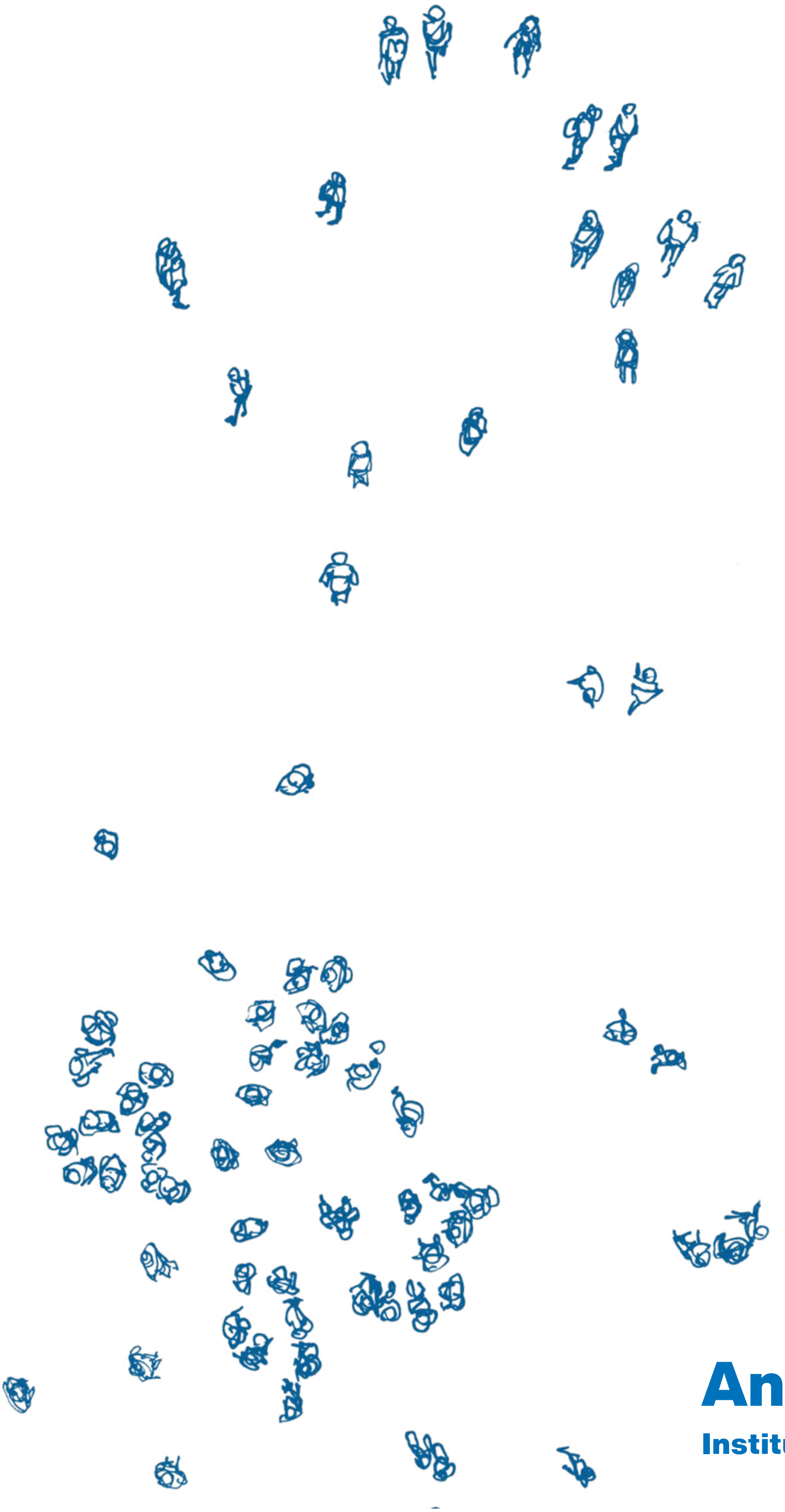
Institute for Advanced Study
Technical University of Munich



2020

Annual Report

Institute for Advanced Study

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TUM President's Foreword

For more than a year, our lives have been in the firm grip of the Covid-19 pandemic. Nonetheless, the Technical University of Munich (TUM) has taken great leaps through turning current challenges into new opportunities of purposeful development.

Taking in stride the necessary restrictions on in-classroom instruction, our university community of professors, staff, and students succeeded in switching to digital teaching formats, adapting laboratory courses and online examinations in a timely and quality-oriented fashion. This enabled us to continue providing our international student body with the full range of high-quality courses offered by our university.

Simultaneously, we have been continuing to implement our TUM AGENDA 2030 by activating our most valuable asset – our people – a diverse pool of talents with a mindset for change. We have been embarking on a journey to increase their capabilities via supporting framework conditions, lifelong learning offerings, transdisciplinary and transnational networking, as well as entrepreneurial action. In addition, we have made sustainability a strategic priority of TUM in all its mission agendas. Beyond expanding our wide range of research and teaching activities in climate research, clean energy, smart mobility or prevention and health, we introduced the TUM Sustainability Office to implement an institutional strategy to lower CO2 footprint and energy consumption and increase resource awareness across the entire university. In just one year, we have achieved great progress, despite of the pandemic.

We have started to remodel our organization into a matrix structure comprising seven TUM Schools and Integrative Research Centers (IRCs) cutting across these schools, in order to better shape new fields of scientific progress. Among our seven schools, the new TUM School of Social Sciences and Technology, set to launch on October 1 of this year, will play a key role in our agenda to implement our "human-centered engineering" approach towards responsible research and innovation. We have initiated a major recruitment program to re-enforce the faculty of this school by up to ten additional professors. At this point, I would like to express my sincere thanks to our TUM-IAS Director Prof. Michael Molls, who chaired the structural committee for faculty recruitment with a truly wholehearted passion and commitment.

Founded as the most recent IRC, the Munich Data Science Institute (MDSI) is the central interface and innovation platform for complex challenges and future-oriented questions in data science, machine learning, and artificial intelligence. Associated with the MDSI is the TUM Georg Nemetschek Institute (GNI) on Artificial Intelligence for the Built World. The GNI uses modern computer technologies, AI, and machine learning to develop fundamentally new solutions for the ecologically and economically sustainable construction environment. It is going to collaborate with the TUM-IAS and build new synergies through thematically oriented Hans Fischer Fellowships. While the GNI is going to be responsible for defining specific research fields for these Fellowships and providing their funding, the TUM-IAS will cover the application and evaluation process, connect the international Fellows to its large and multidisciplinary scientific community, and provide comprehensive professional support during the Fellowship.

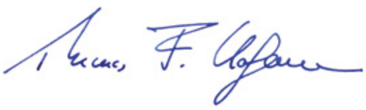
We also initiated the ONE MUNICH strategy to synergize leading scientific strengths between institutions in the Munich metropolitan area. In conjunction with our partners, the LMU Munich, the Bavarian Academy of Sciences and Humanities, the Fraunhofer Society, and the Max Planck Society, TUM will continue to promote the development of quantum science and technology in the Munich Quantum Valley Network over the next ten years. Building on the strengths of our Cluster of Excellence Munich Center for Quantum Science and Technology (MCQST), cooperation projects are going to range from quantum simulators and computers to help search for new materials, to methods of quantum

metrology for high-precision measurements of electric or magnetic fields, to methods for tap-proof quantum cryptography.

To accelerate the translation of new discoveries and technologies into transformative businesses, TUM and its affiliated start-up incubator UnternehmerTUM have initiated the TUM Venture Labs. These labs will support tech entrepreneurs with office and lab space matching the needs for specific tech areas like robotics/AI, quantum engineering or molecular assemblies, professional advice for start-up projects from idea creation to market growth and networking support concerning global enterprises and venture capital investors.

Founded in 2005, as a cornerstone of TUM's institutional plan in the first round of the excellence strategy, the TUM Institute for Advanced Study has been developing to become a natural cauldron for nurturing new ideas with benefits for TUM as a whole. TUM-IAS has expanded its radius, has taken up new focus areas, and is destined to go on doing so. Issues of social and political science have become essential priorities because of new Fellows. Research fields such as data science, artificial intelligence, and robotics in the built environment are going to become internationally subjects of expertise with a strong draw through a state-of-the-art Fellowship program. Since this year, the TUM-IAS plays an important role in establishing the so-called TUM Innovation Networks, which consist of transdisciplinary "high risk/high gain" collaborative projects involving professorships across the various disciplines of TUM. As a result of this new format, TUM-IAS helps to identify and pursue future-oriented and high-potential research focus areas that can later lead to large-scale, far-reaching research consortia. The first three TUM Innovation Networks have been introduced in 2021 and are up and running.

If there is one lesson from the pandemic that we should carry on into the future it is this: The unprecedented and breathtaking speed in developing an entirely new class of vaccines and thus delivering the first signs of hope in fighting and containing the virus, was made possible through scientific collaboration. In this sense, our leitmotif of cooperation, knowledge exchange and excellence in research have been inspiring TUM-IAS and its Fellows for years and will continue to do so in the future. ■



Prof. Thomas F. Hofmann
President

TUM-IAS Director's Message

The first year in my responsibility as the new TUM-IAS Director has presented our Institute for Advanced Study, our university, and the entire globe with enormous challenges in the pandemic that will certainly be judged later in retrospect as a turning point in time.

Like all institutions of higher education, TUM and the Institute for Advanced Study had to convert their operations to online formats. Our international Fellows could not join us, or only under very difficult conditions. We had to cancel workshops, conferences, lunches, and annual meetings or move them to digital formats. Yes, all of this impacted and complicated our collaborative work. But the innovative spirit of our Fellows and hosts overcame this too, and the research work continued.

Our TUM-IAS team and I look forward to seeing you all again in the coming weeks and months, and to renewing our exchanges in person.

But much more than that. In response to our 2020 Call for Fellowships, we have invited 14 new Fellows from more than 10 countries to the TUM-IAS, with topics ranging from catalysis research to digital business and platform capitalism. At the same time, the strategic development of TUM is picking up immensely, and this is also reflected in the plans, activities, and measures of the TUM-IAS.

Expansion of the social sciences and humanities as well as increased interdisciplinary and transdisciplinary research are strategic focal points of TUM, and data sciences will encompass almost all TUM disciplines like a web.

Accordingly, our TUM-IAS has expanded its radius to include new topics. Topics in social and political science became visible focal points with new Fellows. Sustainability is and will continue to be a guiding theme across all disciplines, thus strategically supporting TUM's course. What is needed with sustainability is overarching thinking in terms of effects, not individual measures, and I expect the inclusion of economics in a way that has not been seen before to provide a further boost.

Hans Fischer Senior Fellowship of the Georg Nemetschek Institute

Research areas such as data, artificial intelligence, and robotics in the built environment will become an internationally visible complex with high attractiveness via a new Fellowship.

New Mößbauer Professorships

The Rudolf Mößbauer Tenure Track Assistant Professorships, which are equally affiliated with the TUM-IAS as Fellowships, were not advertised completely openly, as in an open-field call, but according to focus areas that also address the thematic expansion of TUM. Five new professors are appointed in these fields:

- Social and Educational Sciences for Technology Transformations
- Organoids and Tissue Engineering
- Prevention and Health Care

Innovation Networks

Innovation Networks are a new instrument of our institutional TUM strategy. With them, we want to identify and promote topics across Schools and Departments that can only be successfully addressed through interdisciplinary research approaches. The Innovation Networks will later give rise to large-scale priority programs or comprehensive funding projects that will strategically complement TUM in the long term. The TUM-IAS, an echange place of knowledge with its experienced and proven evaluation system at the top international level, is exactly the right place to conduct selection and competition on the Innovation Networks. (➔ see more on page 10)

"Food for thought" – brainstorming for the post-pandemic world

In light of the Covid-19 pandemic this anthology, the most elaborate work of the TUM Senior Excellence Faculty and the TUM-IAS to date, stands for the need to initiate radical change in politics, business, and society. More than 90 authors, including many from the TUM-IAS, produced this anthology in just six weeks. The German version was published in July 2020; the English version has just arrived. In 70 transdisciplinary contributions on sustainability, politics and society, basic research, technology and IT, living spaces (urban, rural, mobility), economics, health and medicine, education and the world of work, and with a special emphasis on Africa, they take up the "change" idea and describe the need for action as well as possible solutions. Topics will always refer to TUM-IAS for our programs and conferences. (➔ see more on page 12)

The German Research Foundation has also called on German federal and state governments to strengthen knowledge-driven research in the aftermath of the Covid-19 pandemic. Research generates knowledge repositories that enable evidence-based solutions to be found quickly in the event of short-term and unforeseen research needs. A point of view that we at TUM-IAS can only but support.

