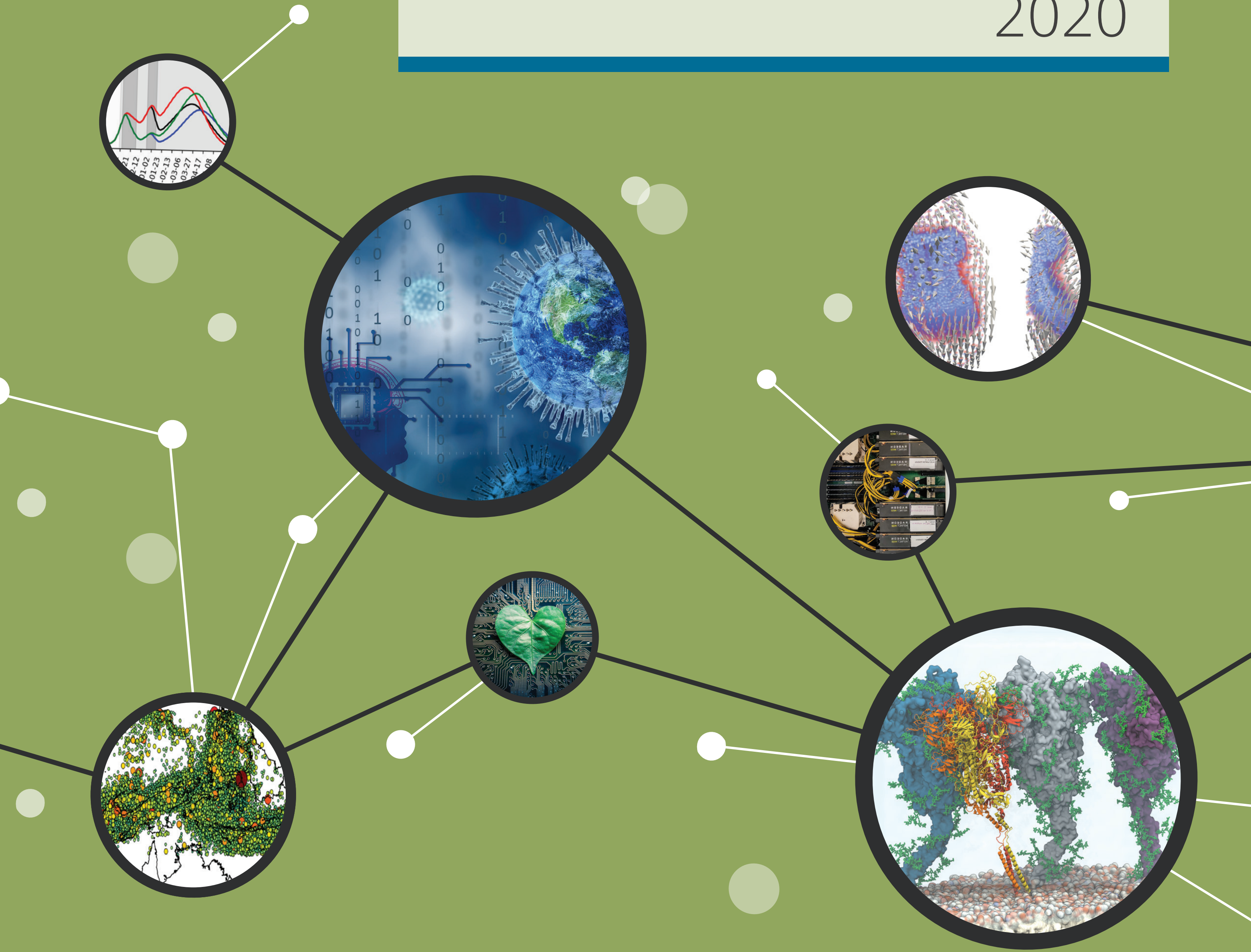
FIAS Frankfurt Institute for Advanced Studies

2020



Content

FIAS

science for the reality of tomorrow

Dear colleagues,
Dear friends and supporters of our science,
Dear knowledge seekers,

2020 was an eventful year! A virus has strongly influenced all of our lives, challenged our flexibility, but also promoted collaborative thinking and inspired virtual action.

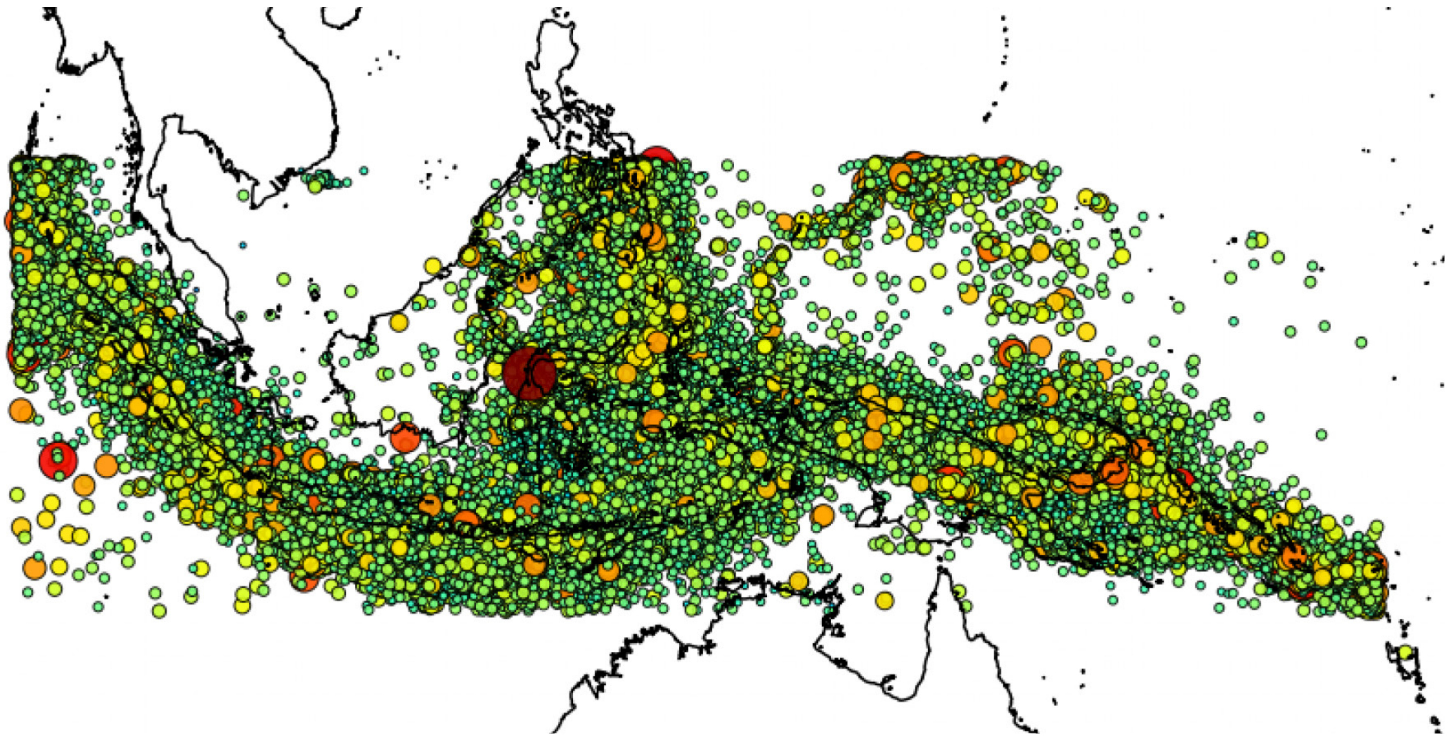
Nevertheless, FIAS can also look back on great successes in 2020! Six new junior group leaders have started their work and built up their research group, five renowned scientists have been recruited as FIAS Fellows and will strengthen us with new projects, first symposia have been organized in virtual form and our research, also in the research focus Covid-19, has successfully set accents.

With the year 2020, the chairmanship of my predecessor Enrico Schleiff has ended. As the new President of Goethe University, he will be a member of our Board of Trustees and will therefore continue to be closely associated with FIAS. We wish him all the best and look forward to our future together!

On behalf of all FIAS members

Prof. Dr. Volker Lindenstruth
Chairman of the Board

HIGHLIGHTS 2020



Seismology and artificial intelligence

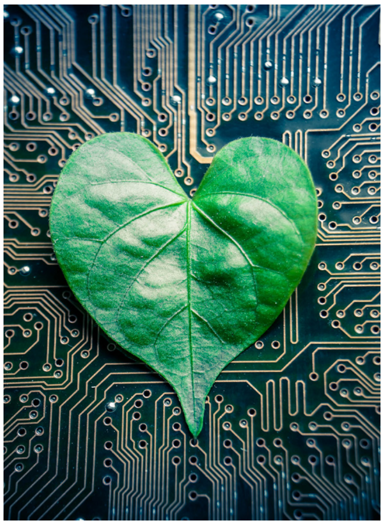
Dr. Nishtha Srivastava, head of the research group "Seismology and artificial intelligence"

Among all forces of nature, earthquakes are considered one of the most devastating threats. They cause enormous human and structural losses worldwide. Even though analysis and measurement methods have been further developed over the past decades, reliable predictions are still not possible today. Although many indications of an increased earthquake probability are known, they do not allow an exact prediction of the location and time of catastrophic earthquakes. From 2020-2024, a new research group at FIAS, headed by Dr. Nishtha Srivastava, will be established. The project is funded by the German Federal Ministry of Education and Research (BmBF) with more than 1.6 million euros as part of the "Promotion of female AI junior scientists" program. Nishtha Srivastava will use methods of artificial intelligence (AI), the application of which in geosciences, especially in seismology, is still in an early stage of research, to expand our understanding of the origin of earthquakes and improve predictions.

LOEWE CMMS

CMMS is the Frankfurt center for multi-scale modeling, analysis, and simulation of biological processes. The long-term goal of CMMS is a comprehensive understanding of both simple molecular biological processes, such as the mode of action of an enzyme, as well as the complex behavior of organisms. Such an understanding is the basis for the adaptation of cell functions for biotechnological use as well as for the development of biomedical, pharmacological, and agricultural applications. The merging of theoretical competencies and their interlinking with data from diverse experiments carried out independently on several scales is essential to develop new concepts for describing biological systems and deciphering the causes of diseases.

CMMS took up his work in May 2020 as a Loewe Schwerpunkt of FIAS together with Panters from the Goethe University Frankfurt, Max Plank Institut for Brain Research, and Max Plank Institut for Biophysics (both Frankfurt). In this function, it will bundle and decisively advance the various activities in the field of multi-scale modeling.



Awards:

Prof. Dr. Rudolf Steinberg receives Federal Cross of Merit

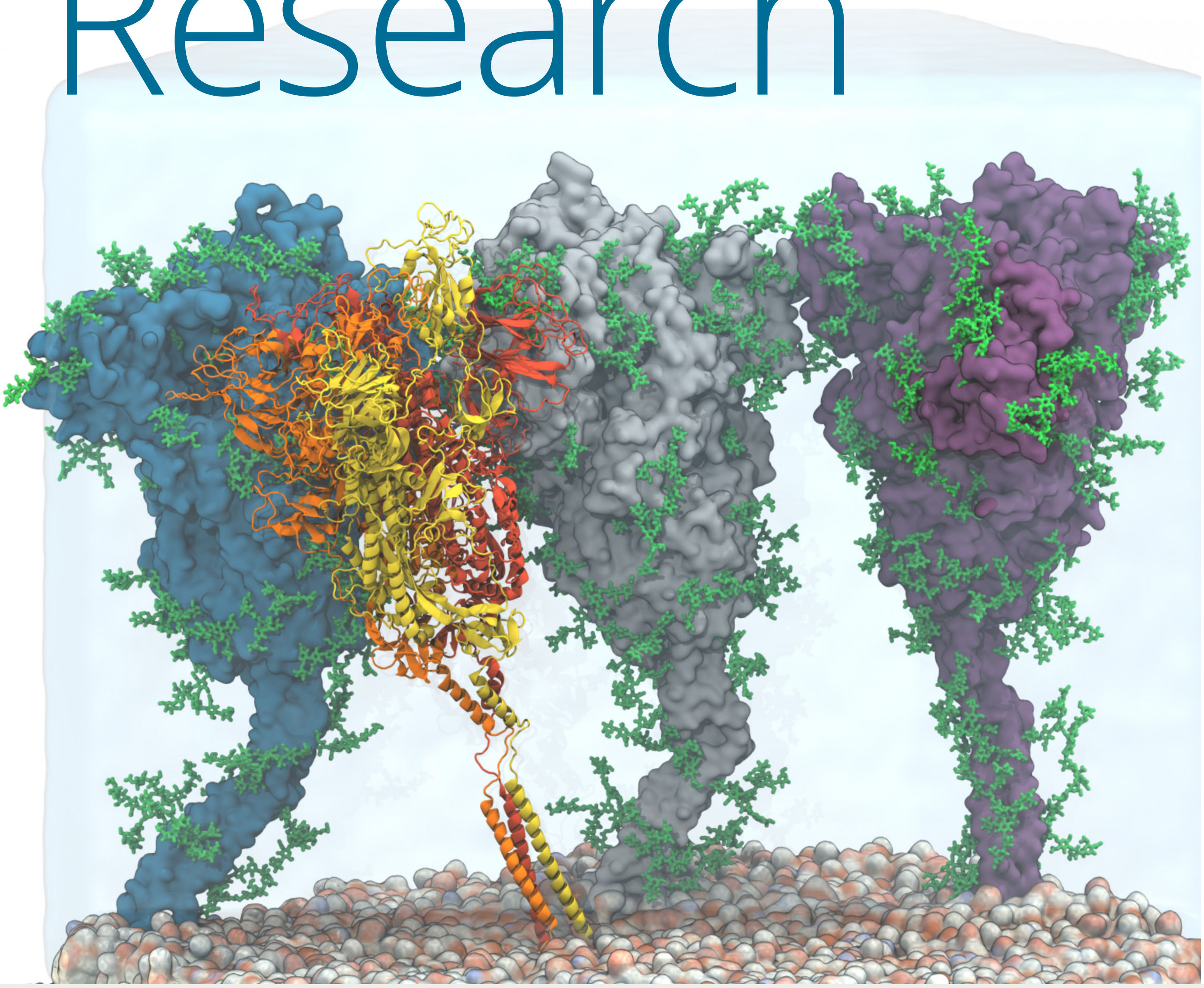
The Chairman of the FIAS Board of Trustees, Prof. Dr. Rudolf Steinberg, has been awarded the Federal Cross of Merit with Ribbon. During a ceremony, he was presented with the award by Volker Bouffier, the Prime Minister of the State of Hesse.

"The interest of young people in Frankfurt as a place to study is great. This is also due to the wide range of subjects offered by the university. A tribute to the former president Prof. Dr. Rudolf Steinberg. He had a decisive influence on the University of Frankfurt and made it a flagship in Germany. Today I am very pleased to present him with the Cross of Merit on Ribbon of the Federal Republic of Germany." said Volker Bouffier, the State Premier of Hessen. Steinberg was also honored by the German President for his extensive honorary commitment.

Horst Stöcker becomes honorary member of the Academia Română

The Romanian Academy of Sciences (Academia Română) has appointed Prof. Dr. Dr. h.c. mult. Horst Stöcker as honorary member in recognition of his work on hot, dense elementary matter in heavy ion research and astrophysics, as well as his many years of commitment to the international scientific community. He is thus one of 91 foreign scientists who are entitled to bear this title.

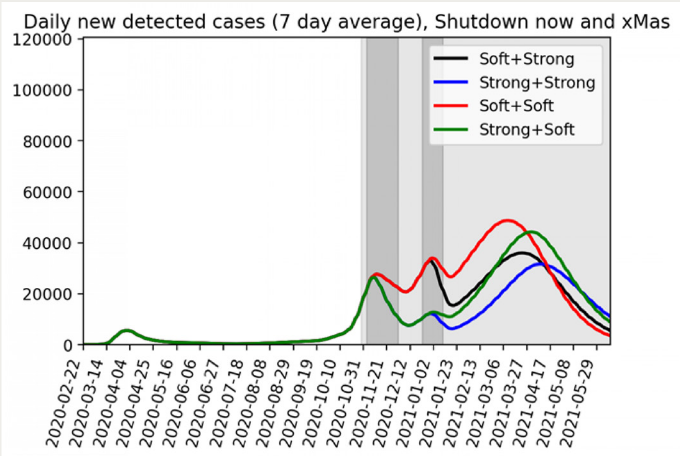
COVID-19 Research



The SARS Covid-19 pandemic has changed everyday research around the world. Many scientists from a wide variety of fields have put aside their actual research to devote themselves to a common larger goal: To help combat the novel virus. FIAS scientists with expertise in the field have joined in. We would like to present some of their results here.

Covid Forecast simulations

Right at the start of the pandemic, scientists from FIAS and Forschungszentrum Jülich joined forces with the University of Heidelberg and the HZI to investigate the impact of various measures on the development of the corona epidemic in Germany. To describe the spread of the disease agent more precisely, Maria Barbarossa and Thomas Lippert, and their collaborators extended a classical model from mathematical epidemiology to include SARS-CoV-2-specific factors. By incorporating information on the number of patients admitted to hospitals and receiving intensive care into the model, they can predict the burden on the German healthcare system in various spread scenarios. These data have also been incorporated into a statement by the Helmholtz Initiative "Systemic Epidemiological Analysis of the COVID-19 Epidemic" for the German government. The results of the model developed at the Jülich Supercomputing Centre (JSC) and FIAS are also included in the Forecast Hub initiated by the Karlsruhe Institute of Technology (KIT).



Selected Publications:

Fuhrmann, J., Barbarossa, M.V. The significance of case detection ratios for predictions on the outcome of an epidemic - a message from mathematical modelers Arch Public Health 78, 63 (2020). https://doi.org/10.1186/s13690-020-00445-8

Modeling the spread of COVID-19 in Germany: Early assessment and possible scenarios MV Barbarossa, J Fuhrmann, J Meinke, S Krieg, HV Varma, N Castelletti, and Th Lippert PLOS ONE 15(9): e0238559 (2020), https://doi.org/10.1371/journal.pone.0238559

Spike Protein Simulations

To ease the development of a protective vaccine, FIAS scientists Gerhard Hummer and Roberto Covino use advanced computer simulations to identify weak points on the surface of the S protein that could be attacked by antibodies. In collaboration with scientists from the Max Planck Institute for Biophysics, EMBL, the Paul Ehrlich Institute (PEI), and other research institutions, they have comprehensively analyzed and modeled the spike protein. In the online edition of Science from August 18, 2020, they report on their research and the finding that the spike protein is much more mobile than first assumed.

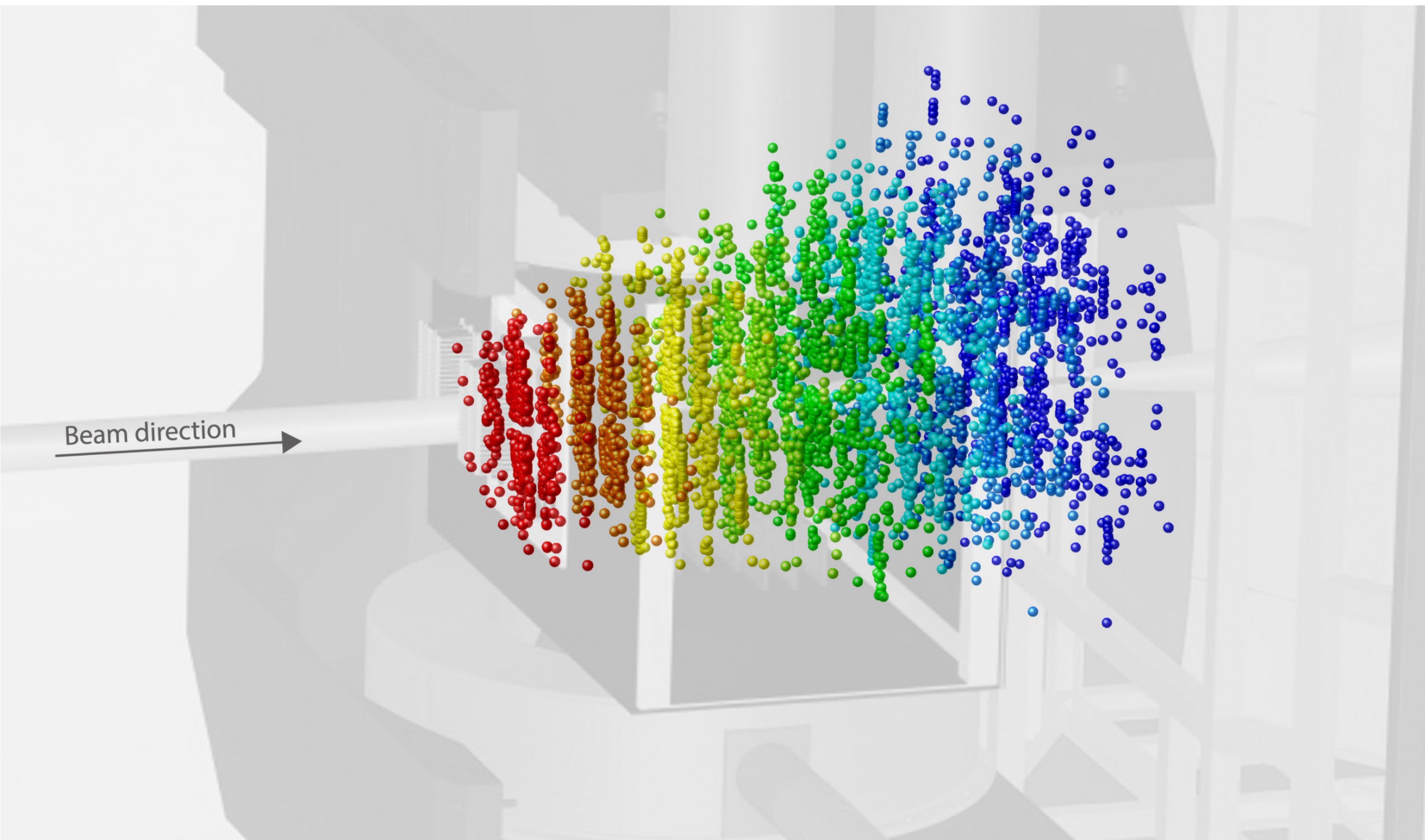
Due to the collaboration of various expertise, the protein could be analyzed in its natural environment with imaging techniques as well as with computer simulations. To determine the dynamics and structure of the spike, the biophysicists and Gerhard Hummer and Roberto Covino, together with their colleagues from the MPI for Biophysics, applied computer model simulations from membrane dynamics to the protein. At the same time, researchers at the PEI extracted SARS-CoV-2 particles from the supernatant of infected cells, which were then accurately mapped in situ (on the virus) by EMBL and MPI scientists using cryo-electron microscopy. These 3-dimensional images of the protein on the surface of the virus were then integrated with the theoretical model of the Frankfurt group to elucidate the structure and dynamics of the protein in detail.

From the models and images, the researchers were able to conclude that the protein is much more flexible than previously assumed. This property enables the virus to dock to human cells like an anchor hook and enter them. Also, the interdisciplinary collaboration has discovered sugar-like deposits on the protein. These so-called glycans hide the protein structure from the immune system and make it difficult for the antibodies to dock to the protein. Such information is important for assessing the effectiveness of vaccines or antibody therapies.

