biotechnology.

Internal rededications and successful acquisition of third-party funds has made it possible for the number of scientists working here to rise to such an extent that the previous laboratory capacities were no longer adequate. The construction of a new laboratory building for the CeBiTec has been going on since 2004. This is the largest university construction measure undertaken in Bielefeld since the erection of the main building more than 30 years ago. The very fact that this was possible in these times of extremely tight public budgets is evidence of the value placed on the research conducted at the CeBiTec from outside the university as well.

Whether in medicine, agriculture or environmental protection (to mention only a few areas) – the research questions being examined at the CeBiTec ultimately concern every single human being, in one way or another. What is more, the CeBiTec makes an important contribution to the furtherance of young scientists by providing diverse opportunities for employment for young researchers and through the International Graduate School in Bioinformatics and Genome Research.

Since it was founded, the CeBiTec has always proven to be a powerful organizational structure for pioneering research of extraordinary impact for all of society. I hope and expect that major stimuli for developments in key areas of natural sciences will continue to originate here in the future as well. This brochure gives you an insight into the diversity of the research being conducted at the CeBiTec.

Dr. Dieter Timmermann

Rector, Bielefeld University, October 2005

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CeBiTec – Center for Biotechnology

The Center for Biotechnology (CeBiTec) at Bielefeld University dedicated to interdisciplinary research in Life Sciences, encourages and supports the development of innovative projects crossing discipline boundaries. Scientists from the Faculties of Biology, Chemistry, Physics and from the Faculty of Technology collaborate in various research projects supported by the German Research Foundation (DFG), the Federal Ministry of Education and Research (BMBF), the State Northrhine Westfalia and the European Union.

As outlined on the right hand side the Senate of the Bielefeld University initiated in 1998 the establishment of the interdisciplinary research center CeBiTec. During the first years, the scientific members of the CeBiTec were heavily engaged in defining joint research projects. It turned out that the combination of Bioinformatics and Genome Research was of highest importance for the further development of the CeBiTec. In the year 2000 a grant proposal in the frame of the German Research Foundation (DFG) program Bioinformatics was positively evaluated. Its support together with a matching fund from the university allowed the establishment of two CeBiTec institutes, the Institute for Bioinformatics (inauguration in 2002) and the Institute for Genome Research (inauguration in 2003). The detailled structure of the institutes is presented in Figure 1. It is of special importance that both institutes host several junior research groups which use the CeBiTec infrastructure for independent research. In this respect, it is worth to mention that the Bielefeld University Bioinformatics Server (BiBiServ) is incorporated into the Institute for Bioinformatics as a technology platform providing more than 30 software tools and various education media. On the other hand, the Institute for Genome Research is equiped with the technology platform Systems Biology supporting all the high-throughput technologies playing a role in genomics, transcriptomics, proteomics and metabolomics. In the year

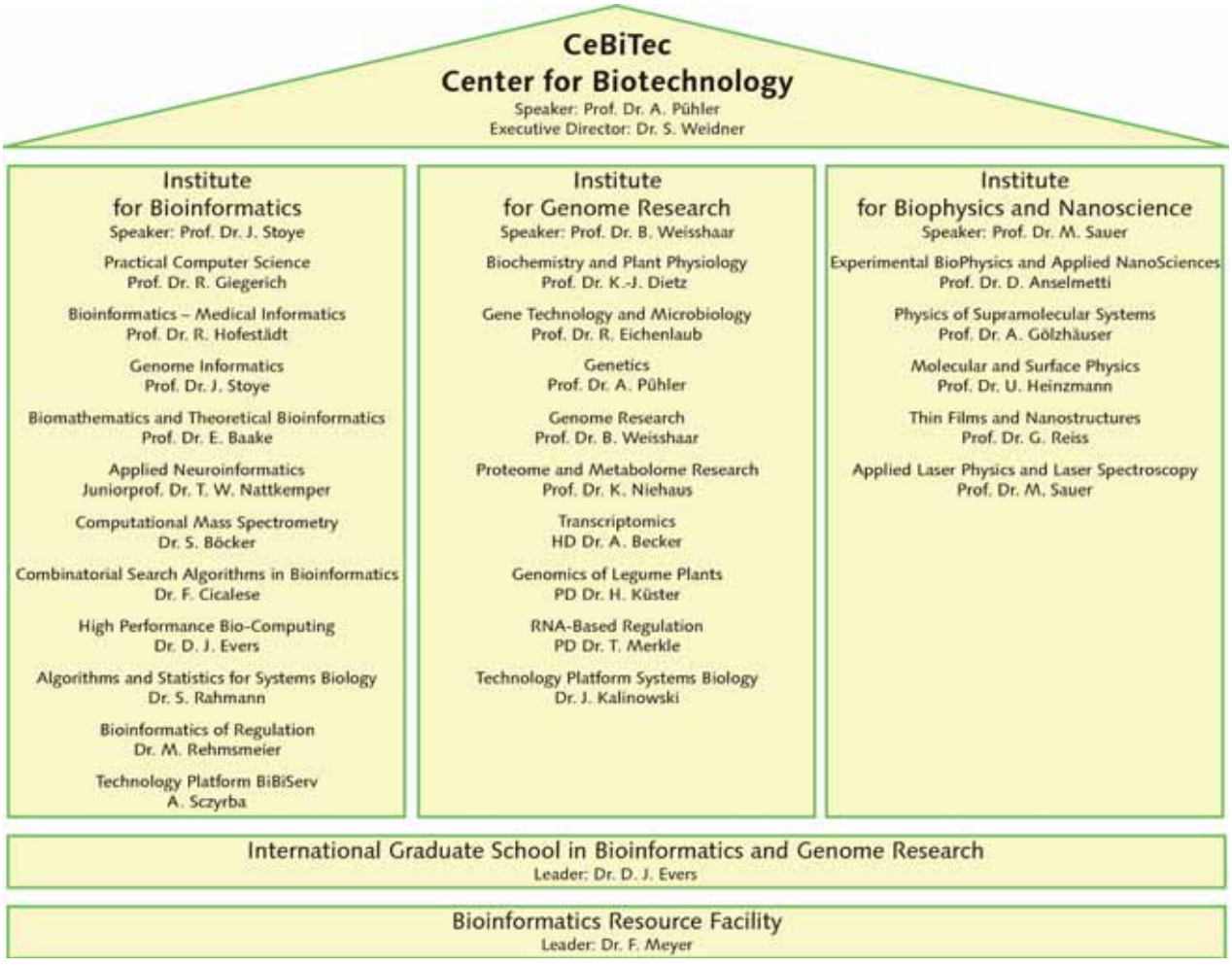


Fig. 1: Current organization chart of the CeBiTec.

2000, a further successful project was funded by the German Research Foundation (DFG). This time, the Research Training Group Bioinformatics could be established which finances three groups of Ph.D. students for a period of nine years.
The year 2001 turned out to be very successful for the scientific members of the CeBiTec since they were able to acquire several large scale research projects. First of all, the International Graduate School in Bioinformatics and Genome Research fincanced by the State Northrhine Westfalia, could be established.

This Graduate School (see Figure 1) planned for five years, educates in the meantime more than 40 Ph.D. students, many of them coming from abroad. Second, the Federal Ministry of Education and Research (BMBF) installed for five years the Competence Network 'Genome Research on Bacteria relevant for Agriculture, Environment and Biotechnology'. Within this network more than 20 groups from universities,

Developmental steps concerning the CeBiTec at Bielefeld University

25.09.98	Establishment of the CeBiTec through the Senate of the Bielefeld University, adoption of the first Statute
21.12.98	First meeting of the Executive Board, election of Prof. Dr. J. Lehmann as CeBiTec-Speaker
08.12.99	Publication of the first CeBiTec brochure
14.09.00	Grant from the German Research Foundation (DFG) for the establishment of Institutes for Bioinformatics and Genome Research at Bielefeld University
01.10.00	Grant from the German Research Foundation (DFG) for the establishment of a Research Training Group Bioinformatics
21.06.01	Grant from the Ministry of Education and Research (MSWF) of the State Northrhine Westfalia for the establishment of an International Graduate School in Bioinformatics and Genome Research
15.08.01	Grant from the Federal Ministry of Education and Research (BMBF) for the Competence Network Genome Research on Bacteria relevant for Agriculture, Environment and Biotechnology
03.12.01	Grant from the German Research Foundation (DFG) for the establishment of the Collaborative Research Center SFB 613 Physics of Single Molecule Processes and Molecular Recognition in Organic Systems
05.12.02	Inauguration of the Institute for Bioinformatics
13.02.03	Inauguration of the Institute for Genome Research
03.12.03	Adoption of the modified Statute by the Senate of Bielefeld University
27.02.04	General meeting of the CeBiTec and election of the current Executive Board, election of Prof. Dr. A. Pühler as Speaker of the CeBiTec Executive Board, appointment of Dr. S. Weidner as Executive Director of the CeBiTec
17.03.04	Laying of the cornerstone for the CeBiTec laboratory building at the Bielefeld University
17.03.04	Establishment of Coordination Committees for the Bioinformatics Resource Facility and the International Graduate School in Bioinformatics and Genome Research by the Executive Board
22.04.04	Inauguration of the Bielefeld Institute for Biophysics and Nanoscience (BINAS)
15.11.05	Publication of the second CeBiTec brochure

research institutes and industry collaborate in the field of bacterial genome research. Combined with this network the establishment of a Competence Center at Bielefeld University dedicated to '-omics' technologies took place. Finally, at the end of the year 2001 the German Research Foundation (DFG) installed the Collaborative Research Center SFB 613 entitled Physics of Single Molecule Processes and Molecular Recognition in Organic Systems. This was a further important step for the CeBiTec since scientists of the Faculty of Physics got in closer contact with the CeBiTec and discussed the possibility of establishing a third institute. Such an institute termed BINAS, an abbreviation of Bielefeld Institute for Biophysics and Nanoscience, was finally inaugurated in the year 2004.

By the end of 2003, the CeBiTec statutes were modified and adopted by the Senate of Bielefeld University. In a general meeting organized in February 2004, the Executive Board was elected. The members of this board are shown in Figure 2. The highlight of the year 2004 was without doubt the beginning of the construction of the CeBiTec laboratory building. The corner stone ceremony took place in March 2004 (see Figure 3). This new building which will provide lab space of around 2100 square meters, will further unify the different research directions of the three CeBiTec institutes. A model of the CeBiTec building is shown in Figure 4. Last but not least, in the year 2005 an Advisory Board consisting of six distinguished scientists was formed which will meet for the first time in November, 2005.

The slogan 'From Molecules to Living Systems' presented on the cover of this brochure describes very well the general topic of the CeBiTec. Recently, this topic was even more focussed and it was agreed that the research groups collaborating in the CeBiTec will develop the emerging field of Systems Biology. In particular, Systems Biology based on genome research is already very well covered by the existing research groups since genome research, bioinformatics and nanoscience represent the pillars on which this discipline is built. It should be mentioned too, that as a first step towards Systems Biology a master

Fig. 2: First meeting of the executive board of the CeBiTec with Prof. Dr. J. Stoye, Prof. Dr. A. Pühler, Prof. Dr. R. Giegerich, M. Stiens, Prof. Dr. B. Weisshaar, Dr. S. Weidner, Dr. J. Kalinowski, A. Neumann.

Fig. 3: Lying of the cornerstone in March 2004 with the CeBiTec speaker A. Pühler, BLB director U. Günther, rector of the Bielefeld University D. Timmermann, chancellor of the Bielefeld University H.-J. Simm, and burgomaster H. Grube.

study course designated Genome Based Systems Biology has been initiated at the beginning of this winter term. This master study course is looking forward very much to the new CeBiTec building since practical courses as well as experimental research work for master theses are planned for the new building.

Evidently, the development of the CeBiTec research center represents a success story. In the meantime, it represents a location where research groups from three different faculties of Bielefeld University collaborate intensively. In addition, the CeBiTec also helped to establish a whole bunch of new technologies. It also facilitated the implementation of up-to-date instrumentation. The members of the executive committee are satisfied with this development and look forward very much to a scientifically successful future.

Prof. Dr. Alfred Pühler

Fig. 4: Model of the new CeBiTec building.

Prof. Dr. Alfred Pühler
Speaker of the Executive Board
Genetics
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

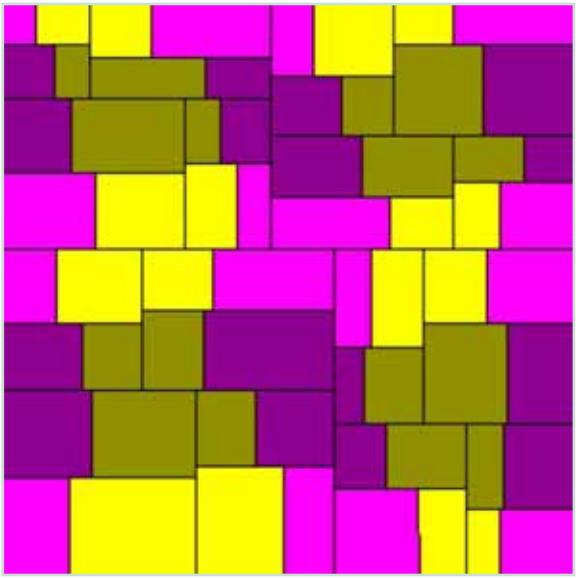
phone +49-521-106 5607
fax +49-521-106 5626
email puehler@genetik.uni-bielefeld.de

Dr. Stefan Weidner
Exective Director
CeBiTec – Center for Biotechnology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 2034
fax +49-521-106 5626
email stefan.weidner@cebitec.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de

The Institute for Bioinformatics

Modern molecular biology requires mathematical models and efficient algorithms to interpret the mass of observations generated by current experimental techniques. This necessity has given birth to the new discipline of bioinformatics.
Bioinformatics can roughly be split in two branches: ***Algorithmic Bioinformatics*** is concerned with new methods of data analysis, resulting in new or better models, algorithms and tools. This branch needs input from biology, but is mainly a computer science activity with its typical cycle of algorithm development, implementation and evaluation.
Applied Bioinformatics is the actual interpretation of biological data with the tools developed in the algorithmic branch of the field. This requires close cooperation between biologists and bioinformaticians, in particular when novel experimental techniques or novel tools are involved. The Institute for Bioinformatics is engaged in both kinds of activities.
The institute was founded in 2002 as a consequence of the successful application of Bielefeld University in the DFG Initiative in Bioinformatics. It was incorpo-



A microarray carrier is partitioned based on a 2-dimensional gray code in order to allow optimal probe-to-spot assignments when designing a new chip. Improving microarray design in order to increase data quality is one of the research projects currently carried out at the Institute for Bioinformatics.

Prof. Dr. Jens Stoye
Institute for Bioinformatics
Center for Biotechnology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 3852
fax +49-521-106 6495
email stoye@techfak.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/IfB

rated into the Center for Biotechnology (CeBiTec) after its new constitution in 2004.
The institute is a forum for communication and joint research in Bioinformatics and Biomathematics at Bielefeld University. The main tasks of the institute are the coordination of interdisciplinary research projects, the organization of workshops and seminars, and the presentation of the activities and results of the involved research groups. One of the largest activities was the organization of the German Conference on Bioinformatics, GCB 2004, with about 280 participants, 28 scientific presentations, and 60 posters.
As of summer 2005, the Institute for Bioinformatics hosts four senior research groups, six junior research groups and one technology platform, the Bielefeld University Bioinformatics Server (BiBiServ), that provides web access to bioinformatics tools and educational material developed in Bielefeld.

Contributing Units

Practical Computer Science;
Prof. Dr. R. Giegerich

Bioinformatics – Medical Informatics;
Prof. Dr. R. Hofestädt

Genome Informatics;
Prof. Dr. J. Stoye

Biomathematics and Theoretical Bioinformatics;
Prof. Dr. E. Baake

Applied Neuroinformatics;
Juniorprof. Dr. T. W. Nattkemper

Computational Mass Spectrometry;
Dr. S. Böcker

Combinatorial Search Algorithms in Bioinformatics;
Dr. F. Cicalese

Higt Performance Bio-Computing;
Dr. D. J. Evers

Algorithms and Statistics for Systems Biology;
Dr. S. Rahmann

Bioinformatics of Regulation;
Dr. M. Rehmsmeier

Technology Platfrom BiBiServ;
A. Sczyrba

Practical Computer Science

The Faculty of Technology was founded in May 1990 and has particularly committed itself to interdisciplinary cooperation in research and teaching.
The research group Practical Computer Science headed by Prof. Dr. R. Giegerich is especially involved in the courses Applied Computer Science in the Natural Sciences and Bioinformatics and Genome Research. 14 students received their Ph.D. and three former group members are now professors for Bioinformatics at German universities.

Research Interests
Programming languages and compilers were the original field of work when the group was first established. Although the research focus has shifted considerably since, the group still holds an interest in this field and persues active research. The use of declarative (functional) programming languages is propagated in computer science education, as well as in program development for bioinformatics applications. A long term goal here is the realization of a declarative language for dynamic programming, which is of tantamount importance in biosequence analysis.
For large scale analysis, variety of tools has been developed, such as REPuter (for fast computation of degenerative repeats in complete genomes) and GENlight (an interactive system for high-throughput sequence analysis and comparative genomics), e2g (matching ESTs to genomic sequences), and MGA (multiple genome alignment). The group has made several contributions to make suffix trees and suffix arrays practical as index data structures for sequence analysis.
For RNA structure analysis, the group provides tools that define the state of the art in several respects, such as RNAforester (structure comparison and multiple structure alignment), pknotsRG (folding structures with pseudoknots), and RNAhybrid (miRNA target prediction). The method of abstract shape analysis was introduced and the group explores its manifold consequences. Recent tools based on this approach are RNAshapes (shape analysis) and RNAcast (consensus structure prediction).
In programming methodology, the discipline of Algebraic Dynamic Programming (ADP) has been developed. It raises dynamic programming over sequence data to a higher level of abstraction, considerably enhancing programming productivity, program reliability and reusability. Several of the aforementioned

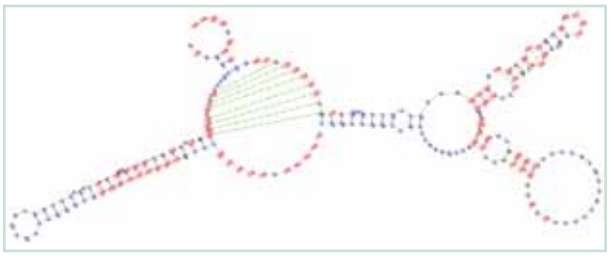


Fig. 1: RNAforester: Structure alignment of the human ferritin 5'UTR and the *Drosophila melanogaster* succinate dehydrogenase 5'UTR. Bases printed in black show structure elements that occur in both structures with the same sequence. Sequence variations are displayed by using red letters. Bases or base pairs that can only be found in ferritin are printed in blue, while bases that only occur in succinate dehydrogenase are printed in green.

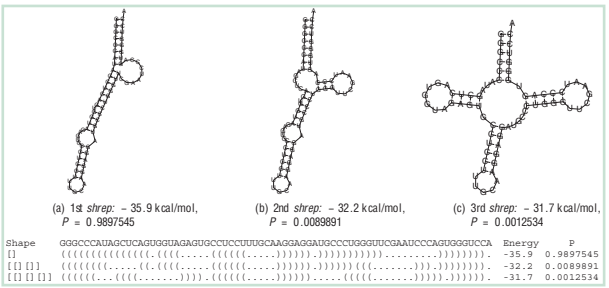


Fig. 2: A common problem in RNA secondary structure analysis is the huge number of very similar suboptimal structures. RNAshapes classifies structures upon their composition from structural elements. For each shape class only one representative structure is reported, providing a synoptic overview of the near-optimal structure space.

Prof. Dr. Robert Giegerich
Practical Computer Science
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 6953
fax +49-521-106 6411
email robert@techfak.uni-bielefeld.de
url www.techfak.uni-bielefeld.de/ags/pi

tools were implemented with this technique.

Involvement in Courses of Study

The research group contributes courses to the programs Applied Computer Science in the Natural Sciences, Bioinformatics and Genome Research, Molecular Biotechnology, and Media Design. Prof. Dr. R. Giegerich is the Speaker of the International Graduate School in Bioinformatics and Genome Research, which was established at Bielefeld University by a grant from the Ministry of Education and Research (MSWF) of the State Northrhine-Westfalia. He is also speaker of the Research Training Group Bioinformatics, financed by the German Research Foundation (DFG). Both programs currently support 37 Ph.D. scholarships.

```
affineGlobalSimilarity alg f = axiom alignment          where
   (nil, d, i, r, dx, ix, h) = alg

   alignment = tabulated ( nil <<< char '$'              |||
                 d   <<< achar  ~~~ xDel                 |||
                 i   <<<          xIns       ~~~ achar   |||
                 r   <<< achar  ~~~ alignment ~~~ achar  ... h)

   xDel      = tabulated ( alignment                     |||
                           dx <<< achar  ~~~ xDel        ... h )

   xIns      = tabulated ( alignment                     |||
                           ix <<< xIns ~~~ achar         ... h )
```

Fig. 3: Algebraic Dynamic Programming (ADP) is a new method to design and implement, tune, test and teach Dynamic Programming algorithms. Compared to the traditional style, ADP provides a much higher level of abstraction, helping to solve more sophisticated problems with better chances of success. The figure shows executable ADP code for Gotoh's algorithm for global sequence similarity under an edit model

Curriculum Vitae

Study of Informatics and Mathematics at the TU Munich and Stanford University, USA
1981: Ph.D. at TU Munich with a dissertation in the area of compiler generating systems
Since 1989: Professor for Practical Informatics, Faculty of Technology, Bielefeld University
1989: Interdisciplinary curriculum 'Naturwissenschaftliche Informatik'
1992: Establishment of Bioinformatics as a new area of research and teaching
1995/97: Two multimedia awards for educational activities (Virtual Sequencing Laboratory, International Virtual Course in Biocomputing)
1996: Establishment of the Bielefeld University Bioinformatics Server, currently with approx. 10 000 users per month
Since 2000: Speaker of the Research Training Group Bioinformatics
Since 2001: Speaker of International Graduate School in Bioinformatics and Genome Research
Steering committee German Conference on Bioinformatics (GCB), and Bioinformatics Research and Education Workshops (BREW)

Members

S. Abdul-Hak | K. Gkogkoglou | Dr. M. Höchsmann | T. Höchsmann | R. Homann | Dr. E. Möllmann | Ch. Peters | B. Quisbrok | Janina Reeder | Jens Reeder | M. Rüther | P. Steffen |

Publications

Malde, K. and Giegerich, R. 2005. **Calculating PSSM probabilities with lazy dynamic programming.** J Funct Programming 16, 1-7
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Bioinformatics – Medical Informatics

The research group Bioinformatics – Medical Informatics headed by Prof. Dr. R. Hofestädt was established in 2001 at the Faculty of Technology. The research topics concentrate on biomedical data management, modelling and simulation of metabolic processes, parallel computing and multimedia implementation of virtual scenarios. Within the scope of these topics different national and international cooperations and research projects have been created and successfully finished.

Research Interests

The group has worked on the development of integrative methods for the modelling and simulation of metabolic processes. For example, a complex information system has been developed, which represents three levels: tools for the data integration of molecular databases, tools for the automatic implementation of user-specific databases and a rule-based method for the simulation of metabolic processes. Additionally, the group participated in several research projects (BMBF, DFG, Volkswagen Foundation and EU) and organized more than 20 national and international conferences, workshops and summer schools in the area of Bioinformatics and Medical Informatics.

Further research interests are signaling pathways, which play a major role in many cellular processes. In short from cell birth to cell death, involving lot of complexity but functioning with robustness. Sometimes perturbation of these pathways leads to a disease such as cancer. The group is interested in modelling and simulation of signaling pathways and would like to know more about their robustness and behavior using different tools and techniques. An additional example of the work is the development of the text mining system ONDEX that maps concepts of ontologies to the words of biomedical texts. Different ontologies (e.g. GO, MeSH terms, CellOntology Wordnet, EC nomenclature) are aligned into one ontology. Then concepts of this merged ontology are mapped to the words of the texts. Due to the use of natural language processing tools (NLP) like part-of-speech tagging (POS) and word stemming, this mapping fits even if the words appear in different grammatical forms.