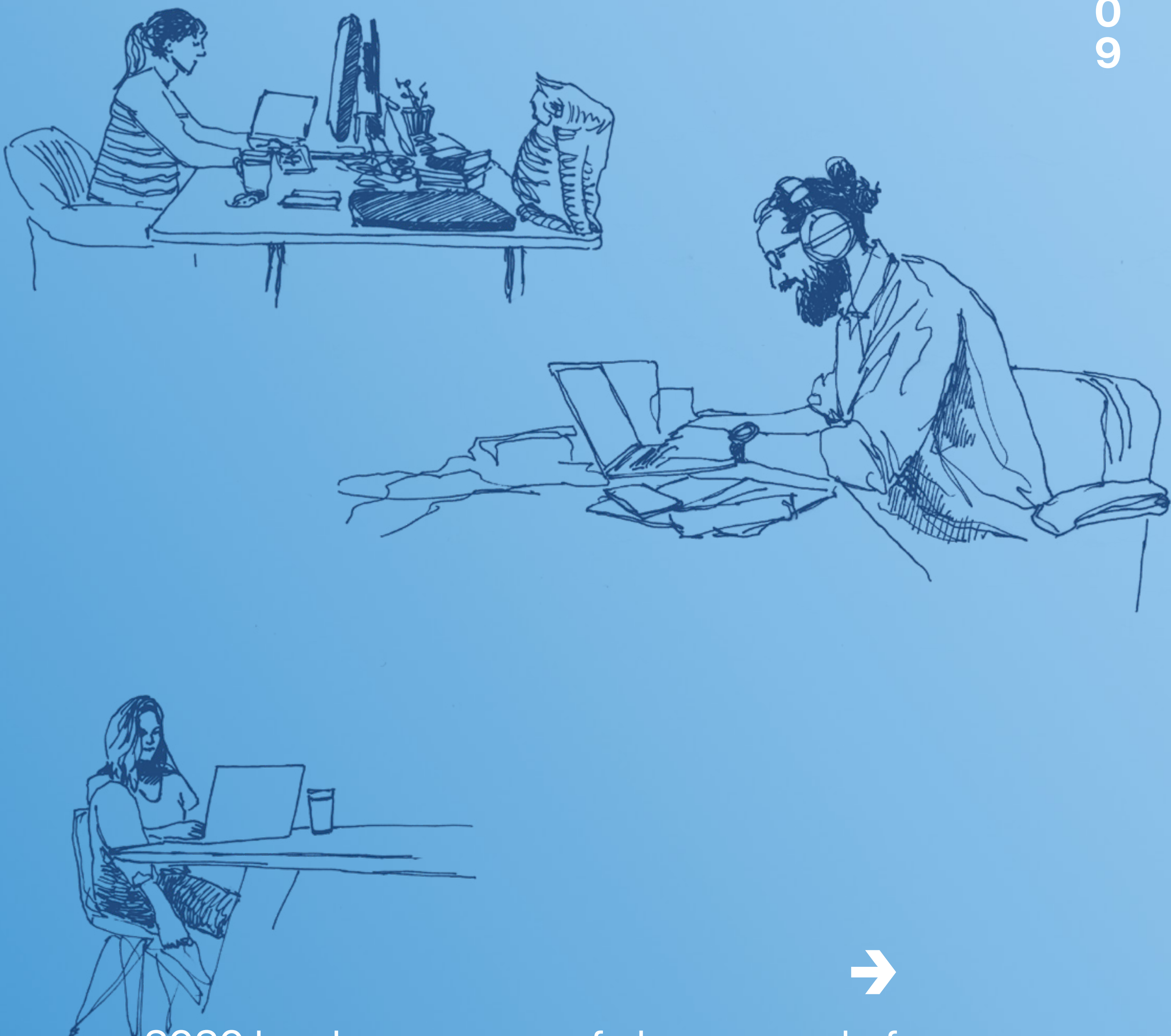
Immediately before our annual report went to press, the German Science Council, Germany's highest-ranking advisory body, took a close look at the various Institutes for Advanced Study in Germany and affirmed their positive impact on the German science system as a whole. It recommends that German IAS make greater efforts to adopt an international perspective in which, for example, science from the global South can be strengthened. The TUM-IAS has long embraced this perspective and sees itself strengthened in its orientation. We will continue on this course, and in addition further intensify our links with IAS in Eastern Europe.

As I write this down, in early May, news reaches me from NATURE that to date 1.2 million coronavirus genome sequences from 172 countries and regions have been shared in the Global Initiative on Sharing Avian Influenza Data. Sequence data have been critical to scientists studying the origins of SARS-CoV-2, the epidemiology of Covid-19 outbreaks, and the movement of viral variants across the planet. What better demonstrates of the spirit and success of international collaboration, which we are part of? ■

M. Molls

Prof. Michael Molls
Director

Actions, Awards, Events



2020 has been a year of change, and of progress. It gave us ample opportunity for actions and new ventures.

Actions

TUM Innovation Networks

With the cross-disciplinary TUM Innovation Networks as part of our excellence strategy TUM AGENDA 2030, we aim to achieve several goals at once: On the one hand, the Innovation Networks are intended to promote the pioneering spirit of our scientists in new fields. After all, curiosity is one of the most important drivers for producing scientific and technological innovations.

Secondly, we want to address high-potential topics that can only be successfully addressed through interdisciplinary research approaches. That is why we exclusively support collaborations of researchers from different disciplines and departments in order to strengthen the bridges between them and to intensively investigate transdisciplinary areas for several years.

Thirdly, we want to identify and take up promising and high-potential research foci at an early stage for TUM, in order to later pave the way for elaborate and extensive research proposals in Germany or at EU level.

As TUM, we are also consciously taking a risk. This means that we knowingly accept that projects can also fail, but at the same time create the conditions for truly groundbreaking innovations. The TUM-IAS as a knowledge exchange center with its experienced and proven evaluation system at the highest international level is exactly the right place to hold the competition for the best ideas and then to permanently accompany the Innovation Networks and evaluate them later.

Transdisciplinary teams, collective creativity, new ideas

In the first round between July and September 2020, a total of 32 teams from TUM submitted project proposals. A specially established Innovation Network Board deliberated on these proposals in October. Its members included Prof. Gerhard Kramer as Senior Vice President Research and Innovation, Prof. Barbara Wohlmuth as Director of TUM's International Graduate School of Science and Engineering (IGSSE), and Prof. Michael Molls as Director of TUM-IAS.

12 days of intensive science – TUM-IAS as a fairground of knowledge

In an elaborate process, the Innovation Network Board selected various groups, which then had the opportunity to further condense and refine their proposals by Christmas 2020. The main element of this was the total of six two-day Exploratory Workshops in November and December, which were prepared and conducted in close cooperation with the TUM-IAS team. Each group presented and discussed different questions and aspects of the proposal and was expertly accompanied in this process by mentors. Such mentors were found, for example, among the TUM-IAS Fellows or the TUM Distinguished Affiliated Professors.

The first successful round – 3 Innovation Networks

In January 2021, the Innovation Network Board had to make a selection from the six highly complex and transdisciplinary proposals that had been elaborated and shaped during the Exploratory Workshops and had been reviewed by TUM external scientists. The TUM university management had the final say in this, and the selected three successful projects are already underway. They deal with

- Neurotechnology for Mental Health (NEUROTECH), Prof. Simon Jacob, Medicine
- Artificial Intelligence powered Multifunctional Material Design (ARTEMIS), Prof. Alessio Gagliardi, Electrical Engineering
- Robot Intelligence in the Synthesis of Life (RISE), Prof. Job Boekhoven, Chemistry, Prof. Friedrich Simmel, Physics

Neurotechnology for Mental Health (NEUROTECH)

Disorders of mental health are amongst the most pressing medical problems that our society faces. Phenomena such as cognitive deficits, depression or chronic pain are caused by disorders of the brain and nervous system, but the mechanisms remain unclear. The TUM Innovation Network for Neurotechnology in Mental Health (NEUROTECH) develops new approaches and technologies to improve the precision of clinical diagnoses and the success of treatments for mental dysfunction.

The team uses electrophysiological methods to record and modulate brain activity at an extraordinary level of detail and combines them with cutting-edge tools from data science. The aim is not only to better understand and differentiate mental disorders, but also to create new, individualized technology based treatment modalities for patients. The researchers are following strict ethical guidelines in all steps of their work and also investigate the ethical implications of disruptive technological innovations in mental health for the individual and entire societies.

Artificial Intelligence powered Multifunctional Material Design (ARTEMIS)

Creating sustainable energy storage solutions and at the same time producing novel materials for regenerative medicine: Both is possible when using the right supramolecular chemical compounds. The TUM Innovation Network for Artificial Intelligence powered Multifunctional Material Design (ARTEMIS) is aiming at the guided discovery of such molecules and at developing them as a unique toolbox for different applications, using Machine Learning and Additive Manufacturing. Potential applications range from electrocatalysis for hydrogen production to guided tissue regeneration and ‘smart’ coating of medical implants. Data-driven prediction represents a novel and powerful way to boost the discovery, synthesis and the design of new multi-functional materials, as well as for scaling-up and fabrication of devices.

Robot Intelligence in the Synthesis of Life (RISE)

How did life emerge? Could it exist elsewhere? Could we even synthesize life – a system that is self-sustaining, self-replicating and evolving? The TUM Innovation Network for Robot Intelligence in the Synthesis of Life (RISE) aims to develop a radically new approach to these centuries-old questions, combining machine learning and robotics with chemical and biophysical experiments.
Robots will not only take tedious tasks out of the scientists’ hands, but actually become part of the experiments. By allowing the robots to observe data in real-time, let them analyze experiments, and, via artificial intelligence, change the course of the experiments, the scientists anticipate that a self-learning experiment evolves towards a system that displays the essential hallmarks of life. It is a development with the potential to revolutionize research and development in both industry and academia.

Outlook

Over the next four years, seven to ten Principal Investigators (PIs) will work closely together across disciplines in each Innovation Network. The teams will further consist of up to ten PhD students and postdocs in addition to the PIs. The total volume of each project is approximately 3 million euros. The next round of calls for proposals will begin in 2021. ▸

Publication CHANGE

Food for thought – answers for the world after Corona

The Covid-19 pandemic was and is a fundamental dislocation for the entire globe, the likes of which we have not known since 1945. It affects our common life in states, but also the relations between states, alliances, economic areas and the entire state system. It affects our economic and social system as well as our education and health systems, mobility, and global trade.

What we suspected in the summer of 2020 is now a certainty: the Corona pandemic confronts the international community with transnational challenges of historic proportions. As a result, the world is undergoing a fundamental transformation.

In this global change process lies the opportunity to transform the standstill that has arisen into progress for society as a whole. The past months have shown the value that science can have in analyzing and overcoming crises.

The anthology "Food for Thought for the Post-Corona Era" is the most elaborate work to date by the TUM-IAS and the TUM Senior Excellence Faculty. Over 90 authors, including many TUM-IAS members, produced this anthology in just six weeks in the summer of 2020, and it was published in English in May 2021. In light of the Corona pandemic, it stands for the need to initiate a radical change in politics, economy and society. From a professional perspective, the authors want to contribute to making the future more people-friendly, also for generations to come.

Central questions

The central questions are: What do "responsibility" and "sustainability" mean in political, economic and social action? What are sustainable innovations in technology, communication and education? How can digitization and artificial intelligence contribute to solving these grand challenges? In 70 transdisciplinary chapters on the topics of sustainability, politics and society, basic research, technology and IT, living spaces (urban, rural, mobility), economy, health and medicine, education and the world of work, and with a special emphasis on Africa, the authors take up the "change" idea and describe the need for action as well as possible solutions.

The book with its theses and proposals aims not only to create awareness for change and "responsible innovation", but also to identify concrete, implementable projects, to work on them, and also to hand them over as clear recommendations for action to political mandate holders, science and society.

The publication CHANGE can be downloaded here:

→ "Wissenschaft, Vernunft & Nachhaltigkeit – Denkanstöße für die Zeit nach Corona" https://mediatum.ub.tum.de/1548492

→ "Science, Reason & Responsibility – Forward Thinking for the Post-Corona Era" https://mediatum.ub.tum.de/1578813

Fellowship Calls

New Fellows at the TUM-IAS

In 2020, we again succeeded in appointing outstanding research personalities as TUM-IAS Fellows. Our 14 new Fellows in the categories Anna Boyksen Fellowship, Hans Fischer (Senior) Fellowship, and Rudolf Diesel Industry Fellowship come predominantly from Europe, including for the first time from Austria, Belgium, Denmark, Ireland and Sweden. At TUM, they will be visiting nine different faculties and the University Hospital rechts der Isar. Two Fellowships for scientists specialized in the fields of Simulation and Digital Twin and Future of Autonomous Systems and Robotics and are funded by the Siemens AG. One of the Hans Fischer Senior Fellows is working in the Cluster of Excellence e-conversion.

The topics of our Fellows not only strengthen our own research, but also open new paths and opportunities for further cooperation. The Fellows' fields of research range from catalytic research to mathematical models for digital twins, from optimization of nonlinear dynamical systems to new semiconductors for diodes and solar cells to the electronic structure of metal-organic frameworks, from metabolism research to high precision genome editing in health research, and from deep fakes to platform economics and its political consequences.

New Rudolf Mößbauer Tenure Track Assistant Professorships

Introduced in 2012 as the first university in Germany, TUM Faculty Tenure is the performance-oriented career model for young scientists with international experience. TUM appoints promising talents as tenure track assistant professors (W2) – and offers them the realistic prospect of advancing to a tenured W3 professorship from the very beginning.

Within this faculty career system, the TUM-IAS has been inviting applications for the prestigious Rudolf Mößbauer Tenure Track Assistant Professorship. The Fellowship is named after TUM professor Rudolf Mößbauer (1929–2011), who was awarded the Nobel Prize in Physics in 1961 for his research concerning the resonance absorption of gamma radiation and his associated discovery of the effect that bears his name. It is intended for outstanding, high-potential early-career scientists who have already achieved a major scientific or technological breakthrough and who have the ambition of developing a new field of endeavor when joining TUM as a Tenure Track Assistant Professor. As the emphasis of the professorship lies on the creative development of a new field of science and/or technology, and as we intend to offer those young researches the best start in their career possible, they are equally affiliated with the TUM-IAS as Fellows. Besides the development of their research, Fellows are expected to participate in TUM-IAS programs and organize activities in order to contribute to the intellectual life of the Institute and the university.

This year's report is featuring recently appointed Rudolf Mößbauer Tenure Track Professors specializing in:

- Structural Design (Prof. Pierluigi D'Acunto)
- Machine Learning (Prof. Reinhard Heckel)
- Functional Nanomaterials (Prof. Barbara Lechner)
- Theoretical Methods in Spectroscopy (Prof. Frank Ortmann)
- Brain Circuit Function and Dysfunction (Prof. Ruben Portugues)
- Biomedical Magnetic Resonance (Prof. Franz Schilling)

→ see more at the Chapter Welcoming Our New Fellows at page 21 ■

Awards

Even though the year 2020 presented us all with special challenges and we had to forego and adjust to many familiar things, we also had uplifting and joyful moments. The prizes and awards to our Fellows are clearly among them.