Publication: https://science.sciencemag.org/content/early/2020/08/17/science.abd5223

picture (left page): Sikora et.al; Map of SARS-CoV-2 spike epitopes not shielded by glycans

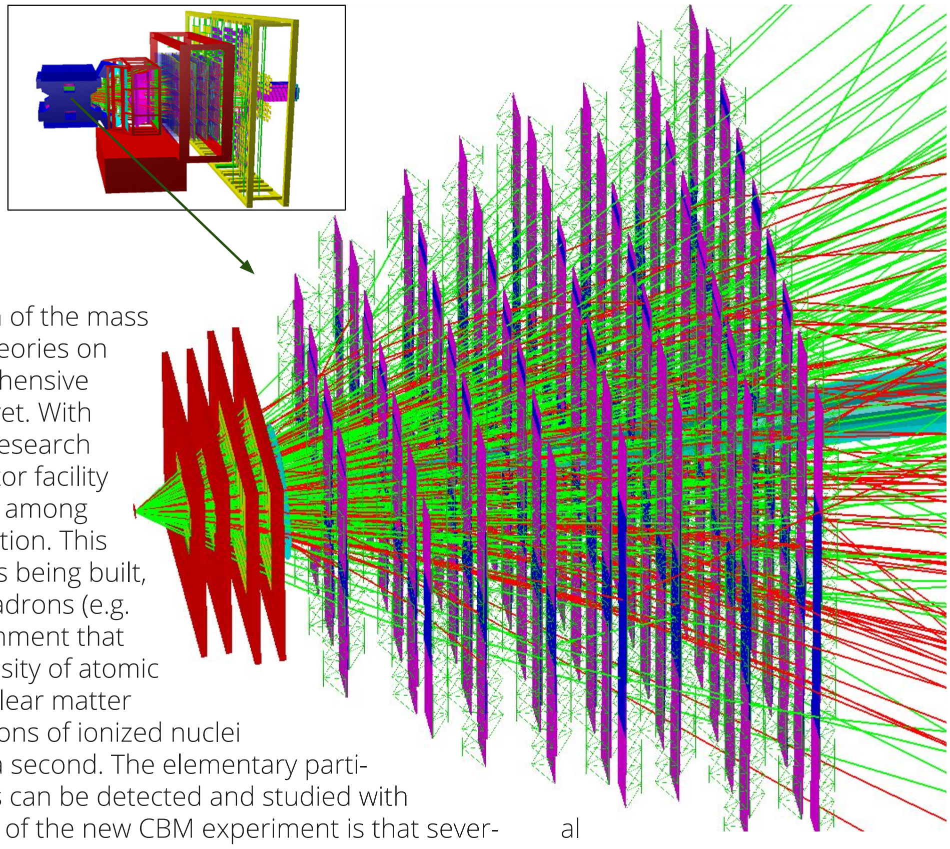
Theoretical Sciences



Methodological research in the field of AI is already proving groundbreaking in the area of theoretical natural sciences for the treatment of problems in theoretical physics. One focus is on high-energy and heavy-ion research and related astrophysical issues, such as the study of neutron star collisions and the phase structure of the hot, dense matter produced there, as well as field theory. AI methods developed at FIAS are also used to describe condensed matter properties, hydrodynamic and electrodynamic flow fields in large networks, and sustainable energy research. In addition, FIAS 2020 initiated the transfer of methods to geophysics, e.g., for the description of seismic earthquakes; here, two outstanding new fellows, Prof. Dr. Georg Rümpker and Dr. Nishtha Srivastava were recruited. The area of atmospheric and climate research was also further established under the leadership of Dr. Alexander Kies.

Deep learning in heavy ion physics

In order to make better use of the amount of data generated by high-energy experiments, scientists at FIAS have developed a new Deep Learning (DL) analysis method. The models based on the PointNet architecture enable a fast online analysis of collision events at event rates of several million collisions per second. For this purpose, the determination of the centrality of heavy-ion collisions at the Compressed Baryonic Matter Experiment (CBM) of the FAIR facility, which is currently under construction at the GSI Helmoltzzentrum für Schwerionenforschung in Darmstadt, was exemplarily investigated.



The CBM experiment is designed to answer one of the central questions in physics, the generation of the mass of atomic nuclei. There are many theories on this subject, but there is no comprehensive experimental confirmation for this yet. With the Facility for Antiproton and Ion Research (FAIR) in Darmstadt, a new accelerator facility is currently being built with the aim, among other things, of answering this question. This is also where the CBM experiment is being built, which will study the properties of hadrons (e.g. neutrons and protons) in an environment that corresponds to many times the density of atomic nuclei. Such highly compressed nuclear matter is only created in high-energy collisions of ionized nuclei and exists only for tiny fractions of a second. The elementary particles generated from these collisions can be detected and studied with the CBM detector. A unique feature of the new CBM experiment is that several million such collision events per second can be generated and recorded. This extremely large data stream requires ultra-fast real-time analysis. This requires completely new analysis methods. FIAS scientists have now developed a new method for event characterization based on deep learning methods. This new method of event classification proves to be more accurate and less model-dependent than conventional methods and uses state-of-the-art GPU processor units to improve performance.

The PointNet models used by Manjunath Omana Kuttan and his colleagues are based on a deep learning architecture optimized for learning from point cloud data. Point clouds are collections of disordered points in space, where each point represents the multi-dimensional properties of an element that contributes to the cloud's collective structure. In the case of a heavy-ion collision, for example, these points correspond to the properties of particle tracks in the CBM detector (picture on the left).

For their study, the researchers used the UrQMD model, also co-developed at FIAS, and the detector simulation of CBM to generate gold-gold collision events at an energy of 10 AGeV. These could then be used to train the PointNet-based architectures. The models were trained using features such as the trajectories of particles in the CBM detector planes.

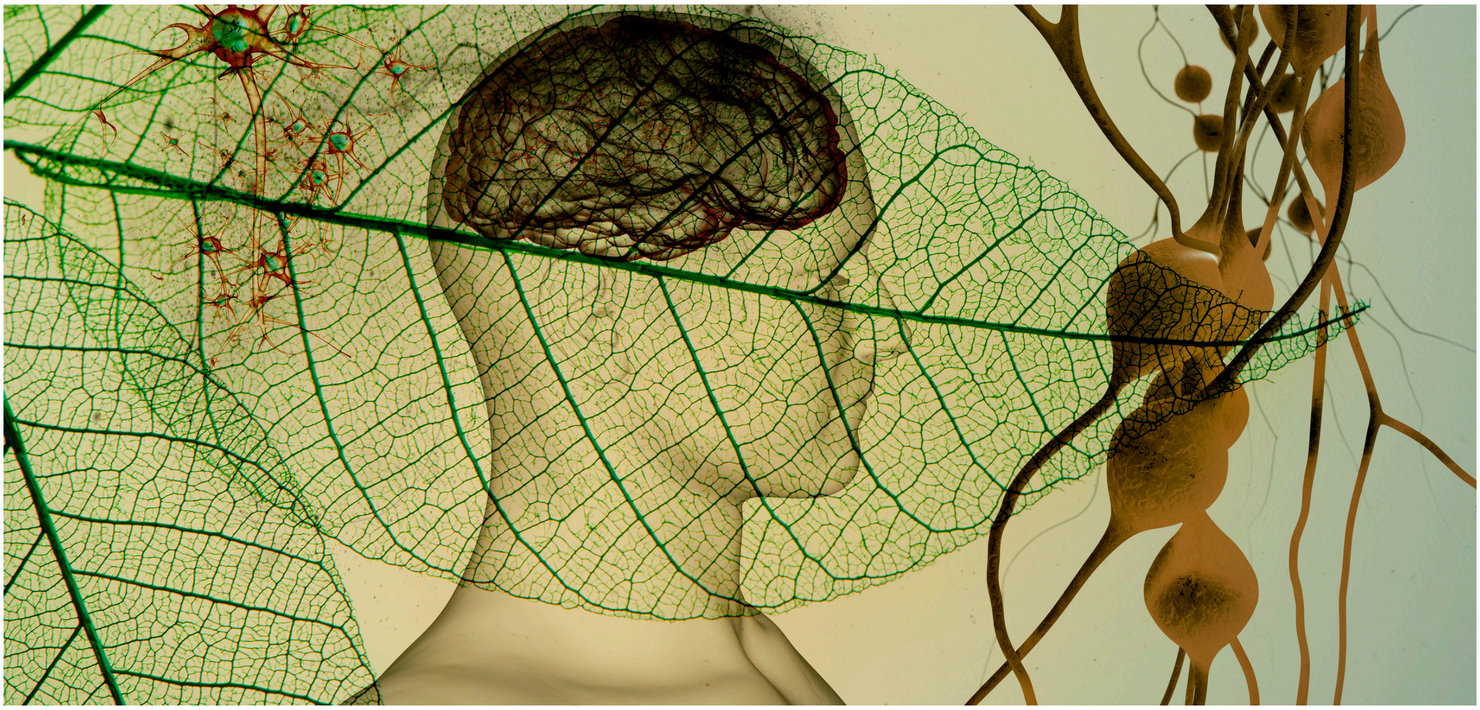
In the future, it should be possible to use the developed model architectures in other heavy-ion collision experiments, e.g.: ALICE at the Large Hadron Collider (LHC) or HADES at GSI's SIS18. The researchers hope to generalize the developed deep learning models for the analysis of a variety of different properties of nuclear collisions.

Publication:

This is a collaborative Project of Manjunath Omana Kuttan, Jan Steinheimer, Kai Zhou, Andreas Redelbach and Horst Stoecker.

"A fast centrality-meter for heavy-ion collisions at the CBM experiment", Physics Letters B, Volume 811, 2020, 135872, ISSN 0370-2693, https://doi.org/10.1016/j.physletb.2020.135872

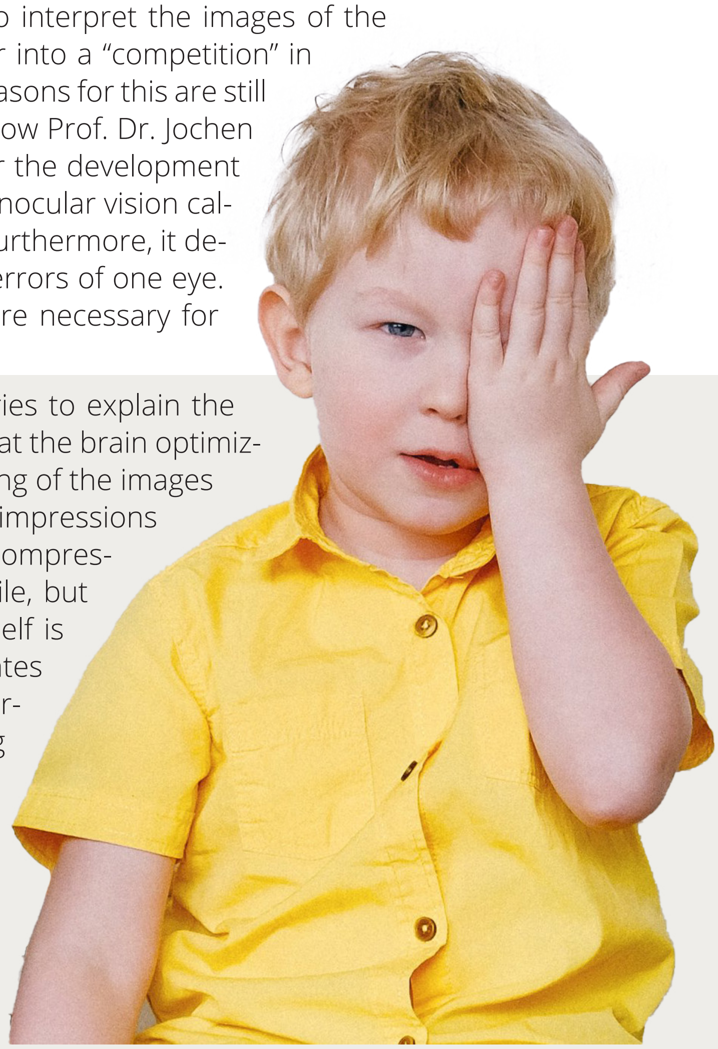
Theoretical Life- & Neuro Sciences



Biological and medical research depends on theoretical approaches to the analysis of complex data structures and the description of highly interconnected biological processes. In the field of theoretical life sciences, the FIAS develops methods taking into account the different scale levels for modeling biological systems and in the interdisciplinary theoretical neurosciences. The standardized integration of theoretical methods is also implemented in medical and pharmaceutical research, such as cancer research and drug development. In all fields, theoretical and experimental approaches and methods for the analysis of heterogeneous data sets are (further) developed - for the standardization of data acquisition and processing, for the development of detailed multi-scale models and their simulation using high-performance computing resources, and the application of AI methodologies. The FIAS follows the principle of integrative experiment design, which integrates experimental and theoretical competencies equally. With the LOEWE focus CMMS, which started its work in May 2020, 4 new junior research groups could be established at FIAS. This enables FIAS scientists, even more, to focus on the transfer of their theoretical competencies to the experimental research community.

Active efficient coding explains the development of binocular vision and its failure in amblyopia.

We view the world with our two eyes from slightly different perspectives. The small differences between the images projected onto the left and right retina are used by our brain to see spatially. However, amblyopia a widespread early childhood developmental disorder, which affects up to 5% of all children, leads to visual impairment in one eye (or in rare cases both eyes). The brain does not learn to coordinate the two eyes correctly and to interpret the images of the two eyes in three dimensions. Instead, the eyes enter into a "competition" in which one eye "suppresses" the other. However, the reasons for this are still poorly understood. The group around FIAS Senior Fellow Prof. Dr. Jochen Triesch has now proposed a new computer model for the development of binocular vision. The model explains how precise binocular vision calibrates itself automatically under healthy conditions. Furthermore, it describes why amblyopia develops in case of refractive errors of one eye. Interestingly, the model also shows conditions that are necessary for successful treatment.



The now presented "Active Efficient Coding" theory tries to explain the learning mechanism for binocular vision. It suggests that the brain optimizes both eye movements and the subsequent processing of the images of both eyes simultaneously to represent the visual impressions as compactly as possible. This works similarly to a compression algorithm that reduces the size of a computer file, but by learning coordinated eye movements, the data itself is optimized. Under healthy conditions, the model calibrates itself to precisely coordinate eye movements and interpret the visual sensations in three dimensions. During this process, nerve cells develop which register small differences between the images of the two eyes, so-called disparities.

The model uses this to align the eyes to the same point. However, in the case of an isometry, in which the refractive power of the two eyes is different, the model develops an amblyopia-like state in which the information of one eye is not processed but suppressed.

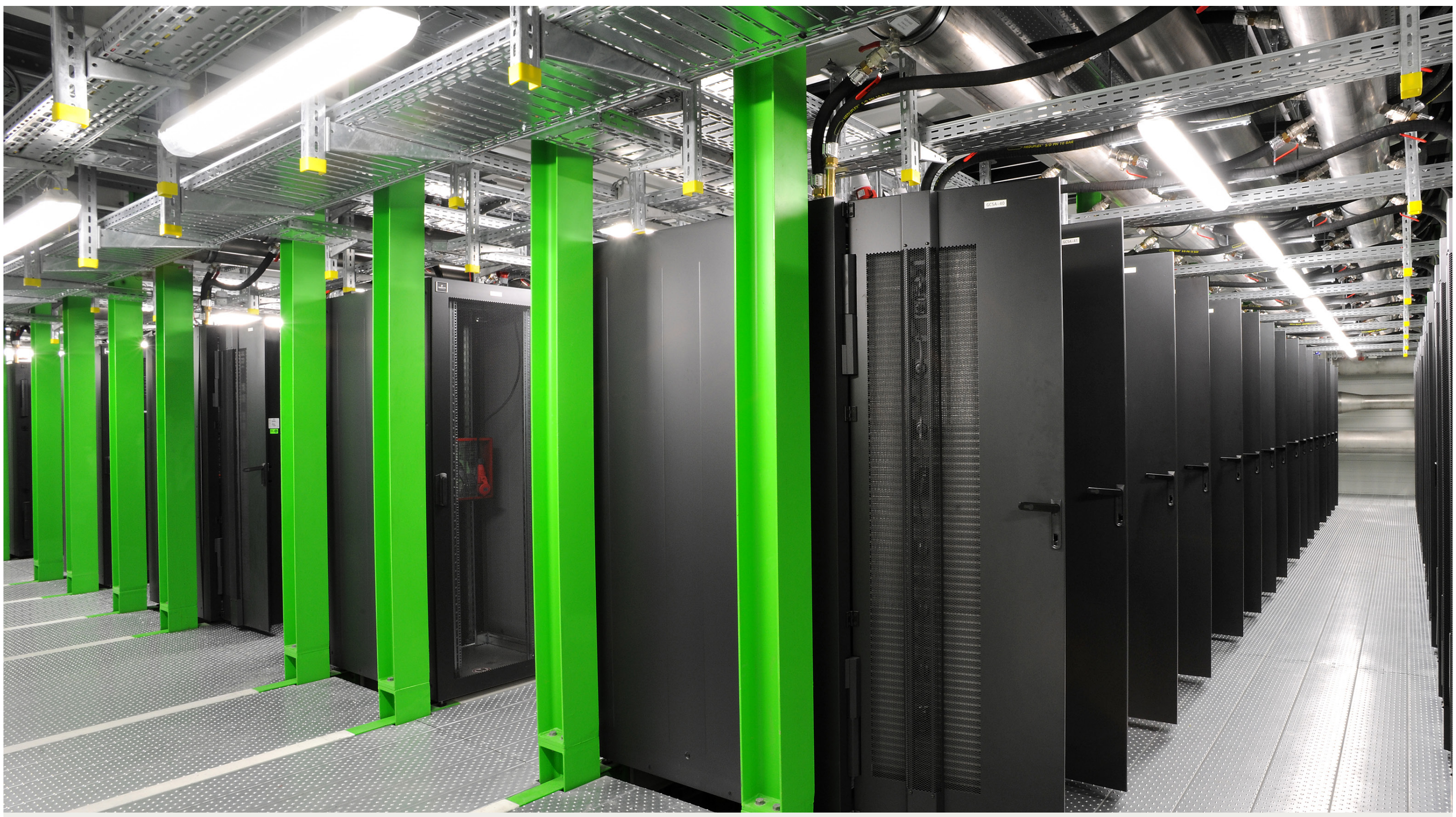
This leads to the development of nerve cells that only process information from the healthy eye. Hardly any disparities can be registered. The visual sensory impressions can therefore no longer be interpreted in a normal spatial manner. In addition, the model shows that a cure for this condition is only possible if the nerve cells are still able to change their processing of sensory impressions, a process known as plasticity. Overall, the model offers a consistent explanation for the development of binocular vision and its failure in the case of amblyopia.

Publication:

Active efficient coding explains the development of binocular vision and its failure in amblyopia Samuel Eckmann, Lukas Klimmasch, Bertram E. Shi, Jochen Triesch

Proceedings of the National Academy of Sciences Mar 2020, 201908100; DOI:10.1073/pnas.1908100117

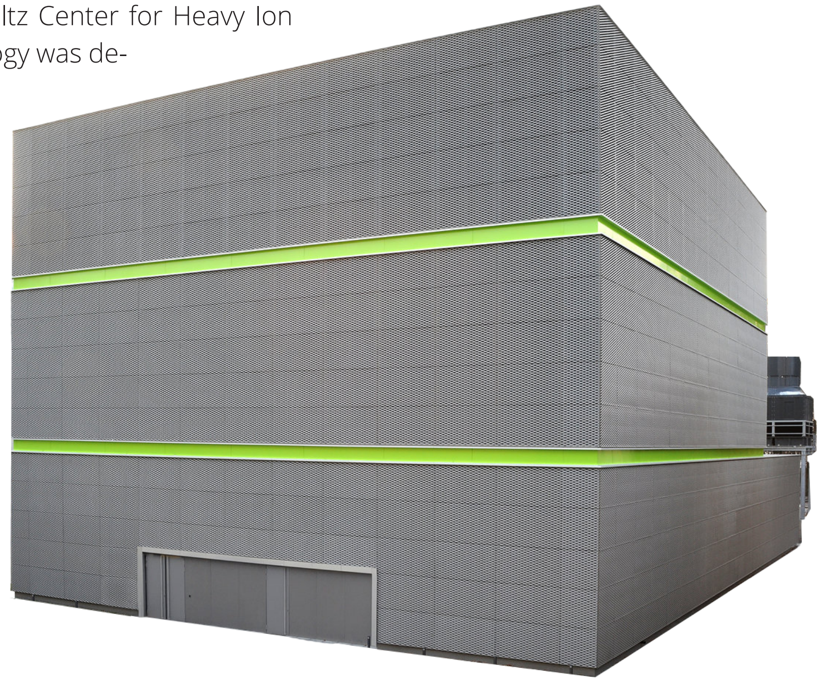
Computer Science & AI Systems



In the area of Computer Science & AI Systems, the already established work in the field of GREEN-IT is complemented by strategies of quantum computing and AI. Highly efficient computer architectures and program libraries are developed. In the past, computer architectures designed at FIAS achieved top positions in the worldwide ranking list for energy-efficient computers (Green500). The patented, highly efficient computer center architecture also allows a drastic reduction of construction costs. The use of GPU-based systems provides an ideal basis for the implementation of AI algorithms. The areas of application cover a very broad spectrum, ranging from tumor diagnostics to elementary particle physics and industrial problem-solving. With the new Senior Fellow Prof. Thomas Lippert, the existing systems will be expanded to include a quantum computer and related research. Developments in these areas will also find applications in the social, natural, and life sciences.

The Green IT Cube receives the Blue Angel eco-label

The FAIR and GSI high-performance computing center developed in cooperation with FIAS is particularly energy-efficient thanks to its special cooling system. This makes it the first computer center to be awarded the Federal Government's eco-label. The Green IT Cube, one of the most powerful scientific computing centers in the world was built at the GSI Helmholtz Center for Heavy Ion Research in Darmstadt. The novel cooling technology was developed by FIAS board members Volker Lindenstruth and Horst Stöcker.



The enormous amounts of data that will be generated during experiments at the accelerator facilities at GSI and, in the future, FAIR must be processed efficiently. In conventional data centers, more than a third of the power consumption is used for cooling, while less than seven percent is needed for the Green IT Cube. The data center uses an innovative air-water process, which makes it possible to accommodate the computers in an extremely space-saving manner. The 27 x 30 x 22 cubic meter cube-shaped building can accommodate a total of 768 computer cabinets on six floors. At present, two of the six floors have been extended with a maximum cooling capacity of four megawatts, which will allow a maximum cooling capacity of 12 megawatts in the final stage of construction.

The cooling technology was developed by FIAS board members Volker Lindenstruth and Horst Stöcker. Volker Lindenstruth is Professor at the Goethe University Frankfurt and was at that time Fellow at FIAS and Professor in Heidelberg. Horst Stöcker, who has been a member of the FIAS since its founding in 2004 and is also a professor in Frankfurt, was vice president of the Goethe University and scientific director at GSI at the time the technology was developed. The powerful concept has already won several awards for innovation and environmental friendliness.