After indexing with ontology concepts text will become searchable by concepts and not only by simple string-string comparisons. Also homonym detection (i.e. discrimination between different meanings of a

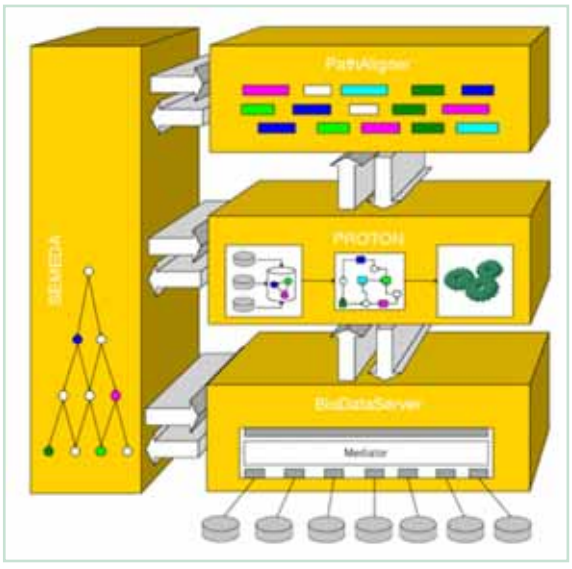

Fig. 1: Overall architecture of MARGBench. In the center of this approach a process called Integrative Modelling of Biochemical Networks has been developed. Modelling starts at the fusion of data from heterogeneous data sources. BioDataServer (BDS) is an integration service based on the mediator approach. Data fusion can be supported by semantic data integration by SEMEDA, the Semantic Meta Database. The fact that the fusion of data from different databases often leads to semantic conflicts, e.g. homonyms and synonyms, makes it hard to model integrated schemata. The interactive modelling environment PROTON has been developed to reconstruct models from databases. PathAligner is designed to reconstruct / retrieve metabolic pathways and process alignments of them.

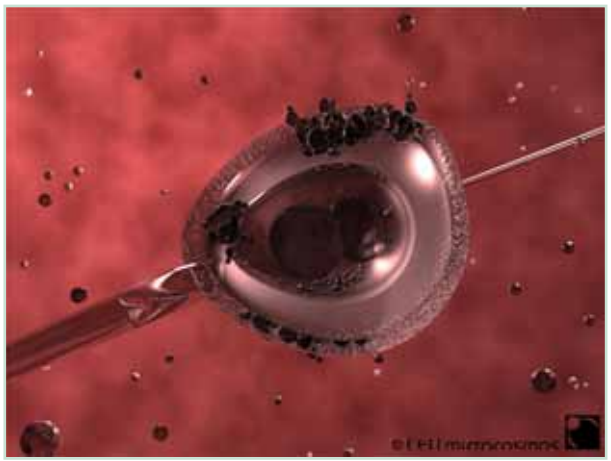

Fig. 2: The aim of the CELLmicrocosmos project is the interactive stereoscopic visualization of biological cells for a better understanding of their internal structures and their functioning. Based on microscopic datasets, biological cells are reconstructed in 3D models. *Via* Virtual Reality (VR) techniques they can be explored interactively for educational and scientific purposes. In this figure the insertion of molecular fragments (e.g. DNA) into the cell *via* microcapillary direct injection is visualized.

Prof. Dr. Ralf Hofestädt
Bioinformatics – Medical Informatics
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5283
fax +49-521-106 6488
email hofestae@techfak.uni-bielefeld.de
url cweb.uni-bielefeld.de/agbi/home/index.html

word, e.g. between mouse as organism and mouse as computer device) is achieved.

Involvement in Courses of Study
The research group is involved in several Bachelor and Master courses at the Faculty of Technology, e.g. Bioinformatics and Genome Research and Applied Computer Science in the Natural Sciences. Therefore, regular basic and special lectures are provided like Database Systems, Medical Knowledge Engineering, Parallel Algorithms in Bioinformatics, Interactive Visualization of Biological Cells and Modelling and Simulation of Metabolic Networks.

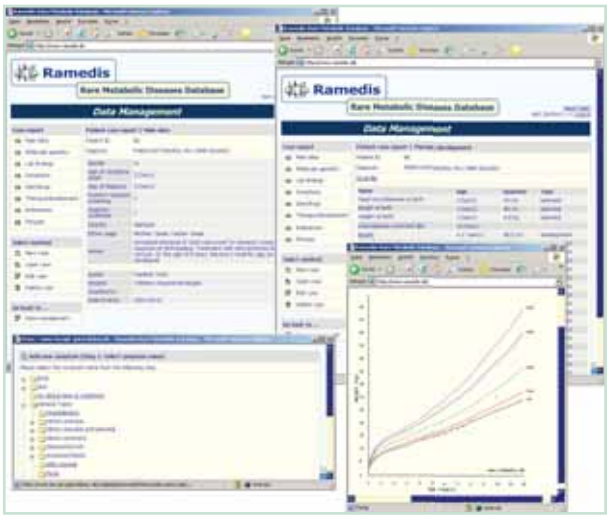

Fig. 3: The RAMEDIS system is a platform independent, web-based information system for genetic diseases on the basis of separate case reports. It was developed in close cooperation with clinical partners and collects information on rare metabolic diseases with extensive details, e.g. about occurring symptoms, laboratory findings, therapy and molecular data. By using RAMEDIS the group expects advances in epidemiology, combination of molecular and clinical facts, generation of rules for therapeutic intervention and identification of new diseases.

Curriculum Vitae

Study of Computer Science and Biology at the University of Bonn
1990: Ph.D. in Computer Science at the University of Bonn
1990-1994: Assistant professor at the University of Koblenz (Practical Computer Science)
1995: Habilitation in Applied Computer Science – Bioinformatics at the University of Koblenz
1995-1996: Professor for Medical Informatics at the University of Leipzig
1996-2001: Professor for Applied Computer Science at the University of Magdeburg
Since 2001: Professor for Bioinformatics – Medical Informatics at Bielefeld University

Members

S. Hariharaputran | S. Klusmann | Dr. D. Lorenz | T. Möller | M. Niemann | B. Prins | A. Rüegg | Dr. T. Töpel |

Publications

Freier, A. *et al.*, 2005. **Investigating the effective range of agents by using integrative modelling.** In Handbook of Toxicogenomics, J. Borlak (ed.). Wiley-VCH, 233-252
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Genome Informatics

The research group Genome Informatics was newly established in March 2002 in response to the growing activities in genome research at Bielefeld University and its need for genome oriented bioinformatics. Initial funding for the group was provided by the DFG Initiative in Bioinformatics. In December 2002, the research group was one of the three founding members of the Institute for Bioinformatics. Within the first three years of existence, three junior research groups became affiliated with the group.

Research Interests

The research area of the group is the development and analysis of efficient algorithms in computational biology and genome research. Currently the main interests are in protein and DNA sequence analysis, and in comparative genomics.

The detection of remote homologues for a given protein or set of proteins remains a challenging bioinformatics task. Using family information often increases the sensitivity, and therefore methods for multiple sequence alignment like the Divide-and-Conquer alignment algorithm and the QAlign program have been developed. Building upon those the group is working on protein classification methods like the Jumping Alignments algorithm and, using in addition to sequence also secondary structure information, the Passta database and search method.

In DNA sequence analysis, often the problem is more the handling of the large amounts of data than the sensitivity of the search method. Using efficient data structures for preprocessing genome-size DNA sequences, the research group works on filtration algorithms for rapid DNA search like the SWIFT algorithm. Based on this, very fast EST clustering is possible, as well as EST to genome mapping for splice site detection or EST-based expression analysis. Visualization of the results of such searches is another topic of research in the group. More theoretically, the group is also interested in better representations and faster algorithms for construction of string indices like suffix trees or suffix arrays. Using such data structures, methods have been developed for the detection of repeats in genomic sequences, in particular tandem repeats, and for elucidating their evolutionary history.

Another general direction of research is the development of algorithms and computer programs for genome comparison. The group developed methods for finding clusters of co-located genes and for com-

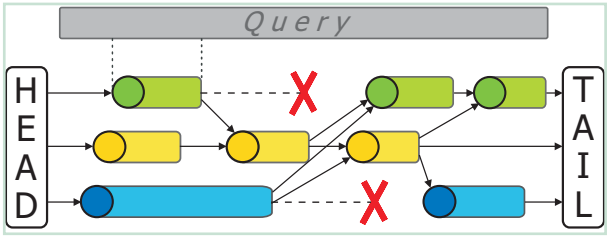

Fig. 1: The figure shows a directed, acyclic graph that is used in the Passta project. The aim is to find the best path from head to tail. The vertices represent alignments of protein secondary structure elements (SSEs) with the Query. Solid arrows are edges, the dashed lines are exemplary edges that were removed due to constraints in the edge definition of the graph.

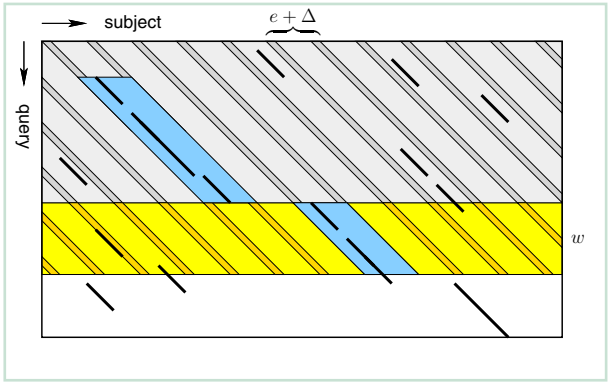

Fig. 2: The SWIFT algorithm for fast local alignment search exploits that word-hits of alignments matching the search parameters are guaranteed to occur within a well-defined region of the dynamic programming matrix. The figure illustrates the filtration step where such regions (blue parallelograms) are located. At any time, the only word-hits (thick diagonal lines) considered are those occurring in the intersection (shaded yellow) of the subject sequence and a sliding window on the query sequence.

Prof. Dr. Jens Stoye
Genome Informatics
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 3852
fax +49-521-106 6495
email stoye@techfak.uni-bielefeld.de
url gi.cebitec.uni-bielefeld.de

puting distances between genomes under different evolutionary models.

Involvement in Courses of Study
The group contributes to the Bachelor, Master, and Ph.D. programs in Bioinformatics and Genome Research, as well as in all other computer science related programs in Bielefeld. The focus is on theoretical subjects like algorithms and data structures, sequence analysis, and algorithms in genome research. The head of the research group is Dean of Studies in Applied Computer Science in the Natural Sciences and of the Ph.D. program in Bioinformatics and Genome Research.

Fig. 3: QAlign2 - panta rhei: a tool to automatically generate multiple alignments (middle of left border) and to visually control the results (top-right area of the main panel). A guided editing function allows changes done by hand (marked boxes), and phylogenetic trees can be inferred on every alignment layout (bottom).

Curriculum Vitae

Diploma and Ph.D. in Applied Computer Science in the Natural Sciences at Bielefeld University
Postdoctoral studies at UC Davis and the German Cancer Research Center, Heidelberg
2001: Head of the Algorithmical Bioinformatics Group, Department of Computational Molecular Biology, MPI for Molecular Genetics, Berlin
Since 2002: Professor for Genome Informatics at Bielefeld University
Since 1999: Member and since 2002 vice speaker of the board of directors of the Bioinformatics Section of the German Society for Computer Science (GI)
Since 2003: Speaker of the Institute for Bioinformatics, Bielefeld University
Member of several program committees (WABI, RECOMB, ISMB, ECCB, GCB, CLS, RECOMB-CG, CPM) and of the editorial board of the IEEE/ACM Transactions on Computational Biology and Bioinformatics

Members

J. Amgarten Quitzao | C. Bannert | P. Husemann | J. Mixtacki | K. Rasmussen | Dr. M. Sammeth | H. Samuel | Dr. T. Schmidt | K.-B. Schürmann |

Publications

Rasmussen, K.R. *et al.*, 2005. **Efficient q-gram filters for finding all epsilon-matches over a given length.** In Proc of RECOMB, 189-203

Bergeron, A. *et al.*, 2005. **On sorting by translocations.** In Proc of RECOMB, 615-629

Schürmann, K.-B. and Stoye, J. 2005. **An incomplex algorithm for fast suffix array construction.** In Proc of ALENEX, 77-85

Krause, A. *et al.*, 2005. **Large scale hierarchical clustering of protein sequences.** BMC Bioinformatics 6:15

Cieliebak, M. *et al.*, 2004. **Algorithmic complexity of protein identification: Combinatorics of weighted strings.** Discrete Appl Math 137, 27-46

Gusfield, D. and Stoye, J. 2004. **Linear time algorithms for finding and representing all the tandem repeats in a string.** J Comput Syst Sci 69, 525-546

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Stoye, J. and Gusfield, D. 2002. **Simple and flexible detection of contiguous repeats using a suffix tree.** Theor Comput Sci 270, 843-856

Biomathematics and Theoretical Bioinformatics

The research group Biomathematics and Theoretical Bioinformatics, led by Prof. Dr. E. Baake, was established at Bielefeld University in July 2004. Its work is devoted to the young discipline of mathematical biology, which develops the theoretical side to biology, akin to theoretical physics one century ago.

Research Interests

The group's main area of research is the mathematical theory of biological evolution, in particular population genetics, which is concerned with the dynamics of genes in populations under the joint influence of mutation, selection, recombination and genetic drift. A fundamental model that describes these evolutionary forces is the Moran model, a so-called interacting particle system (Fig. 1). Here, the backward point of view is particularly interesting, which arises if one picks individuals from the present population and follows their ancestry back into time; one then aims at probability laws for the evolutionary history. If the population is very large, it may be described by a (deterministic) differential equation, which is much easier to treat than the full stochastic model. For example, a variational principle is available that describes the interaction of mutation and selection, and connects the present and the past; the recombination dynamics even has a closed solution. But populations of moderate size require the full-fledged stochastic approach to also capture the effect of genetic drift, and pose many open problems. Another recent activity concerns probability models in immunobiology. Here, one of the fundamental questions is the recognition of foreign antigens against a self background (Fig. 2). Recent models and their analysis reveal that this recognition is possible on the grounds of a purely mathematical principle.

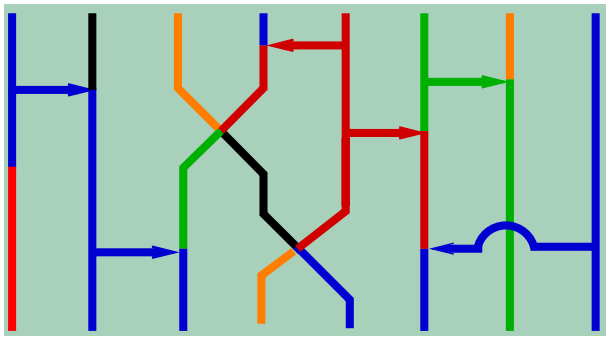


Fig. 1: The Moran model describes the time evolution of a population of constant size. Each individual is represented by a vertical line, and time runs in the vertical direction. Every individual is characterized by a type (its color), and can perform three different actions at any instant of time: it can mutate (change color); it can reproduce (where the offspring replaces a randomly chosen individual, as indicated by an arrow), or two individuals may recombine (cross over), which results in two new, 'mixed' types.

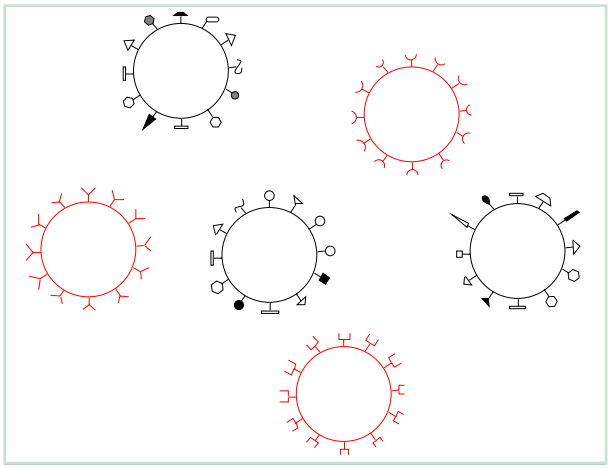


Fig. 2: T cells (red) at work, trying to recognize foreign antigens in a mixture of foreign and self molecules on the surface of antigen-presenting cells (black).

Biomathematics and Theoretical Bioinformatics

Mathematical Population Genetics | Mathematical Immunobiology

Prof. Dr. Ellen Baake
Biomathematics and Theoretical Bioinformatics
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4869
fax +49-521-106 6490
email ebaake@techfak.uni-bielefeld.de
url www.techfak.uni-bielefeld.de/ags/bm/

Involvement in Study Courses

The group is involved in the mathematics education for the Bachelor, Masters, and Diploma programs at the Faculty of Technology, and in courses in mathematical biology.

Curriculum Vitae

1985: Diploma in Biology, University of Bonn
1989: Ph.D. in Theoretical Biology, University of Bonn
1989-1992: Research associate at the Mathematics Institute, University of Augsburg
1992-1996: **Research associate at the Max Planck Institute for** Developmental Biology, Tübingen
1996: Research fellowship at the Institute for Cell, Animal, and Population Biology, University of Edinburgh (UK)
1996-2000: **Research associate at the Zoology Department, University** of Munich
1999: Habilitation for Zoology and Theoretical Biology, University of Munich
2000-2001: 'Oberassistentin' (C2) at the Zoology Department, University of Munich
2001-2004: PostDoc at the Department of Mathematics and Computer Science, University of Greifswald
WS 2001/02: Temporary full professorship (C4) in Genome Informatics, Faculty of Technology, Bielefeld University
SS 2004: Visiting professorship at the Faculty of Mathematics, University of Vienna
Since 2004: Professor (C3) for Biomathematics and Theoretical Bioinformatics at the Faculty of Technology, Bielefeld University

Members

I. Hildebrandt | N. Zint |

Publications

Baake, E. *et al.*, 2005. **An asymptotic maximum principle for essentially linear evolution models.** J Math Biol 50, 83-114
Georgii, H.-O. and Baake, E. 2003. **Supercritical multitype branching processes: The ancestral types of typical individuals.** Adv Appl Prob 35, 1090-1110
Baake, M. and Baake, E. 2003. **An exactly solved model for mutation, recombination and selection.** Can J Math 55, 3-41
Hermisson, J. *et al.*, 2002. **Mutation-selection balance: Ancestry, load, and maximum principle.** Theor Pop Biol 62, 9-46
Baake, E. and Gabriel, W. 2000. **Biological evolution through mutation, selection, and drift: An introductory review.** Ann Rev Comp Phys VII, 203-264
Baake, E. *et al.*, 1997. **Ising quantum chain is equivalent to a model of biological evolution.** Phys Rev Lett 78, 559-562

Applied Neuroinformatics

The junior research group Applied Neuroinformatics was established in October 2002. Since then it is led by Juniorprof. Dr. T. W. Nattkemper and has become a vital member of the CeBiTec, the International Graduate School in Bioinformatics and Genome Research, the Research Training Group 'Strukturbildungsprozesse', and the Faculty of Technology. The group cooperates with other university groups in Bielefeld (like the Neural Networks group, the Theoretical Physics group, the Faculty of Biology and the Department of Public Health), local medical service centers (like the City Hospital, the Institute for Neuropathology and the Gilead Hospital) as well as international partners (like for instance the Institute of Cancer Research (UK), Unilog IT Services (Swiss), the Universidade Federal do Caera (Brazil) and the Florida State University (USA)). The group currently consists of seven Ph.D. students and eleven undergraduates.

Research Interests

Nowadays a growing number of computer science applications from the field of computational intelligence in the domains of bioinformatics and medical data analysis can be observed. The applied algorithms are rooted in the fields of pattern recognition, artificial neural networks (ANN) or machine learning (ML) and image processing. ANN and ML algorithms can learn non-linear mappings from even noisy labelled data sets and have the potential to analyze complex data structures in high-dimensional spaces. The research of the Applied Neuroinformatics group aims at exploring these promising potentials for the analysis of data from biology and biomedicine as well as clinical data. One focus of the group's attention is the development of approaches that support the explorative data analysis by non-computer-expert users. This can be achieved for instance by developing software tools which can be used more intuitively based on the primary expertise of the biologist. Using these software tools the user can explore data in data driven visualizations (see Fig. 1) or analyze digital images using algorithms which have been tuned based on expert knowledge (see Fig. 2). Other works apply novel dimension reduction and clustering techniques to find hidden regularities in biomedical data (see Fig. 3). The fascinating advantage of ANN and ML algorithms is the way they are adapted to new environments, data sets or imaging parameters. To tune the algorithm to a change in the environment or in the experimental parameters, a new training set has to be supplied. In the generation of the training set, the user can use his primary expertise or background knowledge to label

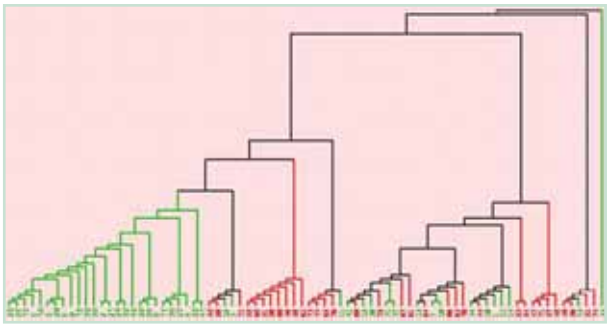


Fig. 1: New clustering approaches are applied to data sets from microarray experiments. In this case, gene expression patterns from 78 patients suffering from breast cancer are clustered. The cluster structure is visualized as a dendrogram showing a good separation of cases building metastases (red) and those who do not (green). The bottom number is the case index. Such visualization is used by biologists and public health researches to browse data for hidden relations to other clinical parameters.

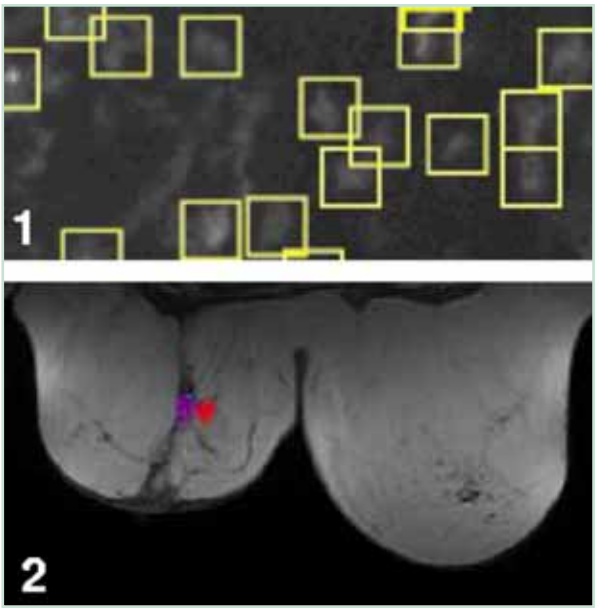


Fig. 2: Supervized learning algorithms are trained to detect biologically significant objects in multivariate image data. In image 1 a system has been trained to detect immunofluorescent lymphozytes in a fluorescence micrograph. Image 2 shows an axial slide in a dynamic contrast enhanced magnetic resonance image (DCE MRI) of a female breast. Machine learning algorithms were applied to detect and classify suspicious tissue to show characteristics of a malignant tumor (red) or a benign one (blue).

Juniorprof. Dr. Ing. Tim W. Nattkemper
Applied Neuroinformatics
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 6059
fax +49-521-106 6011
email tnattkem@techfak.uni-bielefeld.de
url www.techfak.uni-bielefeld.de/ags/ani

the data with class information (like a sample ID or state of disease) or by marking immunofluorescent cell structures in a digital fluorescence micrograph on a screen. The application of learning algorithms in such frameworks demands further research, since an application of these algorithms in a real world study is not straightforward, which is mainly caused by missing prerequisites. Some of the most frequent problems are for example unbalanced data sets or missing background knowledge like gold standards. All research projects of the group include the development of solutions to these problems. One major prerequisite for solving these problems has always been the close collaboration with partners from biology and medicine.

Involvement in Courses of Study

The group regularly carries out the lectures Biomedical Image Analysis and Information Visualization. In addition the group organizes seminars in Data Mining, Machine Learning in Bioinformatics, Statistical Data Analysis as well as a basic seminar Milestones of Computer Sciences, where students are also taught how to give a talk.