The German Pattern Recognition Award was granted to Alumnus Rudolf Mößbauer Tenure Track **Prof. Matthias Nießner** for his pioneering research on tracking, reconstructing and visualizing photorealistic 3D face models from video with machine learning and AI.

Prof. Jia Chen, Rudolf Mößbauer Tenure Track Professor for Environmental Sensing and Modelling, was included in this year's list of the **"Young Elite – Top 40 under 40"** in the category "Society and Science". The German finance magazine Capital has been presenting this award since 2007. Jia Chen conducts research on topics relating to climate change and urban air pollution. She also develops sensors and mathematical models for the exact determination of greenhouse gas emissions and air quality parameters. The data generated can be used to develop new climate protection measures and to evaluate existing measures.

Prof. Job Boekhoven, Rudolf Mößbauer Tenure Track Professor for Supramolecular Chemistry, started his 5 year project on "From Chemistry to Information: a Model System for the Coupling of Metabolism and Heredity", which was granted by **Volkswagen Foundation**. With partners in Cambridge/UK and at the TUM Physics Department he looks at the interdependency of genetic information storage and propagation (heredity) and chemical energy dissipation (metabolism), which is a hallmark of life. However, how coupling between metabolic and informational systems emerged and sustained has never been explored experimentally in a cross-disciplinary context. Experts in both experimental and theoretical aspects of systems chemistry and synthetic biology will explore these crucial aspects of the emergence of life through synthetic model systems by addressing the following questions: a) How can heredity arise from pools of information encoding polymers? b) How can heredity be coupled to energy dissipation through chemical cycles? c) How can physicochemical transitions such as liquid-liquid demixing drive such cycles? d) How can a coupled metabolic-genetic system sustain itself?

Prof. Kathleen Thelen, TUM-IAS Hans Fischer Senior Fellow and Professor of political science at the Massachusetts Institute of Technology (MIT), has been honored with the **Friedrich Schiedel Prize for Politics and Technology.** The Friedrich Schiedel-Stiftung, TUM and the Bavarian School of Public Policy at TUM award the prize annually to outstanding personalities who have contributed to the understanding of the mutual interactions between politics, society and technology. She works in the field of comparative political economy, where she concentrates on the origins and evolution of political-economic institutions in rich democracies. In the past few years she has pursued an important research agenda on the governance of new technologies, in particular addressing the question of how large technology companies can be regulated. Her widely acclaimed publications include for example "Regulating Uber: The Politics of the Platform Economy in Europe and the United States" and "Are We All Amazon Primed? Consumers and the Politics of Platform Power".

The European Research Council awards not only Europe's most competitive and most prestigious awards, but also its most highly remunerated. Last year, three of our Fellows at the TUM-IAS have been receiving an ERC grant.

Hans Fischer Fellow **Dr. Luca Magri** (University of Cambridge) was awarded the prestigious **ERC Starting Grant** for his project PhyCo. In this project, he combines machine learning methods with the art of constructing physical models, which has the potential to revolutionize the engineering design of multi-physics systems.

Prof. Kathrin Lang, Alumna Rudolf Mößbauer Tenure Track Professor for Synthetic Biochemistry, received an **ERC Consolidator Grant** for her research on the protein called “ubiqutin”. A crucial step in regulating protein functions consists of labeling selected proteins with a small protein called ubiquitin. Due to the ubiquity of this protein, many diseases are associated with disorders of processes it is involved in. In her Ubl-tool project, Kathrin Lang aims at developing a modular and interdisciplinary toolbox using chemical and synthetic biology to investigate widely varying aspects of ubiquitin labeling that cannot be studied by more traditional approaches. Another objective is to find new target points within the ubiquitin system for the discovery of future treatments.

For his research on quantum computers, **Prof. Robert König**, Alumnus Rudolf Mößbauer Tenure Track Professor for Theory of Complex Quantum Systems, has received an **ERC Consolidator Grant.** Quantum computers built to date only use a small number of noisy quantum bits (qubits) and therefore do not match the performance of an ideal quantum computer. Robert König's project EQUIPTNT will explore the potential of such restricted quantum devices. Specifically, algorithms will be developed that make it possible to use such devices in applications. In addition, methods to simulate the behavior of associated quantum systems will be developed. These could be used to create models in order to plan the design of quantum devices, to evaluate them or to identify possible problems of a given system. Simulations should also enable the certification of quantum computers. ■

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European Research Council

Established by the European Commission

Events

Science thrives especially on personal exchange, which became almost impossible in presence after March 2020, due to the Corona restrictions. The consequences of the Covid-19 pandemic were especially noticeable at events of our Fellows, but also in the dialogue with the public. Not only were public issues heavily dominated by Covid-19; it also took a while for online conference formats to be developed and widely used. Nevertheless, TUM-IAS has maintained some high-profile events and regular dialogue with the public.

TUM-IAS International Workshop Report

In 2020, the TUM-IAS Focus Group "Built Environment Digital Twinning", comprising Hans Fischer Senior Fellow Dr. Ioannis Brilakis (University of Cambridge) and his host at TUM Prof. André Borrmann, published a comprehensive report on their International Workshop on Built Environment Digital Twinning. The workshop was organized in December 2019 and co-financed by the TUM-IAS and the Siemens AG.

The concept of a digital twin – a digital replica of a real-world physical entity (El Saddik 2018) – is already widely used in the manufacturing sector. In the built environment sector, digital twins are gradually entering the scientific discussion as they can offer substantial value to all associated stakeholders. The workshop brought together digital twin experts across academia and the private sector, with specialists from the Civil & Environmental Engineering, Computer Science and Architecture disciplines. These experts were given the task to explore the key research and technology transfer challenges in the following areas:

- the digital twin itself,
- from real world to the digital twin,
- from the digital twin to the real world,
- tech transfer and market penetration

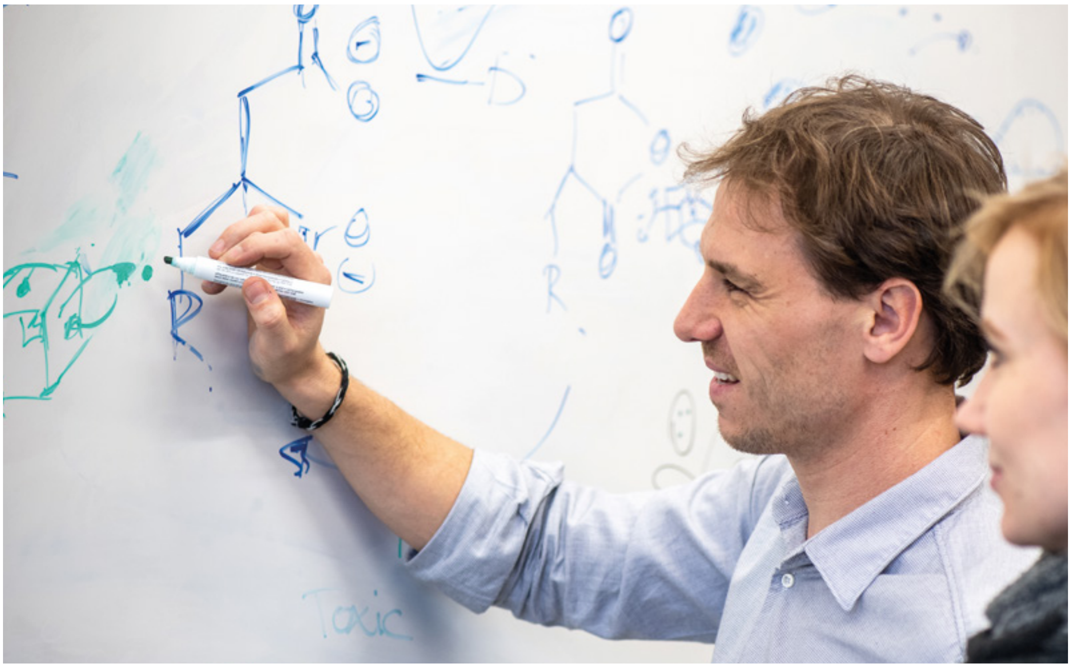
Notable speakers were invited to the workshop to present their vision in one of the aforementioned areas. Their presentations were followed by brainstorming sessions that aimed to provide all attendees an opportunity to brainstorm jointly and derive novel insights.

More information can be found here:

→ information on the workshop: https://www.cms.bgu.tum.de/digital-twinning/

→ workshop videos: https://lnkd.in/dHmGmNw

→ full workshop report: http://go.tum.de/513144



Prof. Job Boekhoven (left) is part of the TUM Innovation Network Robot Intelligence in the Synthesis of Life (RISE).

TUM Exploratory Workshops

TUM Innovation Networks aim to foster innovative, high-risk, high-gain research projects spanning multiple disciplines. They are a central element of our institutional strategy, TUM AGENDA 2030.

The teams who submitted the most promising project proposals by September 2020 were invited to participate in a dedicated, project-specific two-day TUM Exploratory Workshop at the TUM-IAS. During the two-day workshop, the project concept was developed further and finalized. Where necessary, further principal investigators could be included in the initial project team. The goal of the TUM Exploratory Workshop was to prepare for a 10-page concept paper reflecting the TUM-IAS motto “Risking Creativity”.

In November and December 2020, the six TUM Exploratory Workshops covered the following areas in a digital format:

- Neural Engineering for Mental Health
- SynLife - Innovation Network for the Synthesis of Life
- Geometric Deep Learning: Beyond Euclidean Data
- Machine Learning Powered Science: Supramolecular Materials for Sustainable Energy Solutions and Regenerative Medicine
- AID-AM – Artificial Intelligence Empowered Design for Additive Manufacturing
- Materials Platforms for Quantum Engineering

This competition resulted in three TUM Innovation Networks, which started operation in April 2021. (➔ see more on page 10) ▸

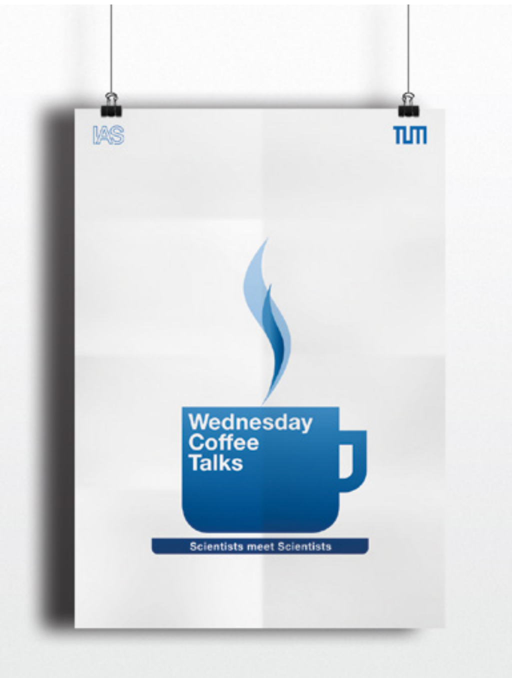
IESP Workshops

In 2020, IESP e.V. (Institute for Earth System Preservation) conducted two events. For the project on Agriculture, Water Management and Climate Change, participants met in the workshop “We stay in dialogue” in person at the Irsee Monastery, March 9-11, 2020, right before the first pandemic lockdown. The November 12-13 workshop “Water for All – Even in the Future?!” took place online due to the then prevailing Covid-19 pandemic.

The March workshop invited farmers, agricultural stakeholders, representatives of the food trade, environmental administration, Bavarian ministries of agriculture and environment, scientists, and representatives of civil society. Its goal was to disentangle the often diffusely expressed conflicts and expectations of the different sides in a protected environment. It identified five issues that future discussions about sustainable agricultural transition must prioritize: transparency, a connecting model agreed upon between agriculture and society, transformation, dialogue, and self-organization. The resulting recommendations for action are available for download at www.iesp.de.

The November workshop was the first ever IESP event in virtual space. Participants from academia, (project) management, and (engineering) practice gathered over two consecutive days to discuss the pressing challenges of the Anthropocene for water management. In addition, the Bavarian State Chancellery's Expert Commission on Water Supply used the framework of this event to brainstorm and discuss creative and innovative measures, as well as conventional proposed solutions, on the basis of existing knowledge. Presentations and rotating small group discussions addressed questions of large-scale or path-dependent processes and structures (such as land drainage via watercourse grading and drainage, or the more decentralized structure of water supply and disposal) and alternatives for uses such as drinking water supply, securing minimum ecological flows, irrigation, cooling water, and navigation. The aim was not only to identify conventional solutions for supply and demand management, but also to explore options for new, unconventional solutions for a sustainable water future in Bavaria. (→ see more on page 92)

Agricultural expert Evelien Verbeij introduces a Dutch model approach to joining cooperative farming and nature preservation.



Wednesday Coffee Talks

We continued our highly successful series of “Scientists Meet Scientists – Wednesday Coffee Talks” during lecture periods. The 12 talks in total, first still in presence in our TUM-IAS premises, after March 2020 in online formats, thematically ranged from cognitive systems in robotics to green technologies in landscape architecture.

A full list of public lectures and events can be found at:

→ https://www.ias.tum.de/events/

“Neighbors” Lecture Series

Also our public talks on Sunday mornings, the TUM-IAS “Neighbors” Lecture Series: “What is it exactly that you do in Garching?” had to be mostly in online-formats, nevertheless reaching a large audience. Talks covered topics such as “The Brain, a Supercomputer on the Back Burner? The Role of Mitochondria in the Nervous System” or “Per Aspera ad Astra: From Accelerators to Neutron Stars and Dark Matter.” ■

Welcoming Our New Fellows

Meet our new Fellows and get inspired by their research projects.