"The label "Blauer Engel" sets high standards for the architecture and operation of a data center,"

says Volker Lindenstruth, pleased with the award of the eco-label to his development. "The requirements are examined very carefully. We are very proud of this award, as it also independently confirms the very good performance data. We look forward to further imitators."

The Blue Angel has been the German government's eco-label and orientation for sustainable purchasing for over 40 years. Independent and credible, it sets demanding standards for environmentally friendly products and services. The Blue Angel guarantees that products and services awarded with it meet high standards of environmental, health, and usage properties. The entire life cycle must always be taken into account in the assessment. For each product group, criteria are developed which products and services labeled with the Blue Angel must fulfill. To reflect technical developments, the Federal Environment Agency reviews the criteria every three to four years. In this way, companies are required to make their products increasingly environmentally friendly. The Green IT Cube is the first data center to be awarded the eco-label based on the criteria, which were changed in 2019.

People at FIAS

Our new FIAS Fellows, youll find more about them and their research on the following pages.

The performance of any scientific institute depends crucially on the people involved with it. This is not different at FIAS – with their enthusiasm and engagement our researchers are the foundation of our success.

Our Fellows are the foundation of FIAS. With their work, they not only provide the scientific operation, but through their applications, they also raise the third-party funds that are so important for the research activities. Therefore, we are pleased that we were able to attract 11 new Fellows in 2020. They will certainly have a lasting impact on the research agenda of the coming years.

While Fellows are usually appointed for at least 5 years, many scientists are only in Frankfurt for a short time: Ph.D. students stay for 3-4 years, and post-doctoral researchers mostly stay for 1-2 years. In addition, we have about 10 guest researchers monthly, they visit FIAS for just a week or up to several months. This means we have new people coming to FIAS every month and we are doing our best to make them feel at home as soon as possible.

Behind all this stands a small, but strong administrative team, organizing everything in the background. Here, too, new employees were hired in 2020. In the area of research promotion, two new employees were hired and another position was filled in IT.

Changes in the Board of Directors:

Enrico Schleiff becomes president of Goethe University.

Prof. Dr. Enrico Schleiff, Senior Fellow, and Chairman of the Board of the FIAS was elected President of the Goethe University on July 8. The term of office is six years and begins on January 1, 2021. For this reason, he has resigned from the position of Chairman of the Board at FIAS as of the end of 2020.

Prof. Dr. Enrico Schleiff

Enrico Schleiff served as Chairman of the Board of FIAS from December 2018 to December 2020. Under his leadership, the institute has made great leaps towards a successful future. He emphasized on the development of a long-term scientific concept for interdisciplinary theoretical basic research until 2030. The financial security of the institute's finances, the promotion of young scientists as well as the restructuring of the administration are also part of his legacy. With the acquisition of the LOEWE-Fokus CMMS a close connection between the theoretical competencies of FIAS and the experimentalists of Goethe University was established. Through this and other research projects in the fields of life sciences and artificial intelligence launched under Enrico Schleiff's leadership, FIAS will continue to establish itself internationally in the coming years.

We congratulate Enrico Schleiff on his new position and would like to express our sincere thanks for his commitment to FIAS. We also look forward to good cooperation in the future. As President of the Goethe University, he is a member of the FIAS Board of Trustees and thus continues to be involved in all important decisions of the Institute.

Prof. Dr. Volker Lindenstruth

Prof. Dr. Volker Lindenstruth was appointed as his successor. The expert for energy-saving high-performance computing centers has been at FIAS since 2007 and was already chairman of the board of our institute from 2012-2018.

Luciano Rezzolla joined the FIAS board

The astrophysisist Prof. Dr. Luciano Rezzolla is part of the FIAS board since Oct 2020. He is also the currunt director of the Institute of Theoretical Physics at Goethe Univeristy.

The FIAS was not only able to win an outstanding scientist as a member of the board but with the current director of the Institute for Theoretical Physics at Goethe University, also an experienced and committed leader.

Prof . Dr. Luciano Rezzolla

Events

Welcome Days

In September, the first event at FIAS took place under corona conditions. Due to the low incidence numbers at that time, we were able to welcome the new Ph.D. students on site.

About 25 participants gathered in the large lecture hall. Due to an extended hygiene concept and a simultaneous online transmission, also Ph.D. students who were ill or in quarantine due to the entry regulations were able to participate.

The two-day event included a diverse lecture program, a welcome by the board of directors, lectures by "experienced" Ph.D. students from the individual research areas, group building concepts, campus walk, and social events. On the morning of the second day, the four junior group leaders and 15 new Ph.D. students of the CMMS project had the opportunity to get to know each other a bit better and present their research topics. The event was concluded by a city tour of Frankfurt.

Scientific Advisory Board

The Scientific Advisory Board is one of the fundamental pillars of FIAS. Its high-profile members from around the world meet every 3 years to evaluate and advise FIAS on its scientific direction. Normally, this evaluation is integrated into our Fellow Conference. Due to the Corona pandemic, this had to be done online and in two phases for the first time in 2020.
In the first phase, all FIAS Fellows recorded a presentation on their scientific work and made it available to the members. In the second part, the FIAS Fellows as well as the Ph.D. students, the Board, and the administrative staff were interviewed by the members of the SAB to get an accurate impression of the work here at FIAS.

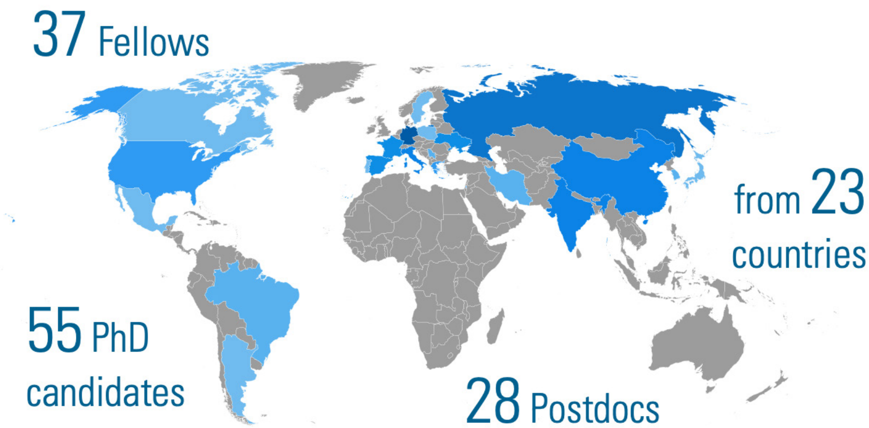
In its final report, the Scientific Advisory Board describes "that FIAS has established itself as a research-strong institute with various thematic areas. [...] Through recruitment at all levels (junior researchers as well as renowned scientists), all research areas could be strengthened in terms of personnel. Several external appointments of FIAS scientists to external professorships at universities also show that FIAS successfully acts as a career springboard and that the concept thus works."
The establishment of the LOEWE focus CMMS, which continues to promote and strengthen the already very good networking with researchers at Goethe University and the surrounding Max-Planck-Institutes, was seen as particularly positive. Concerning the Ph.D. students at FIAS, it was suggested to establish stronger cooperations with other graduate schools at Goethe University and the Max-Planck-Institutes – A suggestion that we will gladly take up.

In the past, many important and successful changes at our institute have resulted from the impulses of the SAB. And we very much regretted not being able to receive the SAB members in person due to the Pandemic. We sincerely thank the members of the Scientific Advisory Board for agreeing to attend this time-consuming online event and thus help FIAS to become an even better research institution.

Since the last evaluation in 2017, we have been able to recruit several new, excellent scientists for the advisory board. In 2020, the SAB consisted of:

Prof. Dr. Ulrich Achatz,
Prof. Dr. Christoph Burchard,
Prof. Dr. Volker Dötsch,
Prof. Dr. Michael Huth,
all from the Goethe University Frankfurt,
Prof. Dr. Wolfgang Bauer (Michigan State University),
Prof. Dr. Theo Geisel (Max-Planck-Institute of Dynamics and Self-Organization),
Prof. Dr. Barbara Jacak (UC Berkley),
Prof. Dr.- Ing. Anke Kaysser-Pyzalla (German Aerospace Center),
Prof. Dr. Edda Klipp (HU Berlin),
Prof. Dr. Stefan Müller-Stach (JGU Mainz),
Prof. Dr. Alexander Reinefeld (Zuse Institute Berlin),
Prof. Dr. Reinhard Schneider (University of Luxembourg) and Prof. Dr. Arndt von Haeseler (University of Vienna).

Currently there are 170 people researching or working at FIAS, including:



Dr.
Maria Barbarossa

Dr. Maria Barbarossa studied mathematics at the University of Perugia, Italy and at the TU Munich. During her doctoral studies (PhD in Mathematics 2013, TU Munich) she started close collaboration with biologists and biochemists at Helmholtz Zentrum Munich. From 2013 to 2015 she was a postdoctoral fellow at the Bolyai Institute, University of Szeged, Hungary. In 2015 she returned to Germany as Margarete von Wrangell Fellow and joined Heidelberg University. Maria is a Fellow at FIAS since Spring 2020.

Home-office improved her multitasking skills

During the pandemic, she learned to draw knight's castels for her son while preparing slides in English and listening to a videocall in German.

Projects @ FIAS: 3

Collaborations

JSC Forschungszentrum Jülich
Heidelberg University
Karlsruhe Institute of Technology
TU Munich
University of Szeged

Immuno-epidemiology

My group works at the development of analytical and computational techniques for the description of processes arising in immunology and infectious diseases. In particular, we work on

i. in-host phenomena at intracellular level (e.g. signaling pathways), or at cellular level (e.g. interactions of immune cells with infected cells or tumor cells)

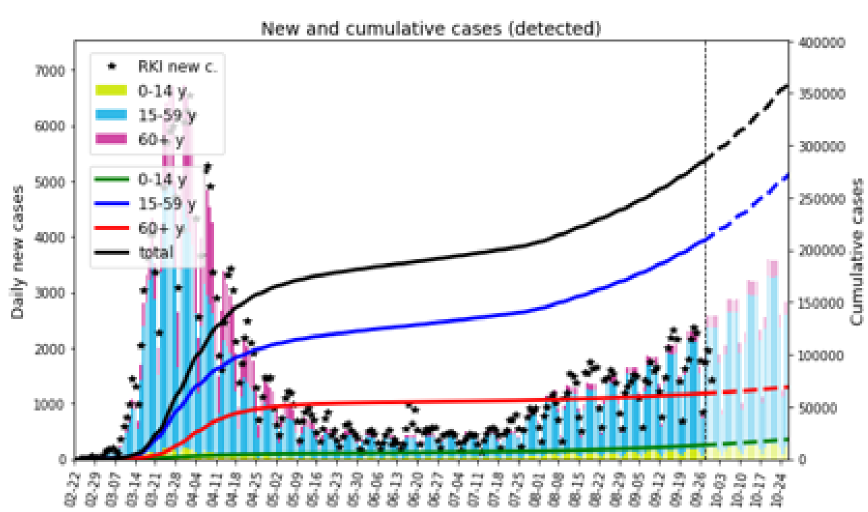
ii. between-hosts dynamics (e.g. pathogen transmission and social dynamics)

and on the coupling of these two scales. This allows, for example, to capture the effects of individual immunity on epidemiological outbreaks in a population, or to study molecular mechanisms and events that influence the dynamic at cellular level (e.g. cell proliferation, death, functionality).

Combining elements of nonlinear and infinite-dimensional dynamics with numerical simulations and optimization, we aim at both qualitative and quantitative understanding of biological phenomena.

In my first months at FIAS I was particularly involved in research work on COVID-19, modeling the biological and social mechanisms leading to the spread of the disease in Germany. The models in their most complex form include age groups, different levels of infectiousness and disease severity (e.g. patients requiring intensive care), and were used among others

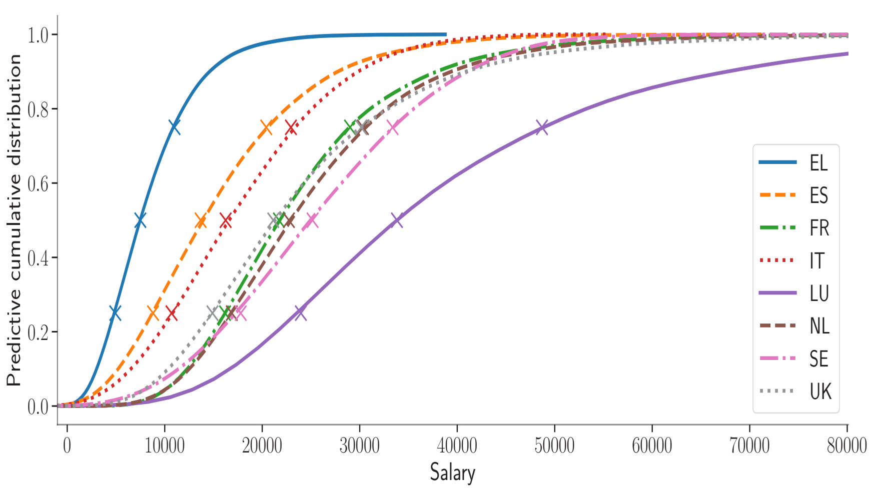
1. to predict the effect of nonpharmaceutical intervention (NPIs) during the first COVID-19 wave
2. to highlight the importance of the assertion ratio (that is, how many cases we detected over the total amount of infected people)
3. to explain the effect of panic behavior just before strict measures (lockdown) are implemented
4. to predict the outcome of short time lockdowns and to propose possible control strategies on the emerging second wave in the autumn of 2020
5. to illustrate the side-effects of noncompliance with NPIs



Systemic Risk

Not least due to the ongoing coronavirus pandemic the last year has been interestingly different. Scientific collaborations had to rely on digital media and modelling of COVID-19 dynamics has become a major focus of research also at FIAS. We were actively engaged in this effort and contributed a small preprint showing that the all important prevalence rate is inherently non-identifiable. Indeed, current epidemic models are consistent with two very different explanations of observed case dynamics: Either lock-down measure are effective at low prevalence or sub-populations start to saturate at much higher prevalence.

At the same time, and most importantly, Rajbir Nirwan has finished his PhD thesis on “Bayesian Machine Learning for Financial Modeling”. Besides Gaussian process based models for the correlation structure of multiple assets -- as already featured previously -- Raj has contributed a novel and rotation-invariant parametrization for probabilistic principal component analysis (PCA). While classical algorithms remove the rotational symmetry of PCA in an ad-hoc fashion more care is needed in the probabilistic case in order to make the model identified. To this end, he developed and implemented an efficient algorithm based on Householder rotations, enhancing the classical PCA solution with principled uncertainty estimates. Furthermore, we proposed a method for estimating distributions from quantile information alone. Especially in economics many data sets are only available in aggregated form as demanded by privacy considerations. For instance, central authorities just release a few selected quantile values of personal income distributions. In contrast to existing approaches, our method starts from the exact sampling distribution based on multivariate order statistics. In turn, we use a fully Bayesian approach for estimating and comparing different distributions thereby making optimal use of the limitedinformation of the data.



Best estimate of cumulative income distbution in different European countries based on just three observed quantile values (marked by X).

Prof. Dr.
Nils Bertschinger

Nils Bertschinger is Helmut O. Maucher-Stiftungsjuniorprofessor for systemic risk. He studied computer science at RWTH Aachen and received his PhD from the Max-Planck Institute for Mathematics in the Sciences about information processing in complex systems. At FIAS he now applies methods from information theory and machine learning to investigate how systemic risks can develop and spread in financial systems.

Systemic Risk Stiftungsprofessur

In 2014, Helmut O. Maucher made the new Systemic Risk research area possible through his endowment.

Projects @ FIAS: 1

Collaborations

Mark Kirstein, LML und MPI MIS
Christian Schlag, SAFE, Goethe University
Martin Hoefer: Goethe University

Dr. Roberto Covino
Roberto Covino studied physics and theoretical physics at the University of Bologna, graduating with a master's thesis on black hole evaporation. He then moved to Trento University for his PhD. Afterwards he joined the newly founded Department of Theoretical Biophysics at the MPI of Biophysics in Frankfurt. During his postdoc, he studied the mechanism of sensing in cellular membranes and developed novel computational methods integrating physics-based models and machine learning. He joined FIAS in April 2020.

Home-office improved his multi-tasking skills

and taught him to make the best use of software to stay in daily touch with his team.

Projects @ FIAS: 1

Collaborations

MPI of Biophysics

Simulation of biological systems

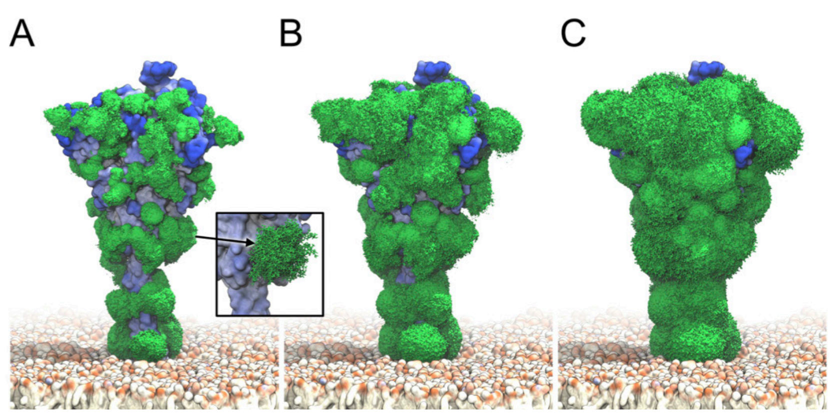
Explaining the emergence of complex self-organization and structures in living cells in terms of general physical mechanisms is an outstanding chal¬lenge. Astounding progress in experimental techniques integrated with ever-increasing computing power and sophisticated theoretical models are bringing us every day a step closer to tackling this challenge. Understanding mechanisms in a quantitative way will facilitate the rational design of therapeutic interventions and bio-inspired nanomachines.

My work integrates closely the development of innovative theoretical and computational methods and their application to uncover fundamen¬tal biological mechanisms. Current research topics are:

- Artificial Intelligence driven scientific discovery of molecular mechanisms
- Computational structural virology: SARS-CoV-2 and HIV
- Molecular mechanisms of sensing and regulation in cellular mem¬branes and the unfolded protein response
- Self-assembly and conformational changes of biomolecules
- Statistical modeling of biophysical experiments and simulations

We recently developed an atomistic model of the spike of SARS-CoV-2 embedded in a realistic membrane. Although produced independently, the agreement with electron tomography imaging of in situ spikes is stunning. Our model aided the interpretation of these images, clarifying the structure of the glycan shields and explaining the dynamic behavior of the long stalk region that connects the spike to the viral envelope. Additionally, by carefully studying the surface of the spike, we identified possible regions that could be targeted by antibodies. We are currently following a similar strategy to understand better the analog of the spike protein in HIV.

I recently co-developed an artificial intelligence (AI) agent that uses deep reinforcement learning to discover the mechanism of molecular self-organization phenomena from computer simulations. The agent adaptively learns how to sample complex molecular events and, on the fly, constructs quantitative mechanistic models. Symbolic regression condenses the mechanism into a human-interpretable form. Autonomous AI sampling like this one has the power to discover assembly and reaction mechanisms from materials science to biology.



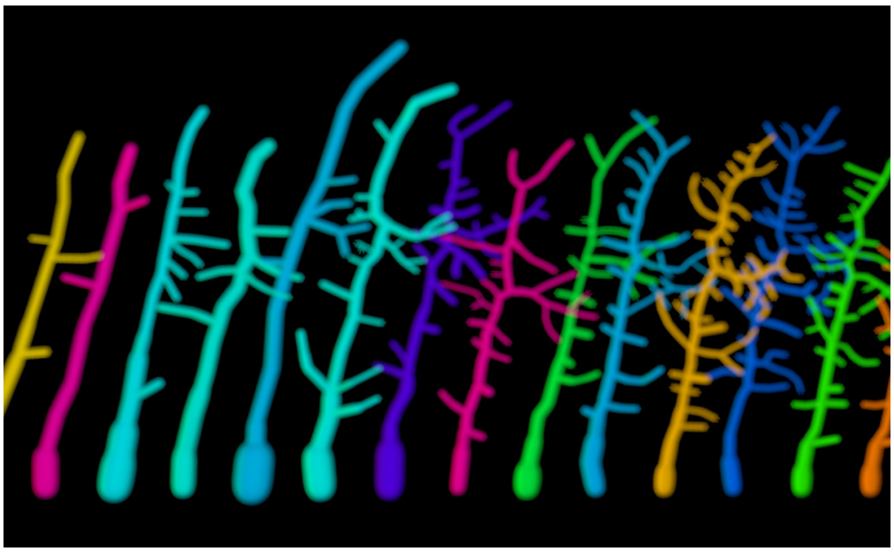
S glycan dynamics from ˜2 μs MD simulations. Time- averaged glycan electron density isosurfaces are shown at high (A), medium (B), and low (C) contour levels, respectively. The blue-to-white protein surface indicates high-to-low acces- sibility in ray analysis. (Inset) Snapshots (sticks) of a bianten- nary, core-fucosylated and sialylated glycan at position 1098 along the MD trajectory.

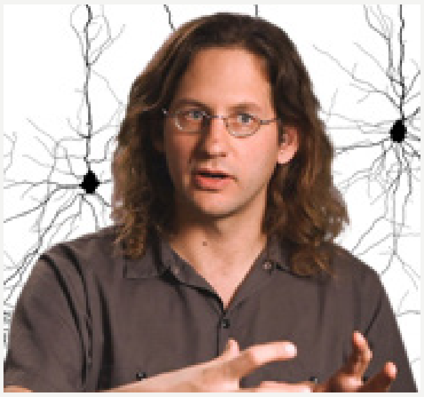
Dendrite growth in fruit fly's comb-shaped neurons

Dendritic growth is the process that ultimately leads to cell type specific morphologies and builds up mature neural circuits that shape the computation they implement. Dendritic trees are known to follow optimal wiring considerations and to determine neuronal function relevant to behaviour. However, the fine regulation of branch outgrowth, pruning and stabilisation that leads to the mature arbour morphology remains largely unknown. We have studied the growth phases of ventral Class I dendritic arborisation (da) neurons of the Drosophila melanogaster larva peripheral nervous system at a high temporal resolution that allows to resolve the fine elements that compose the growth process (see Figure). Being proprioceptive neurons that are known to respond to contractions in the larva body during crawling, Class I da neurons do not obviously gain from satisfying optimal wiring constraints. Therefore, we use this system to study how the specific functional requirements of these cells interfere with optimal wiring constraints during the developmental growth process that leads to the dendritic morphologies of these cells.

In a surprising turn of events we find in the work published in eLife (Ferreira Castro et al, 2020) that a precise sequential activation of two growth programs eventually leads to dendritic trees that conserve total cable and yet are able to implement their specific function optimally. To do this, dendrites first grow out stochastically to fill the available space in a process that we have previously described to be optimal in terms of wiring. In a second phase, the class I da neurons prune and retract stochastically, which in turn selectively preserves the branches that are well arranged to sense the contractions of the fly larva's body. These results are reproduced in a simple computational model and will eventually lead to a better understanding of the various growth programs that shape dendrites in the intricate circuits of the brain.