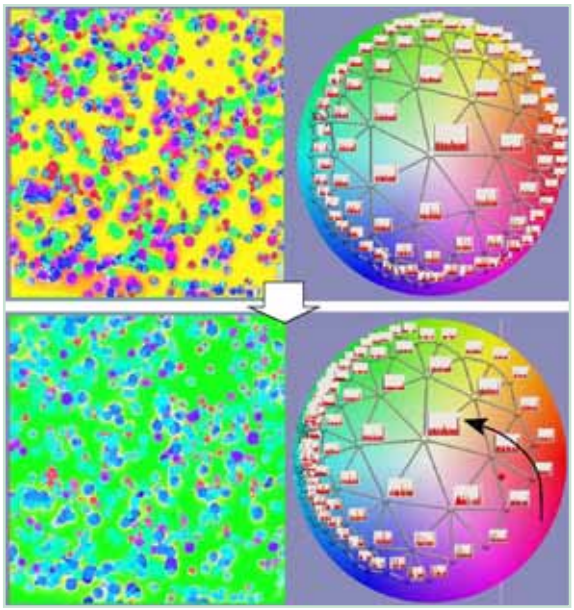


Fig. 3: The HyDE (HYperbolic Data Explorer) system has been invented to assist biomedical researchers in the interactive exploration of multivariate image data. Right: Using the hyperbolic selforganizing map (HSOM), the signal patterns are mapped onto a lower dimensional grid. Left: Interactive pseudocoloring is achieved by mapping color scales on the low dimensional grid.

Curriculum Vitae

1997: Diploma in Applied Computer Science in the Natural Sciences
1997-2001: Scholarship holder from the Research Training Group 'Strukturbildungsprozesse'
2001: Ph.D. about Neural Network-based Analysis of Multivariate Fluorescence Micrographs
Since 2002: Juniorprofessor in Bielefeld with his own junior research group Applied Neuroinformatics
Teaches and works in the field of Biomedical Image Analysis, Machine Learning, Data Mining and Information Visualization

Members

B. Arnrich | H. große Deters | J. Eickmeyer | M. Grahl | B. Hafer | J. Herold | J. Huth | C. Lange | B. Lessmann | C. Loyek | C. Müller | A. Saalbach | P. Schneider | W. Timm | T. Twellmann | C. Varini | D. Voss | Y. Wang | N. Wei |

Publications

Twellmann, T. *et al.*, 2005. **An adaptive tissue characterization network for model-free visualization of dynamic contrast enhanced magnetic resonance image data.** IEEE Trans Med Imag, in press

Saalbach, A. *et al.*, 2005. **Image fusion based on topographic mappings using the hyperbolic space.** Information Visualization, in press

Nattkemper, T.W. *et al.*, 2005. **Evaluation of radiological features for breast tumour classification in clinical screening with machine learning methods.** Artif Intell Med 34, 129-139

Nattkemper, T.W. 2004. **Multivariate image analysis in biomedicine: A methodological review.** J Biomed Inform 37, 380-391

Nattkemper, T.W. *et al.*, 2003. **Human vs. Machine: evaluation of fluorescence micrographs.** Comput Biol Med 33, 31-43

Nattkemper, T.W. *et al.*, 2001. **A neural classifier enabling high-throughput topological analysis of lymphocytes in tissue sections.** IEEE Trans Inform Technol Biomed 5, 138-149

Computational Mass Spectrometry

Computational Analysis of Mass Spectrometry Data for Proteomics | Genomics | Metabolomics

Dr. Sebastian Böcker
Computational Mass Spectrometry
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4755
fax +49-521-106 6495
email sebastian.boecker@cebitec.uni-bielefeld.de
url www.gi.cebitec.uni-bielefeld.de/ims

Curriculum Vitae

Diploma in Mathematics at Hamburg University
Ph.D. in Mathematics at Bielefeld University
2000-2001: Senior scientist Bioinformatics at SEQUENOM GmbH, Hamburg
2002-2003: Senior scientist Bioinformatics at SEQUENOM Inc., San Diego
Since 03/2003: Head of the junior research group Computational Mass Spectrometry
Winner of the DFG Computer Science Action Program (Emmy Noether Program)
Program committee member, ISMB conference 2005

Members

M. Kaltenbach | Dr. Zs. Lipták | Dr. V. Mäkinen | T. Marschall | M. Martin | A. Pervukhin | K. Runte | M. Steinrücken | H. Sudek | W. Timm |

Publications

Böcker, S. and Kaltenbach, H.-M. 2005. **Mass spectra alignments and their significance.** In Proc of CPM, 429-441
Böcker, S. and Mäkinen, V. 2005. **Maximum line-pair stabbing problem and its variations.** In Proc of EWCG, 183-186
Böcker, S. and Lipták, Zs. 2005. **Efficient mass decomposition.** In Proc of ACM SAC, 151-157
Ehrich, M. *et al.*, 2005. **Multiplexed discovery of sequence polymorphisms using base-specific cleavage and MALDI-TOF MS.** Nucleic Acids Res 33, e38
Böcker, S. 2004. **Sequencing from compomers: Using mass spectrometry for DNA *de-novo* sequencing of 200+ nt.** J Comput Biol 11, 1110-1134
Cieliebak, M. *et al.*, 2004. **Algorithmic complexity of protein identification: Combinatorics of weighted strings.** Discr Appl Math 137, 27-46

Computational Mass Spectrometry

The junior research group Computational Mass Spectrometry headed by Dr. S. Böcker was founded in March 2003. Projects are primarily funded by the German Research Foundation (DFG) through the Computer Science Action Program (Emmy Noether Program). Ph.D. students are also supported by the International Graduate School in Bioinformatics and Genome Research.

Research Interests

The group approaches computational problems in mass spectrometry analysis for proteomics, genomics, and metabolomics. For that, a variety of techniques from mathematics and computer science, among them combinatorics and graph theory, algorithm design, statistics, and computational geometry are used. Projects include alignment and statistical analysis of protein mass fingerprints, analysis of DNA mass spectra for pathogen identification, weighted strings and decomposition of masses for high-resolution mass spectrometry, robust recalibration of mass spectra, and prediction of peak intensities using machine learning techniques. Other research interests include phylogenetics and compressed data structures. In-house collaborations have been established with several groups, among them the department of Proteome and Metabolome Research of Prof. Dr. K. Niehaus and the junior research group Applied Neuroinformatics of Juniorprof. Dr. T. W. Nattkemper. Outside Bielefeld University, the group collaborates with the Institute of Computer Science at the Freie Universität Berlin, SEQUENOM Inc. in San Diego, and others.

Involvement in Courses of Study

The group provides the module Algorithms for Mass Spectrometry and other regular courses for the Bachelor and Master of Science programs Bioinformatics and Genome Research and Applied Computer Science in the Natural Sciences. It is also actively involved in courses at the International Graduate School in Bioinformatics and Genome Research.

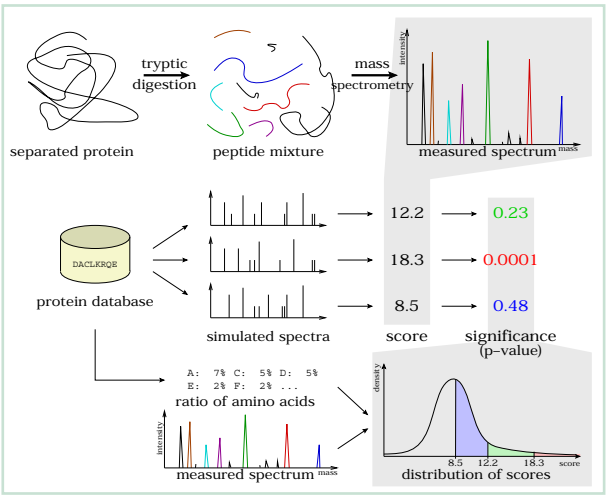


Fig. 1: Identification of proteins using protein mass fingerprints and statistical evaluation of similarity scores *via* p-values.

Combinatorial Search Algorithms in Bioinformatics

The junior research group Combinatorial Search Algorithms in Bioinformatics is funded by the Alexander von Humboldt Foundation and the Federal Ministry of Education and Research (BMBF), within the Sofja Kovalevskaja Program 2004. At the moment, the group includes the group leader and Sofja Kovalevskaja awardee, Dr. F. Cicalese (Italy), a Ph.D. student, L. Ulveland (Sweden), and a student assistant and programmer, M. Rolf.

Research Interests

The main research activity of the group is the design and analysis of efficient algorithms for the solution of combinatorial search problems arising in the field of bioinformatics. The group concentrates on the solution of concrete problems in genetics and proteomics but also on the new theoretical issues that such problems raise in the field of combinatorial search theory, specifically combinatorial group testing. Presently, the group is studying the employment of the group testing machinery to tackle the following problems in molecular biology: splice site detection, MS-protein mixtures identification, q-gram identification. On a more theoretical level, the group investigates efficient procedures for accessing data bases including complex data objects. In-house collaborations have been established with several groups, among them the research group Combinatorics and Information Theory of Prof. Dr. R. Ahlswede and the junior research group Computational Mass Spectrometry of Dr. S. Böcker. Outside Bielefeld University, the group collaborates with the departments of Computer Science at Chalmers University (Sweden), at the Pontifica Universidade do Rio de Janeiro (Brasil) and at the University of Salerno (Italy), as well as with the department of Mathematics at the University of Florence (Italy).

Involvement in Courses of Study

For the academic year 2005-2006, the group provides the modules 'Elements of Combinatorics for Computer Scientists' (1st semester) and 'Complex Interactions in Molecular Systems: A Game Theoretic Approach' (2nd semester) and is also actively involved in courses at the International Graduate School in Bioinformatics and Genome Research.

Dr. Ferdinando Cicalese
Combinatorial Search Algorithms in Bioinformatics
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5163
fax +49-521-106 6495
email nando@cebitec.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/~nando

Curriculum Vitae

1995: Laurea (cum laude) in Computer Science at University of Salerno (Italy)
1996: Visiting researcher at Middlesex University (London) funded by the Italian National Council of Research (CNR)
2001: Ph.D. in Computer Science at University of Salerno
2001: Award for the best Italian Ph.D. thesis in Theoretical Computer Science
2001: Committee member of the international workshop Combinatorics of Search Sorting and Coding 2001 (COSSAC 2001)
Since 03/2001: Research assistant (with tenure) at Department of Computer Science and Applications, University of Salerno
2004: Sofja Kovalevskaja Award of the Alexander von Humboldt Foundation and the Federal Ministry of Education and Research (BMBF)

Members

L. Ulveland | M. Rolf |

Publications

Cicalese, F. and Laber, E. 2006. **On the competitive ratio of evaluating priced functions.** In Proc of SODA, to appear
Cicalese, F. and Deppe, C. 2005. **Perfect minimally adaptive q-ary search with unreliable tests.** J Stat Plan Inference, to appear
Cicalese, F. and Laber, E. 2005. **An optimal algorithm for querying priced information: monotone boolean functions and game trees.** In Proc of ESA, 664-676
Cicalese, F. and Laber, E. 2005. **A new strategy for querying priced information.** In Proc of STOC, 674-683
Cicalese, F. *et al.*, 2005. **Overlaps help: improved bounds for group testing with interval queries.** In Proc of COCOON, 935-944
Cicalese, F. *et al.*, 2005. **Optimal group testing algorithms with interval queries and their application to splice site detection.** In Proc of WBRA, 1029-1037
Cicalese, F. and Vaccaro, U. 2004. **Bounding the average length of optimal source codes *via* majorization theory.** IEEE Trans Inform Theory 50, 633-637

High Performance Bio-Computing

HPC in Genomics | Data Integration in Complex Systems | Visualization of Complex Data

Dr. Dirk J. Evers
High Performance Bio-Computing
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

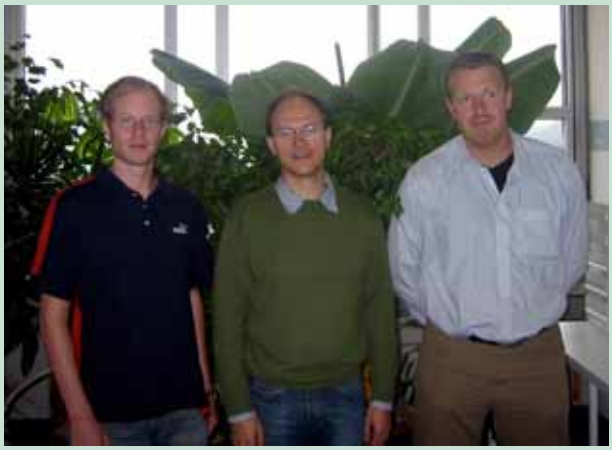
phone +49-521-106 3793
fax +49-521-106 6490
email dirk.evers@cebitec.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/groups/hpbc

Curriculum Vitae

Diploma in Applied Computer Science in the Natural Sciences at Bielefeld University
Ph.D. in Computer Science at Bielefeld University
2001-2003: Informatics Research Scientist at Exelixis Deutschland GmbH, Tübingen
Since 10/2003: Head of the junior research group High Performance Bio-Computing
Since 01/2005: Executive Director of the International Graduate School in Bioinformatics and Genome Research

Members

M. Beckstette | F. Lipsmeier |



Publications

Wedemeyer, N. *et al.*, 2000. **Conservation of the 3'-untranslated region of the *Rab1a* gene in amniote vertebrates: Exceptional structure in marsupials and possible role for posttranscriptional regulation.** FEBS Lett 477, 49-54

Evers, E. and Giegerich, R. 1999. **RNA movies: Visualizing RNA secondary structure spaces.** Bioinformatics 15, 32-37

Stoye, J. *et al.*, 1998. **Rose: Generating sequence families.** Bioinformatics 14, 157-63

Stoye, J. *et al.*, 1997. **Generating benchmarks for multiple sequence alignments and phylogenetic reconstructions.** Proc Int Conf Intell Syst Mol Biol 5, 303-306

High Performance Bio-Computing

The junior research group High Performance Bio-Computing headed by Dr. D. J. Evers was founded in November 2003. The group is funded through the NRW Graduate School Program of the 'Ministerium für Innovation, Wissenschaft, Forschung und Technologie' (MIWFT) of the State Northrhine-Westfalia (NRW) as part of the International Graduate School in Bioinformatics and Genome Research.

Research Interests

The group applies high performance computing strategies to solve problems on large data sets in bioinformatics. Interests focus on parallel algorithms for sequence assembly, data integration in complex systems, interactive problem solving on grid computers, very large scale indexing approaches and parallelization of dynamic programming algorithms. To this end, techniques from bioinformatics, applied computer science, computational geometry, algorithm design and parallel algorithm design are used. In conjunction with message passing or threading toolkits the developed algorithms are tested on the grid- and multi-processor computers available at the CeBiTec. Current projects are parallel genome assembly, high-throughput sequence analysis, and algorithms for massive short-range sequencing. Other research interests include RNA secondary structure visualization, sensitive matching in enhanced suffix arrays, and algorithms for the fast identification of regulatory networks. In-house the group collaborates with the junior research group Genomics of Legume Plants and the Bioinformatics Resource Facility. Outside Bielefeld University, the group collaborates with Darren Platt (Head of Informatics, Joint Genome Institute) on parallel genome assembly pipelines.

Involvement in Courses of Study

The group provides courses mainly for the curriculum of the International Graduate School in Bioinformatics and Genome Research, but also in the B.Sc. and M.Sc. programs Bioinformatics and Genome Research and Applied Computer Science in the Natural Sciences. The course topics cover applied computer science, software engineering, and bioinformatics tool usage, as well as scientific soft skills.

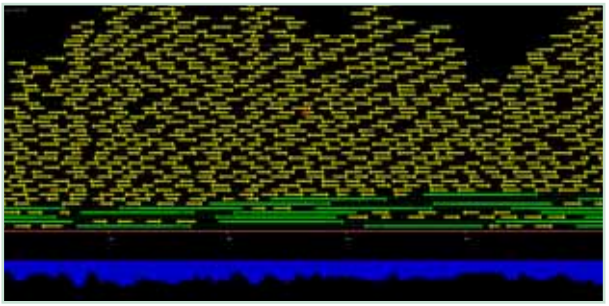


Fig. 1: Visualization of part of a forge/G assembly of *Prochlorococcus*: Conventional sanger sequenced reads with 2X coverage (green) together with short reads from a 454 run (yellow) and the consensus quality (blue).

Algorithms and Statistics for Systems Biology

The junior research group Algorithms and Statistics for Systems Biology headed by Dr. S. Rahmann was founded in March 2004 to approach computational problems in bioinformatics and systems biology from both a stochastic and a combinatorial viewpoint.

Research Interests

The group is interested in modeling transcriptional regulation, e.g. in modeling and efficient discovery of binding site motifs, and in the possibilities and limitations of reverse engineering regulatory networks. Group members also have considerable experience in microarray design and optimization. One project with the aim of modeling and predicting cross-hybridization will help to increase data quality in transcriptomics and to integrate microarray data into whole systems biology projects. The group maintains close links with other junior research groups and with the chair of Genetics, for example, in establishing a regulation database for Corynebacteria. Outside Bielefeld University, the group collaborates, for example, with the Bioinformatics department at the Würzburg University on a biodiversity and species barcoding project, with the Max Planck Institute for Molecular Genetics in Berlin on transcriptional regulation, and with the Riley Hospital for Children (Indiana, USA) on clinical biomarker identification.

Involvement in Courses of Study

The group is actively involved in statistical courses at the International Graduate School in Bioinformatics and Genome Research, as several of the Ph.D. students receive fellowships. The group provides regular courses, like Phylogenetics, and Algorithmic Statistics in Bioinformatics, for the Bachelor- and Master of Science programs Bioinformatics and Genome Research and Applied Computer Science in the Natural Sciences and contributes a mathematical course to the newly established Master program Genome Based Systems Biology.

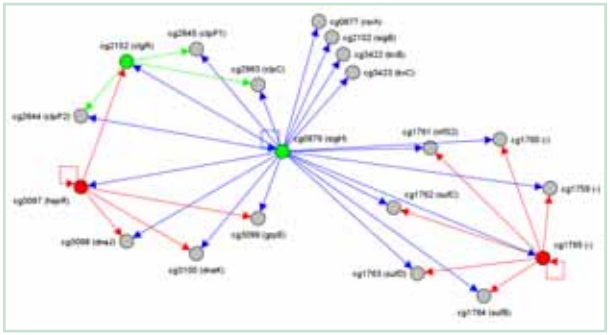


Fig. 1: A small part of the transcriptional regulation network of *Corynebacterium glutamicum*, as represented by CoryneRegNet, a database of regulatory relationships in Corynebacteria, developed in the Algorithms and Statistics for Systems Biology group.

Dr. Sven Rahmann
Algorithms and Statistics for Systems Biology
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 3841
fax +49-521-106 6495
email sven.rahmann@cebitec.uni-bielefeld.de
url gi.cebitec.uni-bielefeld.de/assb/

Curriculum Vitae

2000: Diploma in Mathematics, University of Heidelberg
2004: Ph.D. in Bioinformatics, Freie Universität Berlin, nominated for the GI dissertation award 2005
Pre-doctoral research at the German Cancer Research Center, Heidelberg, and at the Max Planck Institute for Molecular Genetics, Berlin
Since 03/2004: Junior research group leader at the Faculty of Technology, Bielefeld University
Program committee member, IEEE CSB conference 2004
Co-Chair, ACM symposium of applied computing, Bioinformatics track 2005

Members

J. Baumbach | S. A. de Carvalho Jr. | E. Fritzilas | C. Höner zu Siederdissen | S. Schirmer |

Publications

Rahmann, S. 2003. **Fast large scale oligonucleotide selection using the longest common factor approach.** J Bioinform Comput Biol 1, 343-361

Rahmann, S. *et al.*, 2003. **On the power of profiles for transcription factor binding site detection.** Statistical Applications in Genetics and Molecular Biology 2, Article 7

Rahmann, S. 2003. **The shortest common supersequence problem in a microarray production setting.** Bioinformatics 19, ii156-ii161

Bioinformatics of Regulation

Genome Research | Regulatory Elements | RNA Secondary Structure Analysis

Dr. Marc Rehmsmeier
Bioinformatics of Regulation
Faculty of Technology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

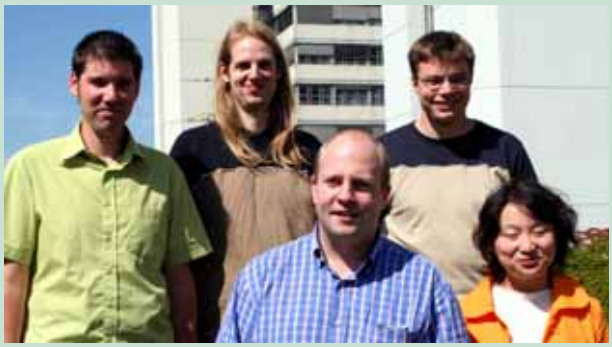
phone +49-521-106 2905
fax +49-521-106 6411
email marc@techfak.uni-bielefeld.de
url www.techfak.uni-bielefeld.de/~marc/

Curriculum Vitae

1990-1996: Study of Applied Computer Science in the Natural Sciences, Bielefeld University
1991: Winner of the 'Bundeswettbewerb Informatik'
1991-1995: Scholarship of the 'Studienstiftung des Deutschen Volkes'
1996: Master's in Computer Science at the senior research group of Practical Computer Science; advisor: Prof. Dr. R. Giegerich
1996-2001: Ph.D. at the department of Theoretical Bioinformatics at the **'Deutsches Krebsforschungszentrum' (DKFZ), Heidelberg;** advisor: Prof. Dr. M. Vingron
2002-2004: Mentor at the International Graduate School in Bioinformatics and Genome Research, CeBiTec, Bielefeld University
Since 2004: Leader of the junior research group Bioinformatics of Regulation, CeBiTec, Bielefeld University

Members

J. Ding | Dr. C. Drepper | T. Fiedler | A. Hauenschild | R. Heinen | G. Obernosterer |



Publications

Rehmsmeier, M. *et al.*, 2004. **Fast and effective prediction of microRNA/target duplexes.** RNA 10, 1507-1517
Alam, I. *et al.*, 2004. **Comparative homology agreement search: An effective combination of homology-search methods.** Proc Natl Acad Sci U S A 101, 13814-13819
Giegerich, R. *et al.*, 2004. **Abstract shapes of RNA.** Nucleic Acids Res 32, 4843-4851
Ringrose, L. *et al.*, 2003. **Genome-wide prediction of Polycomb/Trithorax Response Elements in *Drosophila melanogaster*.** Dev Cell 5, 759-771

Bioinformatics of Regulation

The junior research group Bioinformatics of Regulation was established in July 2004 and is headed by Dr. M. Rehmsmeier. The group is part of the Faculty of Technology and of the Institute for Bioinformatics at the CeBiTec. Currently, the group consists of the head, one PostDoc, five Ph.D. students, a Bachelor student, and a Master student.

Research Interests

The group's main interests are RNA Bioinformatics and Regulatory DNA Elements. In RNA Bioinformatics, the focus is on the analysis of microRNAs and their targets. microRNAs are short RNAs of around 22 nucleotides, which post-transcriptionally regulate the expression of their target genes by binding to the target mRNAs. In cases of perfect or near-perfect complementarity between microRNA and target site, the target mRNA is cleaved and subsequently degraded. In cases of weaker complementarity, translation of the mRNA into protein is inhibited. The microRNA pathway is a complex mechanism of regulation, which importance and even existence has only recently been recognized. The most prominent result of the work so far is the program RNAhybrid which predicts microRNA target genes. RNAhybrid considers binding energies of microRNA/target duplexes, statistical significance of individual and multiple binding sites, and evolutionary conservation of microRNA/target relationships (see Fig. 1). The group is strongly interested in the biological relevance of its work and thus takes care in the experimental verification of predictions, either by its own wet-lab activities or by collaborations with external groups.

Involvement in Courses of Study

The group contributes to the Bachelor and Master courses Bioinformatics and Genome Research with lectures in bioinformatics, e.g. on basic models of sequence analysis, and to computer science curriculae with more fundamental lectures, e.g. on algorithms and data structures.

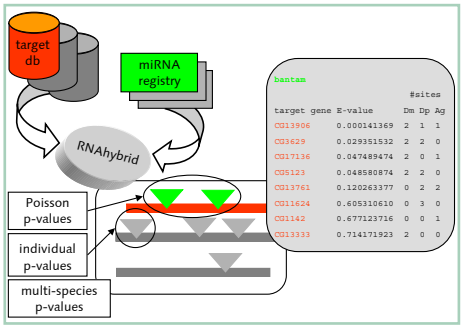


Fig. 1: RNAhybrid takes as input a set of potential target mRNAs and a set of microRNAs. For each microRNA/target pair, energetically favourable binding sites are determined. Statistical significance of binding sites is assessed in a step-wise fashion with p-values of individual sites, p-values of multiple sites (Poisson p-values), and multi-species p-values.

Technology Platform Bielefeld University Bioinformatics Server (BiBiServ)

Bioinformatics WebServices | Educational Media Design

The BiBiServ

The Bielefeld University Bioinformatics Server (BiBiServ) was established in 1996 by the research group of Practical Computer Science at the Faculty of Technology headed by Prof. Dr. R. Giegerich. Since 2001 the BiBiServ is supported by the DFG Initiative in Bioinformatics.