Prof. Ib Chorkendorff

Technical University of Denmark

Fellowship: Hans Fischer Senior Fellowship | **Hosts:** Prof. Ulrich Heiz (TUM Department of Chemistry), Prof. Ian Sharp (TUM Department of Physics) | **TUM-IAS Focus Group:** Light-Induced Molecular Transformations on Cluster-Assembled Materials | **TUM-IAS Research Area:** Surface, Interface, Nano- and Quantum Science

This Focus Group seeks new and efficient catalysts for photoinduced hydrogen and oxygen evolution reactions as well as for the hydrogenation of CO2 by accessing the non-scalable size regime, i.e., the cluster regime and the cluster-nanoparticle transition regime. In most catalytic applications, we are used to working with materials that are scalable. Consider a particle that occupies a certain volume: We would expect that if we double the number of atoms in the particle, then the volume also doubles. We could expect similar effects for a catalytically active surface: Doubling the area should double the number of molecules turned over, if all other parameters remain constant. Nonetheless, this is not the case when the nanoparticles become smaller. Below 2 nm (non-scalable size regime), they also begin to exhibit more molecule-like behavior, with discrete electronic levels. This has strong implications for the reactivity of the individual surface atoms, drastically influencing the overall activity and thus opening up possibilities for tuning reactivity by size.

Prof. Pierluigi D’Acunto

TUM Department of Architecture

Fellowship: Rudolf Mößbauer Tenure Track Assistant Professorship | **Host:** Structural Design | **TUM-IAS Focus Group:** Structural Design | **TUM-IAS Research Area:** Advanced Computation and Modeling

The building industry is a major contributor to the excessive consumption of raw materials, the generation of greenhouse gases, and the production of material waste. Tackling this problem requires devising strategies that effectively mitigate the environmental impact of existing and new buildings. This Focus Group explores novel design and construction approaches that enable more efficient use of material resources by taking advantage of the interplay between form and forces in building structures. The research focuses on new computer-aided design methods at the interface between architecture and structural engineering. In this context, we are exploring equilibrium-based computational design and structural form-finding supported by machine learning. In addition, the Focus Group investigates innovative material systems and construction processes that make use of emerging technologies such as additive manufacturing and robotic fabrication. This includes the development of physical prototypes to validate the effectiveness of design solutions in terms of environmental impact, structural performance, construction feasibility, and architectural potential.

Prof. Michel Géradin

University of Liège

Fellowship: Hans Fischer Senior Fellowship | **Host:** Prof. Daniel Rixen (TUM Department of Mechanical Engineering) | **TUM-IAS Focus Group:** Multibody Systems (joint focus group with Prof. Nachbagauer) | **TUM-IAS Research Area:** Advanced Computation and Modeling

The activities of this Focus Group are centered on the interplay between modeling, simulation, and optimization of nonlinear dynamic systems, with special focus on flexible multibody systems. On the one hand, we will develop new formulations for the modeling of rigid and flexible multibody systems that take floating frames of reference into account. On the other hand, new approaches for the intelligent optimal control of multibody systems for future digital twin technologies will be investigated. Such efficient numerical methods for design and simulation of multibody systems such as robots, for example, represent an important challenge in the engineering dynamics community and are at the center of our scientific collaboration.
Prof. Géradin holds a TUM-IAS Hans Fischer Senior Fellowship awarded by Siemens AG.

Prof. Reinhard Heckel

TUM Department of Electrical and Computer Engineering

Fellowship: Rudolf Mößbauer Tenure Track Assistant Professorship | **Host:** Machine Learning | **TUM-IAS Focus Group:** Machine Learning | **TUM-IAS Research Area:** Advanced Computation and Modeling

My group and I work at the intersection of machine learning and signal/information processing, with a focus on the following areas: 1) Deep networks for imaging. Learning-based methods, and in particular deep neural networks, are starting to be used for important imaging applications, such as the newest generation of medical imaging systems and smartphones. We develop algorithms that yield higher-resolution images at shorter scan times than conventional methods, and we study their performance and limitations. 2) The foundations of machine learning and information processing. We develop learning algorithms and study their theoretical foundations. We are particularly interested in learning from few and noisy examples since, even in the age of big data, training data can often be surprisingly scarce and noisy. 3) DNA data storage. Because of its longevity and enormous information density, DNA is a promising storage medium for digital data. We co-developed the first robust DNA storage system, and we are conducting ongoing research toward future DNA storage systems. We used our technology for the first commercial application of DNA data storage in 2020, and we are now exploring the role DNA can play in information technologies more broadly.

Prof. Ron Heeren

University of Maastricht

Fellowship: Hans Fischer Senior Fellowship | **Hosts:** Prof. Thomas Hofmann (TUM School of Life Sciences Weihenstephan), Prof. Percy A. Knolle (TUM School of Medicine) | **TUM-IAS Focus Group:** Molecular Imaging of Cellular Metabolism | **TUM-IAS Research Area:** Fundamental Natural and Life Sciences

Cellular metabolism is defined by a complex interplay between various molecular classes, molecular signals, and a dynamic cellular environment. This Focus Group investigates the local proteome, lipidome, and metabolome levels to provide detailed insight into the heterogeneity of living systems, with the aim of improving our understanding of the molecular status of health and disease. Innovative single-cell imaging in the native tissue context, using advanced mass spectrometry imaging strategies combined with advanced “omics” approaches, is employed to chart cellular metabolism in unique detail. In particular, we target the translational study of immune metabolism at the cellular level through research on the metabolic state of immune cells within the liver and the central nervous system in settings of sterile inflammation. Our integrated, interdisciplinary approach is augmented with the characterization of contextual lipids and metabolites in the microenvironment surrounding immune cells in these systems. The Focus Group works closely with various collaborators within TUM and at the Maastricht MultiModal Molecular Imaging Institute in jointly targeting the advancement of the fundamental, methodological, and translational impact of molecular imaging in the study of cellular metabolism.

Prof. Lothar Hennighausen

National Institute of Diabetes and Digestive and Kidney Diseases - NIH/NIDDK

Fellowship: Hans Fischer Senior Fellowship | **Host:** Prof. Bernhard Küster (TUM School of Life Sciences) | **TUM-IAS Focus Group:** Gene-Regulatory Mechanisms | **TUM-IAS Research Area:** Medical Natural Sciences

High-precision genome editing tools have the potential to cure human genetic diseases. The most important question now is to learn which gene edits can lead to a cure without risking severe side effects. Multifactorial diseases are often caused by dysregulation of genes rather than dysfunction. It is thus not sufficient to simply inactivate or repair dysfunctional genes. Instead, we need to elucidate and understand how genes are regulated to allow for more fine-grained interventions that restore the gene-regulatory balance found in healthy cells. This is a daunting task, as multiple genes among the more than 20,000 in a mammalian genome, each of which is controlled by several regulatory elements, may be affected in a disease. While the regulation of individual genes has been well studied, we lack a reliable way to predict the presence of genuine biologically relevant regulatory elements. In this Focus Group we seek to use machine learning and artificial intelligence to develop computational tools and methods that offer unprecedented insights into the underlying principles of gene regulation, which will eventually allow more targeted genome-editing studies aimed at curing human diseases.

Prof. Laura Herz

University of Oxford

Fellowship: Hans Fischer Senior Fellowship | **Hosts:** Prof. David Egger (TUM Department of Physics), Prof. Thomas Bein (Physical Chemistry, LMU) | **TUM-IAS Focus Group:** Optoelectronic Properties of Perovskite Semiconductors | **TUM-IAS Research Area:** Fundamental Natural and Life Sciences

Perovskite semiconductors are among the most promising energy materials for new generations of low-cost, highly efficient technological devices such as solar cells and light-emitting diodes. This Focus Group investigates the physical and chemical phenomena that underlie the spectacular optoelectronic properties of perovskite and perovskite-like materials. These include the transport of electric and ionic charge, optical properties, and vibrational characteristics. The goal of the Focus Group is to propose novel perovskite and perovskite-like material compositions that show improved properties, e.g., enhanced stability or reduced toxicity. To this end, the research approach combines a variety of tools from optical spectroscopy, microscopic theory, and material synthesis. Prof. Herz has been awarded a TUM-IAS@e-conversion Hans Fischer Senior Fellowship.

Prof. Barbara A. J. Lechner

TUM Department of Chemistry

Fellowship: Rudolf Mößbauer Tenure Track Assistant Professorship | **Host:** Functional Nanomaterials | **TUM-IAS Focus Group:** Functional Nanomaterials | **TUM-IAS Research Area:** Surface, Interface, Nano- and Quantum Science

This Focus Group aims at expanding our fundamental understanding of dynamic processes occurring on the surface of functional materials. Such dynamic phenomena can strongly influence the functionalitiy and stability of nanomaterials. A particular focus lies on monitoring and guiding the continuous restructuring of catalyst materials under reaction conditions in order to optimize catalyst composition and geometry. For this purpose, we perform scanning tunneling microscopy and X-ray photoelectron spectrosopy for investigations of nano-assembled materials under gaseous atmospheres.

Prof. Karin Nachbagauer

University of Applied Sciences Upper Austria

Fellowship: Hans Fischer Fellowship | **Host:** Prof. Daniel Rixen (TUM Department of Mechanical Engineering) | **TUM-IAS Focus Group:** Multibody Systems (joint focus group with Prof. Géradin) | **TUM-IAS Research Area:** Advanced Computation and Modeling

The activities of this Focus Group are centered on the interplay between modeling, simulation, and optimization of nonlinear dynamic systems, with special focus on flexible multibody systems. On the one hand, we will develop new formulations for the modeling of rigid and flexible multibody systems that take floating frames of reference into account. On the other hand, new approaches for the intelligent optimal control of multibody systems for future digital twin technologies will be investigated. Such efficient numerical methods for design and simulation of multibody systems such as robots, for example, represent an important challenge in the engineering dynamics community and are at the center of our scientific collaboration.

Prof. Nachbagauer holds a TUM-IAS Hans Fischer Fellowship awarded by Siemens AG.

Prof. Shobhana Narasimhan

Jawaharial Nehru Centre for
Advanced Scientific Research

Fellowship: Anna Boyksen Fellowship | **Hosts:** Prof. Johannes Barth (TUM Department of Physics), Dr. Eva Sandmann (TUM Gender Equality Office) | **TUM-IAS Focus Group:** Building Bridges to Promote Gender Inclusivity in Science | **TUM-IAS Research Area:** Gender and Diversity in Science and Engineering

This Focus Group's primary aim is to increase the engagement of TUM with the community of gender minorities in science in the developing world who are in early stages of their careers, as well as to foster their career development. These scientists have to struggle with a lack of basic infrastructure and poor access to scientific equipment and resources. In addition, they frequently have to challenge prevailing societal norms regarding gender roles. We aim to help these scientists build scientific contacts and collaborations with research groups at TUM, help them acquire soft skills that will better equip them to rise in their careers, and aid them in forming a community that can act as a support network. We wish to raise awareness of the challenges they face, as well as the ways in which they have succeeded in overcoming obstacles. We are also interested in studying the factors that affect the participation and retention of gender minorities in science. For example, we have recently discovered interesting (and surprising) correlations between the percentage of women scientists in a country and its per-capita GDP.

Dr. Sani Nassif

Radyalis LLC

Fellowship: Rudolf Diesel Industry Fellowship | **Host:** Prof. Ulf Schlichtmann (TUM Department of Electrical and Computer Engineering) | **TUM-IAS Focus Group:** Machine Learning for Energy Analysis | **TUM-IAS Research Area:** Advanced Computation and Modeling

Integrated circuits (ICs) are the key enablers for all of the smart devices we use in everyday life. The IC powering a modern smartphone has billions of components and represents the combined effort of hundreds of engineers. A key metric for ICs is energy efficiency, since that determines battery life, and managing energy consumption requires accurate models of energy as a function of usage. Portions of IC design are often acquired from external sources to save on development time, and this makes it more challenging to create energy models for those portions. Our research aims to apply advanced machine learning techniques to improve energy models. We leverage known aspects of these energy models to develop guided machine learning techniques for creating accurate and predictive models. This problem is not specific to smartphones or battery-operated devices; large data centers also consume lots of energy and can also benefit from these ideas.

Prof. Frank Ortmann

TUM Department of Chemistry

Fellowship: Rudolf Mößbauer Tenure Track Assistant Professorship | **Host:** Theoretical Methods in Spectroscopy | **TUM-IAS Focus Group:** Theoretical Methods in Spectroscopy | **TUM-IAS Research Area:** Advanced Computation and Modeling

The field of theoretical spectroscopy in chemistry involves research on materials of various types, from single molecules to large semiconductor crystals or nanostructures. We investigate their properties by means of simulations, with the ultimate goal of being able to predict characteristic features on the basis of their atomic or molecular structure alone. Typical examples include questions such as how novel materials will react upon illumination by light (as in a solar cell) or upon application of a voltage. A central research topic is electronic transport in organic semiconductors that are used for organic solar cells or organic LEDs. We investigate, for example, why some semiconductor materials bind the electrons relatively strongly while others conduct them well. The spatial orientation of molecules within the semiconductor material is one important aspect. Interestingly, even the smallest chemical modifications can alter the arrangement of the molecules and thus improve charge transport. The prediction of these properties often involves simulations with supercomputers, because only they can provide the necessary computational power to perform complex simulations.