Original publication: Ferreira Castro A, Baltruschat L, Stürner T, Amirhoushang B, Jedlicka P, Tavosanis G, Cuntz H (2020). Achieving functional neuornal dendrite structure through sequential stochastic growth and retraction. eLife 9(e0920). https://doi.org/10.7554/eLife.60920





Dr. Hermann Cuntz

In the year 2013 he received the prestigious Bernstein Award with a prize money of around 1.25 million Euros to establish a group at FIAS and the Ernst Strüngmann Institute. He is approaching cellular neuroanatomy in a similar comparative manner as Santiago Ramón y Cajal one of the founders of the field of Neuroscience. Instead of using pen and paper as in his beautiful drawings Hermann Cuntz now takes advantage of computer models to reproduce dendritic structures from simple general principles.

Science at Centre Pompidou

His group's virtual reality (written by Marvin Weigand) has made it to the Centre Pompidou for an exhibition.

Projects @ FIAS: 1

Collaborations

Peter Jedlicka
Gaia Tavosanis
Stephan Schwarzacher
Thomas Deller

Prof. Dr.
Hannah Elfner

Hannah Elfner is groupleader at GSI, professor for Theoretical Physics at Goethe University and a fellow at FIAS since 2013. She obtained her PhD degree at Goethe University in 2009 and spent 3 years as a Humboldt fellow and visiting assistant professor at Duke University. In 2016, she received the most prestigious award for young scientists in Germany, the Heinz Maier-Leibnitz prize by the DFG and BMBF. In 2018, she was awarded the Zimanyi medal at the Quark matter conference, the highest recognition of young theoretical heavy ion physicists.

Stand-up paddling event in September 2020

On a beautiful sunny September day, Frankfurt was explored from a different perspective from the river. Some group members even got to look at the water surface from below at the end...

Projects @ FIAS: 2

Collaborations

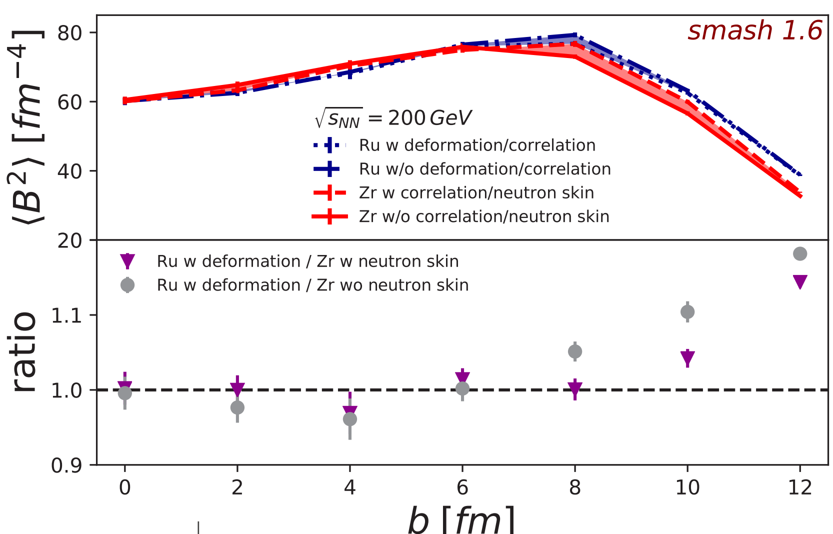
JETSCAPE collaboration, Prof. Charles Gale, McGill University, Dr. Massimiliano Alvioli, Perugia University, Prof. Mark Strikman, Penn State University, Prof. Gabriel Denicol, Rio de Janeiro, Dr. Volker Koch, Lawrence Berkeley National Laboratory, Prof. Marcus Bleicher, GU Frankfurt

Influence of neutron skin on magnetic fields in isobar collisions

The chiral magnetic effect in heavy-ion collisions is proposed to allow for an understanding of fundamental properties of the strong interaction concerning the difference of left-handed and right-handed particles. If vacuum fluctuations lead to asymmetries between quarks with spin and momentum aligned parallel or antiparallel to each other, the large magnetic fields generated by the charged ions moving at the speed of light will generate observable differences in the charge distribution in the final state. This effect is predicted to be rather small and therefore, previous measurements are affected by background contamination and no clear conclusions can be made.

The STAR collaboration at the Relativistic Heavy Ion Collider (RHIC) has recorded events for isobar collisions, Ruthenium and Zirconium, that only differ in their proton number but have the same mass number. The idea is that this will produce a similar background in terms of system size and collective effects while rather different magnetic field strengths are reached. In our study we have explored how the generation of the magnetic field is influenced by well-established nuclear structure effects. Besides ruthenium being deformed, Zirconium is expected to exhibit a so called neutron skin. In nuclei with a larger neutron to proton ratio, it has been observed that the neutron are located more on the outer region of the nucleus while the protons concentrate on the inside. This affects the current that generates the magnetic field. As can be seen from the picture below assuming the maximum possible neutron skin, the magnetic field difference between the two isobar systems is reduced by a significant amount. This calculation is important with regard to the expected experimental results from RHIC.

Associated publication: Phys.Rev.C 101 (2020) 6, 061901



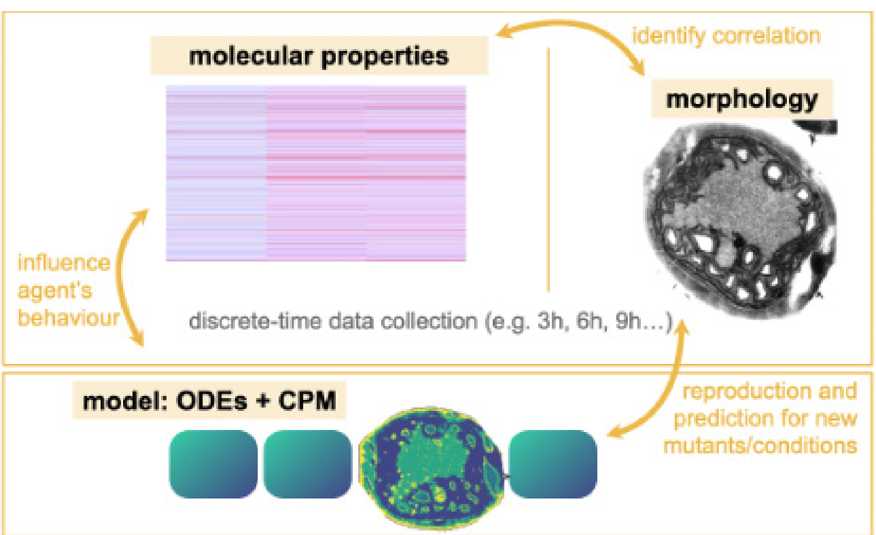
Top: Strength of magnetic field squared for 96Zr (red) with (solid) and without (dashed) neutron-skin and for 96Ru (blue) with (solid) and without (dashed) deformation. Bottom: Effect of the neutron skin on the magnetic field strength squared ratio between 96 Ru and 96 Zr.

Systems Medicine of Infectious Diseases

In 2020 there are two highlights. On the one hand I got a MSNZ (Mildered Sheel Nachwuchs Zentrum) junior group position at the SIP/UKF (Dr. Senckenberg Institute of Pathology/University Hospital Frankfurt) to investigate the correlation between morphology and the underlaying molecular properties. On the other hand Marina Kurtz, my first PhD Student started her work. She is one of the CMMS students and works on modelling heterocyst differentiation in the filamentous cyanobacterium Anabeana PCC7120 to understand how the morphological rearrangements during cell differentiation are steered by the underlaying genetic layer. On average every 10th cell differentiates into a heterocyst under nitrogen depletion (pattern formation).

In our CMMS project (Figure) EM (electron microscopy) images will be acquired of different stages from the developmental process and the corresponding morphological features will be extracted. These features will be correlated to gene expression data. Based on the gene expression we will build a multi scale model, representing the growing filament as an ODE (Ordinary Differential Equation) system. And the morphological rearrangements in the developing heterocyst will be modelled with a CPM (Cellular Potts Model). At the end our model should reproduce the morphological features observed in the EM pictures.

In general there are many published models which reproduce the pattern formation of the complete filament. To find a suited basis for our model, which is not only able to reproduce the characteristic pattern but is also able to regulate the development of the proheterocysts, we checked how far published gene expression data could be reproduced. With the best fitting model we further tested if additional experiments on proheterocyst regression in fragmented filaments could be reproduced. The selected model is able to reproduce the influence of several vegetative cells attached to one side of the proheterocyst qualitatively: The more vegetative cells are attached, the less likely a regression is.



Dr. Nadine Flinner

Nadine Flinner studied bioinformatics and worked on the structure and phylogeny of membrane proteins during the diploma thesis. In her PhD, finished in 2015, she investigated the behaviour of membrane proteins using molecular dynamic simulations.
Nadine Flinner started her PostDoc at FIAS investigating the migration of immune cells and is now interested in understanding the correlation between cell morphology and the underlaying molecular features.

New Research Fellow

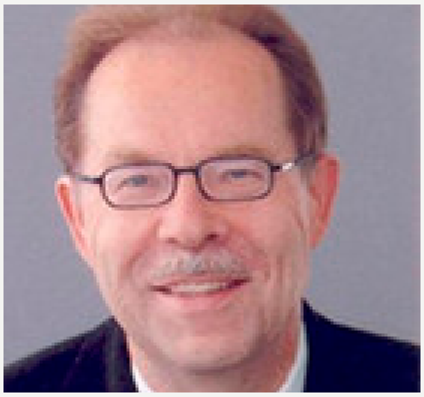
Nadine Flinner became a group leader and FIAS Research Fellow in 2019.

Collaborations

Peter Wild, Goethe University

Olga Goncharova, Dr. Senckenberg Institute of Pathology

General Overview over the CMMS project on modelling heterocyst differentiation



Prof. Dr.
Martin-Leo Hansmann

Martin-Leo Hansmann studied medicine and biology in Bonn. After recieving his diploma in 1974 and his medical state examination in 1977, he received his doctorate in 1982 and habilitated in 1987. From 1990 to 1996 he was Professor at the Institute of Pathology at the University of Cologne and since 1996 Professor at the Senckenberg Institute of Pathology at the Goethe University.
Hansmann joined FIAS in 2016 his main expertise lies in haematopathology, the molecular pathology of malignant lymphomas.

Highlight

In 2001 he was awarded the German Cancer Aid Prize.

Projects @ FIAS: 1

Collaborations

Dr. Wojciech Samek (Frauenhofer HHI), Prof. Dr. Frederick Klauschen (Charite' Berlin), Prof. Dr. Klaus-Robert Müller (TU Berlin)

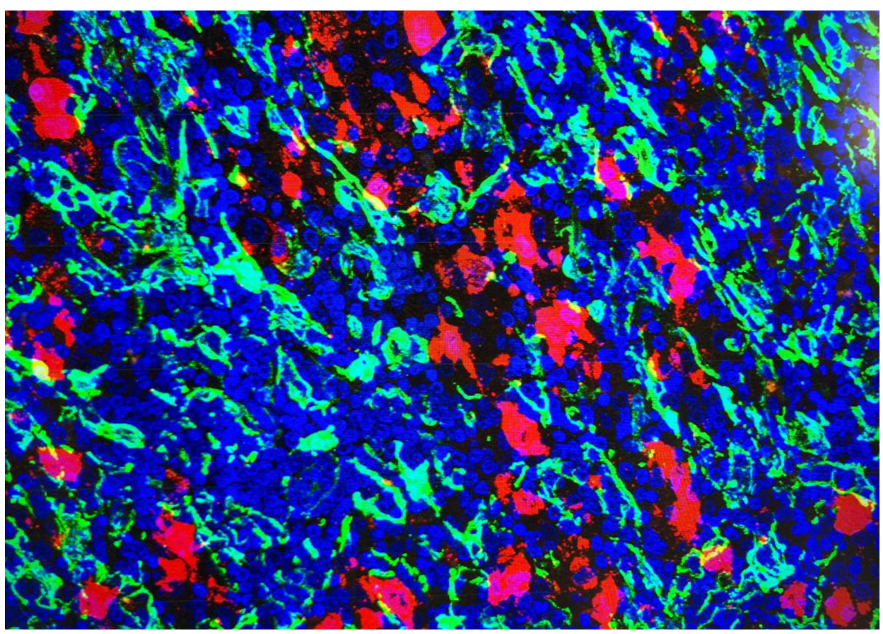
Computational life science on deep learning Biomedicinie

The BMBF funded project made considerable progress, in that we could show, that cell movement is an independent and important factor for classification of different populations of lymphocytes and non lymphoid cells in the immune system. These are quite new findings that have not been reported in humans up to now.

The first paper on cell movement in human lymphoid tissue was published (Donnadieu et al.2020).We could show that PD1 cells, which are a special cell population, needed for germinal center cell reactions, have different speeds in defined compartments of germinal centers. PD1 cells with high speed are found in the periphery and those with low-speed in the centre of germinal centers. So we were able, for the first time, to define movement landscapes of human lymphoid tissue. We started to investigate these phenomena applying bioinformatic and machine learning technologies.

Our group published 17 papers in 2020. Besides movement evaluations, our scientific work was concentrated on 3-D studies in immuno reactions . Laser scanning technologies enabled us to visualize networks in between reticulum cells, as well as T cells and their neoplastic variants, to give new insights in the development of malignant lymphomas. Usually tumours are diagnosed by histology. Our approaches started to construct a new network situation as a basis of lymphoma classification.

The aim for most of our studies is to establish the so called virtuel lymph node. We could visualize lymph node structures in 3D and 4D using laser scanning and include the data in a mathematical model. This model will enable in the near future to calculate qualitative and quantitatively the immuno reactions in a synthetic lymph node setting.



Distribution of macrophages (red) in a lymph node network (green).

A new perspective on dark matter

Galaxies rotate faster than Einstein's theory of General Relativity predicts. This is also true for our own galaxy, the Milky Way. But just exactly why the predictions of General Relativity do not fit with the observations is presently unclear. Most astrophysicists believe that 80% of the matter in our universe is an invisible type of "dark matter". If true, the Milky Way is embedded into a huge cloud of this dark matter, and planet Earth flies through it. Another, alternative, explanation – called "modified gravity" – is that General Relativity isn't quite correct.

One of the projects I have worked on last year with PhD candidate Tobias Mistele is whether the rotation of our Milky Way can be explained by a hybrid theory, that is a combination of dark matter and modified gravity. It is a type of matter which can form a superfluid, and in this superfluid phase it mediates an additional force that mimics gravity. This hybrid theory combines the benefits of both, dark matter and modified gravity, without the disadvantages of either. It was previously shown to work well for other galaxies.

The data from the Milky Way is both better and worse than that of other galaxies. Better because we have more data and it's from nearby. Worse, because we are embedded in the galaxy and move through it. However, our new work shows that the superfluid dark matter can well explain the rotation of the Milky Way.

Dr.
Sabine Hossenfelder

Sabine graduated from Frankfurt in 2003 and was a postdoctoral fellow, among others, at UC Santa Barbara, and the Perimeter Institute in Canada. Before returning to Frankfurt, she held a position as assistant professor at Nordita, in Stockholm, Sweden. Sabine's research is presently supported by the Swedish Research Council, the German Research Foundation, and the Foundational Questions Institute. Besides her research, Sabine is also active in science communication.

Science Communicator

Sabine writes for several magazines, hosts a popular science blog and published her first book in 2019.

Projects @ FIAS: 4

Collaborations

Nordita, Stockholm
Perimeter Institute, Canada
SISSA, Trieste

An example of a spiral galaxy, the Pinwheel Galaxy (also known as Messier 101 or NGC 5457)
Image Credit: ESA/Hubble

Prof. Dr.
Matthias Kaschube

Matthias Kaschube studied Physics and Philosophy in Frankfurt and Göttingen and obtained his doctoral degree in theoretical physics working with Fred Wolf and Theo Geisel at the Max Planck Institute for Dynamics and Self-Organization. From 2006-2011 he was Lewis-Sigler Theory Fellow at Princeton University, working on theoretical neuroscience and developmental biology. In 2011 he joined FIAS and became Professor for Computational Neuroscience at Goethe University.

Vice-Dean

From 2017-2019 he served as Vice-Dean of the Goethe Universitys Department of Informatics and Mathematics.

Projects @ FIAS: 5

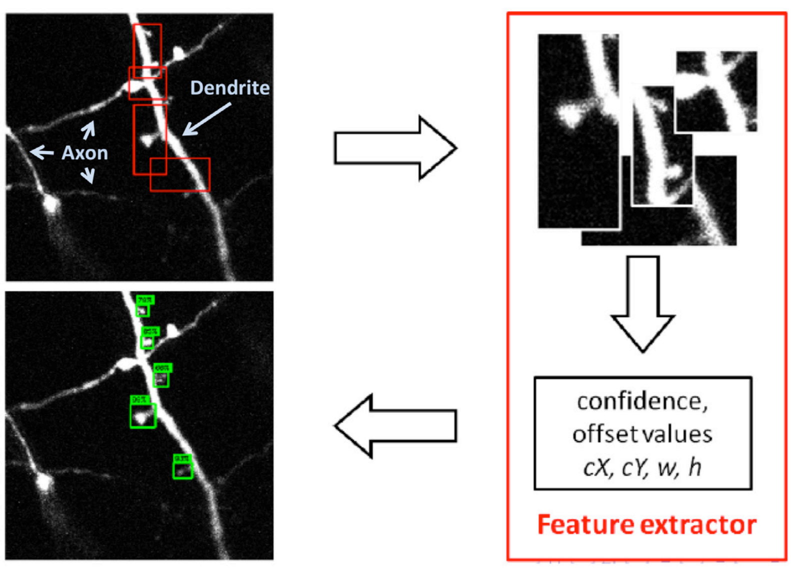
Collaborations

David Fitzpatrick (Max Planck Florida Institute), Simon Rumpel (Univ. Mainz), Gilles Laurent (Max Planck Institute for Brain Research), Kenichi Ohki (Univ. of Tokyo)

Deep learning-based detection of synaptic connections

The functionality of neural circuits in the brain depends significantly on the strengths of synaptic connections between neurons. Recent developments of deep tissue live imaging techniques enable to visualize large numbers of synapses and to monitor them over extended periods of time, from hours up to several weeks. Extracting the strengths of synaptic connections and analysing how they change across time, for instance while an animal acquires the skills necessary to perform a given task, could shed important light on the neural underpinnings of learning. However, measuring the strengths of individual synaptic connections from live imaging data has been a daunting task relying largely on visual inspection and manual annotation and so difficulties in scaling this up to simultaneous measurements of large numbers of synapses has been the bottleneck in such analyses. In collaboration with neurobiologist Simon Rumpel at the University of Mainz, we have made significant improvements towards developing a scalable image analysis pipeline, enabling to automatically detect large numbers of spines (proxies for synapses) in fluorescence imaging stacks and to track them across several days (Figure; Vogel et al., manuscript in preparation). For spine detection we exploited transfer learning, adopting a deep convolutional neural network (CNN) that was pretrained to detect and classify objects in natural images. We combined a Faster R-CNN to generate and refine region proposals of candidate spines with an Inception-ResNet for the recognition step of spines. The detection outperforms previous methods and achieves a near human level performance (F1 score of 0.90 tested on data sets labeled by n=5 experts; for experts, F1=0.94).

The work arose from an excellent bachelor thesis by Fabian Vogel, previously recognized as Hessen's youngest student entering the computer science program at Goethe-University at the age of 16.



Deep learning-based detection of synaptic connections (so-called spines are used as a proxy for synaptic connections): First, using pre-trained convolutional neural networks a large number of candidate regions (proposals of spine locations) are automatically generated (red boxes; only a small subset is shown). Then, each region is evaluated for the presence of a spine and refined in size and position (green boxes). For illustration, only a small dendritic branch is shown. The method can reliably distinguish dendritic spines from axonal structures

Block chain technologies in public administrations

One of the highlights of 2020 is the work done by my PhD candidate Philipp Lang, on blockchain. The main features of a blockchain are the integrity of the data and the use in decentralized networks. Started with the Bitcoin project, which aims to replace intermediary systems such as banks, show that there is a lot of potential in this technology. But there is also still a lot to research and improve, as the discussions on energy consumption and the intended application show. It is precisely the application possibilities that fascinate me and my PhD candidate, Philipp Lang.

Therefore, we are researching the possible fields of application and are trying to develop another field of application with the goal of a promoted single-sign-on system on the physical domain. Similar to a single sign-on on computer systems, users should be able to authorize various devices and building accesses with a single login.

Dialogues with collaborations such as Govdigital (nationwide grouping for the implementation of a blockchain system of public administrations) and IDUnion (alliance of science, public administrations and business with the goal of implementing a worldwide blockchain system) should make it possible to test the in-house development on an overall system across the board and to fully leverage the decentralized characteristic. Another potential collaboration is about to be finalized and will enhance my research team.

In addition, the first course with the content of blockchains took place. As a result of the teaching, exciting master's theses are developing that expand my own research area and support my existing research.

Govdigital: https://www.govdigital.de/

IDUnion: https://idunion.org/

Prof Dr.
Udo Kebschull

Professor Udo Kebschull studied computer science at the Technical University of Karlsruhe (today KIT) and graduated in 1989. From 1989 to 1990 he worked as a scientific employee at the FZI in Karlsruhe. After working in Leipzig and Heidelberg, in 2010 Udo Kebschull became head of the University Computer Center of the Goethe University Frankfurt in connection with a chair for infrastructures and computer systems in information processing.

New FIAS Fellow

His research focuses on the low-latency processing of large amounts of data, such as those generated by experiments in high-energy physics

Projects @ FIAS: 1

Collaborations

Hessische Zentrale für Datenverarbeitung (Hessian center for data processing)

co author
Philipp Lang

Dr. Alexander Kies

Alexander Kies, born 1986 in Bremen, heads the research group FIAS Renewable Energy Systems and Artificial Intelligence (FRESNA) at the Frankfurt Institute for Advanced Studies (FIAS). He obtained his B.Sc. (2007-2010) and M.Sc Physics (2010-2012) at the University of Bremen with a focus on theoretical semiconductor physics. Afterwards, he obtained his PhD in physics at the University of Oldenburg with a cumulative thesis on energy system analysis. He has been employed at the FIAS since 2016 and performs research on energy system modelling, energy markets and artificial intelligence.

Featuerd Project

You will find more about his work in the featured article on page 13 within this issue.