Research Interests

The BiBiServ supports internet-based collaborative research and education in bioinformatics. Currently, more than 30 software tools and various educational media are available. These include tools from different areas such as genome comparison, alignment, primer design, RNA structures, and evolutionary relationships. The BiBiServ makes tools developed at different CeBiTec groups available to the bioinformatics community. The group supports authors in integrating their tools into the server environment and designing both HTML-based interfaces as well as WebServices. WebServices allow an easy integration of remote tools in workflows based on standardized interfaces. Reliable service and user support are provided, where applicable even if the author of the tool left Bielefeld University. BiBiServ is a member of the Helmholtz Open BioInformatic Technologies network (HOBIT). The HOBIT initiative is dedicated to form the core of a network linking bioinformatics centers together. It shall be understood as an initial organizational and technological platform for interconnection of bioinformatics activities. The aim of the network is to concatenate applications and resources in a simple way using WebServices technology.

The BiBiServ Media & Distance Education section supports teaching in bioinformatics with internet-based multimedia courses. Currently, there are five online courses and tutorials available on BiBiServ. The most recent ones are 'Sequence Analysis with Distributed Resources' (a Web-based practical course on sequence analysis using resources from all over the world) and The ADP Pages (interactive pages that allow to study and experiment with classical dynamic programming algorithms).

Involvement in Courses of Study

The group contributes courses to the programs Applied Computer Science in the Natural Sciences, Bioinformatics and Genome Research, Molecular Biotechnology, and Media Design.

Fig. 1: E2G is a WebService which efficiently maps large EST data sets to genomic DNA. The server hosts huge EST databases of a few Gb in size in indexed data structures. This allows users to rapidly detect new genes, verify the exon-intron structure of predicted genes and determine splice variants in a genomic region of interest.

Alexander Sczyrba
BiBiServ
Institute for Bioinformatics
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 2910
fax +49-521-106 6411
email asczyrba@techfak.uni-bielefeld.de
url bibiserv.techfak.uni-bielefeld.de/

Curriculum Vitae

1998: Diploma in Computer Science in the Natural Sciences at Bielefeld University
1999-2000: Guest investigator at The Rockefeller University, New York, USA
2000-2002: Staff member at research group **'Praktische Informatik'**, Bielefeld University
Since 2002: Head of the Bielefeld University Bioinformatics Server (BiBiServ)

Members

S. Hartmeier | A. Kaiser | S. Konermann | J. Krüger | K. Löwenthal | J. Reinkensmeier |

Publications

Sczyrba, A. *et al.*, 2005. **Full length cDNA prediction and cross species mapping in *Xenopus laevis*.** BMC Genomics 6:123

Krüger, J. *et al.*, 2004. **e2g: An interactive web-based server for efficiently mapping large EST and cDNA sets to genomic sequences.** Nucleic Acids Res 32, W301-W304

Taher, L. *et al.*, 2004. **AGenDA: Gene prediction by cross-species sequence comparison.** Nucleic Acids Res 32, W305-W308

Sczyrba, A. *et al.*, 2004. **Identification of 10,500 *Xenopus laevis* full length clones through EST clustering and sequence analysis.** In Proc in GCB

Beckstette, M. *et al.*, 2004. **Genlight: Interactive high-throughput sequence analysis and comparative genomics.** Journal of Integrative Bioinformatics 0008

Sczyrba, A. *et al.*, 2003. **RNA-related tools on the Bielefeld Bioinformatics Server.** Nucleic Acids Res 31, 3767-3770

Morgenstern, B. *et al.*, 2003. **AltAVisT: A WWW tool for comparison of alternative multiple alignments.** Bioinformatics 19, 425-426

The Institute for Genome Research

The Institute for Genome Research was founded in February 2003 when the intensive activities at Bielefeld University in bacterial genomics were extended in the context of the DFG Initiative in Bioinformatics. A new chair for Genome Research was established that complements the research on microbe genomes and plant-microbe interactions with research activities in the field of functional plant genomics (head: Prof. Dr. B. Weisshaar).
The Institute for Genome Research is a forum for communication and joint research in genomics at Bielefeld University that relies on state-of-the-art technology. The increasing automation of modern molecular biology techniques requires complex and expensive equipment. This is especially true for DNA sequencing, clone and library handling, microarray technology for transcriptional profiling, quantitative RT-PCR, 2D-protein analyses, and mass spectroscopy for protein and metabolite analyses. At the Institute for Genome Research, the Technology Platform Systems Biology supports these and other technologies to allow high-level access to transcriptomics,

A robotic device to load the samples for MALDI-TOF (Matrix-Assisted Laser Desorption Ionisation - Time Of Flight; a specific type of mass spectroscopy) analyses onto the target support arrays. The samples are spotted onto a metal support as an array of 96 or 384 spots. The results allow for example the identification of proteins present in the samples on the basis of molecular masses of peptides.

Prof. Dr. Bernd Weisshaar
Institute for Genome Research
Center for Biotechnology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 6873
fax +49-521-106 6423
email genomforschung@uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/IfG

proteomics and metabolomics technology.
At present, four chairs from the Faculty of Biology covering Genetics, Genome Research, Biochemistry and Plant Physiology, Gene Technology and Microbiology as well as the department Proteome and Metabolome Research are located at the institute. In addition, three junior research groups are active in the areas of Transcriptomics, RNA-Based Regulation and Genomics of Legume Plants. The equipment and the research capacity of the institute is used extensively in the demanding education of B.Sc., M.Sc., and Ph.D. students, most prominently for those enrolled in the programs for Bioinformatics and Genome Research as well as Genome Based Systems Biology.

Contributing Units

Biochemistry and Plant Physiology;
Prof. Dr. K.-J. Dietz

Gene Technology and Microbiology;
Prof. Dr. R. Eichenlaub

Genetics;
Prof. Dr. A. Pühler

Genome Research;
Prof. Dr. B. Weisshaar

Proteome and Metabolome Research;
Prof. Dr. K. Niehaus

Transcriptomics;
HD Dr. A. Becker

Genomics of Legume Plants;
PD Dr. H. Küster

RNA-Based Regulation;
PD Dr. T. Merkle

Technology Platform Systems Biology;
Dr. J. Kalinowski

A 96-capillary DNA sequencer from Applied Biosystems for high-throughput DNA sequencing. The 3730xl instrument takes up stacks of 96-well microtiterplates containing sequencing reactions with four different fluorescent terminators, one for each of the four bases in DNA. The sensitive detection of the fluorescent signals allows read lengths up to more than 900 bases per read.

Biochemistry and Plant Physiology

The chair is dedicated to bridging the disciplinary scales of biochemistry, molecular biology, biotechnology and ecophysiology of plants, for example by analyzing the dynamics and function of single molecule processes *in vitro* and *in vivo* with the aim to understand their contribution to the ecological processes of adaptation, maximization of fitness and biomass production. This integrative approach is addressed both in teaching within various B.Sc., M.Sc. and Ph.D. programs and in current research. In addition, the chair organizes a trainee program for technical staff ('Ausbildung von Biologielaboranten').

Research Interests

Current research addresses the biochemical and genetic flexibility of plants to adapt to changing environment and to optimize biomass production (Fig. 1). Most tolerance traits are not expressed constitutively. Therefore, environmental cues first need to be sensed and signal transduction initiated in order to trigger the optimum systems' responses and to achieve maximum fitness and productivity of plants. Investigated environmental factors are salinity, a productivity limiting factor of global scale, heavy metal contaminated soils, soil deficiencies in essential nutrient elements, drought and excess light. Signal transduction within and between cell compartments and subsequent integration of the diverse signalling networks connects the processes of signal perception to gene regulation by specific transcription factors (Fig. 2). The work relies on methods of transcriptome, proteome and metabolome analyses (Fig. 3). Redox-, hormone-, metabolite-dependent regulation of photosynthesis is analyzed on essentially all molecular levels. The specific function and assembly of plant proteins is addressed *in vitro* and *in vivo*. Heterologously produced proteins following site-directed mutagenesis of their amino acid sequences are analyzed for specific functional, catalytic and binding properties. Transgenic approaches are employed to relate gene function to plant performance. Plants are selected in mutant screens that have specific defects in signalling to identify novel regulators. Plants that overexpress or lack specific proteins such as the peroxiredoxins show increased or decreased stress tolerance. A major emphasis is placed on oxidative stress that is involved likewise in animal and plant disease and ageing, but also in stress hardening and tolerance development. Biophysical methods such as fluorescence energy transfer and confocal laser

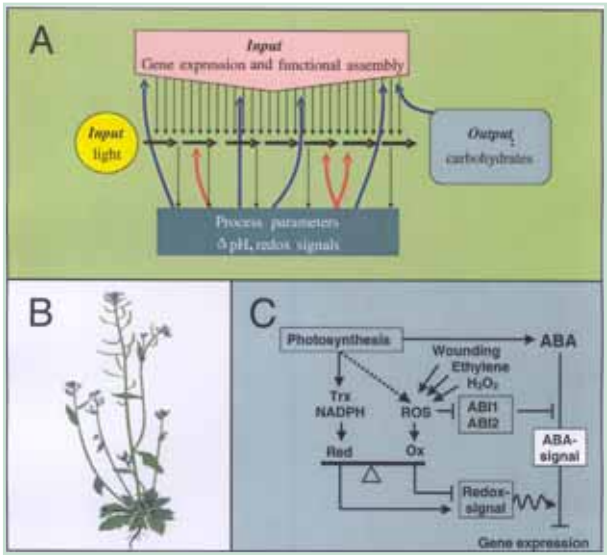


Fig. 1: Photosynthesis sustains life on earth. Exogenous and endogenous factors as input define the photosynthetic activity, measured as carbohydrate production as output. (A) A complex set of monitored parameters control the process. (B) *Arabidopsis thaliana* was the first plant whose complete genome was sequenced and is the genetic model used at the chair. (C) Regulation of gene expression depends on integrated signalling pathways as shown here as a model for a subset of genes.

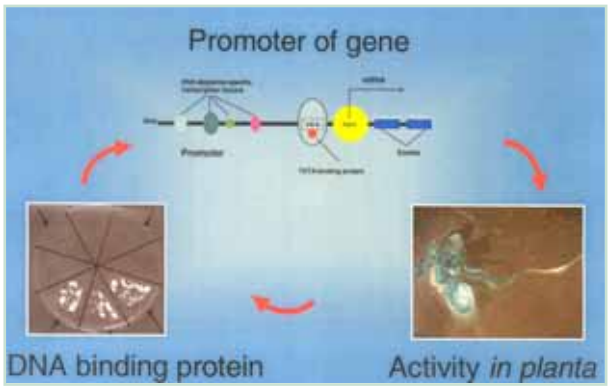


Fig. 2: Regulation of gene expression depends on cis-elements. The chair investigates the specific regulation of genes in response to environmental stress, for instance by reporter gene analysis in transgenic plants. Blue color indicates promoter activity. Specific binding proteins are isolated by using a yeast system. The yeast strains only grow after binding of a regulatory plant protein to the DNA.

scanning microscopy allow to visualize interacting proteins in the cell.

Involvement in Courses of Study
The chair is involved in four Bachelor- and five Master of Science programs, namely Molecular Cell Biology, Genome Based Systems Biology, Ecology and Biodiversity, Molecular Biotechnology and Biochemistry, and the International Graduate School in Bioinformatics and Genome Research.

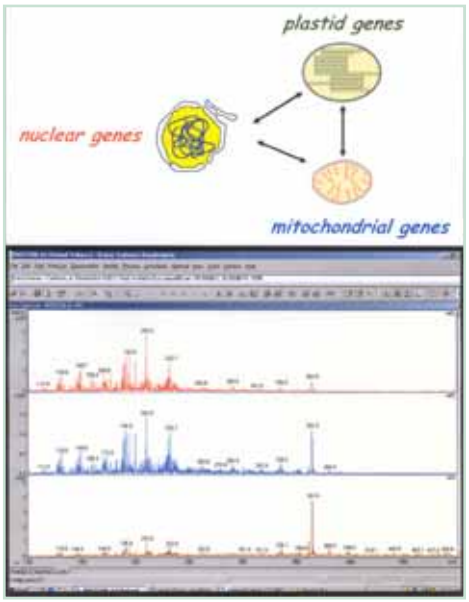


Fig. 3: The state of metabolism controls gene expression in the three genetic systems of the plant cell, the nucleus (>25000 genes), the chloroplast (~100 genes) and the mitochondrion (~60 genes). Deep level of understanding of the regulatory processes links metabolic states to genetic activities. Mass spectrometry in addition to classical biochemical methods is used to analyze the metabolism of plant cells.

Prof. Dr. Karl-Josef Dietz
Biochemistry and Plant Physiology
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5589
fax +49-521-106 6039
email karl-josef.dietz@uni-bielefeld.de
url www.uni-bielefeld.de/biologie/Bio4

Curriculum Vitae

Diploma and Ph.D. degree in Biology at the Julius Maximilian University of Würzburg
1985-1987: PostDoc at Harvard University
1991: Habilitation at the Faculty of Biology, University of Würzburg
1997: Professor and head of the chair of Biochemistry and Plant Physiology at the Faculty of Biology, Bielefeld University
1997: Program organizer and instructor of trainees ('Ausbilder von Biologielaboranten')
2002: Chair of the section Plant Physiology and Molecular Biology and member of the executive board of the German Society of Botany
2004: Dean of Faculty of Biology
2000: Speaker of the Research Unit FOR 387 Redox Regulation in Photosynthesis of the DFG
2002: Advisory Board of the German Academic Exchange Service (DAAD)
Member of the DFG Collaborative Research Centers 176 (1988-98), 251 (1995-97), 549 (1998-2000) and 613 (2002-current)

Members

Dr. M. Baier | H. Bogunovic | P. Gayk | Dr. M. Georgi | Dr. D. Golldack | M. Holt | Dr. A. Kandlbinder | Dr. V. Tognetti | U. Windmeier | P. Witte-Brüggemann |

Publications

Finkemeier, I. *et al.*, 2005. **The mitochondrial type II peroxiredoxin F is essential for redox homeostasis and root growth of *Arabidopsis thaliana* under stress.** J Biol Chem 280, 12168-12180
Baier, M. and Dietz, K.-J. 2005. **Chloroplasts as source and target of cellular redox regulation: A discussion on chloroplast redox signals in the context of plant physiology.** J Exp Bot 56, 1449-1462
Seidel, T. *et al.*, 2005. **Mapping of C-termini of V-ATPase subunits by *in vivo*-FRET measurements.** FEBS Lett 579, 4374-4382
Rouhier, N. *et al.*, 2005. **Identification of plant glutaredoxin targets.** Antioxid Redox Signal 7, 919-929
Dietz, K.-J. 2003. **Plant peroxiredoxins.** Annu Rev Plant Biol 54, 93-107
Dietz, K.-J. 2003. **Redox control, redox signalling and redox homeostasis in plant cells.** Int Rev Cytol 228, 141-193
König, J. *et al.*, 2003. **Reaction mechanism of the 2-Cys peroxiredoxin: Role of the C-terminus and the quarternary structure.** J Biol Chem 278, 24409-24420
Horling, F. *et al.*, 2003. **Divergent light-, ascorbate- and oxidative stress-dependent regulation of expression of the peroxiredoxin gene family in *Arabidopsis thaliana*.** Plant Physiol 131, 317-325
Metwally, A. *et al.*, 2003. **Salicylic acid alleviates the cadmium toxicity in barley (*Hordeum vulgare*) seedlings.** Plant Physiol 132, 272-281
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.** Proc Natl Acad Sci U S A 99, 5738-5743

Gene Technology and Microbiology

The chair of Gene Technology and Microbiology headed by Prof. Dr. R. Eichenlaub was founded in August 1985. Numerous students have successfully completed their Diploma and Ph.D. theses and accepted positions in other research institutions or industry. Associated with the chair is the chair of Prof. Dr. U. Eichenlaub-Ritter.

Research Interests

At present the research interests of the chair focus on two subjects, the ecology of bacterial plasmids and bacteriophages, and the pathogenic interaction of *Clavibacter michiganensis* subsp. *michiganensis* with tomato plants. Plasmids and bacteriophages are considered to play an important role in the genetic adaptation to changing conditions in the environment and the fluctuations of bacterial populations. Thus the abundance of bacteriophages and their bacterial hosts and plasmid-carrying bacteria in natural environments is monitored. The characterization of plasmids and transducing phages is providing data on the possibility of horizontal and vertical gene transfer in natural environments.
Clavibacter michiganensis subsp. *michiganensis* (*Cmm*) is a Gram-positive bacterium which causes bacterial canker and wilt in tomato plants. *Cmm* is the most important bacterial pathogen of tomato plants and causes severe economic losses in agriculture. In the studies, two genes of *Cmm* were identified, which are responsible for the disease in tomato. Both genes are located on plasmids while other genes responsible for a successful infection and growth of the bacteria in the plant are located on the bacterial chromosome. Recently, the complete nucleotide sequence of *Cmm* has been determined here in Bielefeld. This will eventually allow the identification of all the genes of the bacterium involved in the pathogenic interaction by proteome and transcriptome analysis.

Prof. Dr. U. Eichenlaub-Ritter's main research interest is in biology and genetics of reproduction, especially mammalian oogenesis and early embryogenesis. New *in vitro* models are established to analyze the cell biology of oocyte maturation, and the influences of age, hormonal homeostasis and environmental exposures on chromosome segregation and developmental competence, as well as function of gene products in regulation of the cell cycle. The research is relevant for human assisted reproduction,

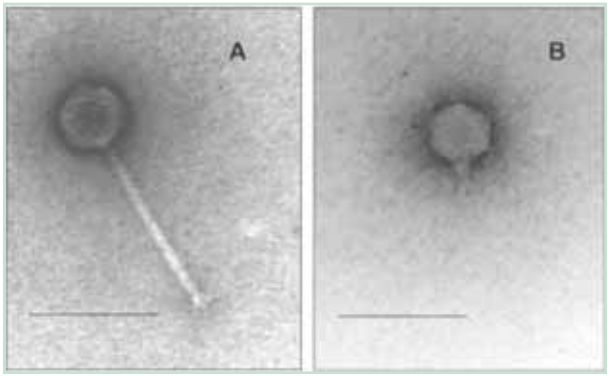


Fig. 1: Electron micrographs of *Brevundimonas vesicularis* phages. Host strains and phages were isolates from ponds in Bielefeld. (A) Phage of the family *Siphoviridae*, (B) Phage of the family *Podoviridae*. Bars correspond to 100 nm.

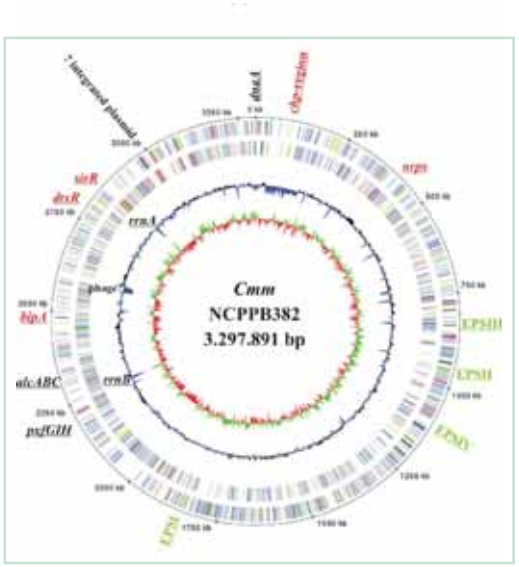


Fig. 2: The chromosome of *Clavibacter michiganensis* subsp. *michiganensis* NCPPB382. The circles represent from outside to inside: leading strand Orfs, lagging strand Orfs, GC-plot, GC-scew.

stem cell research and understanding of adverse environmental influences to preserve and improve fertility.

Involvement in Courses of Study
The chair is responsible for teaching microbiology, microbial genetics and gene technology to Diploma students and more recently is also involved in the teaching of Bachelor and Master students contributing to the Bachelor courses in Biology and in Master courses in Genome Based Systems Biology and Molecular Cell Biology.

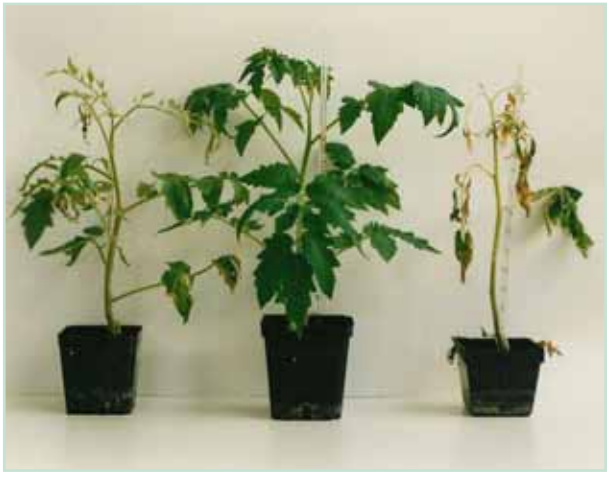


Fig. 3: In the middle a healthy tomato plant. Left and right plants infected with *Clavibacter michiganensis* subsp. *michiganensis* showing severe symptoms of bacterial wilt.

Prof. Dr. Rudolf Eichenlaub
Gene Technology and Microbiology
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5558
fax +49-521-106 6015
email eichenlaub@uni-bielefeld.de
url www.uni-bielefeld.de/biologie/Mikrobiologie/indexd.html

Curriculum Vitae

Diploma in Biology, Ph.D. in Biology and habilitation in Microbiology at the Ruhr-Universität, Bochum
1975-1976: Postdoctoral studies at the University of California, San Diego, USA
1983-1985: Professor for Genetics at the Hamburg University
Since 1985: Head of the chair of Gene Technology and Microbiology at Bielefeld University
1995-1996: Dean of the Faculty of Biology
1992-2000: Speaker of the DFG funded Research Training Group 'Zelluläre Grundlagen biotechnischer Prozesse'

Members

B. Abt | F. Beilstein | Dr. A. Burger | S. Cukurcam | Dr. B. Dreiseikelmann | Prof. Dr. U. Eichenlaub-Ritter | J. Engemann | M. Flügel | Dr. K.-H. Gartemann | I. Gräfen | O. Kaup | E. Vogt |

Publications

Beilstein, F. and Dreiseikelmann, C. 2005. **Bacteriophages of freshwater *Brevundimonas vesicularis* isolates.** Res Microbiol, in press

Kaup, O. *et al.*, 2005. **Identification of a tomatinase in the tomatopathogenic Actinomycete *Clavibacter michiganensis* subsp. *michiganensis* NCPPB382.** Mol Plant Microbe Interact, in press

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Shen, Y. *et al.*, 2005. **High magnitude of light retardation by the zona pellucida is associated with conception cycles.** Hum Reprod 20, 1596-1606

Gartemann, K.-H. *et al.*, 2003. ***Clavibacter michiganensis* subsp. *michiganensis*: First steps in the understanding of virulence of a Gram-positive phytopathogenic bacterium.** J Biotechnol 106, 179-191

Battermann, A. *et al.*, 2003. **A functional plasmid-borne *rrn* operon in soil isolates belonging to the genus *Paracoccus*.** Microbiology 149, 3587-3593

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Jahr, H. *et al.*, **2000. The endo-ß-1,4-glucanase CelA of *Clavibacter michiganensis* subsp. *michiganensis* is a pathogenic determinant required for induction of bacterial wilt of tomato.** Mol Plant Microbe Interact 13, 703-714

Genetics

The chair of Genetics headed by Prof. Dr. A. Pühler was founded in December 1979. During the last 25 years the chair was successfully involved in the education of diploma and Ph.D. students. Altogether, more than 200 students completed their diploma thesis and around 100 graduate students performed research work to receive the Ph.D. degree. Among the scientists employed, ten members were awarded a habilitation. The chair is proud that several of the habilitated scientists recieved professorships at German universities, e.g. at Aachen, Bielefeld, Bochum, Rostock and Tübingen.

Research Interests

Since its foundation the chair was continuously interested in analyzing soil bacteria capable of forming symbiotic or pathogenic interactions with host plants. Concerning symbiosis the nitrogen fixing root nodules induced by *Sinorhizobium meliloti* on the roots of its host plant *Medicago* were analyzed on the molecular level (Fig. 1). In addition, the endomycorrhiza formed by the genera *Glomus* and its host plant *Medicago* constitutes another interesting research topic. For the analysis of the pathogenic interaction, the phytopathogenic soil bacterium *Xanthomonas campestris* pv. *campestris* infecting cabbage was selected (Fig. 2).