Prof. Ruben Portugues

TUM School of Medicine

Fellowship: Rudolf Mößbauer Tenure Track Assistant Professorship | **Host:** Brain Circuit Function and Dysfunction | **TUM-IAS Focus Group:** Brain Circuit Function and Dysfunction | **TUM-IAS Research Area:** Fundamental Natural and Life Sciences

The Focus Group Brain Circuit Function and Dysfunction works on understanding the brain circuitry that underlies behavior, how this is established during development, and how it is affected during natural processes such as learning and disease or injury. We use a highly interdisciplinary approach that stems from neuroimaging experiments we perform, during which we monitor the activity of all 100,000 individual neurons in a larval zebrafish, with single-cell resolution and at a rate of two brains per second. By designing virtual reality environments and behavioral assays during which we present stimuli and monitor behavior, we probe processes such as decision-making, learning, navigation, and attention. These experiments generate large data sets that we analyze and use to generate circuit hypotheses, which we further probe with electrophysiology, optogenetics, modeling, and behavioral experiments. These experiments offer a unique possibility within vertebrate model organisms to investigate neuronal processing from sensory perception to motor action, across scales that range from individual synapses to the whole brain and across multiple behavioral paradigms, while retaining the ability to perturb these circuits and assess their robustness and recovery.

Prof. Meike Schalk

KTH Royal Institute of Technology

Fellowship: Anna Boyksen Fellowship | **Host:** Prof. Benedikt Boucsein (TUM Department of Architecture) | **TUM-IAS Focus Group:** Rethinking Patterns of (In)equity and Diversity in Architecture | **TUM-IAS Research Area:** Gender and Diversity in Science and Engineering

To encourage cultures of equity and diversity at TUM, we are addressing institutionalized patterns that have led to a lack of parity and diversity in architectural departments and workplaces. The Focus Group brings together the chairs of Architectural Design and Conception; History of Architecture and Curatorial Practice; Theory and History of Architecture, Art and Design; and Urban Design in TUM's Department of Architecture, as well as the chair of Sociology and Gender Studies in the Department of Sociology at LMU. Our Focus Group examines how (in)equalities are embedded, produced, and reproduced in architectural representations, discourses, norms, curricula, material conditions, and working regimes. Mainly through a doctoral program in practice-oriented research including a conference and publication, we aim to embed analysis and methods of gender and intersectionality studies, feminist and queer perspectives in architectural history and theory, and critical pedagogical formats into educational and research activities at TUM. The main goals are to raise awareness of existing inequities and to address cultural and structural change within the Department of Architecture.

Prof. Franz Schilling

TUM School of Medicine

Fellowship: Rudolf Mößbauer Tenure Track Assistant Professorship | **Host:** Biomedical Magnetic Resonance | **TUM-IAS Focus Group:** Biomedical Magnetic Resonance | **TUM-IAS Research Area:** Bio-Engineering & Imaging

The research of Prof. Schilling aims at the development of novel methods in the area of biomedical magnetic resonance. He and his group characterize and validate imaging biomarkers to enable a comprehensive characterization of tissue by providing functional, physiological, metabolic, cellular, and molecular information beyond anatomical details. The research focus lies on the development of sensitive hyperpolarized molecules for imaging metabolism and pH as well as advanced diffusion magnetic resonance imaging (MRI) techniques. For this purpose, a multimodal approach is taken, utilizing high-sensitivity positron emission tomography (PET) tracers for simultaneous PET/MRI. Interdisciplinarity is an essential characteristic of this area of research, which combines the development of physical methods, the chemical characterization and synthesis of molecular sensors, and the investigation of biological and medical research questions.

Prof. Mathias Senge

Trinity College Dublin

Fellowship: Hans Fischer Senior Fellowship | **Hosts:** Prof. Willi Auwärter (TUM Department of Physics), Prof. Johannes Barth (TUM Department of Physics) | **TUM-IAS Focus Group:** Molecular and Interfacial Engineering of Organic Nanosystems | **TUM-IAS Research Area:** Surface, Interface, Nano- and Quantum Science

Chemistry at interfaces is very different from that in solution. This Focus Group combines classic chemical synthesis with advances in the construction of functional molecular architectures on surfaces. Our molecules of choice are porphyrins, the red and green pigments of life that give blood and green plants their characteristic colors. Recent breakthroughs in the chemistry, molecular engineering, and physical characterization of porphyrins have opened up tremendous application opportunities for functional nanodevices. We will use a molecular engineering approach, together with unique cube- and propeller-shaped linker structures, to affect a transformational advance in the molecular design and control of nanoconstructs. These systems will have tunable electronic, photonic, and chemical functionalities for the translational development of platform technologies in the materials sciences aimed at new catalysts and sensors.

Prof. Natalia Shustova

University of South Carolina

Fellowship: Hans Fischer Fellowship | **Host:** Prof. Roland A. Fischer (TUM Department of Chemistry) | **TUM-IAS Focus Group:** Photophysics and Electronic Structure of Metal-Organic Frameworks | **TUM-IAS Research Area:** Fundamental Natural and Life Sciences

The study of energy and electron transfer (ET) processes is a cornerstone of modern physical and inorganic chemistry, which is driven by the growing demand for efficient energy conversion. This is necessary to build a sustainable energy society that is not dependent on fossil fuels. Our group focuses on materials with a predesigned pathway for ET, which can address the urgent needs to rapidly enhance material performance in areas ranging from optoelectronic devices to photocatalytic systems and thus could dramatically alter the existing energy and material landscape. Well-defined materials such as the metal-organic frameworks (MOFs) targeted within this collaboration offer significant advantages for achieving directional ET: They provide a high level of control for chromophore arrangement, structural parameters, and photophysical properties. To harness MOFs as a versatile platform for enhancing energy utilization, we first need to elucidate mechanistic and structural aspects governing ET efficiency. Thus, preparation of materials with a predesigned pathway for ET still remains a noteworthy challenge; addressing it is the main focus of our collaborative efforts.

Prof. Thaddeus Stappenbeck

Cleveland Clinic

Fellowship: Hans Fischer Senior Fellowship | **Host:** Prof. Dirk Haller (TUM School of Life Sciences) | **TUM-IAS Focus Group:** Cell Stress in Intestinal Tissue Repair and Microbiome Homeostasis | **TUM-IAS Research Area:** Fundamental Natural and Life Sciences

We are interested in the combined effects of host genetics and the environment on the health of the cells that line the intestine. The lining cells of the intestine have many functions, including nutrient absorption and creation of a barrier that is both physical and chemical. Inherited genes, in combination with environmental factors such as diet, exercise, smoking, and sleep, lead to alterations in the function of these cells. The composition of microbial populations in the intestine (the microbiome) is a target of both the environmental factors and defects in host cellular function. The crosstalk between these factors is an important component of this system. We are interested in how host cells, particularly secretory cells such as Paneth cells that secrete a variety of antimicrobial proteins, fail to function properly. The consequences of genetic and environmental challenges often lead to cell stress, poor function, and cell death. We are interested in understanding the mechanism of poor function and developing new therapies to target these defects.

Prof. Kathleen Thelen

Massachusetts Institute of Technology

Fellowship: Hans Fischer Senior Fellowship | **Host:** Prof. Eugénia da Conceição-Heldt (TUM School of Governance) | **TUM-IAS Focus Group:** Comparative-Historical Perspectives on Platform Capitalism | **TUM-IAS Research Area:** Political, Social and Technological Change

Our research focuses on the origins and evolution of political-economic institutions in the rich democracies, together with the impact they exercise on contemporary political outcomes. New global giants such as Amazon and Google have put competition and antitrust policy at the top of the public policy agenda. A first goal, therefore, is to complete a study that situates research on regulation of these new platform firms within a broader comparative-historical perspective, focusing on a comparison of Germany and the United States. Beyond this, in a wide range of industries the advent of the new platform business model poses a host of new challenges to existing labor relations and collective bargaining regimes. Thus, a second goal is to advance our understanding of cross-nationally divergent responses to the labor issues raised by the growth of platform firms and the growth in various forms of "atypical" employment in a range of industries.

Prof. Luisa Verdoliva

University Federico II of Naples

Fellowship: Hans Fischer Senior Fellowship | **Host:** Prof. Matthias Nießner (TUM Department of Informatics) | **TUM-IAS Focus Group:** Visual Computing | **TUM-IAS Research Area:** Advanced Computation and Modeling

This Focus Group works on the creation and detection of synthetic media, also known as deepfakes. We have already built a large data set of videos that includes different types of face manipulation (FaceForensics++), and we have used it to train effective tools based on deep learning to distinguish between real and fake content. We have also devised few-shot learning strategies to handle scenarios where only a handful of fake examples are available during training. Currently, we are following innovative identity-based approaches where we look at the problem from a different perspective, by focusing on the facial characteristics of a specific identity. We can then reformulate the problem as an authentication task: Is this the person it is claimed to be? Within this framework, we rely not only on classic features based on the biometrics of a specific subject, but also on new features based on emotions. Moreover, we are developing a multimodal approach that relies on both the video and the audio signals. This new approach will help in enhancing generalization with respect to new forms of manipulation and in improving detection performance in realistic scenarios.

In Focus

Pollutants and Sustainability Governance

Dealing with environmental contaminants that know no borders is a global matter demanding international cooperation. Effective solutions also require interdisciplinary analysis, to help governments navigate the maze of tradeoffs involving technology and politics, industry and society. These are the challenges taken up by TUM-IAS Fellows Prof. Noelle Eckley Selin and Prof. Henrik Selin, their host Prof. Miranda Schreurs, and doctoral candidate Fiona Kinniburgh, who talk about their collaboration in an interview.

While multiple intertwined global crises are unfolding now or looming ahead, this moment in human history is also distinguished by unprecedented capabilities for probing, measuring, analyzing, and understanding our world – as well as for communicating the knowledge gained, and for sharing potential solutions.

The TUM-IAS Focus Group on Pollutants and Sustainability Governance examines cases of environmental pollution – centered on substances such as mercury, carbon, and pesticides – with an interdisciplinary approach that integrates public policy and social sciences with natural sciences and engineering. Addressing aspects of human activity that have offered benefits to society but are increasingly viewed as unsustainable, this research extends beyond case studies to the creation of broadly applicable frameworks for understanding and action.

To provide an inside look, the Institute for Advanced Study arranged a virtual interview in May 2021 with all members of the group: Hans Fischer Senior Fellows Prof. Henrik Selin of Boston University and Prof. Noelle Eckley Selin of the Massachusetts Institute of Technology, who during their time with the TUM-IAS co-authored the book Mercury *Stories:* ***Understanding Sustainability through a Volatile Element*** *(MIT Press, 2020); their host Prof. Miranda Schreurs of the Bavarian School of Public Policy at TUM; and doctoral candidate Fiona Kinniburgh, who is jointly advised by all three. Science journalist Patrick Regan conducted the interview and edited it for clarity and length.*

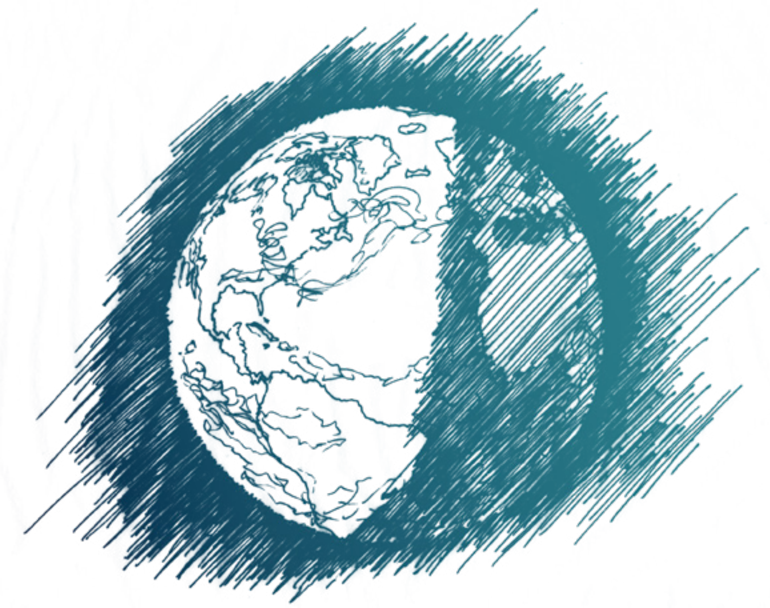
Q: It is not hard to see how your interests and approaches overlap, complement each other, and combine. But how did this collaboration come together?

Schreurs: I work on a range of issues dealing with both political and societal understanding of sustainability. A lot of my work is focused on climate change. The climate change issue is of course a very big issue, and very central in politics today. It's one that we're seeing addressed at the international level in climate negotiations, and at the national level in the form of energy transitions. And it's also an issue at the local level. For the university it's very important because of the role technology can play in addressing climate change.

The idea of working with Noelle and Henrik to explore these issues further was already there when the right opportunity arose. The TUM-IAS, with its interdisciplinary character and its interest in engaging with society, provided a perfect environment for our collaboration, with the added benefit of supporting Fiona's doctoral research.

Many years back, Henrik and I, together with another scholar, co-edited a book on trans-Atlantic environmental cooperation. That book was looking at both similarities and differences between the approaches across the Atlantic on environment and climate issues. I got to know Noelle as well at that time. And their work, which focuses on mercury, is indirectly tied to the other kinds of issues I work on. I spent many years living in Japan, and the entire mercury story that Noelle and Henrik have recently completed their book on begins in Japan. There are many points of connection for us in thinking about the links between technological development, chemical use, and environmental impacts.

Something that's common among the different issues we've been looking at, whether that's greenhouse gases and climate change or mercury pollution or ozone depletion, which Henrik and I worked on in the past, is that these are all global issues. And so they can't be solved by any one country alone.



We really need global cooperation. Another commonality is that they all have to do with chemical processes or gases, and they have industrial connections. So change means it's going to have economic impacts.

It's a wonderfully complex problem that allows us, as social scientists, to think about how we can bring the different pieces together. How do we convince industry of a need to change? How do we convince policy makers of a need to change? Something that is super important is how science is presented to policy makers and to publics. What is the story that we're telling? How are we communicating these problems?