Projects @ FIAS: 4

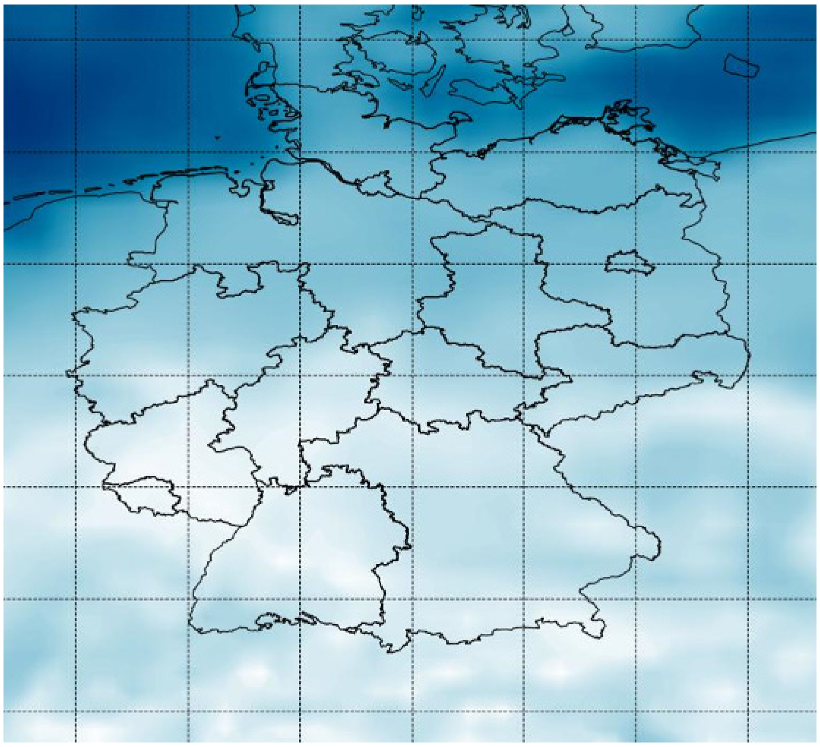
Collaborations

Jakub Jurasz (AGH Krakow),
Tom Brown (KIT),
Bruno Schyska (DLR)

AI research for the energy system of tomorrow

Robust energy system models are necessary for the planning of the energy transition. The Federal Ministry for Economic Affairs and Energy (BMWi) funds research at FIAS as a cooperation of the research groups FIAS Renewable Energy Systems and Artificial Intelligence (FRESNA) and Deep Thinkers for three years within the framework of the new research project EnergiesysAI.

The careful planning of the future energy system is central for the decarbonisation efforts of European economies to tackle the looming threat of climate change. Reliable meteorological data is essential to perform energy system analysis for research and policy advice. However, different datasets show significant differences in the data itself and in the results obtained using them with energy system models and their influence on energy system models is not understood. The aim of this research project is to use artificial intelligence to reduce the uncertainties in energy system optimisation resulting from uncertainties in the input data. For this purposes generative models (GANs) are used to create meteorological data and to produce representative datasets that were trained with respect to reduced uncertainty and can be used within the modelling community. All models and data will be made publicly available under appropriate licensing.



Modelled 10m-wind speeds in January 2015

Algorithms for heavy ion collisions

In 2019 the work of Prof. Dr. Ivan Kisel's group was focused on further development of the algorithms for processing and analysis of heavy ion collisions, which are part of FLES (First Level Event Selection) package of the CBM experiment (FAIR/GSI). The goal of FLES is to provide full data analysis in the CBM experiment in real time at 10^7 heavy ion collisions per second.

At this stage the work was carried out to investigate and improve the accuracy of the algorithms, as well as their reliability in the conditions of working with real data in online mode. For this purpose, we used the data of the experiment STAR (BNL, USA), which is now collecting data in the program BES-II (Beam Energy Scan) on the accelerator RHIC at collision energies close to the energy of the CBM experiment.

The work was carried out within the framework of the FAIR Phase-0 program, which is to participate CBM scientific teams in other experiments in order to test and improve the detector systems and algorithms developed for CBM under real conditions of other experiments already in operation. In this case, the use of such detector systems and processing algorithms is expected to significantly accelerate the start of the CBM experiment itself in the future.

Prof. Dr. Ivan Kisel

Ivan Kisel works on data reconstruction in high-energy and heavy-ion experiments. His approach based on cellular automata allows to develop parallel algorithms for real-time physics analysis using HPC. He received his PhD in physics and mathematics from the Joint Institute for Nuclear Research (Dubna, 1994). Then he worked at the University of Heidelberg, where he gained his habilitation in physics, in 2009, and at the GSI Helmholtz Centre for Heavy Ion Research. Since 2012, he is a professor for software for HPC at the Goethe University and a fellow at FIAS.

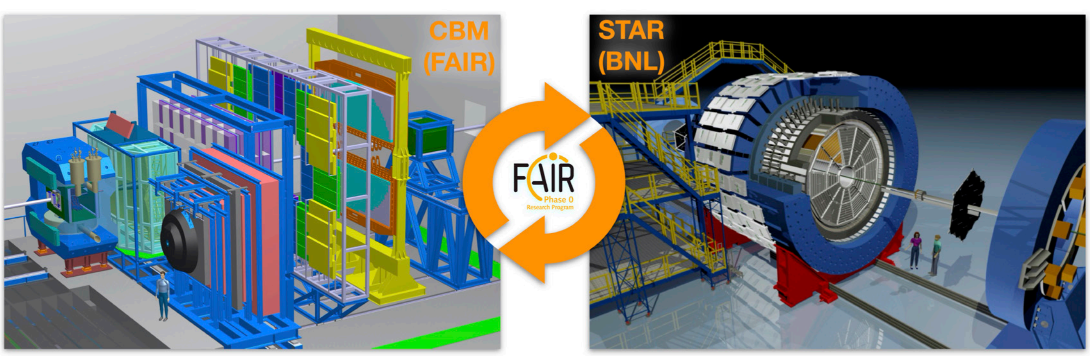
Featuerd Project

You will find more about his work in the featured article on page 13 within this issue.

Projects @ FIAS: 2

Collaborations

CBM
PANDA
ALICE
STAR



Schematical presentation of the FAIR Phase-0 program

Prof. Dr.
Volker Lindenstruth

Professor Volker Lindenstruth studied physics at TU Darmstadt and received his doctorate in 1993 at Goethe University. He spent his Postgraduate years at the UC Space Science Laboratory. In 1998, he returned to Germany as a Professor and department head at the University of Heidelberg. In addition, he has been the head of the ALICE HLT project at the LHC since 2000. In 2007 he joined Goethe University as professor and at FIAS he held the position of Fellow but became a Senior Fellow soon thereafter.

Patentet Technology

The energy-saving high-performance data centers he co-developed were successfully patented.

Projects @ FIAS: 4

Collaborations

CBM
ALICE

ALICE at CERN

ALICE (A Large Heavy Ion Collider Experiment) at the CERN LHC is primarily focused on characterizing the properties of the matter created in high-energy heavy-ion collisions. The final-state particles produced in these collisions stream into the various sub detectors of ALICE. From there various algorithms are used to identify hits in the detectors and combine them to reconstruct the particle tracks. The experiment has been undergoing major upgrades during the LHC's long shutdown 2 in preparation for the increased Pb—Pb interaction rate of the LHC Run 3 (50 times that of LHC Run2). These upgrades not only include major updates to the particle tracking detectors but an upgrade to the computing program, known as ALICE O2 (Online-Offline). ALICE will now read the data continuously, rather than using the classical approach of online triggering. The continuous readout will exceed 3 TB/s and, at these rates, is it impossible to store the data for offline use. It will therefore be compressed, in real time, to a manageable size using the online compute farm. The farm comprises two parts. The first, known as the First Level Processor (FLP), receives data from the detectors via optical links that end in PCI Express cards mounted in general PCs. This data is then transferred to the memory of the host and is then sent via an Infiniband network (throughput of 14.4 Tbit/s) to the Event Processing Nodes (EPN) farm, which provides the majority of the compute power. The data being shipped belong to a particular interaction and must therefore be sent to a single designated processing target computer, and this is guaranteed through the use of a scheduler.

A full system test of data reconstruction on an EPN server was conducted and the performance and reliability subsequently validated. Additionally, the use of GPUs for the compute-intense workloads is fully implemented and established. The baseline solution for the servers was therefore confirmed and the full system has been procured and installed, shown in the image below. The EPN farm consists of 250 servers (totaling 16k cores and 2000 GPUs), that receive up to 600 GB/s of data from the FLP farm and reduce this rate to 100 GB/s in real time, before sending the data to the final storage space. The ALICE experiment has been at the forefront of utilizing FPGAs and GPUs, together with CPUs, for real time data analysis. The use of the aforementioned technologies has pioneered hardware-accelerated real-time computing at the LHC and other new experimental setups.

Modular Supercomputing and Quantum Computing

With the end of "Dennard Scaling" and the beginning of the phase-out of Moore's Law, the fac-tor of scalability in supercomputing became more important in order to maintain the desired growth rates in applicable computing power, especially in data rates. This was promoted by the increasing number of cores per processor, communication channels and SERDES elements as a result of increasing miniaturization, and by the increasing number of processors per system. Exascale – the next performance level – will take us into a completely new area of system paral-lelization, code scalability, reliability requirements for supercomputer technology, energy and processing power requirements and the effective allocation of resources.

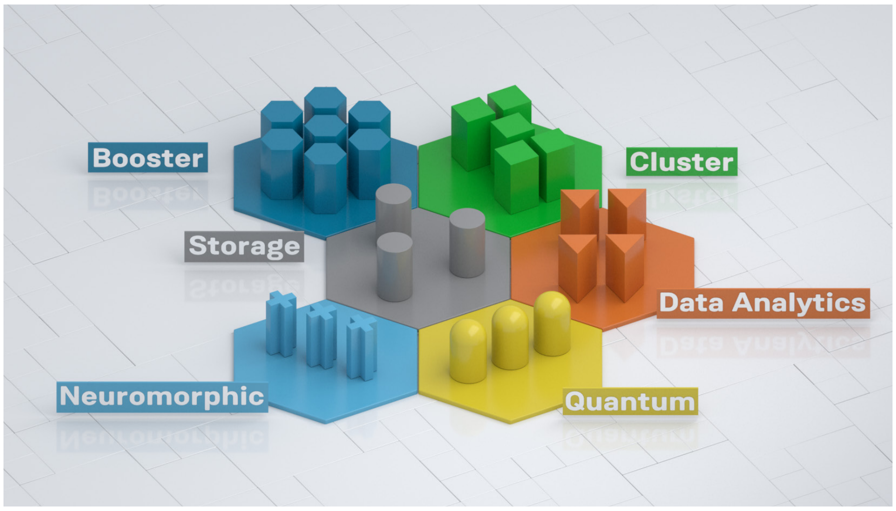
I have been pursuing the Modular Supercomputing Architecture (MSA) since 2000. In 2010 I filed a patent, which has since been granted worldwide. Starting in 2012, I have been co-designing MSA with the DEEP projects, funded by the European Commission. In 2017, a first production system was implemented at the Jülich Supercomputing Centre, JURECA – ranked 29th in the TOP500 list. In 2020, JUWELS, Europe´s most powerful supercomputer, went into operation, based on MSA.

MSA has evolved into a broad concept, capable of integrating future computing systems like quantum computers/annealers and neuromorphic systems into the modular network. At FIAS I do basic research on MSA – involving interaction and optimization of the use of disaggregated computing resources, MSA optimization of fast connection networks, integration of parallel file systems and cloud/high-performance computing mechanisms.

I intend to work closely with users in theoretical astrophysics, nuclear/elementary particle phys-ics, neuroscience and biology. It is my concern that HPC returns to a high application efficiency on the way to Exascale. I plan to integrate the first practical quantum computing devices for hy-brid HPC-QC calculations into a MSA network with the Frankfurt HPC systems, especially for use in first applications for industry and finance.

**Prof. Dr.
Thomas Lippert**

Prof. Dr. Dr. Thomas Lippert received his diploma in Theoretical Physics in 1987 from the University of Würzburg. He completed Ph.D. theses in theoretical physics at Wuppertal University on simulations of lattice quantum chromodynamics and in the field of parallel computing with systolic algorithms at Groningen University. He is director of the Jülich Supercomputing Centre at Forschungzentrum Jülich, member of the board of directors of the John von Neumann Institute for Computing (NIC) and the Gauss Centre for Supercomputing (GCS). Since August 2020 he holds the chair for Modular Supercomputing and Quantum computing at Goethe University Frankfurt and was appointed Senior Fellow at FIAS in March 2020.



Modular Supercomputing Architecture – MSA (Credits: Forschungszentrum Jülich/TRICKLABOR)

**Prof. Dr.
Franziska Matthäus**

Following her studies in biophysics at the Humboldt University of Berlin, including one year research stay at UC Berkeley (USA), Franziska Matthäus spent five years in Warsaw (Poland) on her PhD and scientific research. Between 2005 and 2016, she held two postdoc positions and a group leader position at IWR, University of Heidelberg. In 2016, she received a junior professorship at CCTB, University of Würzburg. Since October 2016, she holds a W2 position in bioinformatics, funded by the Giersch-Foundation.

Plenary Speakers

Zoë Lange and Franziska Matthäus were both invited for (virtual) plenary talks at the 2nd Fluminense Meeting of Women in Biomathematics in Rio de Janeiro.

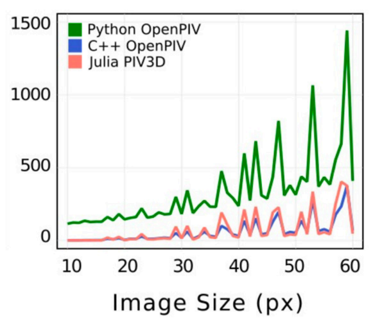
Projects @ FIAS: 1

Collaborations

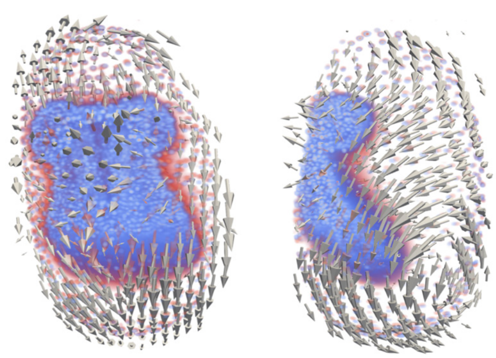
E. Stelzer, M. Windbergs, A. Frangakis (GU), A. Gerisch (TU Darmstadt) K. Painter (Politecnico di Torino), D. Headon, J. Rainger (Roslin Inst. Edinburgh)

Quantitative image analysis – 3DPIV

Advanced microscopy techniques, such as light sheet microscopy, record the dynamics of biological systems in 3D over a long time span. Hereby, images are recorded in stacks from different directions at every time point, and a 3D volume is fused from the set of recordings. This imaging technique is used to study developmental processes in insect organisms, or the dynamics of experimental model systems of organ function (the so-called organoids). However, to gain understanding of the involved processes we need to obtain quantitative data from these movies. To this end we developed 3D particle image velocimetry (3DPIV). PIV is a correlation-based technique to quantify translations, given two consecutive image frames of moving structures. Available software packages were only available for 2D image analysis. Our 3D application is implemented in Julia language, which provides the best trade-off between performance and high-level productive programming experience. Tests on artificially generated data indicate that when applied to 2D data the Julia package outperforms C++ applications due to compiler optimizations brought by Julia's compilation pipeline. As 3DPIV is based on cross-correlation, quantification of movement does not rely on the segmentation of tissue structures or labelling of cellular components. 3DPIV yields vector fields for every pair of consecutive frames, which are then used to compute a variety of quantities, such as the spatio-temporal velocity distribution, divergence, collectiveness, or pseudo-trajectories. The package has been successfully analyzed to study extra-embryonal membrane dynamics in the embryo of Tribolium castaneum, the red flour beetle. The software has been developed by Marc Pereyra and is available at Github (https://github.com/Marc-3d/PIV3D).



	C++	Python	PIV3D
2D	63ms	160.81ms	50.42ms
3D	-	59.72s	18.09s



Top left: Cross-correlation computation in PIV3D achieves speeds of C++ implementations and is significantly faster than OpenPIV implemented in Python. Bottom left: The complete PIV analysis in the Julia framework is about three times faster than Pythons OpenPIV, and outperforms the C++ implementation. Right: Result of 3DPIV applied to a time segment of Tribolium castaneum development. The resulting vector fields indicate a collective cell migration phase during the gastrulation event.

ESA Test-of-Time Award for Ulrich Meyer (FIAS) and Peter Sanders (KIT)

The ESA Test-of-Time Award (ToTA) recognizes excellent papers in algorithms research that were published in the European Symposia on Algorithms (ESA) proceedings 19-21 years ago and which are still influential and stimulating for the field today. For the 2019 Award, given in 2020, papers from ESA 1998 to ESA 2000 were considered.

The award committee selected the following paper for the ESA ToTA 2019 The paper stands for its impact in the design of efficient parallel algorithms for shortest path problems.

Ulrich Meyer, Peter Sanders: Delta-Stepping: A Parallel Single Source Shortest Path Algorithm. Proceedings of ESA 1998, pp. 393-404. Appeared also in J. Algorithms 49(1): 114-152 (2003)

Laudation: The paper presents an ingenious algorithm, dubbed Delta-stepping, for the Single-Source Shortest Path Problem (SSSP). This problem is well understood in the sequential setting (i.e., Dijkstra's algorithm) but its ubiquitous applications call for efficient parallelizations. Most of the sequential SSSP algorithms are based either on label-setting or on label-correcting methods. Label-setting algorithms, like Dijkstra's algorithm, settle at each iteration the distance label of one vertex. Label-correcting algorithms work instead by relaxing edges incident to unsettled vertices: all labels ar z temporary until the final step, when they all become permanent. In spite of the great practical performance of label-correcting methods, label-setting algorithms have been known to be asymptotically superior. In their paper, Meyer and Sanders show how to fill this gap by presenting Delta-stepping, a new label-correcting algorithm for SSSP which runs in optimal linear time with high probability for a large class of graphs with random edge weights. They further provide an efficient parallel implementation of their Delta-stepping algorithm, which has been a reference method and has inspired much subsequent work in parallel algorithms for many years.

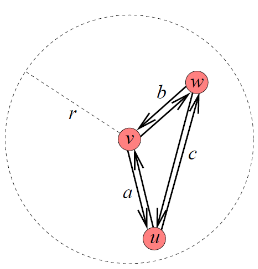
Award Committee: Giuseppe F. Italiano, Uri Zwick, Samir Khuller

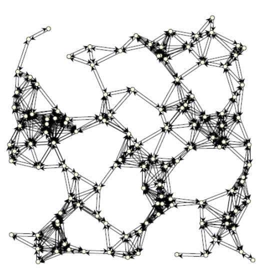
**Prof. Dr.
Ulrich Meyer**
Prof. Dr. Ulrich Meyer joined FIAS in January 2020. He is at full professor at Goethe University Frankfurt since 2007. Since 2014 he is also the spokesperson of the DFG priority program "Algorithms for Big Data" (SPP 1736, www.big-data-spp.de) which spans more than 15 sites allover Germany, Austria, and Switzerland. He received his Ph.D. in computer science from Saarland University in 2002. Subsequently he was a postdoc and eventually senior researcher (W2) at Max-Planck Institute for Computer Science in Saarbrücken.

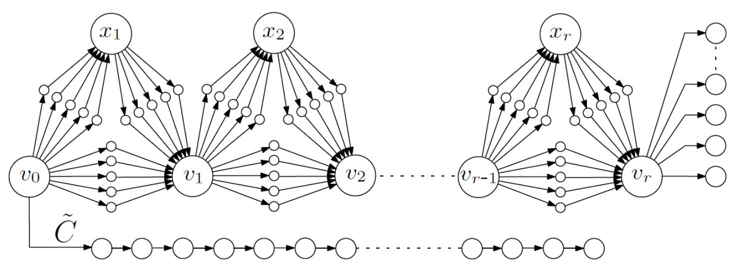
News travels fast

How long did it take for the first 100 students (out of 178) to check their ALGO-2 examination results after they appeared on the group's webpage without any further notice? --- Just 19 minutes!

Projects @ FIAS: 1







Prof. Dr.
Igor Mishustin

Igor Mishustin studied theoretical physics and astrophysics at the Moscow State University. He obtained his PhD and then the Doctor of Sciences degree (habilitation) at the Kurchatov Institute in Moscow. After long-term stays in the Niels Bohr Institute (Denmark) and the University of Minnesota (USA), he joined the newly-established Frankfurt Institute for Advanced Studies, in 2004. Here he leads the group of theoretical subatomic physics and astrophysics.

Medicine Physics

In addition to his work in subatomic and astrophysics, he has done important research on cancer therapy with ion beams.

Projects @ FIAS: 1

Collaborations

Abdel Nasser Tawfik

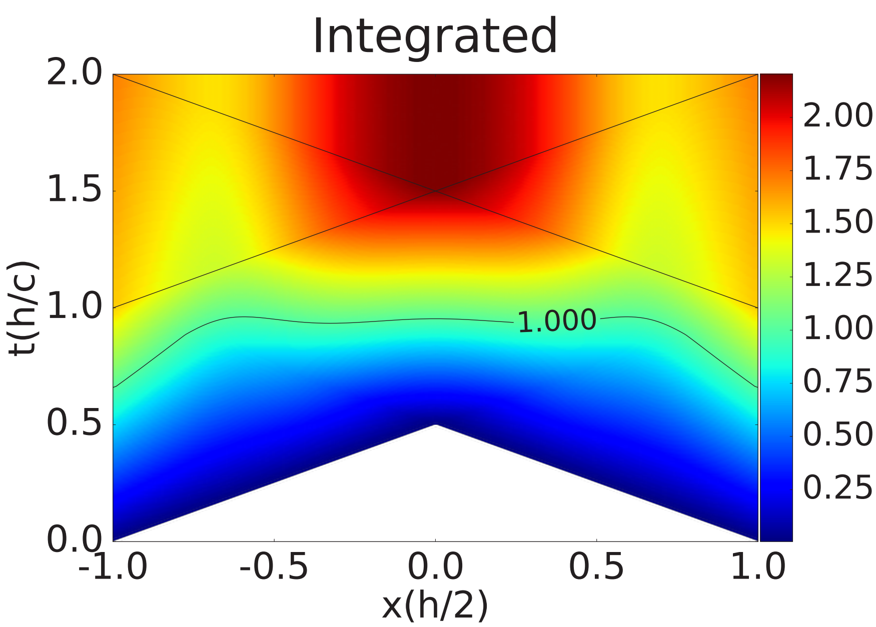
L.M. Satarov

M.I. Gorenstein

L.P. Csernai

Radiation dominated implosion with flat target

Inertial Confinement Fusion is a promising option to provide massive, clean, and affordable energy for humanity in the future. But the progress in research and development in this field is hindered by hydrodynamic instabilities occurring at the intense compression of a spherical target by energetic laser beams. To avoid instabilities the initial compression of the target pellet should be eliminated or significantly decreased. Then a final short and more energetic laser pulse should provide rapid volume ignition. It should be as short as the penetration time of the light across the target. In the present study, we consider a flat fuel target irradiated from both sides simultaneously by two laser beams. To reach ignition conditions in the flat target with a smaller compression, we need to largely increase the temperature. To reach this goal we propose to use plasmonic nano-shells embedded in the target fuel. In this way the reflectivity of the target can be made negligible, but the absorptivity can be increased by one or two orders of magnitude. Thus, the ignition temperature and radiation dominated regime can be achieved. As relativistic fluid dynamics simulations show, under these conditions most of the target interior will reach the ignition conditions almost simultaneously, This will make impossible the development of any kind of instabilities, which up to now prevented the complete ignition of the spherical targets.