Another research topic of the chair concentrates on biotechnology. Two microbial systems employed in industrial fermentation processes are subjected to molecular analysis. One system deals with the amino acid production by *Corynebacterium glutamicum* (Fig. 3) and the other one with the xanthan production by *Xanthomonas campestris* pv. *campestris.*

In recent years, the chair was heavily engaged in the development of genomic and post-genomic techniques. The outstanding projects concerned the sequencing of bacterial genomes. As partner of a world-wide consortium the *S. meliloti* genome sequence was established. In addition, the *C. glutamicum* genome was sequenced in collaboration with an industrial company. The most recent published genome sequence of the chair concerns that of the human pathogen *Corynebacterium jeikeium* K411 strain.

In the meantime, the sequencing of additional bacterial genomes was carried out in the framework of a research network financed by the Federal Ministry of Education and Research (BMBF). In particular, genomes of bacteria relevant for agriculture, en-

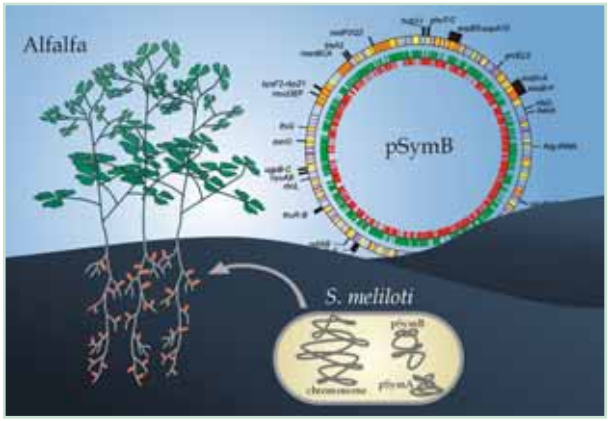

Fig. 1: The symbiosis between Alfalfa and the Gram-negativ soil bacterium *S. meliloti*.
The symbiont is able to induce the formation of nitrogen fixing root nodules. In exchange for ammonium the plant supports the bacteria with carbohydrates. The genome of *S. meliloti* consists of three replicons, namely the chromosome and the two megaplasmids pSymA and pSymB. The *S. meliloti* genome sequenced by a world-wide consortium has a size of 6.69 Mb.

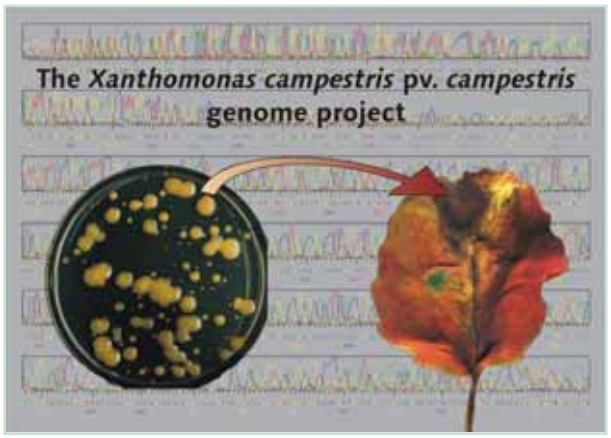

Fig. 2: The phytopathogenic interaction between the Gram-negative soil bacterium *Xanthomonas campestris* pv. *campestris* and its host *Brassica olerecae*.
X. campestris pv. *campestris* is responsible for the so-called black rod desease. On the other hand, *X. campestris* pv. *campestris* produces the exopolysaccharide xanthan, which is used in the food as well as in the cosmetic industry. The genome of *X. campestris* pv. *campestris* was sequenced several times. The most recent sequence was established by the chair of Genetics at Bielefeld University.

vironment and biotechnology were completely sequenced. Beside genomic techniques the chair concentrated on the development of modern post-genomic techniques like transcriptomics, proteomics and metabolomics. All these techniques supported by applied bioinformatics represent a solid base for starting research activities in the field of Systems Biology.

Involvement in Courses of Study

The chair contributes to the Bachelor course in Biology and initiated the Master course Genome Based Systems Biology. In addition, the chair is involved in the Bachelor and Master courses Bioinformatics and Genome Research. Of special interest is also the significant role of the chair in establishing the International Graduate School in Bioinformatics and Genome Research. It should also be mentioned that the chair offers courses at the national and European level to train Ph.D. students and PostDocs in the field of genome sequencing, transcriptomics, proteomics, metabolomics, and bioinformatics.

Fig. 3: Production of L-lysine by the Gram-positive *Corynebacterium glutamicum* ATCC 13032 strain.
The role of *C. glutamicum* in the production of the amino acid L-lysine is shown. The sequence of the *C. glutamicum* genome was established by the chair of Genetics in collaboration with an industrial company. In the post-genomic area improved production strains can now be developed by a rational design using **'-omics'-technologies.**

Prof. Dr. Alfred Pühler
Genetics
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5607
fax +49-521-106 5626
email puehler@genetik.uni-bielefeld.de
url www.genetik.uni-bielefeld.de/Genetik

Curriculum Vitae

Diploma in Physics, Ph.D. degree in Biology and habilitation in Microbiology and Genetics at the E. A. University Erlangen-Nürnberg
Since 1979: Professor and head of the chair of Genetics at the Faculty of Biology, Bielefeld University
1985 and 1986: Dean of the Faculty of Biology
1992-1994: Prorector for research and junior scientists at Bielefeld University
1988-1996: Elected member as a DFG expert in the field General Biology, Genetics and Cell Biology
Since 1995: Member of the Central Commission for Biological Safety
1999-2005: Elected member of the German Science Council
Member of the Northrhine-Westfalian Academy of Sciences (since 1993), member of the German Academy of Natural Scientists Leopoldina (since 1999) and member of the acatech - Convention of Technical Sciences of the Union of German Academies of Sciences (since 2004)

Members

V. Bartelsmeier | S. Castrup | Dr. A. Hüser | Dr. D. Jording | Dr. O. Kaiser | Dr. J. Kalinowski | I. Krahn | S. Malmivaara | Dr. A. Schlüter | Dr. S. Schneiker | Dr. W. Selbitschka | Dr. A. Tauch | Dr. S. Weidner |

Publications

Thieme, F. *et al.* 2005. **Novel insights into genome plasticity and pathogenicity of the plant pathogenic bacterium *Xanthomonas campestris* pv. *vesicatoria* revealed by the complete genome sequence.** J Bacteriol 187, 7254-7266

Tauch, A. *et al.*, 2005. **Complete genome sequence and analysis of the multiresistant nosocomial pathogen *Corynebacterium jeikeium* K411, a lipid-requiring bacterium of the human skin flora.** J Bacteriol 187, 4671-4682

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, 5-25

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

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Genome Research

The chair of Genome Research was founded in 2003 when the head, Prof. Dr. B. Weisshaar, moved to Bielefeld University from the Max Planck Institute for Plant Breeding Research in Cologne. Building on expertise and long standing interests in the analysis of transcription factor networks and functional genomics, several projects integrating molecular biology, high-throughput technology and applied bioinformatics were newly launched at Bielefeld. With additional funding from BMBF, DFG, and EU the chair has now grown to 25 people.

Research Interests

The aim of the chair's research activities is to understand functions of genes and regulatory gene families at the genomic level. As an example the chair uses the biosynthesis of an important class of plant secondary metabolites, the flavonoids. Among these are compounds that give red color to flowers and fruits, or brown color to seeds. Others help plants to defend themselves against pathogens or UV irradiation. The biosynthesis of flavonoids requires coordinated activation of a number of different genes. This is accomplished by a network of co-acting transcription factors, including bZIP, bHLH and MYB proteins. The chair analyzes this network to understand general principles of how plants develop and respond to their environment and to gain knowledge that can be applied in breeding programs. For much of the chair's work the model plant *Arabidopsis thaliana* is used. Plants that carry defined mutations are an essential tool to assign functions to the 29,000 genes predicted in the genome (Fig. 1). With the 'GABI-Kat' project, funded by the German plant genomics initiative GABI, the chair offers the scientific community a flanking sequence tag (FST) -based mutant population of about 80,000 T-DNA mutagenized *A. thaliana* plants (Fig. 2). This resource is used by many researchers around the world.

The chair also contributes to the establishment of a central platform for testing lead gene function in crops based on TILLING (Targeting Induced Local Lesions IN Genomes). TILLING is a 'reverse genetics' approach relying on the detection of small mismatches in double stranded DNA. The focus of the chair's part in the project is to set up a laboratory information management system (LIMS) and to optimize the TILLING technology for increased throughput.

In addition, the chair works on resources and tools for the detection of single nucleotide polymorphisms (SNPs) from EST sequences, SNP-based mapping

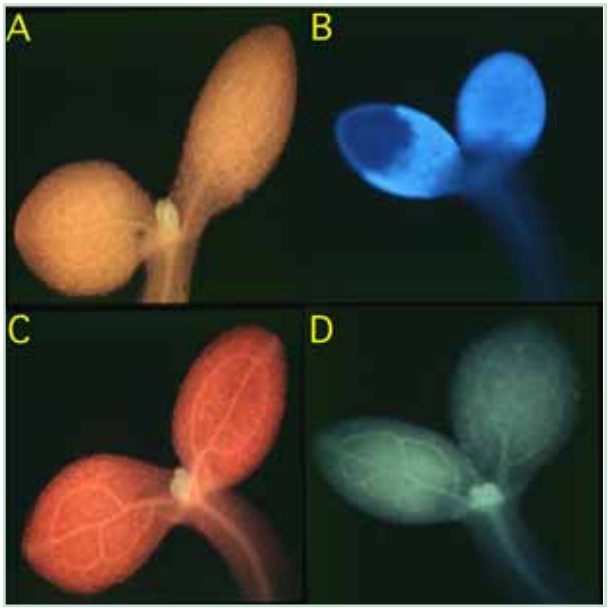

Fig. 1: Seedlings of *A. thaliana* plants mutated in various steps of flavonoid biosynthesis (B-D) in comparison to wild type (A). A specific staining procedure allows to distinguish mutants that accumulate different pathway intermediates based on their fluorescence in UV light. Mutant analysis is the method of choice to assign functions to genes and the corresponding proteins.

Fig. 2: The 'GABI-Kat' insertion mutant resource. A: Result of a query in the 'GABI-Kat' web interface, showing 2 T-DNA insertions (green triangles) in the *A. thaliana* gene *At4g18960*. Numbers refer to positions on chromosome 4, blue arrows represent exons. B: Seed storage. Seeds of lines carrying insertions as shown in A can be ordered to elucidate functions of the affected genes. C: Plants with insertions in *At4g18960* produce flowers inside their flowers, indicating a function of this gene in controlling organ identity.

Prof. Dr. Bernd Weisshaar
Genome Research
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 6873
fax +49-521-106 6423
email genomforschung@uni-bielefeld.de
url www.genomforschung.uni-bielefeld.de

procedures and visualization of SNP data. For sugar beet the chair is involved in the generation of a BAC-based physical map of the genome which will be of central importance for marker assisted breeding and for positional cloning of genes.
Some flavonoids are known to have anti-nutritive effects in animal feed, while others are beneficial to humans and reduce the risk of cardiovascular diseases. To increase their nutritional value, the chair identifies structural and regulatory genes involved in flavonoid biosynthesis in rapeseed and apple. This information is used to generate functional markers for controlling flavonoid accumulation in specific plant parts (Fig. 3). In this way the chair transfers results on gene functions and transcription factor networks gained from the model system *A. thaliana* to 'real world' applications.

Involvement in Courses of Study

The chair contributes to the Bachelor course in Biology and the Master courses Genome Based Systems Biology and Molecular Cell Biology. In addition, the chair is involved in the Bachelor and Master courses Bioinformatics and Genome Research as well as the International Graduate School in Bioinformatics and Genome Research.

Fig. 3: FLAVO Logo. FLAVO is an European Union 6th Framework Project with the aim to provide knowledge, tools and methods to enable development of high quality, consumer-acceptable fruits, vegetables, foods and beverages containing flavonoids at levels that are optimal for human health. Building on data from the model system *A. thaliana* (seeds, upper left), the focus is on grapes, strawberries and apple.

Curriculum Vitae

Diploma in Biology and Ph.D. degree in Genetics and Virology
1991-2003: Senior scientist and group leader at the Max Planck Institute for Plant Breeding Research
1994: Visiting scientist with funding from the DFG and the Royal Society at Glasgow University, Scotland UK
1995: Habilitation in Genetics at the University of Cologne
1995-2005: Head of the DNA core facility of the MPI for Plant Breeding Research
Since 2003: Head of the chair of Genome Research at Bielefeld University
Since 2004: Head of the Scientific Coordination Committee of the German plant genomics program GABI
Since 1998: Member of the American Society of Plant Biologists (ASPB)
Since 2000: Member of the 'Deutsche Botanische Gesellschaft'

Members

J. Brüggemann | U. Bürstenbinder | V. Düttmann | H. Hagemeyer | Dr. D. Holtgräwe | G. Huep | H. Ishihara | B. Kah | A. Kralemann-Köhler | M. Kuhlmann | Y. Li | D. Piekorz | R. Prasad | T. Rosleff Sörensen | M. Rosso | Dr. M. Sagasser | U. Schalk | J. Starmann | Dr. R. Stracke | P. Viehoever | M.-L. Wilke |

Publications

Mehrtens, F. *et al.*, 2005. **The *Arabidopsis transcription* factor MYB12 is a flavonol-specific regulator of phenylpropanoid biosynthesis.** Plant Physiol 138, 1083-1096
Hartmann, U. *et al.*, 2005. **Differential combinatorial interactions of *cis*-acting elements recognized by R2R3-MYB, BZIP, and BHLH factors control light-responsive and tissue-specific activation of phenylpropanoid biosynthesis genes.** Plant Mol Biol 57, 155-171
Zimmermann, I.M. *et al.*, 2004. **Comprehensive identification of *Arabidopsis thaliana* MYB transcription factors interacting with R/B-like BHLH proteins.** Plant J 40, 22-34
Rosso, M.G. *et al.*, 2003. **An *Arabidopsis thaliana* T-DNA mutagenized population (GABI-Kat) for flanking sequence tag-based reverse genetics.** Plant Mol Biol 53, 247-259
Schmid, K.J. *et al.*, 2003. **Large-scale identification and analysis of genome-wide single-nucleotide polymorphisms for mapping in *Arabidopsis thaliana*.** Genome Res 13, 1250-1257
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Proteome and Metabolome Research

The department of Proteome and Metabolome Research headed by Prof. Dr. K. Niehaus was founded in May 2005. The department designation reflects the progression of molecular biology towards a holistic approach that combines the different post-genome techniques and concepts. Guided by this development collaboration with partners in physics, chemistry, biotechnology, bioinformatics and other disciplines is an integral concept of education and research. The department is involved in different Bachelor, Master and Ph.D. programs and frequently hosts students and guests from Argentina, Great Britain, Bulgaria, France, Hungary, India, the Netherlands, Pakistan, Syria and Thailand.

Research Interests

The research of the department is focussed on model organisms. Among these are the plant *Medicago truncatula*, symbiotic bacteria (*Sinorhizobium meliloti*), phytopathogenic bacteria (*Xanthomonas campestris* pv. *campestris*) and other biotechnologically important bacteria. The whole genome sequencing of these model organisms is finished or will be finished in the near future. The logical vision now is to go 'From Genes to Functions'. A central focus of the post-genomic research will be to understand how cellular phenomena arise from the connectivity of genes, RNAs, proteins and metabolites. Realizing the potential of post-genome science will be a highly interdisciplinary process requiring close collaboration between a wide range of disciplines. This requirement should ideally be reflected by a multi-disciplinary structure of the department. Understanding complex biological systems requires the integration of experimental and computational research leading to a systems biology approach. The establishment of an effective symbiosis between plants and bacteria is controlled by a complex network of signals produced by both partners. It has been suggested that successful infection of the host plant may depend on the ability of the bacteria to escape or suppress the induction of structural or chemical defenses that normally serve to prevent infection by pathogenic microorganisms. What enables bacteria to invade host plant cells without eliciting defense responses? And what are the signals that induce plant defence in case of a pathogenic attack? The extracellular matrix (ECM) of microorganisms and plants is essential for the recognition between two symbiosis-partners. Components of the bacterial ECM, e.g. the various extracellular (EPS), capsular (KPS) and lipopolysaccharides (LPS) and certain extracellular proteins function as signals recognized by the plant. One scientific focus will be the role of bacterial (outer) membrane proteins in plant-microbe interactions. Membrane proteins are involved in the export and import of substances and in the signal transduction into the bacterial cell. For this reason, membrane proteins are ideal candidates to analyze plant-microbe interactions. Further aspects are plant GTPases and their role in plant microbe interactions. High end microscopes allow for high content screening and localization of GFP-tagged GTPases in living cells. Further technical developments of the department will concentrate on quantitative proteomics and mapping of post-translational modifications. In order to

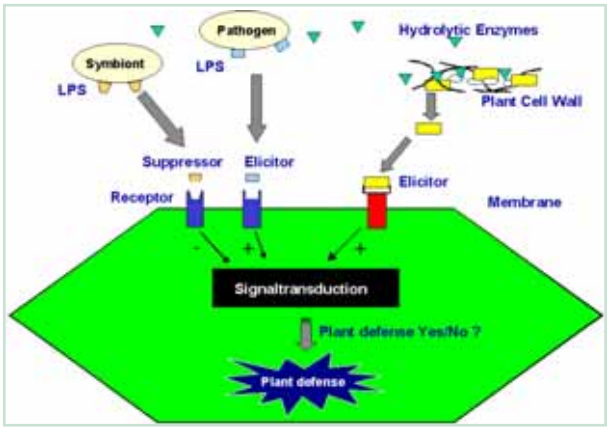

Fig. 1: Recognition of microbes by plants is mediated by a complex network of signals. Compounds of the microbe can induce or suppress the plant defence system. Recognition is controlled by a 'blend' of different molecules forming a Pathogen Associated Molecular Pattern (PAMP) that is evaluated by the infected plant. Depending on the different signals the decision for or against a defence reaction is made.

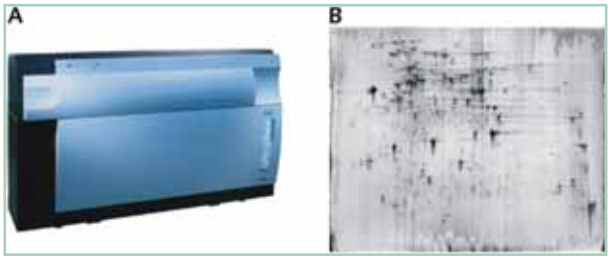

Fig. 2: Matrix Assisted Laser Desorption Mass Spectroscopy (MALDI-TOF MS) is carried out by a Bruker ultraflex machine (A). The proteomics facility is equipped with robots and automated data analysis allowing a throughput of several hundred samples per day. Separation of *Xanthomonas campestris* pv. *campestris* extracellular proteins by 2D-gel electrophoresis and identification of proteins by MALDI-TOF MS (B).

Prof. Dr. Karsten Niehaus
Proteome and Metabolome Research
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5631
fax +49-521-106 5626
email kniehaus@genetik.uni-bielefeld.de
url www.genetik.uni-bielefeld.de/Genetik/phyto/

keep up with the fast technical development in the field of mass spectroscopy a new MALDI-TOF system (Bruker ultraflex) was installed. With this investment the necessary sample throughput and the automated generation of protein sequence information could be achieved. The ProDB software, developed in the Bioinformatics Resource Facility, makes an ideal bioinformatic counterpart for these future perspectives. During the last years it became evident that a holistic analysis of biological systems requires the integration of metabolic data. *In silico* predictions arising from the genome data must be confirmed by qualitative and quantitative metabolome data arising from biological experiments. Integration of metabolomic data is the final step on the way 'From Genes to Functions'. Core facilities for metabolome experiments were installed to serve these needs. The analytical system consists of a capillary gas chromatograph (GC), high performance liquid chromatography (HPLC) and capillary electrophoresis (CE) coupled to ion-trap mass spectrometers (ESI-MSn). A major challenge of this department will be the generation of a new database containing MS-spectra and chromatographic information of biologically relevant metabolites.

Involvement in Courses of Study

The department contributes to the education in Bachelor courses in Biology, Bioinformatics and Genome Research, and Molecular Biotechnology. A special focus is set on the Master program Genome Based Systems Biology.

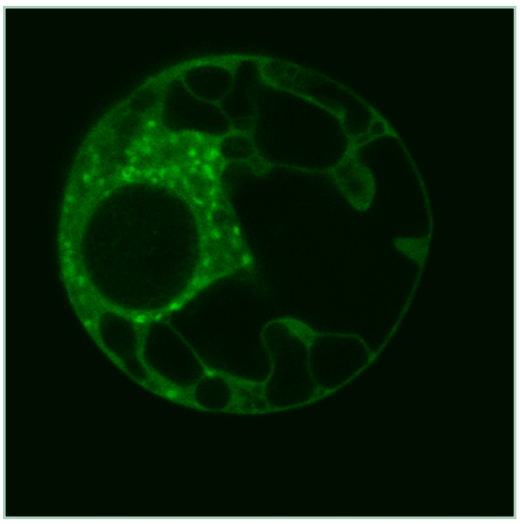

Fig. 3: Localization of the GTPase Rab11f as fusion with the green fluorescent protein (GFP) in a living cell. The GTPase:: GFP localizes in small vesicles and to a lower extend in the cytoplasm but is absent in the plant cell nucleus.

Curriculum Vitae

Diploma in Biology, Ph.D. degree in Biology and habilitation in Genetics and Cell Biology, Bielefeld University
2000-2005: Head of the DFG junior research group for Proteome Research within the DFG program Bioinformatics and Genome Research
Founding member of the 'Gesellschaft für Proteomfor-schung', member of the 'Deutsche Phytomedizinische Gesellschaft' and 'Deutsche Gesellschaft für Zellbiologie'
Since 2005: Professor and head of the department of Proteome and Metabolome Research, Bielefeld University

Members

A. Alici | A. Barsch | M. Brecht | G. Gandhi | N. Jensen | Dr. D. Kapp | N. Küpper | P. Nounurai | Dr. T. Patschkowski | V. K. Sidhu | P. V. Tellström | Dr. S. Watt | T. Watt |

Publications

Yaneva, I.A. and Niehaus, K. 2005. **Molecular cloning and characterisation of a Rab-binding GDP-dissociation inhibitor from *Medicago truncatula*.** Plant Physiol Biochem 43, 203-212

Watt, S. *et al.*, 2005. **Comprehensive analysis of the extracellular proteins from *Xanthomonas campestris* pv. *campestris* B100.** Proteomics 5, 153-167

Kunze, G. *et al.*, 2004. **The N terminus of bacterial elongation factor Tu elicits innate immunity in *Arabidopsis* plants.** Plant Cell 16, 3496-3507

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Albus, U. *et al.*, 2001. **Suppression of an elicitor-induced oxidative burst reaction in *Medicago sativa* cell cultures by *Sinorhizobium meliloti* lipopolysaccharides.** New Phytol 151, 597-606

Meyer, A. *et al.*, 2001. **The lipopolysaccharides of the phytopathogen *Xanthomonas campestris* pv. *campestris* induce an oxidative burst reaction in cell cultures of *Nicotiana tabacum*.** Planta 213, 214-222

Cardinale, C. *et al.*, 2000. **Differential activation of four specific MAPK pathways by distinct elicitors.** J Biol Chem 275, 36734-36740

Schiene, K. *et al.*, 2000. **Transgenic tobacco plants that express an antisense construct derived from a *Medicago sativa* cDNA encoding a Rac-related small GTP-binding protein fail to develop necrotic lesions upon elicitor infiltration.** Mol Gen Genet 263, 761-770

Niehaus, K. *et al.*, 1998. **A *Sinorhizobium meliloti* lipopolysaccharide mutant induces effective nodules on the host plant *Medicago sativa* (Alfalfa) but fails to establish a symbiosis with *Medicago truncatula*.** Mol Plant Microbe Interact 11, 906-914

Transcriptomics

Symbiotic Plant-Microbe Interactions | Microbial Polysaccharide Production | Transcriptomics

HD Dr. Anke Becker
Transcriptomics
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4824
fax +49-521-106 5626
email anke.becker@genetik.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/groups/nwt/

Curriculum Vitae

1991: Diploma in Biology
1994: Ph.D. in Molecular Biology
1999: Research stay at the Massachusetts Institute of Technology
Since 1999: Head of Transcriptomics Facility
2000: Habilitation in Genetics at the Faculty of Biology, Bielefeld University
Since 2001: Leader of the junior research group Transcriptomics
2002-2005: Heisenberg fellow
Since 2002: 'Hochschuldozentin' at the Faculty of Biology, Bielefeld University

Members

C. Bahlawane | Dr. B. Baumgarth | D. Chang | Dr. P.-B. Kamp | A. Knorp | Dr. E. Krol | Dr. M. McIntosh | M. Meyer | J. Mohr | N. Pobigaylo | E. Schulte-Berndt | J. Serrania | Dr. L. Sharypova | A. Tauchen |

Publications

Becker, A. *et al.*, 2004. **Global changes in gene expression in *Sinorhizobium meliloti* 1021 under microoxic and symbiotic conditions.** Mol Plant Microbe Interact 17, 292-203

Sharypova, L.A. *et al.*, 2003. ***Sinorhizobium meliloti acpXL* mutant lacks the C28 hydroxylated fatty acid moiety of lipid A and does not express smooth LPS.** J Biol Chem 278, 12946-12954

Bartels, F.W. *et al.*, 2003. **Specific binding of the regulatory protein ExpG to promoter regions of the galactoglucan biosynthesis gene cluster of *Sinorhizobium meliloti* - A combined molecular biology and force spectroscopy investigation.** J Struct Biol 143, 145-152

Galibert, F. *et al.*, 2001. **The composite genome of the legume symbiont *Sinorhizobium meliloti*.** Science 293, 668-672

Transcriptomics

The junior research group Transcriptomics headed by HD Dr. A. Becker was founded in December 2001. Research projects are primarily funded by the DFG in the framework of the Bioinformatics Initiative and SFB 613 Physics of Single Molecule Processes and Molecular Recognition in Organic Systems as well as by the BMBF in the Competence Network Genome Research on Bacteria relevant for Agriculture, Environment and Biotechnology. Ph.D. students are also supported by the International Graduate School in Bioinformatics and Genome Research.