In their work on mercury, Henrik and Noelle have shown how this story telling played a critical role in slowly, over time, bringing about changes in understanding and overcoming industrial opposition – which you can understand, because industry had invested a lot in old processes. It's similar with climate change. How can we bring people to understand that something they've been doing for decades is a problem now? The only way to help people understand the need for change is to help them really understand what the science is saying. The environmental field is trying to figure out how we can take scientific and industrial questions, including the impact on society, and make them understandable to society.

"So change means it's going to have economic impacts."

PROF. MIRANDA SCHREURS

Q: Noelle, how would you describe the interplay between the natural and social sciences in your own approach to sustainability research?

N. Selin: My current work draws more from the natural science and engineering side, but my background is also very interdisciplinary. I did my PhD in earth and planetary sciences, focusing on atmospheric chemistry, modeling how hazardous substances like mercury travel through the atmosphere, where they're coming from, where they're going, what chemical reactions they undergo, and how to trace their pathways through the environment. But my work is very policy-focused. I initially did a lot of research in the social sciences, thinking about the ways scientific information was used in policy processes. That shaped my approach to scientific research. You can't really understand what's happening in the atmosphere unless you fundamentally understand the influence of humans, and two-way interactions with human societies. And in this era of the Anthropocene, we increasingly need to take that into account when we're trying to understand the fundamentals of what's happening in the atmosphere. At MIT, I'm a faculty member in an interdisciplinary institute – the Institute for Data, Systems, and Society – and jointly ▸

appointed in Earth, Atmospheric, and Planetary Sciences. But I also run the Technology and Policy Program. That's our interdisciplinary two-year master's program, which is similar to the politics and technology program at TUM. There are related programs across the world that are master's programs focusing on the intersection of science, engineering, and public policy.

My research group takes an interdisciplinary perspective on a broad range of sustainability issues, especially those involving hazardous air pollution and their dangers to human health. Mercury is a key focus. My group does a lot of modeling, trying to trace policies all the way to impacts and responses: for mercury as well as ozone, particulate matter, and persistent organic pollutants.

Q: In many fields, researchers have had to develop appropriate ways to deal with gaps in data or reliability concerns. How do such issues affect your modeling work?

N. Selin: I have collaborations with a lot of groups that collect data on mercury and other substances in the atmosphere and in other media. One of the challenges with mercury is that the data are sparse. There are few places in the world where data has been collected, and those are mostly in the northern hemisphere, mostly in developed countries. To help to understand where mercury is traveling and what kinds of processes it undergoes, we go back and forth between the data and the modeling to test hypotheses and generate insights. The data question is also where this intersects with the policy world. Where and when would you collect more data on mercury? Both Henrik and I have worked with the global treaty on mercury, the Minamata Convention, in the context of their process for effectiveness evaluation.

Some questions come up there: Where should mercury be measured? Who will pay for such measurements? Countries are of course interested in having measurements in their own territories and close to the outputs that are most meaningful for them. Those might not be the most optimal measurements from a scientific perspective to constrain some of the processes and scientific understandings of mercury. So there is a necessary interplay between the scientific research and the policy process to really understand where new data can come in, and how to use that both in scientific research and in policy assessments.

In my group, as we do model analyses and actually look at the science and engineering of mercury and related issues, we really try to involve stakeholders and policy considerations in the framing and throughout the research process. So for example we'll be talking to regulators – in the US context, that tends to be state and national regulators – but also non-governmental organizations that have an interest in the research. And that has changed some of the framing of the questions we've asked and the data sources we've used, in order to increase their trust in that process and make the product more usable at the end of the day.

H. Selin: In our book Mercury Stories, Noelle and I take a systems approach to studying mercury and understanding it as a sustainability issue, but then also using that systems framework to think about leverages. If you want to push a system from a less sustainable to a more sustainable state, what are the different levers you can pull? And then to think about what happens if you pull lever A. If you pull lever B, what happens? If you pull lever C? And you can then use that to think about which reverberates most throughout the system. Where do you get the most bang for the buck? If you can only pull one lever, which one should you pull?

Q: And when? Is timing an important factor?

H. Selin: Right. When do you need to take what action? A lot of that is to do with thinking about tradeoffs of different policy options. Most policy options come with tradeoffs. And also how different policies intersect. That is something that Fiona has also done in her work, looking at how international treaties – where global governments come together and write international law – intersect with private sector certification schemes. In an ideal world, they should be complementary, but in the real world they might not be. Fiona can talk more about that. But that's one of the things we've been doing.

Q: What brought you to this field of research, Fiona? And what is your vantage point on the interactions between science and society, between public policy and private enterprise?

Kinniburgh: I started out doing my undergraduate work in biology. I've always been very interested in the scientific side. But through my interest in the environment I came to understand that social science is now a key factor in driving the process. My focus now is on international politics – I have a lot of overlap on that with Henrik and Noelle and Miranda – and also on the use of social science in the policy process. My background too is in climate change, but I have also done a lot of work on biodiversity and agriculture as well. So bringing all those things together is a nice point of contact where chemicals are in the middle of all these issue areas at the same time.
Through the TUM-IAS, I had the opportunity to spend some time at Boston University and MIT last year, which was really special. On top of the work we're doing, our actual collaboration, I think the fact that we have these international perspectives is extremely useful – first because we've all worked on international policy issues, and also because Miranda is a comparative scholar, and that's where my work is now going as well. My current focus is looking at France and Germany from a comparative perspective.
In many ways we have very different empirical cases. That really adds to the richness of the group, because we find we have pretty similar themes that all deal with the complexities of the systems that we are trying to analyze and then bring some insights to. The connection with policy is critical. We know that these are very important issues with real-world implications. The types of things we're thinking about might actually impact some decisions. That makes it both challenging and very exciting.

Q: Henrik and Noelle, where does your book about mercury come in? Do you think insights from your studies of mercury might aid in understanding and dealing with other sustainability issues?

H. Selin: In the book we use the adoption of the global Minamata Convention on Mercury as a sort of a frame. The first story of the book is related to that. And as part of our research, both Noelle and I attended many of the negotiations on site. We were also in Minamata when the convention was adopted in 2013. One of the reasons we found it interesting to use mercury as a case study of sustainability is that people have interacted with mercury and mercury compounds for thousands of years. ►

There's a very long history to draw from, going back to the earliest use of cinnabar. You mine cinnabar, and then you extract mercury from cinnabar. Noelle has a piece of cinnabar behind her. So do I. It's basically a red rock. But this is also cinnabar red. It was being used in coloring and in ancient medicines for thousands of years. And then mercury began to be more actively used around the 1400s and 1500s in Europe. It was used to make mirrors, and then it was used to make hats, and of course they invented the mercury thermometer – that's probably what most people associate mercury with. For about 300 years, it was the dominating technology for measuring temperature, by far the most accurate one.
And then a lot more industrial uses emerged in the 1800s. Mercury became an integral component in chemicals manufacturing. There was continued use in medicines, for hundreds of years. It was used to try to treat syphilis. That didn't go very well. So there's a very long history of both useful interactions with mercury and really bad ones. And along that side you also have active mining of mercury, which was often a very deadly activity. One of the things we talk about in the book is how human well-being has been advanced by mercury. The mercury thermometer is a practical example of that. But then on the flip side, interaction with mercury has also been deadly. An example is the tragedy in Minamata that Miranda mentioned. We tried to unpack the ways in which humans have interacted with mercury, ways it has advanced human well-being, and ways it has severely harmed human well-being. And we tried to do that using the system framework.

N. Selin: A lot of people think about environmental pollution stories as a fairly common narrative. You have a discovery of something, it's found to be harmful, and it's then phased out. There's an arc to it. And one of the surprising things the mercury story shows us is that the history is much more complex than that. This becomes clear once you start thinking about who benefits and who is harmed and how that changes over time, the development of knowledge, the different impacts of institutions along the way, different times at which different uses were thought to be hazardous, to whom and why. Another complicating factor is that mercury has diffused across borders both through trade and through environmental transport.
This is a major insight of our book, that a sustainability challenge can't be fully solved by just saying, for example, let's get rid of mercury. It's an element in the periodic table. And people have been interacting with it in ways that will linger for generations and millennia. Once mercury is released to the atmosphere or into the environment, it continues to circulate. It travels globally. Mercury can be in the air. Most people are familiar with the silvery liquid form, which I have in a small container here. But it goes into the gas phase. It becomes a gas as elemental mercury. And it can travel worldwide. Then it deposits to ecosystems and builds up as methyl mercury, which was the very toxic form in Minamata, Japan, that caused all the poisoning incidents.

Q: It accumulated in the bodies of fish?

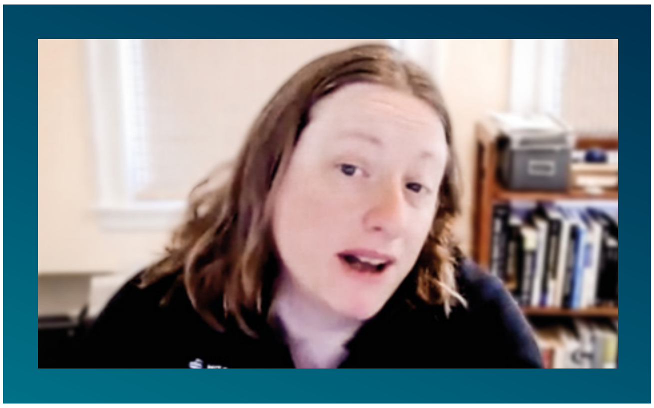
N. Selin: Yes. Mercury can build up along food chains in fish. People across the world

"My group does a lot of modeling, trying to trace policies all the way to impacts and responses: for mercury as well as ozone, particulate matter, and persistent organic pollutants"

PROF. NOELLE ECKLEY SELIN

are exposed to levels of methyl mercury in fish that could result from pollution that's happening today, but also could result from pollution that was happening a few hundred years ago. Mercury continues to circulate in the environment and poses a longer-term challenge. We also found in researching our book that while telling the story of mercury from a scientific perspective would illuminate a lot about environmental transport, the social perspective was important too.
One of the key uses of mercury in the 1500s was in silver mining in the Americas. That mercury came from Europe and was transported over to the Americas. There it was used in silver mining and had very negative consequences for the miners, who had severe health problems, often fatal health issues, because of mercury exposure. But that mercury also could continue to circulate. Today, it could be in South America, but it could also have traveled worldwide. It's a topic of some scientific uncertainty what the legacy of that mercury was, how far it spread globally, but understanding where that mercury came from and ended up really required us to understand the social and societal transport of mercury along with and alongside the environmental transport of mercury. And also how it was perceived over time. It was gaining value for colonial powers and at the same time was really detrimental to indigenous workers.
We see this pattern, unfortunately, echoed as well with the current uses of mercury in artisanal and small-scale gold mining. Henrik and I have a project, along with a colleague at the University of Wisconsin, looking at the continuing use of mercury. This project, funded by the US National Science Foundation, was really a spinoff of the work we did in the book, applying our framework to a specific case study in a region that has a lot of gold mining and a lot of societal problems.

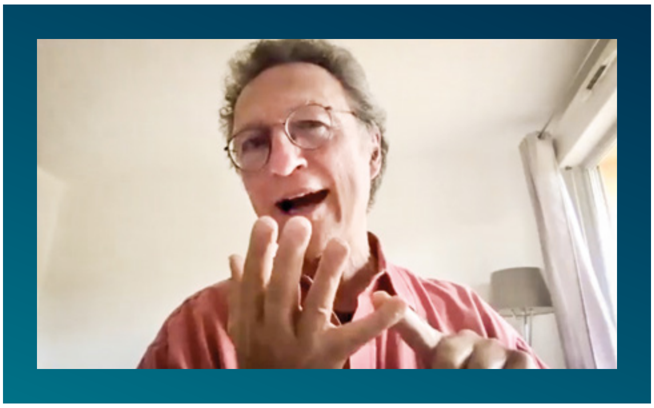
H. Selin: Historically, two of the largest mercury mines in the world have been in Europe. There is Almadén in Spain, which has been in use for about two thousand years at least, and Idrija in what is now Slovenia, which has been used for five or six hundred years. Recently both of them jointly became UNESCO world heritage sites – another way of showing the transition there. We have visited both of them. We've been down in both mines. The nearest large city to Almadén is Seville. If you go to the large cathedral there in Seville, you will see that a lot of the most valuable objects are not made of gold. Typically when you go into a large cathedral, there is a lot of gold. Here there's the silver. They took the mercury to Latin America, they extracted the silver, and then it was brought back home. So it's a cathedral that is much more covered in silver than in gold, and that is directly related to the mercury that came from a few miles up the road.



Prof. Noelle Eckley Selin

N. Selin: We have a chapter that looks at the current challenge of artisanal and small-scale gold mining. We have a chapter that looks at the global cycling of mercury, which gets into some of these issues of transport by air versus transport by ship. But we haven't yet talked about what is potentially the second largest atmospheric source of mercury, and that is coal burning. Mercury is a contaminant in coal, and when coal is burned, it's released to the atmosphere, and a lot of the current industrial mercury pollution is a result of the rapid increase in coal burning. You have a real clear link to climate change in the industrialization that comes out of the mercury case as well.
One of the other things we do in our book is to break down the key findings for different ▸

audiences. In the final chapter we draw some lessons for researchers, people who are studying mercury, as well as decision makers, the policy audience, and also concerned citizens. The lessons are a little bit different for all of those audiences in terms of their understanding, their ability to act, their potential leverage points. So we really try to identify that separately and think about what their interests are and how they can help move toward a more sustainable trajectory.



Patrick Regan (conducted the interview)

Q: So you're tuning the output for people who might have different interests and different capabilities for action. Could you explain a bit more about what you mean, in this context, when you talk about a systems approach?