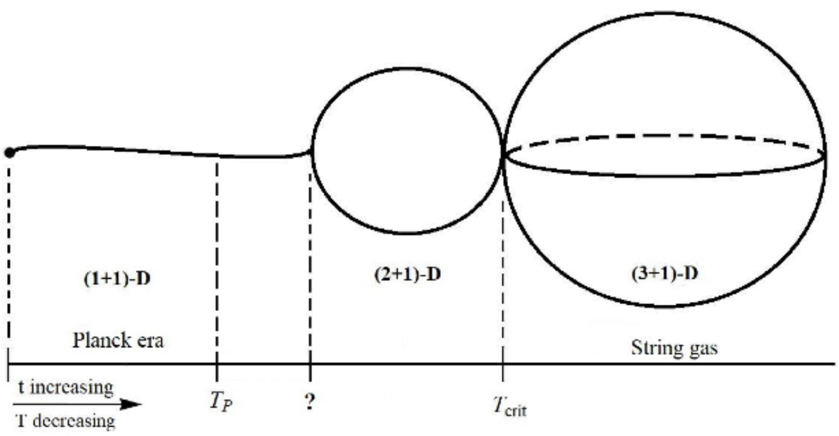


The energy density T(t, x) achieved up to a given time in the flat target. The color strip indi-cates the energy density, T, in units of the critical one, Tc. The contour line T = 1 indicates the critical energy density, Tc, where the phase transition (A) or the ignition (B) in the target is reached. This contour line is almost at a constant time, indicating simultaneous transition or ignition in thewhole target volume.

Classical and Quantum Gravity

The group activity has focused on the physics of the early Universe during the Planck era, an epoch characterized by exotic objects like strings, branes as well as evaporating black holes. The highlight of the research activity of the group has been the proposal of the concept of "dimensional oxidation", namely the dynamical evolution of the pre/post-inflationary Universe dimension from two to four, in a process opposed to the dimensional reduction. Such a proposal has been applied to the quantum decay of de Sitter space. It has been shown that the oxidation can efficiently explain Dark Matter in terms of quantum black hole remnants nucleated after the inflation. In addition the oxidation leads the Universe to a four dimensional state described by a variety of actions grouped under the umbrella of Horndeski gravity. In other words our proposal can be instrumental to understand the current acceleration of the Universe, without invoking additional forms of energy.

Another important result has been the determination of a family of charged and rotating black hole spacetimes able to accommodate the so called gravity self completeness. The latter is a paradigm according to which curvature singularities are inaccessible by any physical process, i.e., matter compression or black hole evaporation. Conventional black hole metrics cannot fulfill the expected bounds on black hole mass and radius the gravity self completeness demands. Indeed short scale quantum corrections must be invoked. The merit of the work of our group has been the first ever derivation of the profile of such greatly sought quantum corrections.



Dimensional reduction/oxidation of the Universe. The spacetime dimension evolves according to the energy scale at which the Universe is observed.

Prof. Dr.
Piero Nicolini

Piero Nicolini received his PhD from the University of Bologna in 2002 and his habilitation from the Goethe University in 2013. After postdoctoral positions in Marseille and in Trieste, he is currently a Research Fellow at FIAS and an Apl. Professor at the Goethe University. His research interests cover quantum gravity, quantum field theory, and theoretical particle physics. Prof. Dr. Piero Nicolini is best known for having first proposed noncommutative geometry as a tool for studying evaporating black holes beyond the semiclassical limit.

Top Editor

Piero Nicolini is in the editorial board for 3 international journals and is serving as editor for 8 journals.

Projects @ FIAS: 1

Collaborations

Prof. Dr. Bernard Carr (Queen Mary University London)
Prof. Dr. Jonas Mureika (Loyola Marymount University & Kavli Institute for Theoretical Physics, University of California, Santa Barbara)
Dr. Konstantinos F. Dialektopoulos (Yangzhou U., China)
Heather Mentzer, MSc, (University of California, Santa Cruz)

Prof. Dr.
Luciano Rezzolla
received his PhD in Astrophysics at the SISSA in Trieste, Italy in 1997. After a number of years at the university of Illinois at Urbana-Champaign, he moved back to SISSA for a tenured position.
In 2006 he moved to the Max-Planck Institute for Gravitational Physics in Potsdam as Head of the numerical-relativity group. In 2013 he moved to Frankfurt and was awarded an ERC Synergy Grant and is the recipient of the 2017 Karl Schwarzschild Prize from the Walter Greiner Foundation. Luciano Rezzola was a Senior Fellow from 2015-2018, he rejoined the institute in September 2020.

New board member

Luciano Rezzolla is the newest member of the board of directors at FIAS.

Projects @ FIAS: 1

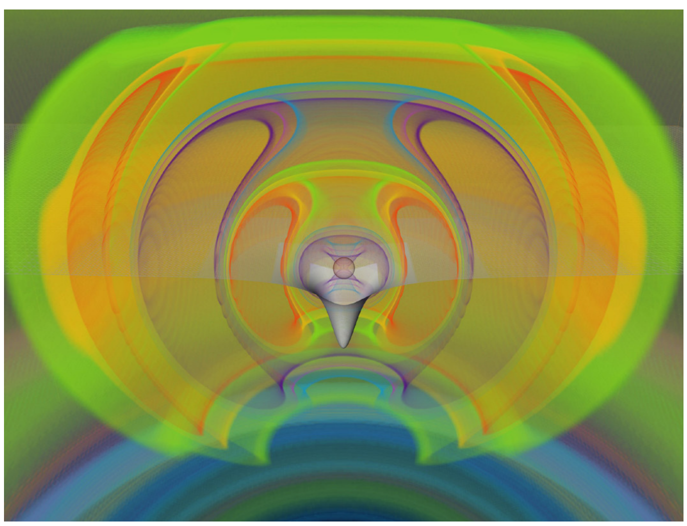
Neutron stars and black holes of stellar mass

Our research is pursued in a fundamentally interdisciplinary manner in which advanced numerical methods are employed for the solution of highly nonlinear equations to widen and deepen our understanding of high-energy astrophysical phenomena and of the state of matter at extreme conditions. Over the years we have considered a wide spectrum of research topics and have performed many pioneering calculations in numerical relativity. For these works I have been awarded a number of prizes and honours: the Karl-Schwarzschild Prize (2017), the Frankfurt Physics Science Prize (2019), the Golden Seal of the University of Bari (2019) and the Andrews Professorship of Astronomy (2019) at Trinity College Dublin, established in 1783. Shared with the EHT, I have received: the Diamond Achievement Award (2019) the 2020 Breakthrough Prize (2019), the Albert Einstein Medal (2020), and the Bruno Rossi Prize (2020).

Starting from 2013 - thanks to the ERC Synergy Grant, shared with H. Falcke and M. Kramer, and as a member of the Executive Board of the EHT Collaboration - I have provided fundamental contributions to the international effort of producing the first image of a supermassive black hole. In particular, the numerical simulations and the theoretical predictions produced by my group have played a fundamental role in understanding the origin of the electromagnetic emission ring and to deduce the properties of the black hole.

Our group also has a long track record in the development and high-performance codes to study black holes and neutron stars. These codes have pioneered the use of advanced techniques in numerical relativity and are now used worldwide in their publicly available versions (Whisky, Whisky-THC, BHAC, ExaHyPE). Some of these works have transformed the field of numerical relativity and have now become the standard in the evolution of non-vacuum spacetimes.

My future research plans and contributions to FIAS will be centered around the physics and astrophysics of compact objects, both in terms of the dynamics and gravitational-wave emission from neutron stars and black holes of stellar mass, and in terms of imaging and modelling accreting supermassive black holes.



Simulation of a collapsing neutron star

Rapid analysis of large seismological data sets

My research focuses on the field of seismology and my current research activities fall into five major areas:

(1) understanding of tectonic processes such as rifting and mountain building, subduction of oceanic plates, and mantle-plume upwellings through the seismological analysis of deformation and flow fields within the Earth's crust and mantle;

(2) studying seismic wave propagation in anisotropic elastic media through waveform modeling and inversion of seismograms;

(3) innovative monitoring of earthquake activity based on temporary deployments of networks and arrays of seismic stations at scales ranging from 10^2 to 10^6 m;

(4) detection, analysis and understanding of seismic and infrasound signals in response to volcanic and magmatic activities;

(5) improvement of seismic recording conditions by removal of noise effects.

In the last 15 to 20 years I have been involved in developing and coordinating seismological research activities in the Middle East, East Africa, and the Indian ocean region. More recently my group has participated in a large-scale European effort to study the Alpine region and related tectonic processes. The vast amounts of seismological data that have and will become available through these and similar research activities conducted by the seismological community require innovative and highly-automized processing and analysis tools to fully exploit the seismic recordings. The new developments in machine and deep learning (ML, DL) based on neural networks over recent years provide a promising base for such automized approaches of data processing.

Through the collaboration with scientists at FIAS and their expertise in applications of ML- and DL-concepts to tackle physical problems, I aim to develop novel tools required for the rapid analysis of large seismological data sets. The ability to utilize the information contained in seismic recordings more completely will significantly improve the imaging and understanding of processes within the earth, which are hidden from direct observations. The new methods also provide opportunities to search for previously undetected patterns that may link subtle waveform changes and earthquake rupturing. As an application for these tools, we are currently developing a proposal for a new AI-based "traffic-light" system to better control the release of induced seismic activity in deep geothermal reservoirs used for electric power generation.

**Prof. Dr.
Georg Rümpker**

After studying geophysics at the University of Münster, Georg Rümpker received his PhD degree in seismology from Queen's University (Canada) in 1996. He continued his career as a postdoctoral fellow at the Carnegie Institution of Washington and later at GeoForschungsZentrum Potsdam as a research scientist. Since 2004, Rümpker has been professor of geophysics at the Institute of Geosciences at Goethe-University Frankfurt, Germany. He joined FIAS in May 2020.

Taunus Observatory

The seismic station at the Taunus Observatory is maintained by the departement of Geophysics at the Institut of Geosciences at Goethe University in Frankfurt together with the BGR (Bundesanstalt für Geowissenschaften und Rohstoffe).

Projects @ FIAS: 1

Prof. Dr.
Enrico Schleiff

Prof. Dr. Enrico Schleiff, studied physics at the Charles University in Prague, and later at the Gutenberg University in Mainz and at the University of Basel. In 1999 he did his PhD at McGill University Montreal, Canada. Later he worked at Christian-Albrechts-University zu Kiel and the LMU, Munich. Since 2007, he has held a W3 professorship for Molecular Cell Biology of Plants at the Institute of Molecular Biology at GU Frankfurt. In 2017 he joined FIAS as Senior fellow and became its chairman in 2018.

Triple threat

In 2020, Enrico not only managed to successfully lead an institute and a research group, but also ran a successful campaign for the position of GU president.

Projects @ FIAS: 1

Collaborations

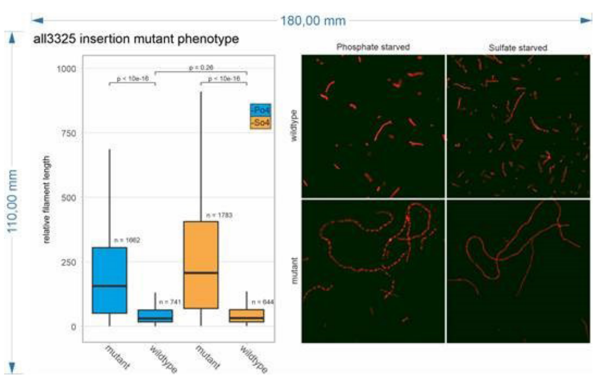
SPOT-ITN
DynaMem
SFB 807 / 902
Nir Keren,
Hebrew Univ. Jerusalem
Arndt von Haesler, CIBIV, Wien

Transcriptional changes in response to environmental stresses

Transcriptional changes in response to environmental alterations is one mechanism of cells to ensure survival. The base of the response are specialized surveillance mechanisms that are essential to maintain the integrity of cells. With our expertise in the analysis of such transcriptional changes, we address reactions in prokaryotic and eukaryotic cellular systems. In general, we apply Principal Component Analysis (PCA) to extract information about the correlation of the transcriptome determined under different conditions. Further, differential expression analysis allows the identification of differential expressed genes (DEGs), which are common under all "stress" conditions or specific to a certain treatment. The functional pathways affected are typically identified through statistical over representation of gene ontology (GO) terms.

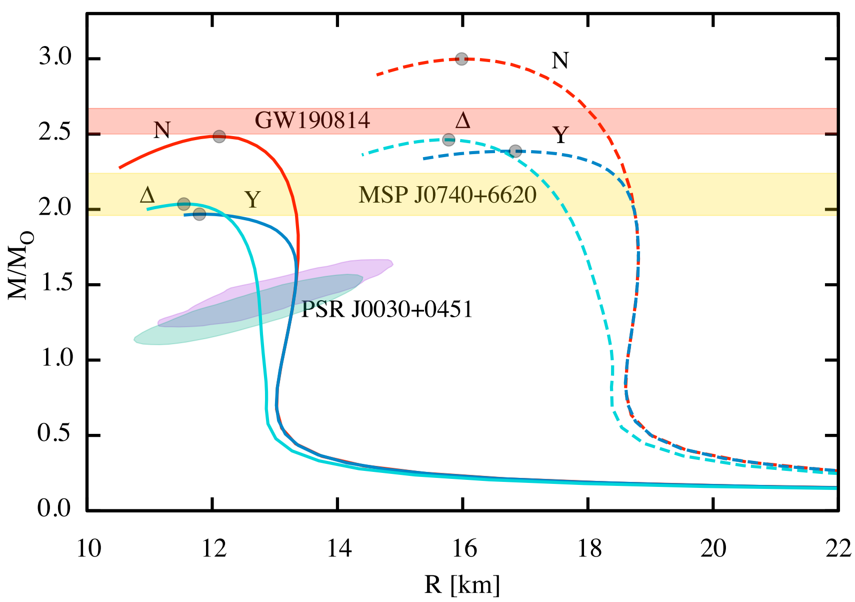
On the one hand, the reaction of the cyanobacteria in response to nutrition alterations is explored. Here, we focus on the analysis of the response to nitrogen fluctuations and to changes in the micro-nutrition supply. We identified a network of genes regulated in short-term response and altered in adapted cells when compared to cells grown under normal nutrition supply. This information is currently linked to morphological and biochemical alterations to draw conclusions on mechanisms of cell differentiation as well as on cell adaptation. This is conducted in collaboration e.g. with the group of Nadine Flinner.

On the other hand, we analyse the specialized surveillance mechanisms that are essential to maintain the genetic integrity of germ cells. Oocytes are the source of all somatic cells and of the germ cells of the next generation. Therefore, DNA damage and chromosomal aberrations affect the entire species. The surveillance of the structural integrity of the DNA is maintained and tightly controlled by the p53 family member TAp63α. We investigated how oocyte death is initiated by TAp63α after gamma-irradiation. The transcriptome of cells was analysed after different time points after gamma-irradiation at different intensities. This approach allows the comparison of the transcription profiles in response to gamma-irradiation dosage and to relate it to the longitudinal observations. In general, we observed 8 clusters of DEGs after high doses irradiation involved in e.g. damage and repair as well as apoptosis. This work is conducted in collaboration with the group of Volker Dötsch.



Equation of state of superdense matter

In 2020, the group of A. Sedrakian continued working on the equation of state of dense matter in the framework of density functional theory. The focus was on the matter which contained heavy baryons (hyperons and delta-resonances). In particular we studied the appearance of heavy baryons at low densities when the matter is heated to high temperature. It was found that cluster states of nuclear matter can also contain heavy baryons. Another aspect of our studies was the effect of rapid rotation on the properties of compact stars and the maximal mass they can have under Keplerian rotation. This topic is of special importance in the context of gravitational wave astronomy, in particular the interpretation of the GW190814 event, where a massive black hole (33 solar masses) and a light object (2.5 solar masses) were observed to merge via their gravitational radiation (see Figure). A further topic that was pursued in 2020 was the transport in the binary neutron star mergers, where we estimated the timescales of damping of matter oscillations due to the deviations from electroweak equilibrium. The work of equation of state was extended further to study the phase transition to quark matter and appearance of twins and triplets of stars in the mass-radius diagram of compact stars. We have explored in detail the parameter space of such models and selected those that are compatible with all the presently available constraints from astrophysics and laboratory physics.



The mass-radius relations for nonrotating (solid lines) and maximally rotating (dashed lines) nucleonic (N), hypernuclear (Y) and Delta-resonance-admixed-hypernuclear stars. The colored areas show the constraints inferred from the most massive pulsar MSP J0740+6620, the mass-radius limits inferred from the NICER experiment and the mass limits from GW190814 (red band). The circlesindicate the maximum masses of the sequences, to the left of which the stars are unstable.

Prof. Dr. Armen Sedrakian

Prof. Dr. Armen Sedrakian received his physics degree from the University of Rostock (1989), PhD at Yerevan State University (1992) and Habilitation from Tübingen University (2006). He held research positions at the Max-Planck Institute for Nuclear Physics (Heidelberg-Rostock), Cornell University (USA), Groningen University (The Netherlands) and Tübingen University. Since 2007, he teaches at Goethe University at the Institute for Theoretical Physics and since 2017, he has the position of Fellow at FIAS. In parallel he holds Professorships at Yerevan State University (2011) and at Wroclaw University (2018).

Academy of Science

Sedrakian is a foreign member of the National Academy of Science of Armenia.

Projects @ FIAS: 1

Collaborations

Prof. M. Alford (Washington U., St. Louis), Prof. Fridolin Weber (San-Diego State U.), Arus Dr. Harutyunyan (Byurakan Astro. Observatory), Peter Rau (Cornell University), Dr. Adraian Raduta (Phys. Eng. Institute, Bucharest), Dr. Micaela Oertel (LUTH, Meudon)

Prof. Dr. Dr. h.c. mult.
Wolf Singer

Wolf Singer, studied Medicine in Munich and Paris, received his PhD from the LMU Munich and his habilitation at the TU Munich.
He was one of the directors of the MPI for Brain Research, as well as founding director of FIAS and the Ernst Strüngmann Institute for Neuroscience.
His research is devoted to the exploration of neuronal foundations of cognitive functions. Central to his research is the question over how many brain areas processes are connected to allow for coherent perception.

Leopoldina Member

Among many other awards, Singer is a member of the National Academy of Sciences.

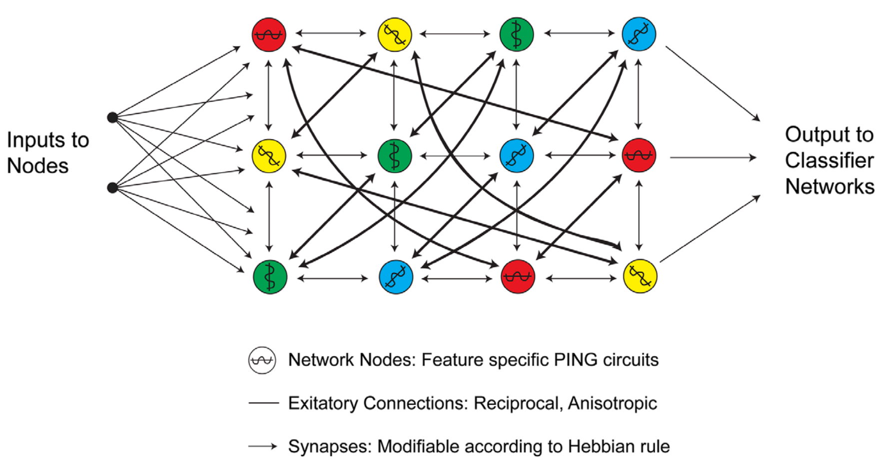
Projects @ FIAS: 2

Collaborations

Dunja Bruder (HZI), Veronika von Messling (PEI), Franklin Toapanta (Maryland University), Yassine Taoufik (Hôpital Bicêtre), Frank Pessler (MHH)

Computations in the high dimensional state space provided by the dynamics of the cerebral cortex

There is still no unifying theory of how the cerebral cortex processes information. Consequently, numerous experimentally identified phenomena, especially the extremely complex dynamics lack a cohesive theoretical framework. We formulated a hypothesis that assigns specific functions to some of these dynamic interactions. As depicted below, the visual cortex can be considered as a recurrent network, whose nodes are feature selective, have a propensity to oscillate, and are coupled through connections whose lay out and efficiency are shaped by experience. Consequently, the architecture of these connections reflects the statistical contingencies of features in the visual world. We are currently testing predictions of our hypothesis by simultaneously recording the activity of numerous network nodes in trained monkeys while these perform cognitive tasks. The results obtained so far support the following predictions. The high dimensional correlation structure of resting activity harbours the priors required for the dynamic binding of features that underlies perceptual grouping. Presenting structured visual stimuli leads to a rapid convergence of network dynamics to low dimensional sub-states with stimulus specific correlation structure. This convergence is more succinct for natural stimuli matching the stored priors than for manipulated stimuli whose statistics do not correspond to prior experience. Thus, sub-states reflect the match between sensory evidence and the stored model of the world. Classification with machine learning techniques of sub-states revealed that these are stimulus specific and better classifiable as well as more sustained if evoked by natural than manipulated stimuli. These observations suggest a mechanism that permits the dynamic representation and parallel read out of a vast amount of priors and the ultrafast comparison of sensory evidence with stored knowledge. These are essential functions of predictive coding strategies.



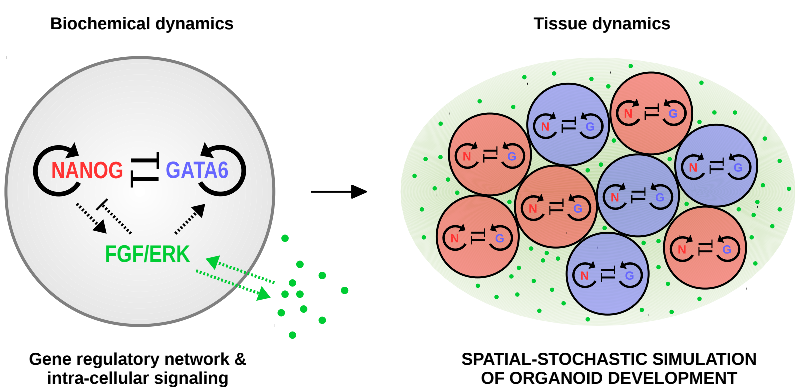
Superficial layers of the cerebral cortex: A delay coupled, anisotropic, recurrent oscillator network Columns coding for related features are coupled preferentially.

Event-driven multiscale biochemical simulations

Living organisms have the capability to process information reliably and efficiently, both inside their cells and at the tissue level. However, to this end they employ biophysical and biochemical processes that are fundamentally stochastic, and therefore limit the reliability of biological information transmission and processing. Nonetheless, cellular information processing can attain astonishingly high precision and reproducibility, in particular in the field of early embryo development. Here, reliable early cell fate assignment is crucial while material and temporal resources are limited, meaning that successful information processing relies on efficient noise-control mechanisms optimized by evolution.

Our emerging group at FIAS aims at unraveling such mechanisms via numerical and analytical models that accurately incorporate the biophysical and resource contraints faced by the cells. Such models chiefly rely on realistic modeling of the fundamental intracellular stochastic processes causing biological noise, which quickly can become intractable both mathematically and numerically. A hallmark of our approach therefore is to employ event-driven simulations, smart mathematical approximations, and problem-specific numerical optimization techniques for reducing the computational cost associated with realistic bio-stochastic models.