Research Interests

Symbiotic nitrogen fixation is profoundly important for the environment. A major source of fixed nitrogen is the rhizobia-legume symbiosis. The group's studies are based on *Sinorhizobium meliloti* that forms a symbiosis with certain genera of leguminous plants. This interaction is investigated by using genome and post-genome approaches. The group's research also focuses on the synthesis and function of bacterial surface polysaccharides and the identification of gene expression patterns that predict the outcome of human breast cancer. The group participates in a Collaborative Research Center on Physics of Single Molecule Processes and Molecular Recognition in Organic Systems and supports a Transcriptomics Facility that provides services and technical support in array production, clone library handling, high-throughput PCR and robot-assisted screening procedures.

Involvement in Courses of Study

The research group contributes to the Bachelor program in Bioinformatics and Genome Research, the Master programs in Genome Based Systems Biology, in Bioinformatics and Genome Research, and the International Graduate School in Bioinformatics and Genome Research.

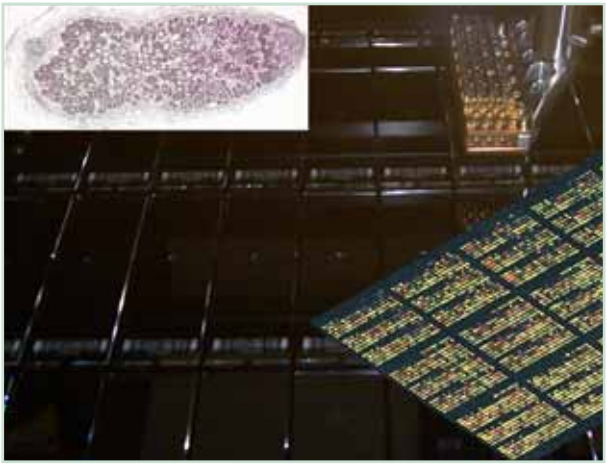

Fig. 1: Microarray spotting robot. Microarrays are applied to investigate the symbiotic interaction between rhizobia and legume plants. Upper left corner: light microscopic image of a *Medicago truncatula* root nodule. Lower right corner: pseudocolor image of a microarray.

Genomics of Legume Plants

The junior research group headed by PD Dr. H. Küster was founded in September 2001. Research projects are primarily funded through the German Research Foundation (DFG) SPP1084 MolMyk: Molecular Basics of Mycorrhizal Symbioses, the EU FP6 Integrated Project GRAIN LEGUMES and the International Graduate School in Bioinformatics and Genome Research.

Research Interests

The research group is interested in the molecular analysis of two symbiotic interactions of legume plants with soil microbes: The formation of root nodules in symbiosis with *Sinorhizobium meliloti* and the arbuscular mycorrhiza interaction with soil fungi of the genus *Glomus*. Whereas nodulation leads to symbiotic nitrogen fixation, arbuscular mycorrhiza improves the uptake of phosphorus and minerals from the soil. Due to the fact that in particular grain legumes are characterized by the formation of protein-rich seeds, the group recently extended its focus to the study of legume seed development. The model legume *Medicago truncatula* was chosen for the studies, since excellent genomics tools are available for this plant. Concerning transcriptomics tools, the group constructs comprehensive microarrays for *M. truncatula* in the frame of the EU and German Research Foundation (DFG) research networks mentioned above.

Involvement in Courses of Study

The group contributes to the Bachelor program in Bioinformatics and Genome Research, the Master program in Genome Based Systems Biology, the Master program in Bioinformatics and Genome Research, and the Ph.D. program in the International Graduate School in Bioinformatics and Genome Research.

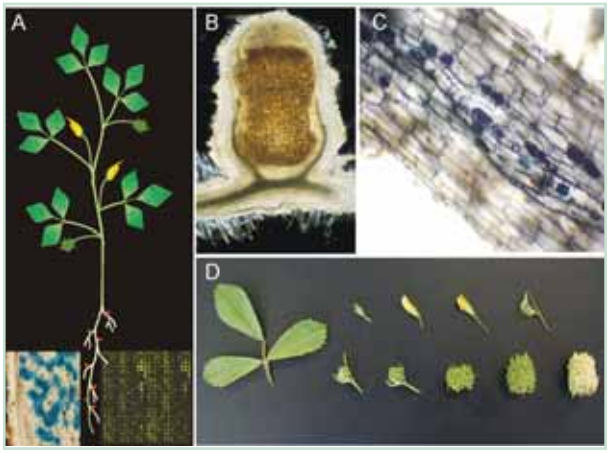

Fig. 1: The model plant *M. truncatula* (A) is used to study key processes of legume biology by applying transcriptome profiling and transgenic approaches: The formation of nitrogen-fixing root nodules in a symbiosis with *S. meliloti* (B), the establishment of an arbuscular mycorrhiza symbiosis with *Glomus* fungi (C), and the development of reproductive tissues (D) as a model for the formation of protein-rich grain legume seeds.

PD Dr. Helge Küster
Genomics of Legume Plants
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4819
fax +49-521-106 5626
email helge.kuester@genetik.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/groups/glp

Curriculum Vitae

1992: Diploma in Biology
1995: Ph.D. in Molecular Biology
2001: Leader of the junior research group Genomics of Legume Plants
2004: Habilitation in Genetics and 'Privatdozent' at the Faculty of Biology, Bielefeld University
Since 2004: Head of the Scientific Committee of the EU FP6 IP GRAIN LEGUMES (GLIP)
Since 2005: Vice president of the GLIP TTP

Members

M. C. Baier | C. Firnhaber | R. Gau | Dr. N. Hohnjec | F. Lenz | M. Meyer | Dr. M. Vieweg |

Publications

Hohnjec, N. *et al.*, 2005. **Overlaps in the transcriptional profiles of *Medicago truncatula* roots inoculated with two different *Glomus* fungi provide insights into the genetic program activated during arbuscular mycorrhiza.** Plant Physiol 137, 1283-1301

Firnhaber, C. *et al.*, 2005. **EST sequencing and time course microarray hybridizations identify more than 700 *Medicago truncatula* genes with developmental expression regulation in flowers and pods.** Planta 222, 269-283

El Yahyaoui, F. *et al.*, 2004. **Expression profiling in *Medicago truncatula* identifies more than 750 genes differentially expressed during nodulation, including many potential regulators of the symbiotic program.** Plant Physiol 136, 3159-3176

Vieweg, M.F. *et al.*, 2004. **The promoter of the *Vicia faba L.* leghemoglobin gene *VfLb29* is specifically activated in the infected cells of root nodules and in the arbuscule-containing cells of mycorrhizal roots from different legume and nonlegume plants.** Mol Plant Microbe Interact 17, 62-69

Manthey, K. *et al.*, 2004. **Transcriptome profiling in root nodules and arbuscular mycorrhiza identifies a collection of novel genes induced during *Medicago truncatula* root endosymbioses.** Mol Plant Microbe Interact 17, 1063-1077

RNA-Based Regulation

miRNAs | Nuclear Export | Signal Transduction | Transcription Factors

PD Dr. Thomas Merkle
RNA-Based Regulation
Faculty of Biology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4806
fax +49-521-106 6423
email tmerkle@cebitec.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/groups/rbr

Curriculum Vitae

Diploma and Ph.D. degree in Biology at University of Freiburg
1992-1996: Postdoctoral research fellow at the Friedrich Miescher Institute in Basel
1994: Guest scientist at the University of Colorado at Boulder
1996-2003: Assistant professor and habilitation in Cell Biology at University of Freiburg
2002-2003: Non-tenured professor for Plant Developmental Physiology at University of Kiel
Since 2004: Leader of the junior research group RNA-Based Regulation, Bielefeld University

Members

L. Alves Jr. | U. Bürstenbinder | S. Niemeier | Dr. R. Palmisano | J. Schleppenbäumer | K. Schmied | J. Starmann |

Publications

Merkle, T. 2004. **Nucleo-cytoplasmic partitioning of proteins in plants: implications for the regulation of environmental and developmental signalling.** Curr Genet 44, 231-260

Ziemienowicz, A. *et al.*, 2003. ***Arabidopsis* transportin 1 is the nuclear import receptor for the circadian clock-regulated RNA-binding protein AtGRP7.** Plant Mol Biol 53, 201-212

Haasen, D. and Merkle, T. 2002. **Characterisation of an *Arabidopsis thaliana* homologue of the nuclear export receptor CAS by its interaction with Importin alpha.** Plant Biol 4, 432-439

RNA-Based Regulation

The junior research group of RNA-Based Regulation headed by PD Dr. T. Merkle was established in 2004. Projects are primarily funded by the DFG through the Computer Science Action Plan (Emmy Noether Program). Ph.D. students are also supported by the International Graduate School in Bioinformatics and Genome Research.

Research Interests

The group is interested in how plants respond to changing environmental cues and how they integrate this into different developmental programs. The group concentrates on two regulatory mechanisms: i) microRNA-directed cleavage of specific mRNAs as a post-transcriptional tool to control mRNA abundance and ii) nucleo-cytoplasmic partitioning of transcription factors as a means to post-translationally regulate signalling. A range of molecular, genetic, biochemical and cell biological methods is applied to gain insight into the functions of selected proteins involved in the regulation of development and in the reaction to environmental signals. MicroRNAs (miRNAs) constitute an important mechanism to regulate endogenous and exogenous signalling, since many mRNA targets encode transcription factors. The group identified novel miRNA targets in *Arabidopsis* that are predicted *in silico* (cooperation with the junior research group Bioinformatics of Regulation) and investigates the regulation by miRNAs of the function of specific transcription factors belonging to the MYB, bHLH, bZIP and homeodomain classes. In Arabidopsis, these are large protein families, and many members of these protein families have plant-specific functions. The group is also interested in the regulated expression of specific miRNA genes themselves. Nucleo-cytoplasmic partitioning also constitutes an important regulatory tool for signalling. Here, the group is investigating the role of nuclear export of *Arabidopsis* transcription factors as a switch-off mechanism for signalling.

Involvement in Courses of Study

The research group contributes to the Bachelor and Master courses in Biology, to the Master course in Genome Based Systems Biology and to the Bachelor course Bioinformatics and Genome Research.

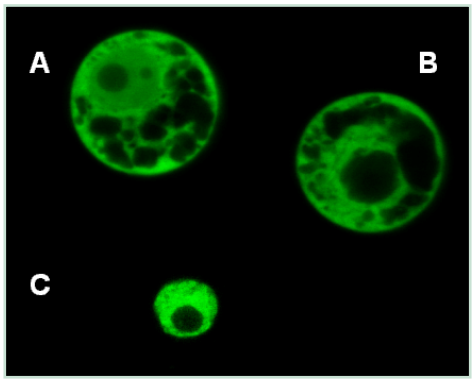

Fig. 1: Nucleo-cytoplasmic localisation of an *Arabidopsis* MYB transcription factor fused to GFP in protoplasts. (A) Localization of the wildtype protein that contains a nuclear localization signal (NLS) and a nuclear export signal (NES) in the nucleus and in the cytoplasm. (B) Almost exclusive cytoplasmic localization of the fusion protein lacking NLS activity. (C) Nuclear accumulation of the fusion protein that lacks NES activity.

Technology Platform Systems Biology

Established with the financial aid of the federal state Northrhine Westphalia under the name 'Zentrum für Genomforschung' and officially opened in April 1999 by the minister of research and education, the technology platform is now an integral part of the Institute for Genome Research at the CeBiTec. The technology platform is headed by Dr. J. Kalinowski and currently comprises three scientists and three technicians. The mission is to provide state-of-the-art equipment, techniques and training to support the research efforts on different fields of genome research. These fields include high-throughput DNA sequencing for the establishment of complete genome sequences (genomics), expression analyses by DNA microarrays (transcriptomics) and by proteomics as well as comprehensive metabolite analysis (metabolomics).

Research Interests

In the recent years the technology platform supported specific research projects of a number of cooperating institutions. These projects are in the field of genome sequencing of bacteria, expression analysis by microarray hybridization in bacteria and plants, proteomics as well as metabolomics of different bacterial species. In particular, two corynebacterial genomes were completely sequenced under the coordination of researchers from the technology platform, that of the industrially relevant amino acid-producer *Corynebacterium glutamicum* ATCC 13032 and that of the human pathogen *C. jeikeium* K411. Based on these and on other sequenced genomes, a number of whole-genome microarrays was manufactured and hybridized in a cooperation with the research group Transcriptomics headed by HD Dr. A. Becker. Further cooperations with the department of Proteome and Metabolome Research headed by Prof. Dr. K. Niehaus exist on the establishment of comprehensive proteomes of bacteria and on metabolic profiling by gas-chromatography coupled to mass-spectrometry. In order to store and analyze the high-volume data coming from all the different techniques, a close collaboration also exists with the Bioinformatics Resource Facility of the CeBiTec.

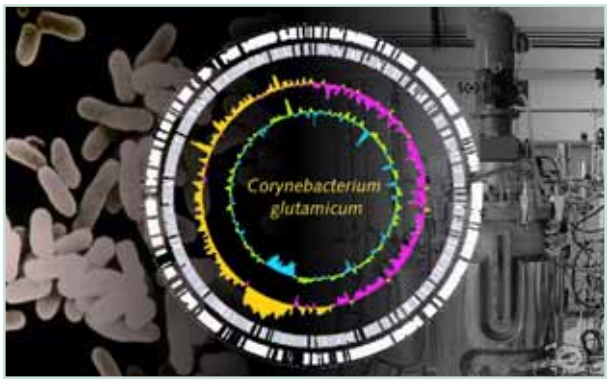

Fig. 1: A plot of the circular chromosome of the industrially relevant amino acid-producer *C. glutamicum* is shown together with a collage showing cells of this bacterium (left side) and an industrial fermentor (right side).

Dr. Jörn Kalinowski
Technology Platform Systems Biology
Institute for Genome Research
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4825
fax +49-521-106 5626
email joern.kalinowski@genetik.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/groups/techsys/

Curriculum Vitae

1985: Diploma in Biology
1990: Ph.D. in Biology at the Bielefeld University
Since 2000: Head of the Technology Platform at the Institute for Genome Research, Bielefeld University

Members

C. Eck | Dr. A. T. Hüser | N. Küpper | E. Schulte-Bernd | Dr. A. Tauch |

Publications

Hansmeier, N. *et al.*, 2006. **The cytosolic, cell surface and extracellular proteomes of the biotechnologically important soil bacterium *Corynebacterium efficiens* YS- 314 in comparison to those of *Corynebacterium glutamicum* ATCC 13032.** Proteomics, in press

Rey, D.A. *et al.*, 2005. **The McbR repressor modulated by the effector substance S-adenosylhomocysteine controls directly the transcription of a regulon involved in sulphur metabolism of *Corynebacterium glutamicum* ATCC 13032.** Mol Microbiol 56, 871-887

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Hüser, A.T. *et al.*, 2003. **Development of a *Corynebacterium glutamicum* DNA microarray and validation by genome-wide expression profiling during growth with propionate as carbon source.** J Biotechnol 106, 269-286

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, 5-25

The Bielefeld Institute for Biophysics and Nanoscience

The Bielefeld Institute for Biophysics and Nanoscience (BINAS) was founded in 2004 to centralize the activities of the Bielefeld University in the areas of nanoscience and biophysics. The establishment was initiated by the physics Professors Dario Anselmetti (Experimental BioPhysics and Applied NanoSciences), Armin Gölzhäuser (Physics of Supramolecular Systems), Ulrich Heinzmann (Molecular and Surface Physics), Günter Reiss (Thin Films and Nanostructures), and Markus Sauer (Applied Laser Physics and Laser Spectroscopy).
Nanoscience and biophysics belong to modern IT relevant research areas that rely critically on the fruitful cooperation between different classical disciplines. Therefore, successful work of BINAS bases upon a close interdisciplinary collaboration between scientists from the Faculties of Physics, Biology, Chemistry, and Technology of Bielefeld University. Besides cooperation with the 'Industrie- und Handelskammern' Ostwestfalen, Bielefeld, Lippe, and Detmold BINAS plays an important role in knowledge transfer from basic to applied sciences. In addition, BINAS aims to help interested companies to solve important and industrially relevant scientific problems. By that, BINAS intends to promote collab-

BINAS
Bielefeld Institute
for Biophysics and Nanoscience

Prof. Dr. Markus Sauer
Bielefeld Institute for Biophysics and Nanoscience
Center for Biotechnology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5450
fax +49-521-106 2958
email sauer@physik.uni-bielefeld.de
url www.physik.uni-bielefeld.de/biophysik/binas

orative research and development projects. Furthermore, BINAS wants to discuss chances and risks of new research developments and future prospects of modern research areas with the local community and politics.
BINAS accommodates five different chairs from the Faculty of Physics and offers various techniques including modern molecular and surface physics, ultrathin films, lithography, supramolecular systems, chemical nanolithography, LEEPS microscopy, laser physics and spectroscopy, single-molecule fluorescence spectroscopy, atomic force microscopy, and molecular nanotechnology. The provided techniques are ideally suited for quality assurance of surfaces, the development of new assays for highly sensitive diagnostics of viral or bacterial infections and tumor detection as well as follow up of malignant diseases, new and refined coating techniques down to the atomic level, structuring of surfaces to improve storage media, to construct optical gratings, or to develop miniaturized circuitry, the development of new magnetic beads for therapeutic applications as well as for data storage.

Contributing Units

Experimental BioPhysics and Applied NanoSciences; Prof. Dr. D. Anselmetti

Physics of Supramolecular Systems; Prof. Dr. A. Gölzhäuser

Molecular and Surface Physics; Prof. Dr. U. Heinzmann

Thin Films and Nanostructures; Prof. Dr. G. Reiss

Applied Laser Physics and Laser Spectroscopy; Prof. Dr. M. Sauer

Experimental BioPhysics and Applied NanoSciences

The chair of Experimental BioPhysics and Applied NanoSciences was founded in July 2000 at Bielefeld University by Prof. Dr. D. Anselmetti with a new interdisciplinary science focus on single molecule biophysics, nanoanalytics, biophotonics and microfluidic lab-on-a-chip.

Research Interests
The Biophysics-Laboratory investigates the structure and function of native biological molecules at the single molecule level, and their interplay and dynamics with complexes, cells and tissue. This new and interdisciplinary research area is commonly termed as NanoBiology and includes the following topics which are all investigated in the Experimental Biophysics group by physicists, chemists and biologists in close cooperation:

- Physics of molecular recognition
- Atomic force microscopy and force spectroscopy
- Single molecule biosensors with optical tweezers
- Single cell analysis / nanoanalytics / lab-on-a-chip
- Biophotonics of single molecules, cells and tissue
- Migration and dynamics of biomolecules
- Ultrasensitive and label-free protein detection
- Molecular binding studies with fluorescence correlation spectroscopy (FCS)
- Single molecule electronics, wires and sensors
- Systems nanobiology

The laboratory is involved in a number of initiatives like the Collaborative Research Center SFB 613 from the German Research Foundation (DFG), a Federal Ministry of Education and Research (BMBF) initiative in Biophotonics and others. Beside the fundamental investigation of physical phenomena at the single molecule level, a considerable effort is put on the development of new, ultrasensitive technologies for microscopical, analytical, and biomedical applications, which leads into close collaborations with a number of industrial partners. The group Biophysics co-founded the Bielefeld Institute for Biophysics and Nanoscience (BINAS) and is actively participating with the other CeBiTec institutes within a new research initiative in the field of Systems Biology. The technology platform of the Experimental Biophysics group includes optical, electron and scanning probe microscopy and spectroscopy, 2-color fluorescence correlation spectroscopy, surface functionalization and micro- and nanofluidic device fabrication,

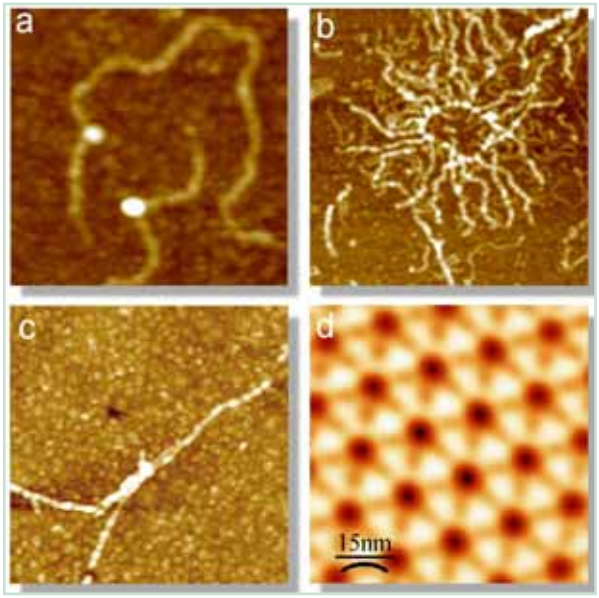

Fig. 1: Imaging biomolecules with atomic force microscopy (AFM) under physiological conditions (a) DNA-protein complexes, (b) proteoglycan cell adhesion molecule, (c) Alzheimer β-amyloid fibril and (d) 2D protein array with bacterial s-layer proteins.

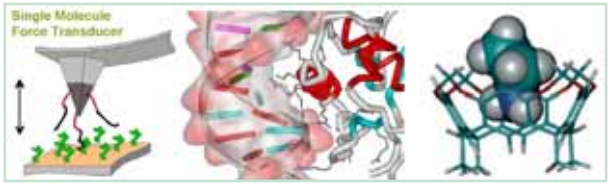

Fig. 2: Quantitative single molecule binding studies with in situ AFM dynamic force spectroscopy reveal the physical basis of specific molecular binding and molecular recognition. Native biological peptide-DNA and synthetic supramolecular complexes can be probed and affinity-ranked at the single molecule level.

Prof. Dr. Dario Anselmetti
Experimental BioPhysics and Applied NanoSciences
Faculty of Physics
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5391
fax +49-521-106 2959
email dario.anselmetti@physik.uni-bielefeld.de
url www.physik.uni-bielefeld.de/biophysik/

cleanroom facilities, multifocus two-photon fs-laser scanning microscopy, optical tweezers, label-free (UV-LIF) gel scanner for proteomics, and many others ...

Involvement in Courses of Study
The chair is involved in the Bachelor, Master and Diploma study courses for Physics, Biophysics and Nanosciences offered by the Faculty of Physics. In addition, the chair contributes to courses of the Faculties of Biology, Chemistry and Technology with lectures and practical exercises in biophysics, nanosciences and nanotechnology, microscopy and spectroscopy, micro- and nanofluidics and biophotonics.