H. Selin: Yes. We are basically setting up a new framework that we call the human-technical-environmental framework, the HTE framework. We're identifying technical components – that could be a coal-fired power plant, or it could be a scrubber that you put in a coal-fired power plant to catch the mercury before it goes into the atmosphere. It involves humans. This could be fishers in Minamata, it could be factory workers, or it could be factory owners. And then there are also environmental components – it could be a small ecosystem, it could be the ocean, it could be the fish. And we're looking at how these three material components – the technology, the humans, and the environment – interact in the context of institutions and knowledge. That's the overall framework.
Through this framework, we are then tying in a matrix-based approach – we think this is one of the major contributions – so there is also basically a roadmap for using and applying the systems framework, which can then be done through a matrix. This is somewhat common in engineering systems but less common in the natural sciences or in the social sciences. So we try to combine insights from the natural sciences and the social sciences and engineering in creating both the analytical framework – the HTE framework – and then also the methods and tools needed for actually applying that framework.

N. Selin: One of the challenges that we encounter in addressing sustainability challenges is the difficulty of trying to break them down and trying to understand them. At first glance, it seems like a really complicated problem, and those in natural sciences and engineering often say: How can I take into account these institutional aspects, and the idea that there's politics involved in this issue? And for the social scientists, there are some physical flows and technologies that have maxima and minima that might not be amenable to the kind of analysis that's traditionally done in their fields.
What we're trying to do is give researchers who have backgrounds in various different domains a common way to talk about these issues and not exclude any of the really critical components. One of the conclusions from looking at these mercury cases across the book was that describing a system and omitting any set of components – whether they be human, technical, environmental, institutional, or knowledge components – wouldn't be a full description of the system. At the same time, then, we're giving you a roadmap to connect some of the analytical ways you would start to break down the problem, looking at how these components interact. And then from a forward-looking perspective, identifying leverage points, highlighting interventions in the systems that can bring about change. It's a four-step process. The first step is categorizing those components, the second is looking at interactions, the

third is looking at interventions, and then the fourth is drawing broader insights into the system.

Q: International treaties must represent some of the more complicated interventions to enact and to evaluate. Are there practical lessons that can be drawn from studying existing treaties? Are there any general insights that might streamline efforts to forge new agreements?

Schreurs: There are parallels between various global environmental agreements. One is just that: They are trying to bring about change globally. And that's important so that you don't have leakage, with industry running off to countries that don't have the same environmental standards. But there are crucial differences as well.

H. Selin: A number of global environmental treaties exist in parallel, but each is also unique and deals with unique issues. The climate change issue is very different from ozone depletion, for instance, in terms of how carbon behaves in the environment compared to the ozone-depleting chemicals, the industries that are involved, the economic interests, and so forth. So just because that one institutional model worked relatively well on ozone depletion – it is often seen as one of the more successful global environmental agreements – that doesn't mean we could solve climate change by copying that approach. One can definitely look at different treaties and try to draw insights and lessons. That's very helpful. But I think one should be really careful about thinking one is a blueprint for another area.

N. Selin: There is also a substantial area of research that links back to Fiona's work on the intersections among these different treaties. Fiona's work looks at the chemicals treaties in particular, also the strong connections they have to the biodiversity convention, as well as to climate change – and the intersections between those issues and how they're dealt with institutionally where you have clear scientific and systems issues that cross those different agreements. You see this, for example, in the cases of mercury and climate change, since both deal with coal in a very substantial way. You have to look at how, institutionally, each agreement carves out its own way of dealing with the problem – in some cases that might be the same countries committing to two very different things. So there might be competition, there might be synergies, there might be interactions. Trying to figure out how all of those things work together in order to move us toward sustainability is a goal of a lot of our work.

Q: Fiona, could you explain more about the current state of things, and the outlook for the future, at the points where biodiversity concerns intersect with the business and practices of the chemical and agricultural industries?

Kinniburgh: Sure, absolutely. I think Noelle introduced it really well. We've had so many international environmental agreements, and for good reason. But there are also historical factors that led to their development over time, often dealing with issues that are very different but do overlap. We know that climate change is a huge problem, and the science on that has been developed and reinforced by the IPCC (the Intergovernmental Panel on Climate Change), but the biodiversity crisis is something that has grown in importance on the international agenda much more recently. We now also have a scientific body for biodiversity, called IPBES (the Intergovernmental Platform on Biodiversity and Ecosystem ▸

Prof. Henrik Selin

Services), that aims to do essentially what the IPCC does: provide scientific knowledge showing us what the state of the problem is. At the same time, on the chemical side, we also have a lot of science showing us that the amount of chemicals we are using and constantly developing is growing unsustainable. Unfortunately there is no science-policy body there yet, though that might be something to come in the future. This is something Henrik has also written about.
So to a certain extent on the scientific side we know that there are a lot of overlapping issues. When it comes to institutions, we're not necessarily equipped to handle these things together. So that's where my work on agriculture comes in. The approach is to say yes, we know what a lot of the environmental and sometimes social problems are. Maybe we also need to focus on sectors. So, for example, focusing on agriculture as a sector then allows us to zoom in on those institutions and actors that can drive change, which are of course impacting the environment but have their own interests, their own place in national economies and the international economy. From a political perspective, this enables us to look at what's going on in a way that an entry point purely from the environmental side doesn't always allow. For agriculture specifically – even on pesticides, which I work on – we have this issue where substitution is not always an obvious answer. Even between one pesticide and another, you actually have to consider different solutions, different scales, and different contexts.
I think what all of our work shows in the end is that the systems perspective is critical. You have to link the scientific side, the material side, and the institutions. But what the science in all of the domains tells us is that, as a whole society, we need to transform our economies. So our question then is: What does that look like? What kinds of knowledge can we use to inform the decisions we need to make?

Q: And how do you see these gears meshing – scientific understanding, public communication, governmental policy, international law and cooperation? Does what you've learned make you optimistic that human civilization can or will be put on a more sustainable foundation in the future?

Schreurs: A lot of the progress we have seen came from interactions, and little steps that eventually added up. So that you saw a lot of different institutions acting, you saw for example a lot of regional efforts to start putting into place some models, some increasing knowledge, with separate efforts feeding into each other. We've seen the magnitude of changes add up over time and really make people's lives better. But there wasn't one magic way that that happened.

H. Selin: I can build on that. Looking at governance and the global environmental agreements, I think that they are very useful for bringing countries together, setting common goals, common rules, common standards. As Miranda said, no country alone can address the sustainability crisis, including the environmental component of that. We definitely need global cooperation. I'm also the first one to acknowledge that these global treaties are limited. Global cooperation and global treaties themselves will not solve the sustainability crisis. That's where we're getting into, especially in Europe, regional cooperation under the European Union, or national action, or even local action. This then is where I see the global level setting the common standards, and then countries need to figure out what works for them. The approach in the United States might not work in Canada, which might not work in Germany, which might not work in Brazil. Each country needs to be figuring out their own way.

Schreurs: I think what we see across these different issues we're looking at is the crisis of an industrial structure that was focused on economic growth but not on long-term

"… no country alone can address the sustainability crisis…"

PROF. HENRIK SELIN

Prof. Miranda Schreurs

Fiona Kinniburgh

well-being, whether planetary or human. And that has led to really serious problems in all these areas we're looking at, whether it's mercury pollution and human health problems or agricultural pesticides and their ecological and human impacts, or greenhouse gases and climate change. And what we're seeing across all these areas is growing pressure for change. Steam is in the pot, and the pot's about to explode. So I think we're hitting the point where we'll start to see bigger, deeper changes in industrial policy and technology policies because of these growing pressures. Notice what just happened in Germany, with the constitutional court's decision that Germany is not doing enough on climate change to protect future generations. The court basically told the government: 2050 is too late. This kind of decision came a few years ago from the Dutch courts, to say the social movements that are demanding more action from the government are justified. And now we see what's going on with the pressures in the United States on the Biden administration to take climate change more seriously – and not just climate change. The message behind the Green New Deal and the European Green Deal is that we need a new structure. We need to rethink our economies. And that's what I'm hoping is happening, that all of these pressures are really indicating it's time for a big change.

Kinniburgh: Many times across these different issue areas, what we've seen in a lot of cases is development that has been for human well-being or has contributed to economic growth, and now we're understanding that maybe human well-being for a majority of the people on the planet has to look somewhat different. This inertia has been building up, especially since the 1950s but even for centuries. The way we've developed as a society is not possible in the same way any more. What that also means is that there's a lot of inertia in the system, so there will need to be a lot of, let's say, energy in the other direction to really motivate change.
I think it's also really exciting, especially for a lot of the younger people pushing for change, to think: Well, we need to imagine something completely different moving forward. And that's why the work that we're all doing ties into these bigger policy questions, such as what could a Green (New) Deal look like? What does this new overall project for society mean for human well-being, for sustainability, for the environment, and for society? ■

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Focus Group Cellular Protein Biochemistry

Prof. Matthias J. Feige (TUM), Alumnus Rudolf Mößbauer Tenure Track Professor | **Nicolas Blömeke, Joao Coelho, Karen Hildenbrand, Susanne Meier, Yonatan Mideksa, Stephanie Müller, (TUM),** Doctoral Candidates | Host: Cellular Protein Biochemistry, TUM

Prof. Matthias J. Feige

How cells make their proteins – from insights to engineering

This is the final annual report from our Focus Group for Cellular Protein Biochemistry at the TUM-IAS. Matthias Feige, heading the group as a Rudolf Mößbauer Tenure Track Assistant Professor, has just obtained tenure and now continues his career as Associate Professor for Cellular Protein Biochemistry at TUM. This provides the opportunity to summarize some our achievements during the Fellowship as well to provide a few glimpses of the path ahead.

In complex organisms, cells need to communicate and interact with each other. This communication is the basis of growth, development, memory formation, and immune defense. Key players in all cellular communication processes are proteins secreted from cells or displayed on the cell surface. Within every mammalian cell, like our human cells, a specialized sub-compartment exists that is responsible for the production of these proteins: the endoplasmic reticulum (ER). Its name stems from its microscopic appearance: a net-like structure within the interior of the cell. Proteins are not only produced in the ER, but also controlled. Only proteins that have acquired their correct, biologically active structure are allowed to leave the cell or to be displayed on the cell surface as membrane proteins. Faulty proteins are recognized by dedicated molecular quality control machinery and degraded. Insights into protein structure formation and its control in the cell are of immediate medical relevance for human pathologies such as Alzheimer's or Parkinson's disease – but may also inspire new approaches in medicine and biotechnology. Both of these avenues motivate our research in the laboratory for Cellular Protein Biochemistry (CPB lab). We want to understand principles of protein biogenesis in the cell, understand why these fail in many human diseases, and also provide new biomedical approaches for therapy. In other words: We are driven by curiosity, but also by purpose. To achieve our goals, we use an interdisciplinary approach from biochemistry to mammalian cell biology to understand and ultimately engineer the underlying processes.

Current work in the CPB lab focuses on two major topics. The first is the quality control of membrane proteins, where principles are still mostly unknown yet have immediate biomedical relevance. Failures in membrane protein biogenesis are associated with a large number of diseases, including neurological disorders. One such example is X-linked Charcot-Marie-Tooth disease, which is caused by mutations in Connexin 32. Charcot-Marie-Tooth disease is the most common genetic disorder of the peripheral nervous system. In our work we were able to show that mutations in Connexin 32 can disturb its proper structure formation and integration into the lipid bilayer [1], a defining step for every membrane protein (Figure 1). This compromises formation of Connexin 32 gap junctions, nano-channels that allow the transport of small molecules within and between cells and are essential in our nervous system. As a consequence, Schwann cells, which form an insulating layer around nerve cells, die and signal transmission in the nervous system is compromised. Our insights thus provide a molecular explanation for certain types of Charcot-Marie-Tooth disease, which may ultimately help in developing new therapeutic approaches. On the basis of these findings, we have meanwhile significantly expanded our scope and our team working on membrane protein biogenesis. A team of five doctoral candidates within our lab is currently performing systematic analyses on cellular quality control machinery for membrane proteins and on the structural biology of these molecular machines. This team has recently uncovered entirely new mechanisms of how the cell handles misfolded membrane proteins. These insights, some of which will be published shortly, help us in understanding at a molecular level how cells produce a major protein class that allows them to interact and build complex multicellular organisms. Also, the newly identified machines for membrane protein quality that we are analyzing may provide targets for future pharmacological treatment.

The second major research focus of the CPB lab is the biogenesis and engineering of interleukins (ILs), key signaling molecules in our immune system. In humans, more than ▸

[1] J. Pl. L. Coelho et al., “A network of chaperones prevents and detects failures in membrane protein lipid bilayer integration”, Nature Communications, vol. 10, no. 1, 2019.

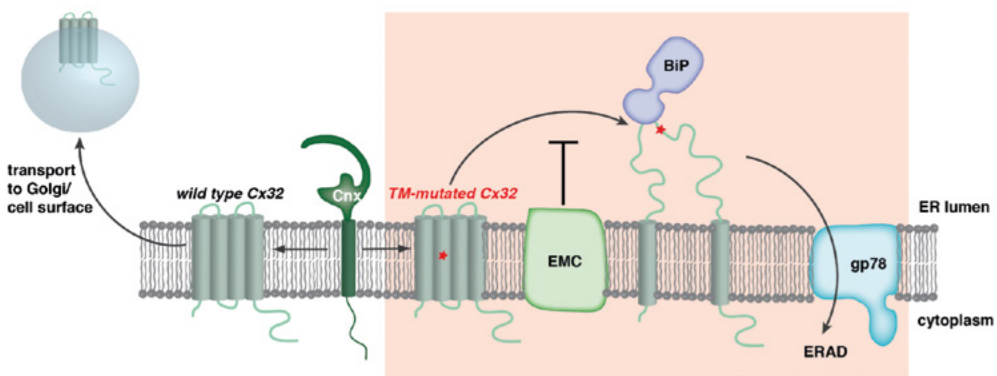

Figure 1, Connexin 32 (Cx32) is normally transported to the cell surface to form gap junctions. If mutated in its transmembrane (TM) regions, membrane integration can be compromised, which is counteracted by the ER membrane protein complex (EMC), a quality control machine for membrane proteins. Misintegrated TM sequences are recognized by the molecular chaperone BiP, and faulty proteins are ultimately targeted for ER-associated degradation (ERAD) by the ubiquitin E3 ligase gp78. Figure taken from [1].