In 2020 we started a new project that will create a generically applicable, numerically efficient event-driven tissue simulator capable of stochastically simulating the mechanical tissue growth, intracellular biochemical dynamics, and cell-to-cell communication governing tissue development. While versatile, the simulator will be concretely applied to elucidate the role of stochastic cell fate assignment and subsequent intercellular comminication in ICM organoids representative of early mouse embryos. To this end we link our efforts with the Matthäus, Stelzer and Fischer (Uni Würzburg) groups, combining their experimental and modeling work on this system by our expertise on spatial-stochastic gene regulation. This work will mainly be carried out by PhD student Michael Ramírez Sierra, who joined the group in September 2020.



Dr. Thomas Sokolowski

Thomas studied physics and mathematics at Saarland University. But soon took the path towards theoretical biophysics he completed his P.h.D. in 2013 from Vrije Universitet Amsterdam (VU). Afterwards he stayed as a postdoc at IST Austria from 2014 until 2020, where he focused on optimizing complex spatial-stochastic models of biophysically constrained cellular information processing, mainly in developmental biology. In April 2020 he started as a group leader and fellow at FIAS.

New research paths

We co-developed a concept combining biophysical optimization and classical inference that ultimately was exemplified by theoretical neuroscientists, which somewhat unexpectedly made us co-authors of a paper in Neuron in early 2021.

Projects @ FIAS: 1

Collaborations

Prof. Dr. William Bialek, Princeton

Prof. Dr. Thomas Gregor, Princeton / Institut Pasteur (Paris)

Prof. Dr. Gašper Tkačik, IST Austria

Prof. Dr. Sabine Fischer, Uni Würzburg

Prof. Dr. Sebastian Maerkl, EPFL (Lausanne)

**Dr.
Nishtha Srivastava**

Nishtha Srivastava finished her Bachelor's in Mathematics and Masters in Exploration Geophysics at Banaras Hindu University, India. Afterwards Srivastava joined the Advanced Computational Seismology Laboratory at the Indian Institute of Technology (IIT) Kharagpur, India where she was part of various seismological projects and wrote her doctoral thesis in seismology to study the site effects due to the impact of both near and far field earthquakes. In 2018 she joined FIAS as a postoctoral researcher and became a Research Fellow in September 2020.

Promoting Women in AI

Her research is funded by a BMBF program to promote women in AI, and she is also personaly involved in promoting young women in AI.

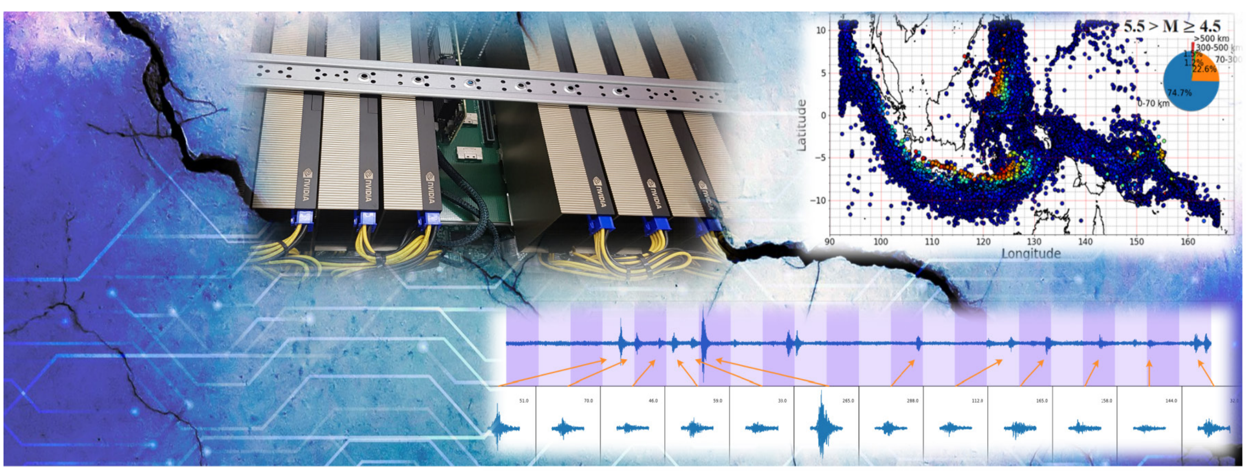
Projects @ FIAS: 1

Seismology and Artificial Intelligence

My freshly started research group seeks to apply novel Deep Learning and Machine Learning based algorithms on seismic signals to improve Earthquake Early Warning System (EEWs) and Seismic Signal Analysis. Additionally, by implementing distinct Artificial Intelligence driven models, supported by the statistical analysis based on classical models we are also trying to better understand the pattern associated with Seismic stress release. Earthquakes are inevitable and considered extremely difficult to predict. Analyzing and interpreting the ever-increasing abundant seismological dataset is most time consuming and is a herculean task. The implementation of Artificial Intelligence powered by Deep Learning algorithms for earthquake signal analysis has the potential to out-perform classical approaches such as STA/LTA.

Seismic Event Detection and Seismic phase picking are two most crucial task for seismologist. Specially in the case of low signal-to-noise ratio small magnitude seismic events are extremely hard to be detected by classical methods and researchers try to identify such microearthquakes manually. We are working on a simple yet powerful Deep Learning architecture based on an encoder-decoder algorithm comprised of 1-Dimensional Convolutional Layers with skip connections and Self- & Multi-Attention mechanism. This architecture is currently being applied and tested on various seismic datasets from different regions to check its performance. Owing to its higher sensitivity, this model is expected to perform better than classical approach.

Furthermore, we are attempting to improve the existing EEWs models by reducing the length of data used as input as well as the needed number of stations. Various combinations of Convolutional Neural Networks and Bi- & Uni-directional Long-Short Term Memory and Gated Recurrent Unit are being tried and tested to obtain the best performing model with optimal hyperparameters. This study is likely to help seismologists in issuing quicker warnings, thus providing increased time window to the local authorities.



The state of matter

from heavy ion collisions to neutron star mergers

The recent years mark the beginning of an exciting new era in the study of super-dense and hot fundamental matter. Since the first observation of astronomical signals from the collision of two neutron stars, we know that such kind of matter is also formed in these cosmic events as well as in relativistic heavy ion collisions.

In our group at FIAS, and especially through the work of Mr. Anton Motornenko, a model was developed that is able to describe the properties of matter produced in such violent collisions: the Chiral Mean field Model (CMF). What makes the CMF model particularly relevant is that it is based on the results of first principle latticeQCD simulations which are usually only valid in the domain of low density and high temperature matter as observed at the LHC-CERN and early universe. This model therefore, for the first time allows a direct comparison of matter produced on the largest earth collider experiments as well as cosmic neutron star mergers.

The CMF model is being employed in large scale simulations of such neutron star merger events. First results from the application of the CMF model for di-lepton production in Heavy Ion collisions at the SIS18 accelerator have already been made public. The simulated evolution of such a collision with the CMF model is shown in the figures below. We were able to show explicitly the effects of a possible QCD-phase transition on the measured di-lepton multiplicities.

Importance of new ML methods to interpret the corresponding data:

The experimental studies at particle colliders and of neutron star mergers require the development of novel technology and have been the driver of technological innovation for decades. Experimental signals are often small compared to the background and though short lived very data intensive. This combination requires the use of modern machine learning methods for their analysis and interpretation. Simultaneous to developing new theoretical models of matter our group also has made progress in the development of deep-learning algorithms for fast event characterization as well as possible detection of outliers (containing new physics) from these experiments. These endeavors are highly complementary and possible due to the interdisciplinary foundation of FIAS.

A. Motornenko, J. Steinheimer, V. Vovchenko, S. Schramm and H. Stoecker, Phys. Rev. C 101, no.3, 034904 (2020)

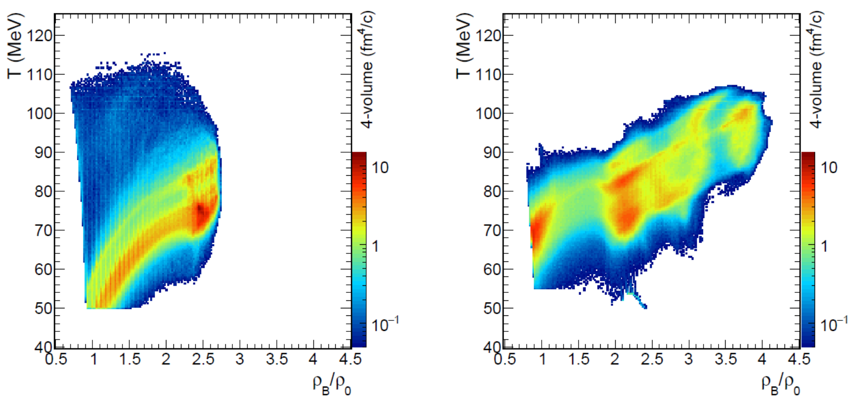


Fig. 1: Distributions of the contributions in fireball temperature and baryon density in central gold+gold collisions at HADES. Calculated with ideal fluid dynamics with the CMF model and two phase transition scenarios (left: crossover, right: first order transition).

Dr. Jan Steinheimer-Froschauer

Dr. Jan Steinheimer-Froschauer graduated in physics in 2008 with a diploma in theoretical physics from Goethe University Frankfurt. After three more years, he earned a PhD from the Goethe University. He then received a postdoctoral position at FIAS from 2011-2012, before moving to the Nuclear Science Division of the Lawrence Berkeley National Laboratory, Berkeley, USA. Since 2013, he has been working at FIAS as a postdoc and was appointed Research Fellow in 2017.

Collaboration with China

Jan Steinheimer is one of the initiators of the Xidian FIAS International Joint Research Center established 2019.

Projects @ FIAS: 3

Collaborations

HADES collaboration

Ralf Rapp, Texas A&M Universit

Abhijit Bhattacharyya, Calcutta University

Christoph Herold, Suranaree University

Volker Koch, LBNL Berkeley, USA

Yasushi Nara, Akita International University

Prof. Dr. Dr. h. c. mult. Horst Stöcker

Following his doctorate 1979 at GU Frankfurt, he first became a guest researcher at GSI Darmstadt.
In 1980 Stöcker joined the Lawrence Berkeley Laboratory of the University of California, Berkeley, USA. From 1982 to 1985, he was an Assistant Professor at the Department of Physics and Astronomy at Michigan State University and NSCL.
In 1985 Horst Stöcker accepted a professorship in Theoretical Physics at the Johann Wolfgang Goethe University in Frankfurt am Main.

At FIAS since 2004

Horst Stöcker is part of FIAS since its foundation in 2004 and was its first chair of the board of directors.

Projects @ FIAS: 4

Deep Learning in theoretical Sciences

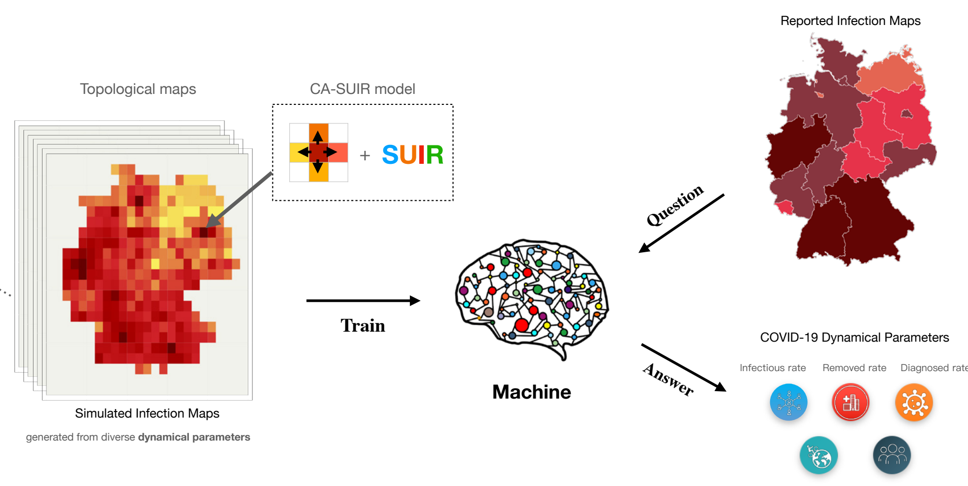
The DL and theoretical physics groups are further extending, also by new strategic hires, their expertise in Machine Learning and Artificial Intelligence, AIML, applications in science and technology.

In the area of theoretical heavy-ion physics and nuclear astrophysics, we strengthened the MAGIC connection between Astrophysics and Gravitational Waves from Binary Neutron Star Mergers and Relativistic Heavy Ion Collisions - Lattice QCD and the EoS of dense matter (with the groups of Dr. Jan Steinheimer and Prof. Dr. Luciano Rezzola)

By bringing the Seismology and AI project to FIAS, we have achieved a long-term commitment to the geosciences. With the Observation of a strongly increasing number of devastating earthquakes M>6 at the Pacific Ring of Fire in Indonesia using AIML (with the group of Dr. Nishtha Srivastava) we have first results in that area.

Another focus was to approach the EU's Green Deal using artificial intelligence to reduce the uncertainties in energy system optimisation resulting from uncertainties in the input data (with the group of Dr. Alex Kies).

Together with the research group of Dr. Kai Zhou, we transferred our physics and AI experience into COVID-19 risk spatio-temperal evolution studies for Germany, by developing a Cellular Automata (CA) coupled with SIUR epidemiological model together with transfer deep learning technique (see figure).



COVID-19 risk spatio-temperal evolution studies for Germany, see [arXiv: 2012.00082] with Dr. Lingxiao Wang, Prof. Yin Jiang, Till Stoecker, Tian Xu and Dr. Kai Zhou

Covariant Canonical Gauge Theory of Gravitation

The action principle establishes the basis for our successful derivation of a Palatini-type gauge theory of gravitation in the extended Hamiltonian formalism of field theories. The ensuing canonical transformation theory ensures, by construction, that the form of the action functional is maintained and thus complies with the requirement of diffeomorphism invariance -- historically referred to as the "Principle of General Relativity". The resulting Hamiltonian system describes self-consistently the coupled dynamics of matter fields and spacetime. This way, it is unambiguously determined how spin-0, spin-1, and spin-1/2 particle fields couple to spacetime.

The Covariant Canonical Gauge Theory of Gravitation (CCGG) introduces an important feature into the theory of gravitation, and adds novel dynamic aspects into cosmology: Einstein's general theory of relativity contains only a linear term, the Ricci scalar, in the Lagrangian. Therefore, spacetime lacks in its description a conjugate momentum field, which is required to enable a dynamical response to deformations of the metric. This is different in the CCGG theory: spacetime itself has a conjugate momentum and thereby a proper dynamical quality of its own. This changes the description of compact astrophysical objects and of relativistic collapse dynamics, with significant impact on the description of binary neutron star structure, mergers and pulsar dynamics. The CCGG modifications of the Friedman equation suggests, for example, a non-standard running cosmological constant and a new interpretation of Dark Energy, and hence change the standard evolution scenario of the universe. Moreover, the spin-coupling of fermions entails a curvature-dependent effective mass term in the ensuing Dirac equation. Its implication on neutron star physics is currently studied in the master thesis of Julia Lienert, which will be submitted in 2021.

Prof. Dr. Jürgen Struckmeier

After finishing his diploma in physics 1978, Jürgen Struckmeier got an appointment as staff scientist at GSI in Darmstadt, where he obtained his PhD in 1985. In 2002, his habilitation thesis was accepted at the Physics faculty of the Goethe University Frankfurt. Having worked as a lecturer, he was appointed there as "Extracurricular Professor", in 2010. In 2016, he joined FIAS as Fellow.

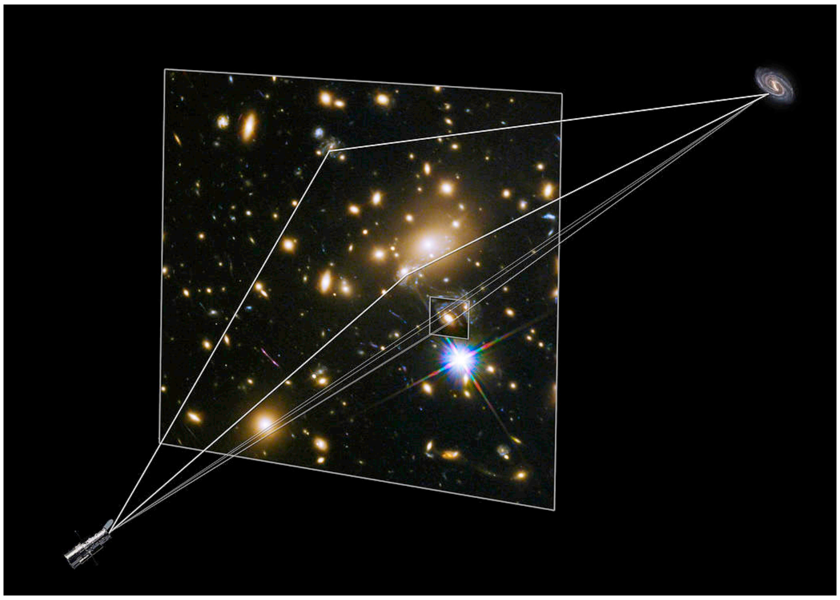
Highlight

Before he focused on gravitational theory, Jürgen Struckmeier successfully carried out theoretical research in the field of beam dynamics in particle accelerators.

Projects @ FIAS: 1

Collaborations

Eduardo Guendelman, Ben-Gurion University of the Negev;
Peter Hess, Instituto de Ciencias Nucleares, Universidad Nacional Autonoma de Mexico;
Johannes Muench, University of Regensburg;
Friedrich Wilhelm Hehl, University Cologne;
Frank Antonsen, Copenhagen



This sketch by NASA shows paths of light from a distant galaxy that is being gravitationally lensed.

Dr. Tatjana Tchumatchenko

Dr. Tatjana Tchumatchenko is a theoretical neuroscientist whose research focuses on modelling signal processing, synaptic, and subcellular dynamics in biological circuits. After receiving her PhD in Computational Neuroscience from the Göttingen Graduate School for Neurosciences, Biophysics, and Molecular Biosciences (Göttingen University, 2010), she completed a postdoctoral fellowship at the Center for Theoretical Neuroscience (Columbia University, 2011-2013) which was funded by the Volkswagen Computational Sciences fellowship (2011). As of 2013, Dr. Tchumatchenko is a Group Leader at the MPI for Brain Research and she became a FIAS fellow in 2017.

YAE Fellow

The Young Academy of Europe selected Tatjana Tchumatchenko as a new fellow in 2019

Projects @ FIAS: 1

Collaborations

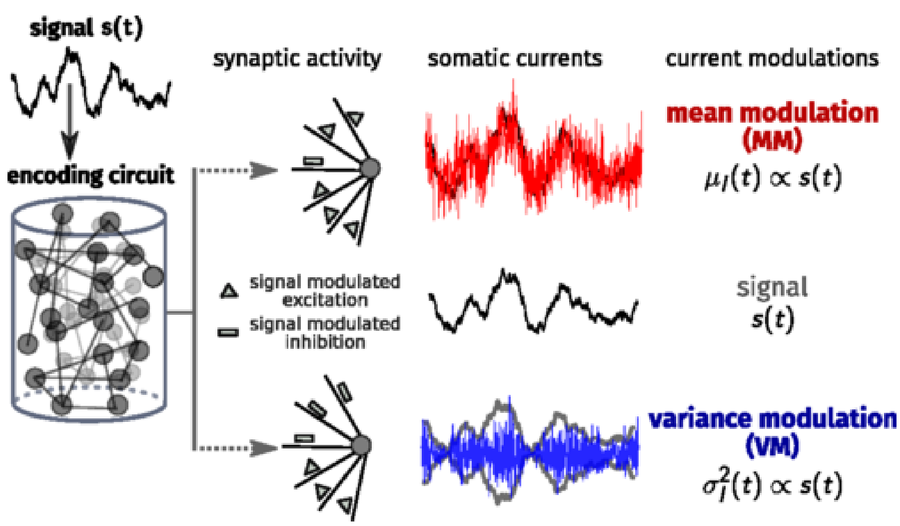
Prof. Schuman, MPI Brain
Prof. Busse, LMU
Prof. Bittner, Univ. Mainz

Theory of Neural Dynamics

My group "Theory of Neural Dynamics" at the Max Planck Institute for Brain Research is collaborating with Prof. Dr. Meyer from the Institute for Computer Science at the Goethe University as part of a project for the Center for Multiscale Modelling in Life Sciences (CMMS) of the FIAS Loewe Schwerpunkt program. This cooperation allows us to develop multi-scale analysis approaches to new and existing biological network models.

By combining mathematical, numerical and computational methods, we aim to better understand complex biological mechanisms, and to evaluate the stability and accuracy of existing models that describe these. We also work on existing models to improve their capacity to be implemented in experimental setups.

Our joint project "Construction, analysis and dimensional reduction for binary networks" is embedded in a larger interdisciplinary collaboration between various institutes in Frankfurt, whose goal is to combine multi-scale modelling and high performance computing to develop models that can be used for experimental applications.



Encoding signals by modulating either the mean or the variance of somatic input currents.
T Herfurth and T Tchumatchenko
Information transmission of mean and variance coding in integrate-and-fire neurons. Phys Rev E (2019)

Development and Characterization of Pharmacological Probes

The in-depth microscopic understanding of the interactions between small molecules and proteins is crucial for the improvement of existing drugs and the development of new drugs. In the past years, several developments of the popular coarse-grained force field Martini opened the way towards efficient high-throughput screening of ligand libraries as well as towards in silico fine tuning of protein-ligand interactions. These developments are all based on the re-parametrization of the force field which significantly improves the chemical specificity of molecular interactions.

In addition, the realistic representation of the molecular shape and of the free pocket volume as well as improved protein flexibility using Martini with a Gō-like model are important methodological improvements making the current state of the Martini force field applicable for structure-based drug design. Unbiased millisecond simulations of protein-ligand interactions recently highlighted the performance of the re-parametrized Martini 3 force field for its use in computer-aided drug design without a priori knowledge of the binding pockets or pathways. Very good quantitative agreement for the benchmark system T4 lysozyme as well as successful identification of binding pockets, binding poses, and binding pathways for different receptors and enzymes were achieved.

During setting up my own research group in the field of pharmacological probe development, I envision a fruitful collaboration with Dr. Roberto Covino to unravel drug binding pathways. In addition, I aim to study protein-drug interactions in collaboration with experimental research groups in the Faculty of Biochemistry, Chemistry and Pharmacy at the Goethe University Frankfurt. Potential target systems include – but are not limited to – selective kinase inhibitors and characterization of allosteric drug binding sites. Moreover, I aim to study photoswitchable pharmaceuticals in collaboration with experimental research groups.