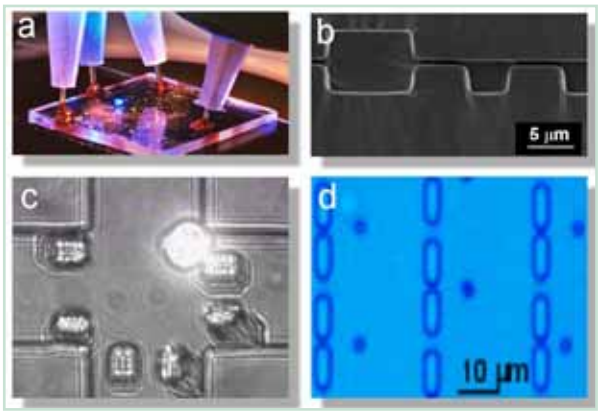

Fig. 3: Lab-on-a-chip and microfluidic devices will revolutionize the future by integrating pumping, separation and analytics of minute amounts of analyte biomolecules within biochips. (a) polymeric microchip device, (b) structured microfluidic channel geometries, (c) single fluorescent, GFP-transfected insect cell captured in a physical cell trap, and (d) colloidal particles in a periodic microstructure array.

Curriculum Vitae

1987: Diploma in Physics at University of Basel
1990: Ph.D. in Physics at University of Basel
1990: PostDoc at IBM-Research (Rüschlikon)
1992: Project leader in Nanobiology (University of Basel); Collaboration: Hoffmann-LaRoche
1994: Visiting scientist at the Joint Research Center for Atom Technology in Tsukuba (Japan)
1994-1999: Project leader for biological nanophysics within Ciba-Geigy AG / Novartis AG
1998: Habilitation in Physics at the Faculty of Natural Sciences at University of Basel
1998: Novartis Leading Scientist Award
1999: Manager of Nanophysics / Bionanoanalytics within Solvias AG in Basel
2000: Head of the chair of Experimental BioPhysics and Applied NanoSciences at Bielefeld University
Since 2002: Dep. chairman/project head in SFB 613
Since 2004: Research Council Member of Bielefeld University
Since 2004: Co-founder of the Bielefeld Institute for Biophysics and Nanoscience (BINAS)
Since 2005: Appointed Full Member of the Northrhine-Westfalian Academy of Sciences

Members

T. Damberg | T. T. Duong | R. Eckel | Dr. H. Frey | A. Fuhrmann | S. Gerkens | W. Hellmich | H. Höfemann | T. Kahre | A. Körnig | K. Leffhalm | G. Krome | J. Martini | Ch. Pelargus | K. Recker | J. Regtmeier | Dr. A. Ros | Dr. R. Ros | A. Sischka | Dr. K. Tönsing | V. Walhorn | D. Wesner |

Publications

Ros, A. *et al.*, 2005. **Brownian Motion: Absolute negative particle mobility.** Nature 436, 928

Eckel, R. *et al.*, 2005. **Single molecule experiments in synthetic biology - a new approach to the affinity ranking of DNA-binding peptides.** Angewandte Chemie (Int. Edition) 44, 3921-3924

Baumgarth, B. *et al.*, 2005. **Detailed studies of the binding mechanism of the *Sinorhizobium meliloti* transcriptional activator ExpG to DNA.** Microbiol 151, 259-269

Eckel, R. *et al.*, 2005. **Supramolecular chemistry at the single molecule level.** Angewandte Chemie (Intl. Edition) 44, 484-488

Hellmich, W. *et al.*, 2005. **Single cell manipulation, analytics and label-free protein detection in microfluidic devices for systems NanoBiology.** Electrophoresis 26, 3689-3696

Sischka, A. *et al.*, 2005. **Molecular mechanisms and kinetics between DNA and DNA-binding ligands.** Biophys J 88, 404-411

Streek, M. *et al.*, 2005. **Two-state migration of DNA in structured microchannel.** Phys Rev E Stat Nonlin Soft Matter Phys E 71, 11905

Rögener, J. *et al.*, 2003. **Ultrasensitive detection of unstained proteins in acrylamide gels by native UV fluorescence.** Anal Chem 75, 157-159

Schwesinger, F. *et al.*, 2000. **Unbinding forces of single antibody-antigen complexes correlate with their thermal dissociation rates.** Proc Natl Acad Sci U S A 97, 9972-9977

Physics of Supramolecular Systems

The chair of Physics of Supramolecular Systems headed by Prof. Dr. A. Gölzhäuser was established in October 2003. The research efforts are focussed on the characterization of structural, electrical and mechanical properties of supramolecular assemblies and their technological applications.

Research Interests

Supramolecular systems are aggregates of organic or biological molecules that self-assemble into larger entities (membranes, vesicles, protein complexes) *via* multiple weak interactions. One of the main objectives of the chair is the fabrication and characterization of artificial supramolecular systems. An important first step towards this goal is the development of simple and rapid techniques for the site-specific immobilization of single molecules or molecular aggregates on surfaces. Such chemical surface structures play important roles in the definition of contacts in 'molecular electronics' and the miniaturization of high throughput assays in molecular biology as well as in biosensors and tissue engineering. To fabricate chemically patterned substrates on a molecular length scale, it is necessary to modify the surface in a controlled manner with nanometer resolution. Molecular structures are created by utilizing electron beam lithography to pattern self-assembled monolayers. Focussed electron beams convert the terminal nitro functionality in self-assembled monolayers of nitrobiphenylthiol to amino groups, defining thus spatially confined reactive sites on a surface. By this electron induced chemical nanolithography ultrahigh resolution (<5 nm) templates for the site selective immobilization of molecules are created (Fig. 2). This patterning strategy is compatible with standard microfabrication techniques and allows the efficient patterning of large areas and mass fabrication.

State-of-the-art microscopic and spectroscopic techniques (Fig. 3) are used to study specific interactions between supramolecular entities, as well as between molecules and ionizing radiation. This knowledge is utilized in the process of nanofabrication of surface patterns, in which individual molecules occupy distinct locations.

Such artificial surfaces mimic biological functions, and are used in biosensors or biochips. More complex supramolecular entities (membranes, pores, molecular motors) can be built *via* a 'guided' self-assembly on such surfaces. In technological applications, such artificial supramolecular systems can be tailored to perform specific tasks in molecular electronics, biosensors, and nanobiotechnology.

The understanding of the complex interactions in supramolecular systems also requires an in-depth knowledge of the structural, mechanical and electrical properties of the involved entities. In contrast, there is a significant deficiency of methods suitable

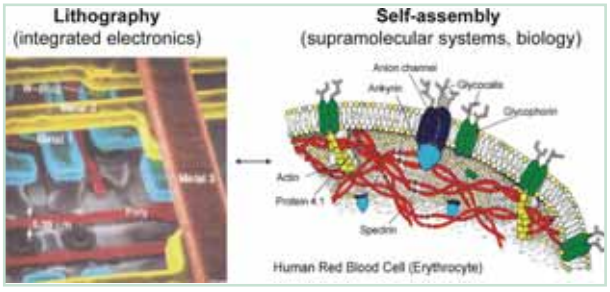

Fig. 1: Two concepts of nanostructure fabrication: Left: Integrated electronic circuits are made by lithography, i.e. a locally controlled exposure of a polymeric resist with light or electrons and a subsequent pattern transfer into silicon. Right: Biological systems spontaneously form vial self-assembly of weakly interacting molecules. The chair works towards the fabrication and characterization of artificial supramolecular systems by using a combination of lithography and self-assembly.

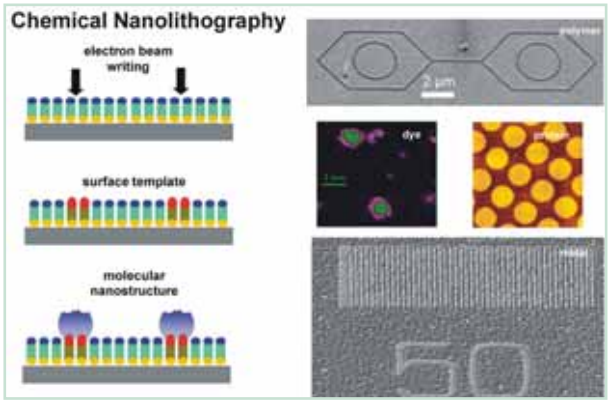

Fig. 2: Left: A self-assembled monolayer is locally exposed by electron beam lithography to create a surface template of reactive surface sites. Molecules can couple to these sites creating a molecular surface nanostructure. Right: Images of nanostructures (polymer, dye, protein, metal) built by chemical nanolithography.

Prof. Dr. Armin Gölzhäuser
Physics of Supramolecular Systems
Faculty of Physics
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5362
fax +49-521-106 6002
email goelzhaeuser@physik.uni-bielefeld.de
url www.physik.uni-bielefeld.de/experi/goelz

to characterize matter on the supramolecular level. Imaging with coherent electrons from Low Energy Electron Point Sources (LEEPS) is a novel method that has this potential. The point source is realized by a metal tip with a radius of atomic dimensions. The source is placed close (~100 nm) to a thin molecular object and a voltage sufficient for electron emission is applied. A part of the electron's wave function is then scattered by the object and interferes with the unscattered part. Hence, a holographic interference pattern is generated that contains information on the object's structure.
The microscopes can image and reconstruct single polymer strands like DNA, nanotubes and nanowires. Coherent low energy electrons are sensitive probes for electrical and magnetic properties of small objects. Hence, there are numerous applications, like mapping of electrostatic charge or magentic impurities and it is a long term objective to explore these capabilities.

Involvement in Courses of Study

The chair is involved in the Bachelor, Master and Diploma study courses for Physics, Biophysics and Nanosciences offered by the Faculty of Physics. In addition, the chair contributes to courses of the Faculties of Chemistry and Technology with lectures and practical exercises in nanosciences and nanotechnology, microscopy and spectroscopy.

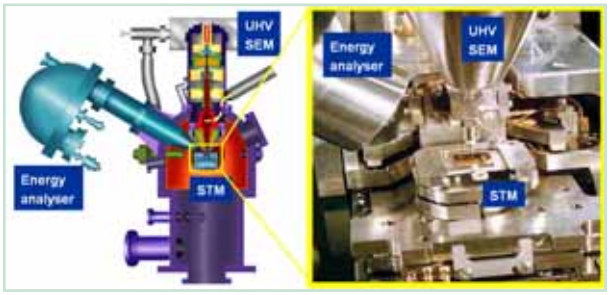

Fig. 3: Left: Schematic view of a surface analytical instrument used in the fabrication and characterization of supramolecular systems. The electron beam of a scanning electron microscopes (SEM) can modify molecular structures while they are simultaneously imaged by a scanning tunnelling microscope (STM). Right: Photograph of the interior of the ultra-high-vacuum chamber.

Curriculum Vitae

1982-1989: Studies of Physics at the University of Heidelberg
1986-1987: Physics Department, Arizona State University
1988-1989: Diploma in Physics at the Max Planck Institute for Medical Research
1989-1993: Doctorate in Physical Chemistry, at the University of Heidelberg
1993-1996: Feodor Lynen Fellowship, Department of Materials Science, University of Illinois at Urbana-Champain
1996-2001: Habilitation; title: Characterization and manipulation of materials at the molecular and atomic levels; University of Heidelberg
2001-2003: Lecturer (C2), Physical Chemistry; University of Heidelberg
2003: Professor (C3) for Physical Chemistry, Philipps University of Marburg
Since 10/2003: Professor (C4) for Experimental Physics, Bielefeld University
Since 2004: Co-founder of the Bielefeld Institute for Biophysics and Nanoscience (BINAS)

Members

Dr. A. Beyer | Dr. A. Turchanin | Dr. B. Völkel |

Publications

Eck, W. *et al.*, 2005. **Free-standing nanosheets from cross-linked biphenyl self-assembled monolayers.** Adv Mater, in press
Biebricher, A. *et al.*, 2004. **Controlled threedimensional immobilization of biomolecules on chemically patterned surfaces.** J Biotechnol 112, 97-107
Küller, A. *et al.*, 2003. **Nanostructuring of silicon by electron beam lithography of self-assembled hydroxybiphenyl monolayers.** Appl Phys Lett 82, 3776-3778
Schmelmer, U. *et al.*, 2003. **Surface-initiated polymerization on self-assembled monolayers: Amplification of patterns on the micrometer and nanometer scale.** Angewandte Chemie (Int. Editi-on) 42, 559-563
Gölzhäuser, A. *et al.*, 2002. **Optimization of the low energy electron point source microscope: Imaging of macromolecules.** Micron 33, 241-255
Gölzhäuser, A. *et al.*, 2001. **Chemical nanolithography with electron beams.** Adv Mater 13, 803-806
Felgenhauer, T. *et al.*, 2001. **Electrode modification by electron-induced patterning of aromatic self-assembled monolayers.** Appl Phys Lett 79, 3323-3325
Geyer, W. *et al.*, 2001. **Electron induced chemical nanolithography with self-assembled monolayers.** J Vac Sci Technol B 19, 2732-2735

Molecular and Surface Physics

The chair of Molecular and Surface Physics headed by Prof. Dr. U. Heinzmann was founded in October 1984. Many students have worked in the experimental molecular and surface physics laboratories for their diploma theses. More than 50 graduate students have carried out research to attain their Ph.D. degree. Several PostDoc scientists have been awarded Professorships at German Universities, e.g. Dortmund, Düsseldorf, Hamburg and Mainz.

Research Interests

In the last two decades the research interests of the chair have 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 towards applications in nanotechnology and nanobiotechnology. Ultra-thin nanometer layer deposition techniques and related analysis methods have been developed towards EUVL (extreme ultraviolet lithography) and x-ray optics for attosecond time resolved spectroscopy. The application of soft x-ray radiation such as scattering, diffraction and imaging techniques as well as of electron microscopy (TEM, SEM, STM and PEEM) on organic and bio-organic systems has come to play an increasingly important role in the research activities of the group over the past few years. Two projects in the Collaborative Research Center SFB 613 Physics of Single Molecule Processes and Molecular Recognition in Organic Systems have been established; these work with soft x-rays and use them to study the dynamics of molecular conformation in organic and bio-organic molecular systems, time-resolved.

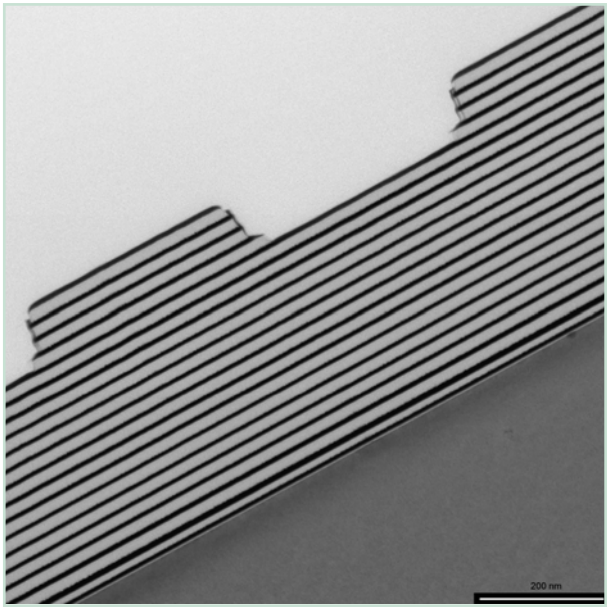

Fig. 1: Cross-section of a nanometer-multilayer x-ray mirror by means of transmission electron microscopy (TEM).

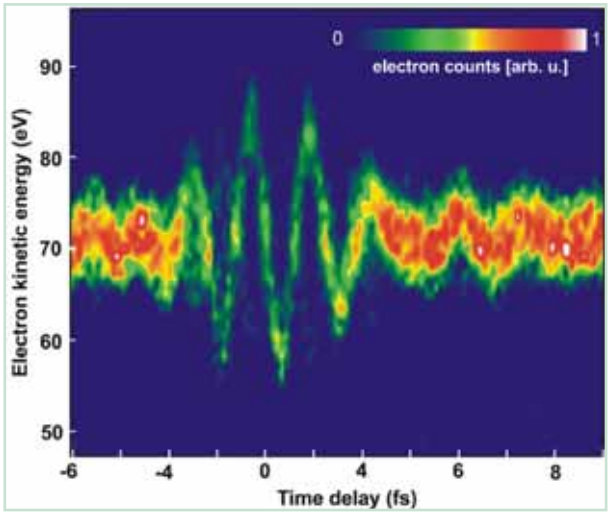

Fig. 2: The world fastest-streaking camera: Direct observation of a 4 Femtosecond short light pulse by use of x-ray pulses of 250 Attoseconds duration *via* the photoelectron energy distribution within the light field oscillation (Goulielmakis, E. *et al.*, 2004).

Prof. Dr. Ulrich Heinzmann
Molecular and Surface Physics
Faculty of Physics
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5469
fax +49-521-106 6001
email uheinzm@physik.uni-bielefeld.de
url www.physik.uni-bielefeld.de/experi/d4

Involvement in Courses of Study

The chair is involved in the Bachelor, Master and Diploma courses for Physics, Biophysics and Nanosciences offered by the Faculty of Physics and contributes to courses of the Biology, Chemistry and Technology Faculties with lectures and practical exercises/experiments in molecular and surface physics, x-ray radiation physics, nanotechnology, microscopy, spectroscopy and ultra-fast phenomena techniques.

Curriculum Vitae

Diploma in Physics at the Technical University Karlsruhe
Ph.D. in Physics and habilitation at the University of Münster
1980: Visiting lecturer at Imperial College London, U.K.
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
1995-2002: Chairman of the DFG-Research Group Nanometer Layer Systems
Since 2002: Chairman of DFG SFB 613 (Collaborative Research Center)
Since 2004: Founding member of the Bielefeld Institute for Biophysics and Nanoscience (BINAS)
1981: Award ('Physikpreis') of the German Physical Society
1998: Gold Medal of the Slovak Academy of Sciences
2000: Member of the European Academy of Sciences and Arts

Members

Dr. T. Andres | P. Bartz | Dr. A. Brechling | S. Cunovic | Prof. Dr. M. Drescher | Dr. W. Hachmann | Dr. F. Hamelmann | S. Hendel | Prof. Dr. N. Kabachnik | R. Kalms | Dr. U. Kleineberg | Dr. J. Lin | A. K. Lofthouse | | M. Michelswirth | Dr. N. Müller | Dr. U. Neuhäusler | V. Schimmang | J. Slieh | T. Uphues | K. Wisotzky |

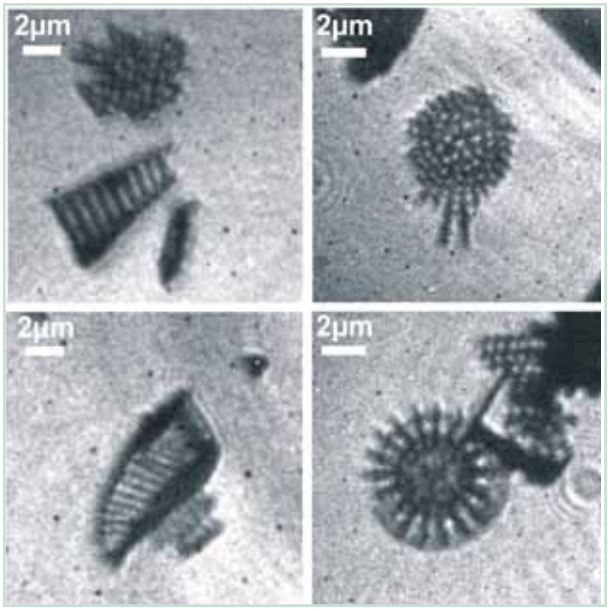

Fig. 3: Soft x-ray microscopy of diatom samples with a resolution of 200 nm by means of a pulsed laser-based coherent table-top radiation source (Wieland, M. *et al.*, 2005).

Publications

Wieland, M. *et al.*, 2005. **Towards time-resolved soft x-ray microscopy using pulsed fs-high-harmonic radiation.** Ultramicroscopy 102, 93-100
Goulielmakis, E. *et al.*, 2004. **Direct measurement of Light Waves.** Science 305, 1267-1269
Lischke, T. *et al.*, 2004. **Circular dichroism in valence photoelectron spectroscopy of free unoriented chiral molecules: Camphor and bromocamphor.** Phys Rev A 70, 022507
Brechling, A. *et al.*, 2004. **Structural organization of DMPC lipid layers on chemically micropatterned self assembled monolayers as biomimetic systems.** J Biotechnol 112, 115-124
Hütten, A. *et al.*, 2004. **New magnetic nanoparticles for biotechnology.** J Biotechnol 112, 47-63
Siffalovic, P. *et al.*, 2004. **Large-scale homogeneous molecular templates for femtosecond time-resolved studies of the guest-host interaction.** J Biotechnol 112, 139-149
Kienberger, R. *et al.*, 2004. **Atomic transient recorder.** Nature 427, 817-821
Brechling, A. *et al.*, 2003. **Characterization of DMPC bilayers and multilamellar islands on hydrophobic Self-Assembled Monolayers of ODS/Si (100) and mixed ODS-DDS/Si (100) by nc-AFM and X-ray reflectometry.** Thin Solid Films 433, 281-286
Kienberger, R. *et al.*, 2002. **Steering attosecond electron wave packets with light.** Science 297, 1144-1148
Drescher, M. *et al.*, 2002. **Time-resolved atomic inner-shell spectroscopy.** Nature 419, 803-807
Böwering, N. *et al.*, 2001. **Asymmetry in photoelectron emission from chiral molecules induced by circularly polarized light.** Phys Rev Lett 86, 1187-1190
Kleineberg, U. *et al.*, 2001. **STM lithography in organic self-assembled monolayer.** Advanced Functional Materials 11, 208-212
Hentschel, M. *et al.*, 2001. **Atto-second metrology.** Nature 414, 509

Thin Films and Nanostructures

The chair of Thin Films and Nanostructures headed by Prof. Dr. G. Reiss was founded in October 1997. In the meantime, it was fully established and equipped and already looks back to a successful development. More than 40 students worked in the laboratories and successfully finished their Diploma and Ph.D. thesis. Already two of the scientists employed were able to habilitate and got highly ranked positions in research institutes.

Research Interests

The chair's focus are new magnetic materials, magnetic nanostructures and their applications in new sensors, memories and logic devices. With the findings of new and large dependences of the resistance of nanoscale ultrathin film systems on an external magnetic field, Magneto- and Spinelectronics appeared as new and vital research fields. Within these topics the activities of the chair span from finding new materials and analyzing fundamental properties to prototyping new sensors and electronic logic devices. This research is done in intensive collaboration both with chemistry and biology as well as with industrial partners.

Within the last years, the field of chemically produced nanoparticles evolved to an exciting new research topic. The chair has successfully entered this area with alloyed particles (Fe/Co) with large magnetic moment. Merging this with the biochip targets now to complete lab-on-the-chip systems.

The equipment covers the complete route from thin film coating and analysis systems (MBE, sputtering, Auger, TEM, AFM etc.) to optical and e-beam lithography for complex micro- and nanopatterned electronic devices.

Since five years, one main activity at the chair is the development of magnetoresistive biochip sensors using the Giant Magneto Resistance (GMR) and the Tunneling Magneto Resistance (TMR). Whilst these effects are frequently discussed to be a new paradigm for the post CMOS era, the application of such highly integrated devices for sensing magnetic particles attached to biomolecules is an exciting and challenging task for cross disciplinary scientific work. The markers are specifically attached to the target molecules, and their magnetic stray field is picked up by an embedded magnetoresistive sensor as a change of the electrical resistance. Compared to established, e.g. fluorescent, detection methods, magnetic biosensors have low molecular detection

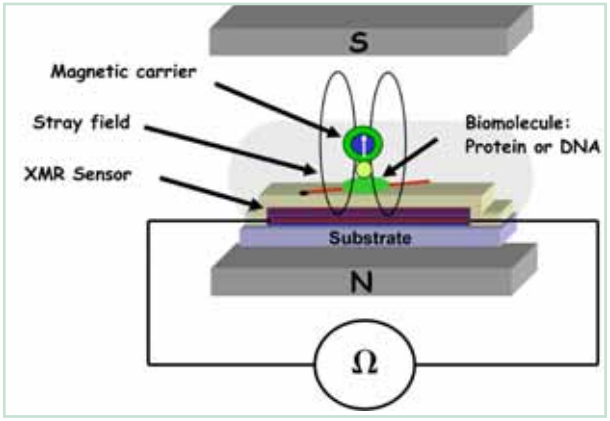

Fig. 1: Principle of the magnetic biochip: Biotin marked DNA-molecules hybridize with complementary strands attached to the surface. After that, streptavidin coated beads bind to the biotin. By applying a magnetic field perpendicular to the sensor surface, only the *in-plane* components of the dipole stray field of the beads are detected.