Dr. Sebastian Thallmeier

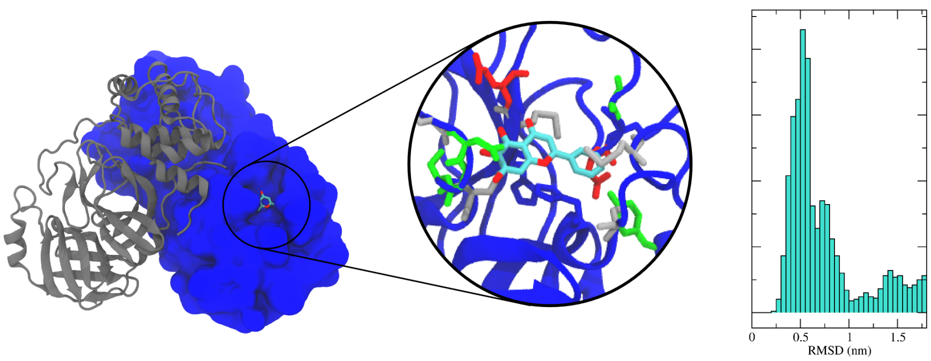
Sebastian Thallmair studied chemistry and biochemistry at the LMU Munich, where he completed his PhD in theoretical chemistry in 2015. After a short period as postdoctoral researcher in Munich, he joined the University of Groningen (The Netherlands) in 2016. His research focused on modeling of biological processes and method development for coarse-grained molecular dynamics. He was appointed as a Fellow in October 2020.

Horizon2020
He was awarded an Individual Fellowship of the Marie Skłodowska-Curie Actions (Horizon2020) in 2017.

Projects @ FIAS: 1

Collaborations

Faculty of Biochemistry, Chemistry and Pharmacy, GU Frankfurt



Binding pose of a small molecule inhibitor to the main protease of SARS-CoV-2 in the crystal structure (left) and the RMSD of the ligand calculated from an unbiased coarse-grained molecular dynamics simulation

**Prof. Dr.
Jochen Triesch**

Jochen Triesch is the Johanna Quandt Professor for Theoretical Life Sciences at FIAS. He also holds professorships at the Dept. of Physics and the Dept. of Computer Science and Mathematics at Goethe University Frankfurt. Before joining FIAS in 2005, he was Assistant Professor at UC San Diego, USA. Originally trained as a physicist, he discovered his passion for studying the brain already during his graduate education.

Explaining Frankfurts research In 2019 he organized a public lecture series, financed by the Stiftung Polytechnische Gesellschaft.

Projects @ FIAS: 7

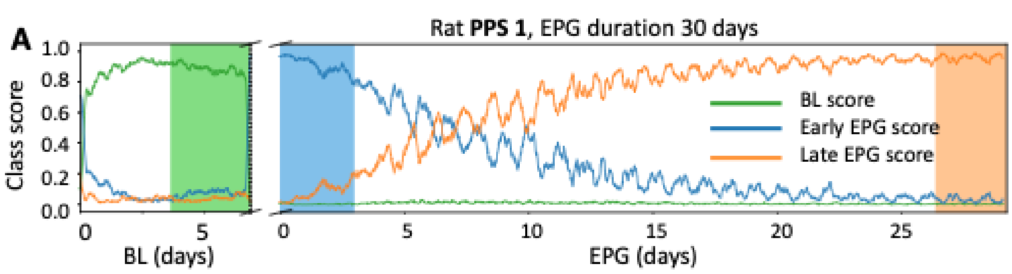
Collaborations

Bert E. Shi (Hong Kong)
Maria Fronius (Frankfurt)
Felix Rosenow (Frankfurt),
Elke Hattingen (Frankfurt),
Frederic von Wegner (Sydney)

Staging Epileptogenesis with Deep Neural Networks

Epilepsy is a common neurological disorder characterized by recurrent seizures due to excessive synchronous brain activity. The process of structural and functional brain alterations leading to increased seizure susceptibility and eventually spontaneous seizures is called epileptogenesis (EPG) and can span months or even years. For example, spontaneous seizures may develop years after a brain trauma. Detecting and monitoring the progression of EPG before the occurence of any seizures could allow for targeted early interventions that slow down disease progression or even halt its development. We have proposed a novel approach for staging EPG using deep neural networks. This approach can detect a developing epilepsy before any seizure has occured and it automatically identifies electroencephalography (EEG) biomarkers to distinguish different phases of EPG. Specifically, together with our collaborators from the university hospital in Frankfurt we have recorded continuous intracranial EEG recordings from a rodent model where epilepsy is induced by a so-called electrical perforant pathway stimulation (PPS). For this, electrodes are implanted into a rat's brain that allow to a) stimulate the brain to trigger the process of EPG and to continuously record the animal's brain activity for several weeks as the EPG unfolds. We have trained a deep neural network (DNN) to distinguish EEG signals from before stimulation (baseline), shortly after the PPS (early EPG) and long after the PPS but before the first spontaneous seizure (late EPG). Our results show that our proposed method can classify EEG signals from the three phases with good accuracy. To the best of our knowledge, this represents the first successful attempt to stage EPG prior to the occurence of any seizures using DNNs. In future work, we hope to translate this approach to humans who have experienced a brain trauma and are at high risk of developing epilepsy.

Reference: ELu, D., Bauer, S., Neubert, V., Costard, L. S., Rosenow, F., & Triesch, J. (2020, September). Staging Epileptogenesis with Deep Neural Networks. In Proceedings of the 11th ACM International Conference on Bioinformatics, Computational Biology and Health Informatics.



Class scores from two PPS rats

Systems Medicine of Infectious Diseases

Throughout history, we have witnessed alarming high death tolls derived from infectious diseases around the globe. Last year 2020 has uncovered one of the biggest pandemics in history, the novel coronavirus SARS-CoV-2 that was first reported in Wuhan, Hubei Province, China in December 2019 (CDC, 2020). While China did a large effort to shrink the outbreak, COVID-19 developed into a pandemic in more than 210 countries moving the epicentre from China to Europe and consequently to America.

The spread of viruses between infectious and susceptible hosts can be orchestrated via close physical interactions. Understanding disease transmission remains a central vexation for science as it involves several complex and dynamic processes. The link between the infection dynamics within an infected host and the susceptible population-level transmission is widely acknowledged. However, several technical aspects of the interface of within- and between-host are still in their infancy. Fusing interdisciplinary activities, the groundbreaking ambition of our research is to apply mathematical modeling and computational simulations to in vivo experiments to

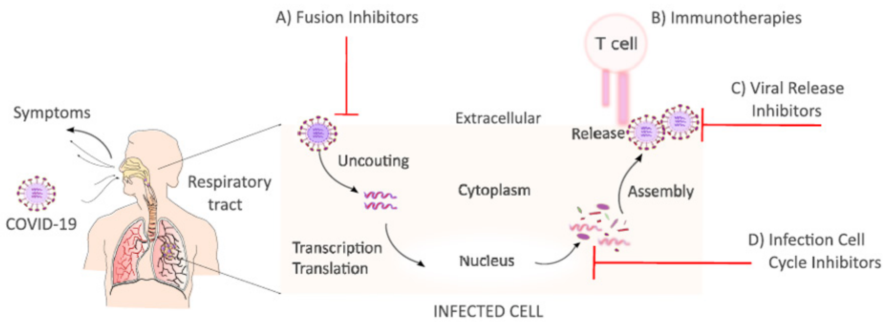
(i) dissect host immune-regulatory mechanisms during acute and chronic infections, and their respective shift in the elderly;

(ii) develop mathematical models for decision making to influence the use of vaccines and drugs; and

(iii) develop multiscale epidemiological models in SARS-CoV-2 as a virtual disease tool to evaluate therapies and public health policies.

Our research group has a special interest in viral infections. Our collaborators are testing our simulation predictions in laboratory experiments. With the aid of the established models, it will be possible to predict rational combinations of antivirals as well as immune modulators and test them specifically. Thus, it is also conceivable that the insights gained from our research could result in therapeutic alternatives in the coming years.

Reference: In-host Mathematical Modelling of COVID-19 in Humans. EA Hernandez-Vargas, JX Velasco-Hernandez. Annual Reviews in Control, 2020



After the binding to receptors of the host cell, the virus RNA is uncoated in the cytoplasm. Then, transcription/translation processes take place to generate new viral RNA material and proteins. Virus assembly occurs within vesicles followed by virus release. Once the virus is released can infect other cells.

Dr. Esteban A. Hernandez-Vargas

FIAS Fellow Esteban Hernandez-Vargas obtained a PhD in Mathematics at the National University of Ireland. Esteban held a three-year postdoc position at the Helmholtz Centre for Infection Research, Braunschweig.
In the same place, he established the Systems Medicine of Infectious Diseases research group. Since March 2017, he holds a Research Fellow funded by the Alfons und Gertrud Kassel-Stiftung, at FIAS Frankfurt.

International Group

His lab members are living at three different continents working together by zoom.

Projects @ FIAS: 2

Collaborations

Dunja Bruder (HZI, Germany)
Franklin Toapanta (Maryland University, USA)
Alejandro Hernan Gonzalez (CONICET, Argentine)
Sorin Olaru (CentraleSupelec, France)
Xin Du (Shanghai University, China)

Prof Dr.
Christoph von der Malsburg

Christoph von der Malsburg studied physics at the universities of Göttingen, Munich and Heidelberg, with PhD work at CERN, Geneva. He worked as research scientist at a Max-Planck-Institute in Göttingen, served as professor for computer science, neuroscience and physics at USC in Los Angeles, co-founded the Institute for Neural Computation at Ruhr-University in Bochum and, since 2007, is Senior Fellow at FIAS. He co-founded two companies and received a number of national and international awards.

Visiting Professor

Invitation as visiting professor et ETH, Zürich (due to Covid postponed to 2022).

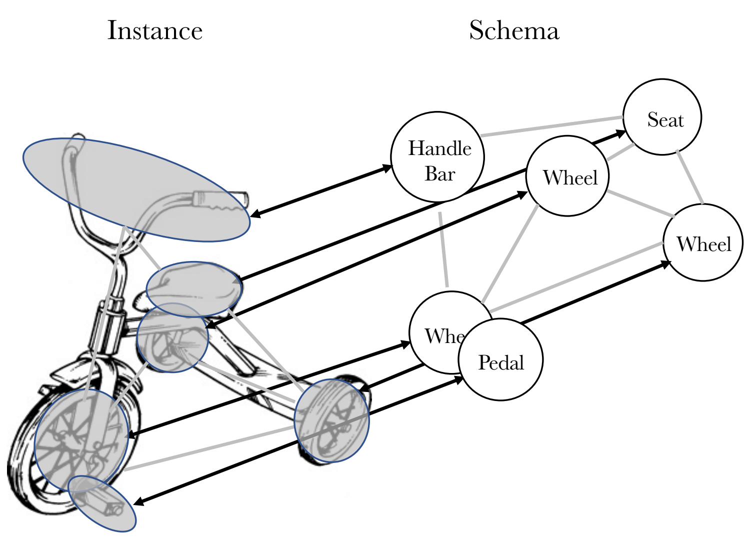
Collaborations

Rodney Douglas,
Benjamin Grewe, both INI, Zürich.
Irving Biederman, USC, Los Angeles.
Tomas Fernandes, Hongshi Technologies, Wuhan.

Fundamental structure of active brain states

In spite of tremendous world-wide efforts and activities, the age-old quest to understand brain and mind seems presently at a standstill. Essential for bringing existing ideas together on a common ground are answers to the questions how mental states are represented by physical brain states and how these physical states arise. I have developed and am further evolving answers to these questions in the form or a cognitive architecture based on dynamic nets. The decades-old stand-off between cognitive science and classical artificial intelligence (AI) on the one hand and neuroscience and neural AI on the other (symbols vs. neurons) is overcome therein by structured networks, "nets". During development and learning, net fragments of growing size are formed by constrained network self-organization, and these net fragments form building blocks which assemble spontaneously into brain-spanning nets that represent the current situation. Network self-organization has been studied four decades ago by experiments and, by myself and colleages, by computer simulations and theoretical formulations. It is the answer to the riddle how complex brains are generated on the basis of in comparison minute amounts of genetic and environmental information, and it answers the question about the fundamental structure of active brain states.

This conceptual framework I have developed in the context of applications to vision, providing, for instance, an answer to the fundamental problem of invariant object recognition. This has led to industrial applications. The principle is based on homeomorphy, and can be applied to the recognition of abstract schemata, giving meaning to individual objects or situations in terms of general structure, as invoked by ethologist to account for animals' purposeful behavior.



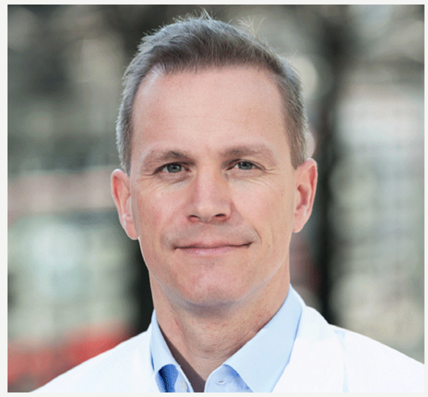
Objects acquire meaning relative to schemata. A schema is abstract in terms of position, size, pose, exact shape, color, material and other properties. It thus fits many instances. Sensory representation of object and schema and the homeomorphic projection between them are composed of net fragments, which spontaneously assemble to form the interpretation.

Systems Pathology

Building accurate models for cancer is a challenging task due to high levels of intra-tumor heterogeneity (ITH) displayed by human cancers. Tumor samples typically consist of a mixture of cells (tumor, stromal, immune and vascular cells), and cancer sub-clonal populations that coexist together and evolve through competition for resources and survival. Genomic heterogeneity generates large clinical variability in major clinically important phenotypes such as the ability to metastasize or resistance to therapy. Particularly, distinct diagnostic signatures can be found in different biopsies from the same tumor, and different clonal populations may exhibit different sensitivities to drugs.

The clonal evolution of e.g. malignant pleural mesothelioma (MPM) is poorly understood. The Systems Pathology Lab lead by Peter Wild investigated the sub-clonal genomic alterations and characterized the intra-tumor heterogeneity in MPM samples through whole exome sequencing and targeted ultra-deep sequencing. MPM is a rare but fatal lung cancer and is associated with asbestos exposure. Due to the lack of many alternative treatment options, standard clinical therapy regimens include a platinum-based therapy in combination with an antifolate. However, chemotherapy only shows effectiveness in about a third of all MPM patients, exposing two thirds of them to unnecessary and mostly severe side effects. In our project, we screened a cohort of 67 MPM patients undergoing similar cisplatin-based treatment for a genetic marker predictive of response to chemotherapy and found that alterations in BAP1 were a negative predictor of MPM outcome. Using different MPM cell lines, we demonstrated that the absence of BAP1 in vitro is causative for cisplatin resistance. We, therefore, suggested that BAP1 mutational status could be used for patient stratification before chemotherapeutic treatment.

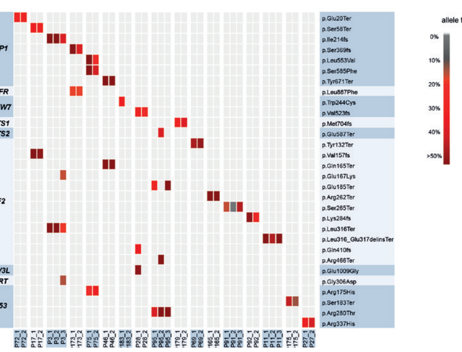
For some of the MPM patients, the genetic composition of the tumor varied between the different phases, reflecting the spatial and temporal heterogeneity in MPM. For a better visualization of the data (Fig. A), we modeled the tumor evolution of two patients from the amplicon sequencing data (Fig. B). The models are based on the assumption that mutations of a high allele frequency are present in a higher fraction of tumor cells and are, therefore, of early clonal origin. Thus, in patient 1, the BAP1 mutation arose before the NF2 mutation and both mutations did not change during chemotherapy (Fig B, left panel). In the relapsing phase, two other mutations in TERT and NF2 occurred. In patient 2, by contrast, TP53 was mutated rather early during MPM development, followed by an NF2 mutation (Fig B, right panel).



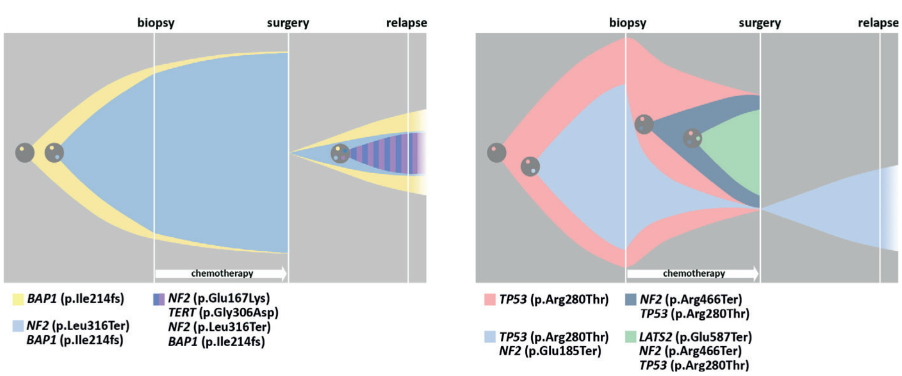
**Prof. Dr.
Peter Wild**

After finishing medical school and residency in pathology in Regensburg, Hamburg-Eppendorf and Zürich, Peter Wild did a postgraduate training at the University of Heidelberg. He became assistent professor in 2012 at ETH Zürich. In 2016, he became a Full-Professor for Systems Pathology at the University of Zürich. In April 2018 he was appointed director of the Dr. Senckenberg Institute of Pathology (SIP), at the University Medical Center Frankfurt and joined FIAS in September 2020.

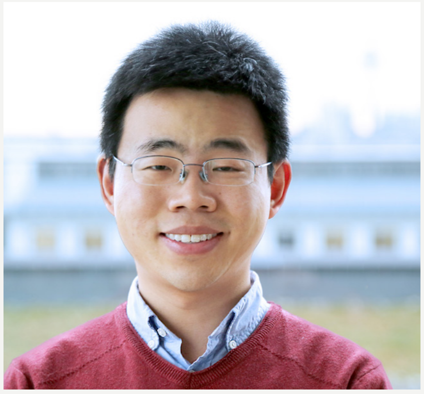
A



B



A and B: Results of deep sequencing (A) and graphical illustration of the clonal evolution of two MPM patients (B). The allele frequency of the mutations was taken as a measure for emergence of the respective clone and is depicted in the width of the diagram (Permission by Clinical Cancer Research 2021).



Dr.
Kai Zhou

Dr. Kai Zhou recieved the BSc degree in Physics from Xi'an Jiaotong University, in 2009, and his PhD degree in Physics with 'Wu You Xun' Honors from Tsinghua University, in 2014.
Afterwards he went to Goethe University Frankfurt to do postdoctoral research work at the Institute for Theoretical Physics (ITP) . Since August 2017, he is a FIAS Research Fellow focusing on Deep Learning (DL) application research.

COVID-19 Research

We transferred our physics and AI experience into COVID-19 risk spatio-temperal evolution studies .

Projects @ FIAS: 3

Collaborations

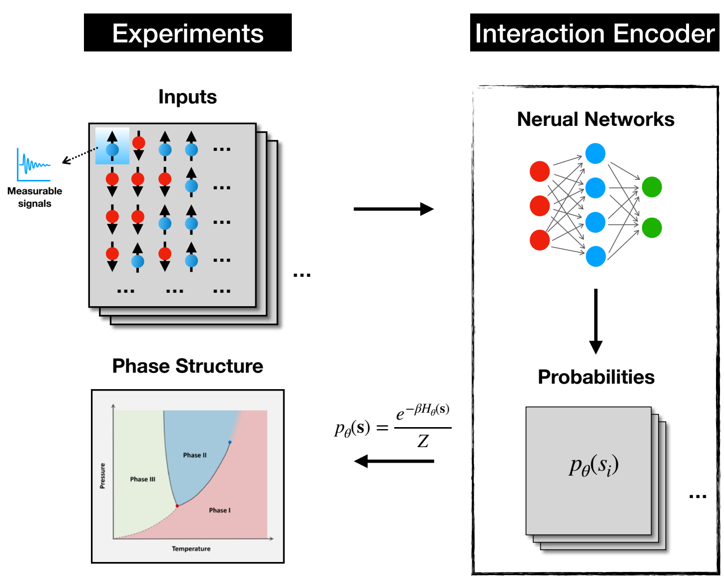
XinNian Wang, Berkeley & Wuhan
Long-Gang Pang, Berkeley,
Carsten Greiner, GU
Moritz Greif, GU
Gergely Endrődi, GU
Bao-yi Chen, GU and Ti'jin
Zhe Xu, Tsinghua, Beijing
Pengfei Zhuang, Tsinghua, Beijing

AI for many-body statistical physics

In theoretical science side, besides a further deepened exploration of our ongoing project "AI for Heavy Ion Collisions" to hot and dense matter EoS study and experiment detector data analysis, I further proposed and led a more general AI for many-body statistical physics project in my group:

To tackle a many-body physical system in general one needs to consider continuous degree of freedom and continuous symmetry. 2D XY model act as an elegant concrete example which is with continuous spins living on lattice and shows unconventional topological phase transition. Although one can sample configuration for the system with Markov Chain Monte Carlo (MCMC) method starting from the Hamiltonian, its expandability and efficiency are limited because of the Critical Slowing Down (CSD) near the critical point. To this we developed continuous autoregressive network inside a variational calculation framework to provide generative modeling for XY system and demonstrated its efficient ability in generating configurations for phase structure study.

Based on the above project we further developed a general approach to extract microscopic interactions from raw configurations with deep neural networks unsupervisedly, thus the Hamiltonian modeling can be achieved by neural networks as encoded in Fig.1. As proof-of-principle study, neural networks with autoregressive property shows remarkable representation ability in 2D discrete and continuous spin systems as shown in our papers . As another concrete example for reconstructing interaction for the system we considered heavy Bottomonium at finite temperature, to which first principle lattice QCD calculation can access its mass and width at different temperatures. We devised a neural network technique with Bayesian point of view to solve the inverse problem through Shroedinger equation on the bound state system and provide the T- and r-dependence interaction potential for Bottomonium which is critical important in understanding the QGP properties and heavy flavor production in heavy ion collisions.



An end-to-end machine can be trained with data from experiments or Ab initio computations, from which the evaluation of the probability on each configuration at fixed external parameters (e.g. Temperature) is possible and revealing the effective Hamiltonian for the many-body system. One can naturally extrapolate it to explore the phase structures of the system.

Donors and Sponsors

In order to ensure the greatest possible independence and flexibility, FIAS was established as a foundation. A large part of the research activities is funded by the public German and European research sponsors, but without the extraordinary commitment of private sponsors, foundations and companies, FIAS would not have come into being and could not continue its work. In recent years, various endowed professorships have been made possible at FIAS and Goethe University. In 2020, 3 junior research groups were funded by private donors.

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Dr. Maria Barbarossa

Quandt Research Group on Mathematical Immuno-Epidemiology

Dr. Roberto Covino

Quandt Research Group on Simulation of Biological Systems

Dr. Sebastian Thallmair

Kassel-Schwiete Research Group on Development of phamacological Probes

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2014: Helmut-Maucher-Stiftungsprofessur Prof. Dr. Nils Bertschinger
2007: Johanna-Quandt-Stiftungsprofessur Prof. Dr. Jochen Triesch

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Publisher
FIAS Frankfurt Institute for Advanced Studies
Chairman Volker Lindenstruth

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www.fias.uni-frankfurt.de

Postal adress
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Ruth-Moufang-Straße 1
60438 Frankfurt am Main

Editorial Staff: Patricia Vogel

Pictures:
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