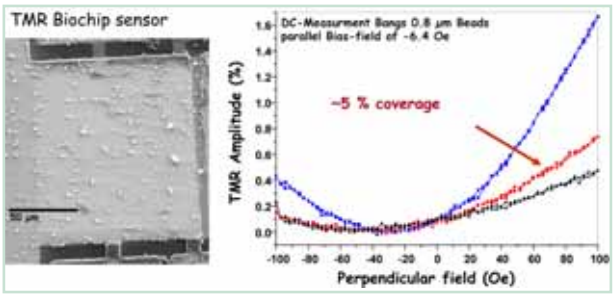

Fig. 2: A TMR sensor surface covered by magnetic beads (left) and the TMR signal measured during applying a magnetic field perpendicular to the sensor surface and an *in-plane* field which is close to the switching field of the soft electrode.

Prof. Dr. Günter Reiss
Thin Films and Nanostructures
Faculty of Physics
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5412
fax +49-521-106 6046
email reiss@physik.uni-bielefeld.de
url www.physik.uni-bielefeld.de/experi/d2

limits, flexibility and the direct availability of an electronic signal suitable for further automated analysis. Most of this work was done within the Collaborative Research Center SFB 613 Physics of Single Molecule Processes and Molecular Recognition in Organic Systems of the German Research Foundation (DFG).

Involvement in Courses of Study
The chair contributes to the Bachelor and Master course in Physics and initiated a Bachelor and Master course Nanoscience. In addition, the chair is involved in the Bachelor and Master courses Biophysics and in the lecture program for cross disciplinary studies.

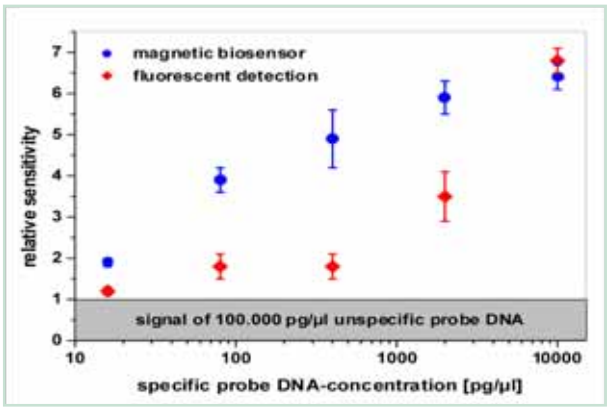

Fig. 3: Comparison of the sensitivity of a GMR based biosensor and the fluorescence method for different DNA probe concentrations. The signal is normalized to that produced by a 150 nM unspecific probe DNA solution.

Curriculum Vitae

Diploma and Ph.D. degree in Physics and habilitation in Experimental Physics at the University Regensburg
1992: PostDoc at the IBM T.J. Watson Research Center, Yorktown Heights, NY USA
1993-1997: Department manager of the Thin Film Division at the Institute of Solid State Research and Materials Science (IFW), Dresden
Since 1997: Professor and head of the chair of Thin Films and Nanostructures, Faculty of Physics, Bielefeld University
Since 2005: Dean of the Faculty of Physics

Members

Dr. S. Herth | Dr. A. Hütten | Dr. X. Kou | Dr. N-N. Liu | Dr. M. Panhorst | K. Rott | Dr. J. Schmalhorst | Dr. A. Thomas | A. Windmann |

Publications

Reiss, G. *et al.*, 2005. **Magnetoresistive sensors and magnetic nanoparticles for biotechnology.** J Mater Res, in press
Reiss, G. and Hütten, A. 2005. **Magnetic nanoparticles – applications beyond datastorage.** Nature Materials – News and Views 4, 725-726
Schmalhorst, J. *et al.*, 2005. **Inelastic electron tunneling spectroscopy and bias voltage dependence of magnetic tunnel junctions with polycrystalline Co_2MnSi electrode.** Appl Phys Lett 86, 052501
Panhorst, M. *et al.*, 2005. **Sensitive bondforce measurements of ligand-receptor pairs with magnetic beads.** Biosens Bioelectron 20, 1685-1689
Brzeska, M. *et al.*, 2005. **Detection and manipulation of biomolecules by magnetic carriers.** J Biotechnol 112, 25-33
Kämmerer, S. *et al.*, 2004. **Co_2MnSi Heusler alloy as magnetic electrodes in magnetic tunnel junctions.** Appl Phys Lett 85, 79-81
Reiss, G. *et al.*, 2004. **Arrays of magnetic tunnelling junctions for field programmable logic gates.** J Magnet Magnet Mater 272–276, E1497-E1498
Hütten, A. *et al.*, 2004. **New magnetic nanoparticles for biotechnology.** J Biotechnol 112, 47-63

Applied Laser Physics and Laser Spectroscopy

The chair of Applied Laser Physics and Laser Spectroscopy headed by Prof. Dr. M. Sauer was new realigned towards the direction of single-molecule sensitive optical techniques in 2003. In the last two years more than five students worked in the laboratories for their diploma thesis and around eight graduate students carry and carried out research to receive the Ph.D. degree. In addition, five talented PostDocs perform partly independent research to promote their own scientific career in the highly interdisciplinary field of biophysics and single-molecule spectroscopy.

Research Interests

The interdisciplinary group focuses on the development of new single-molecule sensitive fluorescence microscopy and spectroscopy techniques and their application in life science. Systems studied involve the development of unidirectional photonic wires, the investigation of energy transfer pathways and photophysics of higher excited states in synthetic light harvesting systems (multichromophoric dendrimers), the implementation of multi-FRET to reveal the assembly of biomolecular machines, the development of new techniques for simultaneous topographic and fluorescence imaging, the design of electron transfer probes for (i) diagnostic applications, (ii) the study of the conformational flexibility of biopolymers, and (iii) protein folding at the single-molecule level with submicrosecond temporal and subnanometer spatial resolution (and direct comparison with Molecular Dynamic Simulations), new fluorescence labeling techniques, switchable fluorophores, live cell imaging with one- and two-photon excitation, precision distance microscopy in the resolution-gap of far-field microscopy, as well as the development of a cellular positioning system (CPS).

Development of Unidirectional Photonic Wires

In contrast to molecular electronic wires which transport electrons (or holes) a photonic wire is a molecular device that conveys excited-state energy from an input to an output unit. In contrast to conductive nanowires, photonic wires are addressable at a distance without the need of physical contacts. The chair is developing molecular photonic wires based on (i) the use of conventional chromophores with high fluorescence quantum yield, (ii) an energy cascade as the driving force for the excited-state energy to ensure unidirectionality, and (iii) an arrangement of the chromophores for optimized energy flow. The chair uses DNA as a rigid scaffold along which the single molecule compatible fluorescent dyes are arranged. Energy flow can be achieved with an efficiency of up to 90% over more than 13 nm based on quadruple FRET over five dyes. Multistep FRET is not only interesting in the context of developing nanoscale optical devices (see above) but can also be used to investigate biomolecular interactions between more than two molecules or to correlate movements of two different segments of the same molecule. However, whenever more than one FRET process occurs, the assignment of the energy transfer pathway becomes ambiguous. Therefore, the chair develops a technique to analyze multistep FRET based on triple alternating laser excitation (TRALEX). Here, an acousto-optical filter rapidly switches between three excitation colors so that the different fluorophores and individual energy transfer steps are probed individually. Alternatively, the energy transfer pathway can be assigned using additional fluorescence parameters such as the fluorescence lifetime. The newly developed technique is applied to the investigation of V-ATPase and to investigate gene regulation on the level of transcription (within the framework of the Collaborative Research Center SFB 613, projects No. A5 and D8).

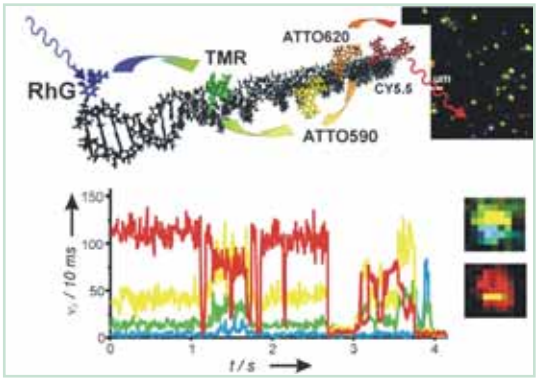

Fig. 1: Fluorescence trajectory of a single immobilized photonic wire bearing five different fluorophores (excitation at 488 nm, emission of four spectrally-separated avalanche photodiodes).

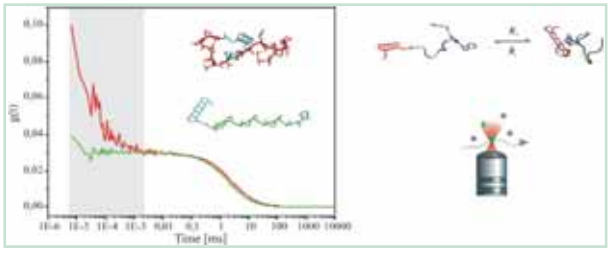

Fig. 2: Fluorescence correlation spectroscopy (FCS) curves measured for flexible and stiff peptides carrying a single Trp residue. Peptides were labelled with the oxazine dye MR121. Contact induced fluorescence quenching results in the appearance of an amplitude in the nanosecond range of the FCS curve.

Applied Laser Physics and Laser Spectroscopy

Prof. Dr. Markus Sauer
Applied Laser Physics and Laser Spectroscopy
Faculty of Physics
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 5450
fax +49-521-106 2958
email sauer@physik.uni-bielefeld.de
url www.physik.uni-bielefeld.de/experi/d3

Curriculum Vitae

Diploma in Chemistry at the University of Heidelberg
1997: Victor Meyer Award of University of Heidelberg
1998: BioFuture Award of the BMBF
1999: Stay abroad in the group of Prof. Dr. S. Weiss at LBNL, Berkeley
2002: Ph.D. in Physical Chemistry and habilitation in Physical Chemistry at University of Heidelberg
2002-2003: 'Privatdozent' (C2) at the Institute of Physical Chemistry at University of Heidelberg
Since 2003: Professor and head of the chair of Applied Laser Physics and Laser Spectroscopy, Faculty of Physics, Bielefeld University
Since 2004: Founding member of Bielefeld Institute for Biophysics and Nanoscience (BINAS)
Since 2005: Speaker of BINAS

Members

Dr. R. Böttner | Dr. S. Doose | Dr. D. Feldmann | Dr. C. Müller | Dr. H. Neuweiler | R. Pätzmann | Dr. P. Tinnefeld | Dr. G. Wiebusch | S. Wörmer |

Studying Conformational Dynamics of Biopolymers Using Selective Fluorescence Quenching of Organic Dyes by Amino Acids and Nucleobases

The formation of intramolecular contacts within polypeptide chains and nucleic acids is of fundamental importance for biological function. Knowledge about the rates of intrachain contacts within peptides is essential for the understanding of fundamental steps of protein folding. On the other hand, conformational flexibility and formation of single-stranded DNA hairpins play a key role in, for example, gene expression and regulation.
The chair found that certain classes of fluorophores (i.e. oxazine and rhodamine dyes) are fluorescence-quenched efficiently upon contact formation with the amino acid tryptophan (Trp) as well as with the nucleobase guanine (G). The fluorescence quenching mechanism is assumed to be a photoinduced electron transfer reaction. Intramolecular dye / quencher contact formation and dissociation in fluorescently modified flexible peptides and oligonucleotides yield non-fluorescent and fluorescent 'off' and 'on' states, whose interconversion kinetics are driven by random biopolymer chain diffusion. Fluorescence correlation spectroscopy (FCS) with nanosecond time resolution is applied to reveal rates of intrachain contact formation and dissociation, measured under thermodynamic equilibrium conditions.

Involvement in Courses of Study

The chair is involved in the Bachelor, Master and Diploma courses for Physics, Biophysics and Nanosciences offered by the Faculty of Physics and contributes to courses of the Faculties of Biology, Chemistry and Technology with lectures and practical exercises/experiments in optical spectroscopy, fluorescence microscopy, optical near-field techniques, energy transfer pathways and light-harvesting, and photophysics.

Publications

Sauer, M. 2005. **Reversible molecular photoswitches: A key technology for nanoscience and fluorescence microscopy.** Proc Natl Acad Sci U S A 102, 9433-9434
Tinnefeld, P. and Sauer, M. 2005. **Branching out of single molecule fluorescence spectroscopy: Challenges for chemistry and influence on biology.** Angewandte Chemie (Int. Edition) 44, 2642-2671
Heinlein, T. *et al.*, 2005. **High-resolution coclocalization of single molecules within the resolution gap of far-field microscopy.** Chemphyschem 6, 949-955
Neuweiler, H. and Sauer, M. 2005. **Exploring life by single-molecule fluorescence spectroscopy.** Anal Chem 77, 179A-185A
Tinnefeld, P. *et al.*, 2005. **Design of molecular photonic wires based on multistep electronic excitation transfer.** Chemphyschem 6, 217-222
Heilemann, M. *et al.*, 2005. **Carbocyanine dyes as efficient reversible single-molecule optical switch.** J Am Chem Soc 127, 3801-3806
Heilemann, M. *et al.*, 2004. **Multistep fluorescence resonance energy transfer in single photonic wires.** J Am Chem Soc 126, 6514-6515
Neuweiler, H. and Sauer, M. 2004. **Using photoinduced charge transfer reaction to study conformational dynamics in biopolymers at the single-molecule level.** Curr Pharm Biotechnol 5, 285-298
Hofkens, J. *et al.*, 2003. **Revealing competitive Förster-type resonance energy transfer pathways in single bichromophoric molecules.** Proc Natl Acad Sci U S A 100, 13146-13151

International Graduate School in Bioinformatics and Genome Research

Bioinformatics and Genome Research at Bielefeld University have an excellent international reputation in research and education. One of the first curricula, world-wide, for Bioinformatics was established 1989 with the study program Applied Informatics in the Natural Sciences and has been the basis for many M.Sc. programs in and outside of Germany. Genome Research was successfully established in Bielefeld by participating in the yeast genome project in 1990. Numerous bacterial genomes have been sequenced in Bielefeld to date. Today, the Center for Biotechnology serves as the hub for projects in the Life Sciences at Bielefeld University. In acknowledgement of the outstanding achievements of the research groups at CeBiTec, the Ministry of Education and Research (MSWF) of the State Northrhine-Westfalia (NRW) awarded the establishment of the International Graduate School in Bioinformatics and Genome Research in 2001. The English language Ph.D. program Bioinformatics and Genome Research under the auspices of the NRW Graduate School is based on broad and interdisciplinary cooperation at the CeBiTec. Through an intensive process of recruiting, selection, supervision, and evaluation it ensures a successful Ph.D. education of the highest international standards.
Meanwhile, the faculty of the NRW Graduate School has grown to over 40 members and seven distinguished researchers of the International Faculty. Overall, 48 students have been admitted to the study program of the Graduate School, 32 with scholarships. On average 40% of enrolled students are from abroad.

International Activities
The NRW Graduate School has appointed seven international faculty members of the highest scientific reputation, all of which hold lectures on a regular basis in the Ph.D. program.
The Bioinformatics Research Education Workshop (BREW) series, initiated by Bielefeld University, brings together first-year Ph.D. students from Ph.D. programs across Europe to promote international cooperation and exchange by networking the graduate students and introducing them to the scientific review process. The participating programs are:

- ComBi program of Helsinki University, Finland
- EBI Ph.D. program of the European Bioinformatics Institute, Hinxton, UK
- Ph.D. Program of Bergen University, Norway
- International Graduate School in Bioinformatics and Genome Research, Bielefeld University, Germany
- Max Planck Research School for Computational Biology and Scientific Computing, MPI for Molecular Genetics, Berlin, Germany

Ensuring the Highest Standards
Every graduate student is assisted by a team of at least two supervisors, who are informed of the state of the Ph.D. project and who give advice on questions regarding the study program. Ph.D. students write project reports every year that are disseminated to the Faculty. Twice a year faculty and students meet at a retreat to hold presentations and have discussions on the current state of the students' research projects. The large number of peer-reviewed publications by students to date shows the success of the strategy of intensive supervision and reporting, as well as continuous discussion of the content and aim of research projects.

The NRW Undergraduate Science Awards
The NRW Graduate Schools have jointly announced an undergraduate award to foster the early development of research experience and practice during undergraduate studies. Every NRW Graduate School awards an annual prize of 1,500 € for an outstanding research paper in the corresponding field of research

Members of the Faculty and Ph.D. students participating in the fall retreat 2005 at 'Haus Reineberg'.

(www.undergraduate-awards.de).

Key Characteristics of the Program
This study program combines the areas of Bioinformatics and experimental Genome Research allowing students to aquire a Ph.D. in either Biology or Computer Science within 3 years. In addition to the scientific research work, students must complete a study program during the first 5 semesters taking into account the scientific background of the students and the subject of the doctoral thesis. The sixth semester is reserved for writing the doctoral thesis. In order to foster competence in research discussion, all graduate students have to present their current research to the faculty of the Graduate School at a retreat twice a year.
Key Features: All seminars, practical courses, and lectures are taught in English. The scientific background of the supervisors is in the fields of computer science, biology, mathematics, chemistry, and physics. Currently, there are 28 Ph.D. scholarships, seven scientific, technical and administrative staff positions. The course program tailored to students' profiles, accompanied by a series of workshops and a guest program.
Program Goals: Graduates of this program will be prepared to make novel contributions to the field of bioinformatics and genome research. The training is rigourous, candidates are expected to have a solid background in some of the following: bioinformatics, computer science, mathematics, statistics, genetics, genomics, biochemistry. Candidates will have a broad understanding of bioinformatics and/or genome research with specialization in a specific area. This program emphasizes communications skills both verbal and written. Graduates are expected to present and publish in peer-reviewed conferences and journals. Graduates of this program will be fully prepared for careers in bioinformatics or genomics, in academia as well as industry.

Dr. Dirk J. Evers
Executive Director
International Graduate School
in Bioinformatics and Genome Research
Center for Biotechnology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4914
fax +49-521-106 6490
email dirk.evers@cebitec.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/GradSchool

Coordination Committee
Prof. Dr. Robert Giegerich (Speaker)
Prof. Dr. Alfred Pühler **(Speaker)**
Prof. Dr. Jens Stoye **(Dean of Studies)**
Dr. Sebastian Böcker
Dr. Jörn Kalinowski

The International Faculty
Prof. W. Atchley, Dept. of Genetics and Center for Computational Biology, North Carolina State University, USA
Prof. V. Brendel, Dept. of Genetics, Development, and Cell Biology, Iowa State University, USA
Prof. D. Cook, Dept. of Plant Pathology, UC Davis, USA
Prof. G. Myers, Dept. of Electrical Engineering and Computer Science, UC Berkeley, USA
Prof. C. Sensen, Dept. of Biochemistry and Molecular Biology, University of Calgary, Canada
Prof. R. Overbeek, Genomics and Applied Bioinformatics, Argonne National Labs, Chicago, USA
Prof. A. Dress, Director, CAS-MPG Partner Institute for Computational Biology, Shanghai, PR China

Mentors
Dr. Susanne Schneiker
Dr. Matthias Höchsmann

INTERNATIONAL GRADUATE SCHOOL
BIOINFORMATICS & GENOME RESEARCH

Bioinformatics Resource Facility

High-throughput genome analysis techniques like whole genome shotgun sequencing, transcriptomics, proteomics, and metabolomics provide researchers with a flood of data and a wealth of information. For storing, analyzing, and integrating all these data sets, applied bioinformatics is an essential tool for bridging the gap between biologists and informatics scientists.
The Bioinformatics Resource Facility provides hardware and software support for genome and post-genome research in general and in addition to that, the group actively develops a number of larger software applications, widely used in several national and international projects.
As a basis for all further analysis, the DNA sequence of a genome of interest is usually obtained e.g. by whole genome shotgun sequencing. For analyzing the individual sequence reads and for monitoring the assembly process, we have developed SAMS, a sequence analysis and management system.
Once the complete DNA sequence is obtained, researchers are interested in the extraction, definition, and interpretation of functional regions on the genome sequence. For such purposes, the group has been developing the **GenDB** open source genome annotation system for prokaryotic genomes for more than five years now. Given a genome sequence, the system integrates numerous tools to perform a gene prediction and a functional annotation of the genome. Subsequently, the genome can be inspected and gene annotations can be manually improved *via* the GenDB web interface (Fig. 1).
For transcriptome data analysis the **EMMA** software platform has been developed that also includes a LIMS component (ArrayLIMS). Data can be uploaded in standard formats and linked to the GenDB data. The system provides customizable pipelines for data processing (Fig. 2) and has a modular architecture that can easily be extended. Several visualization methods like scatter-plots or heat maps are also available. EMMA features detailed reports about spots, genes, and their corresponding measurements.
ProDB is software for large-scale analysis of proteome data including a LIMS component. ProDB stores experimental data like images of 2D gels or mass spectra (MS) and allows automated data analysis and annotation of mass spectra.
Each of the described applications can be used stand-alone, but they can also be linked *via* the **BRIDGE** integration layer. Using this layer, data objects from different projects can be linked so that e.g. information originating from a GenDB project can be shown in the EMMA or ProDB web interface. The group is in the process of tightly integrating the different applications to provide the user with the benefit of having all useful information present at each step of the analyses.

Hardware and Software Support for Genome and Post-Genome Research
Being a part of the Bioinformatics Resource Facility, the Support Team runs the infrastructure necessary

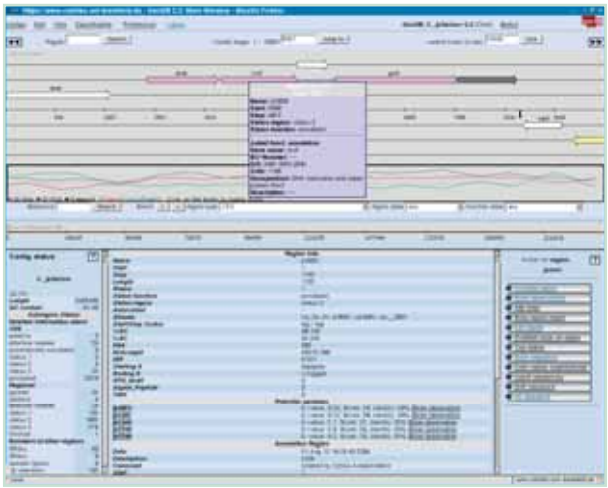

Fig. 1: This screenshot of the GenDB web interface depicts the first few genes of *Corynebacterium jeikeium*. Coding sequences (CDS) are displayed as arrows using different color codes according to the functional classification. By clicking on a CDS, detailed information is displayed, e.g. the gene length, GC content, molecular weight, or a list of potential paralogs.

Fig. 2: The EMMA software provides a user friendly interface for the configuration of individual data analysis pipelines. The screenshot shows the pipeline configuration dialog that allows a step by step creation of reusable data analysis workflows.

for providing the bioinformatics services outlined above. Apart from providing computer workstations for local scientists, this includes the installation, operation, and maintenance of the storage, database and compute systems. At the time of this writing these core facilities comprise a redundant file service with a total storage capacity of approx. 22 terabytes, a backup system, and a compute cluster consisting of 500 CPUs.
Further, the team provides mechanisms for maintaining local mirrors of a number of international sequence databases which are the mandatory basis for most of the computations performed at the CeBiTec. Providing first and second level support for the users of the CeBiTec computer systems as well as Bioinformatics Resource Facility software developers by installing and maintaining a variety of scientific and auxiliary tools adds to the team's field of responsibility. The monitoring and tuning of the infrastructure so that the whole system meets the constantly evolving requirements completes the list of tasks.

Involvement in Courses of Study

The group contributes to the Bachelor program in Bioinformatics and Genome Research, the Master programs in Genome Based Systems Biology and in Bioinformatics and Genome Research. Concerning Ph.D. studies, the group participates in the International Graduate School in Bioinformatics and Genome Research and in the Research Training Group Bioinformatics.

Fig. 3: A part of the CeBiTec compute cluster and storage systems including 128 SunFire V20z dual Opteron servers and several Sun StorEdge 351x and A3500FC cabinets.

Dr. Folker Meyer
Executive Director
Bioinformatics Resource Facility
Center for Biotechnology
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

phone +49-521-106 4827
fax +49-521-106 6419
email fm@cebitec.uni-bielefeld.de
url www.cebitec.uni-bielefeld.de/groups/brf

Coordination Committee

Prof. Dr. Bernd Weisshaar (Speaker)
Prof. Dr. Alfred Pühler
Prof. Dr. Jens Stoye
HD Dr. Anke Becker
PD Dr. Helge Küster
Alexander Sczyrba

Members

Dr. J. V. Choudhuri | Dr. A. Goesmann | T. Kasch | A. Neumann | Dr. V. Mittard-Runte |

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CeBiTec
Bielefeld University
Universitätsstraße 25
33615 Bielefeld
Germany

url www.cebitec.uni-bielefeld.de