40 different ILs exist. They constitute the language of immune cells. Depending on the individual IL, these mount, sustain, or suppress immune reactions in health and disease. Understanding interleukin biogenesis in the cell in more detail can thus provide avenues toward rationally modulating immune responses: dampening immune responses in autoimmunity, but also augmenting them when needed, e.g., to fight cancer wcells. Our work mostly focuses on the interleukin 12 (IL-12) family, which comprises four members (IL-12, IL-23, IL-27 and IL-35, Figure 2A) that span a broad range of biological functions [2] – from activating immune responses to suppressing immunity. As such, IL-12 family members are involved in a large number of human diseases including autoimmune disorders, cancer development, and sepsis [3]. Several studies from our lab in the past five years have revealed the molecular mechanisms of how cells produce IL-12 family members [4-9]. In one of these, in close collaboration with colleagues in the Bavarian NMR Center, TUM Medicine, and the Bioengineering Department at Stanford University, we were able to reveal mechanistic and structural details how cells produce IL-23 [5] (Figure 2B). This study now helps understanding how cells regulate and control protein interactions for signaling molecules (IL-23 consists of two parts), but also provides insights into this pro-inflammatory molecule that already is a successful target of antibody therapies in the clinics. In another study, in close collaboration with TUM Medicine and TUM Physics as

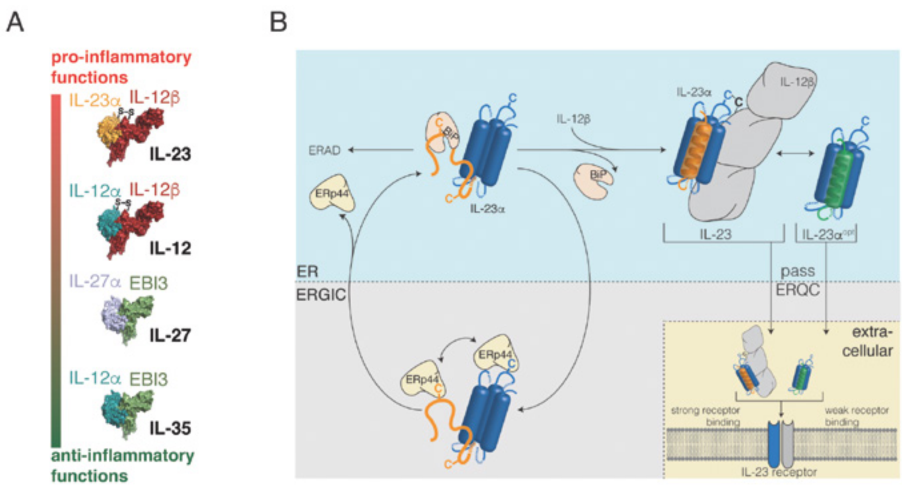

Figure 2, A) Schematic of the IL-12 family. Each family member is a heterodimer, consisting of one α and one β subunit, and performs distinct roles in regulating immune responses. IL-12 and IL-23 are covalent dimers, connected by a disulfide bond (S-S), whereas IL-27 and IL-35 are non-covalent dimers. B) The molecular basis of IL-23 biogenesis. IL-23α is retained in the cell by molecular chaperones that recognize its unstructured first α-helix. Once IL-23α assembles with its partner, IL-12β, it can be secreted and signal via its receptor. In silico optimization of IL-23α allows it to pass ER quality control (ERQC) without IL-12β and act as a signaling molecule on its own. Figure in (B) taken from [5].

[2] D. A. Vignali and V. K. Kuchroo, "IL-12 family cytokines: immunological playmakers", Nature Immunology, vol. 13, no. 8, 2012.

[3] E. D. Tait Wojno, C. A. Hunter and J. S. Stumhofer, "The Immunobiology of the Interleukin-12 Family: Room for Discovery", Immunity, vol. 50, no. 4, 2019.

[4] S. Bohnacker et al., "Influence of glycosylation on IL-12 family cytokine biogenesis and function", Molecular Immunology, vol. 126, 2020.

[5] S. Meier et al., "The molecular basis of chaperone-mediated interleukin 23 assembly control", Nature Communications, vol. 10, no. 1, 2019.

[6] Y. G. Mideksa et al., "Site-Specific Protein Labeling with Fluorophores as a Tool To Monitor Protein Turnover", ChemBioChem, 2020.

[7] S. I. Müller, I. Aschenbrenner, M. Zacharias and M. J. Feige, "An Interspecies Analysis Reveals Molecular Construction Principles of Interleukin 27", Journal of Molecular Biology, vol. 431, no. 12, 2019.

well as with immunologists in Paris, we were able to gain detailed insights into how IL-27 acquires its native structure and how cells monitor structure formation of this protein [8]. These studies contribute to the basis of current research in the lab. Here a team of doctoral candidates and postdoctoral researchers is advancing our understanding of hitherto hardly understood IL-12 family members (namely IL-35) and is now using these insights for the rational engineering of interleukins with desired properties: Using these insights, we engineered a new human interleukin, extending the language of human immune cells. Currently we are further developing this rationally engineered biomolecule from our lab as a potential new treatment for sepsis, one of the deadliest diseases in developed countries without any good causal treatment options. Our first patent on the development of this new molecule was awarded with the Innovationspreis 2019 der BioRegionen in Deutschland. Funded by the BMBF and the Else-Kröner-Fresenius Stiftung, we have now built an interdisciplinary team in protein biochemistry, molecular immunology, pharmacology, and medicine, including an expert in the biotech business, to ultimately bring our engineered interleukins to the clinics. Within a few years, we have thus taken the step from basic science to (pre-)clinical translation, which was possible due to the broad range of expertise present at TUM. ■

[8] S. I. Müller et al., "A folding switch regulates interleukin 27 biogenesis and secretion of its alpha-subunit as a cytokine", Proceedings of the National Academy of Sciences of the United States of America, vol. 116, no. 5, 2019.

[9] S. Reitberger, P. Haimerl, I. Aschenbrenner, J. Esser-von Bieren and M. J. Feige, "Assembly-induced folding regulates interleukin 12 biogenesis and secretion", Journal of Biological Chemistry, vol. 292, no. 19, 2017.

Focus Group Computer Vision and Machine Learning

Prof. Michael Bronstein (Imperial College / University of Lugano / Intel / Twitter), Alumnus Rudolf Diesel Industry Fellow | **Prof. Daniel Cremers (TUM),** Carl von Linde Senior Fellow | Host : **Prof. Daniel Cremers,** Computer Vision and Artificial Intelligence, TUM

Prof. Michael Bronstein

Prof. Daniel Cremers

Machine learning in non-euclidean spaces

The activities of our Focus Group are primarily centered on the interplay between geometry, machine learning, and computer vision. Analysis of geometric objects has been a topic of computer vision and pattern recognition since the inception of the field, and geometric principles of symmetry and invariance underpin the success of modern deep learning methods.

Members of the group have both academic and industrial experience. Michael Bronstein was until 2019 a principal engineer at Intel responsible for the development of RealSense range-sensing technology, and following the acquisition of his startup Fabula AI in 2019 is the head of Graph Learning Research at Twitter. Daniel Cremers is the founder and Chief Scientific Officer of the autonomous driving startup Artisense.

“Geometric deep learning” (a term coined by Michael Bronstein) tries to approach machine learning problems from the position of geometric priors such as symmetry and scale separation. Modern machine learning systems need to routinely deal with data in thousands or even millions of dimensions, running into a phenomenon colloquially known as the “curse of dimensionality.” Incorporating prior knowledge about the structure of the data (typically expressed through the symmetry group of the underlying domain) turns out to be a powerful geometric principle that finds its realization in the majority of popular deep representation learning architectures dealing with all sorts of data: convolutional networks ubiquitously used for image analysis (emerging from the translational symmetry of the grid); graph neural networks, deep set, and Transformer architectures (based on principles of permutation equivariance); and gated recurrent neural networks (time warping).

Graph neural networks have recently taken the spotlight of the machine learning community, with successful applications ranging from novel antibiotic drug discovery to traffic prediction in Google Maps services. We believe the rapid movement of these methods from a niche interest to the spotlight of research are in part thanks to our contributions and the activities of our Focus Group.

Of particular interest to our Focus Group is bridging the gap between geometric and deep learning by generalizing neural architectures and the underpinning mathematical models to non-Euclidean domains, as well as developing next-generation machine learning methods capable of dealing with geometric data such as meshes and point clouds.

In collaboration with a startup company Ariel AI (founded by Iasonas Kokkinos, who was a visitor in summer 2018 and participated in the TUM-IAS Workshop on Machine Learning for 3D Understanding), we developed a hybrid pipeline for 3D hand pose estimation with an image CNN-based encoder and a geometric decoder. A demo of this system presented at CVPR 2020 allowed the creation of realistic body avatars with fully articulated hands from video input on a mobile phone faster than real-time. Ariel AI was acquired by Snap in 2020.

Another paper [2] co-authored with the team of Nassir Navab (TUM Chair for Computer Aided Medical Procedures & Augmented Reality) and presented at MICCAI 2020 developed a new graph neural network architecture with latent graph learning for automated diagnosis of neurological disorders.

In a new book preview on Geometric Deep Learning [3] authored by Michael Bronstein with Joan Bruna (NYU), Taco Cohen (Qualcomm), and Petar Veličković (DeepMind), we provide a geometric unification for a broad class of machine learning problems and show how to derive some of the most popular deep representation learning architectures from first principles.

Efficient deep learning architectures developed in the group of Daniel Cremers [4] formed the core engine for the project Slow Down COVID-19 at Harvard, allowing the detection of COVID-19 in X-ray scans. ▸

[1] D. Kulon, R. A. Guler, I. Kokkinos, M. M Bronstein and S. Zafeiriou, "Weakly-supervised mesh-convolutional hand reconstruction in the wild", 2020, arXiv:2004.01946.

[2] L. Cosmo, A. Kazi, S.-A. Ahmadi, N. Navab and M. M. Bronstein, "Latent-graph learning for disease prediction", in Medical Image Computing and Computer Assisted Intervention – MICCAI 2020, Lecture Notes in Computer Science, Martel A. L. et al., Eds., Cham: Springer, 2020, vol. 12262, pp. 643-653.

[3] M. M. Bronstein, J. Bruna, T. Cohen and P. Veličković, "Geometric Deep Learning: Grids, Groups, Graphs, Geodesics, and Gauges", 2021, arXiv:2104.13478.

[4] F. Pasa, V. Golkov, F. Pfeiffer, D. Cremers and D. Pfeiffer, "Efficient Deep Network Architectures for Fast Chest X-Ray Tuberculosis Screening and Visualization", Scientific Reports, vol. 9, no.1, 2019.

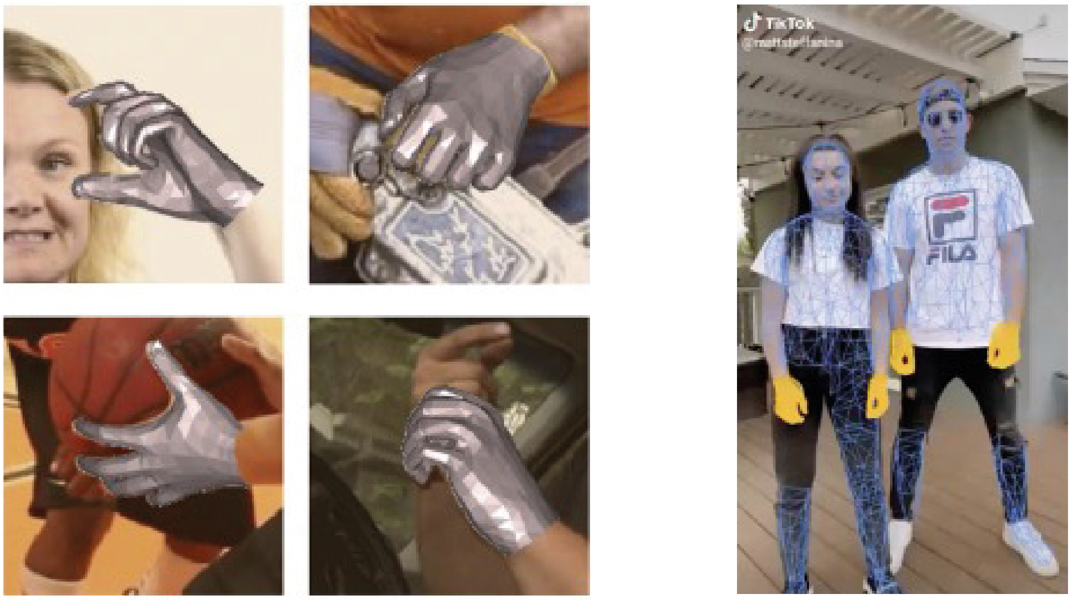

Figure 1, Examples of complex 3D hand poses reconstructed from 2D images in the wild (Figure from [1]) and a demo presented at CVPR 2020.

[5] P. Wenzel, R. Wang, N. Yang, Q. Cheng, Q. Khan, L. von Stumberg, N. Zeller and D. Cremers, "4Seasons: A Cross-Season Dataset for Multi-Weather SLAM in Autonomous Driving", 2020, arXiv:2009.06364.

[6] F. Wimbauer, N. Yang, L. von Stumberg, N. Zeller and D Cremers, "MonoRec: Semi-Supervised Dense Reconstruction in Dynamic Environments from a Single Moving Camera", IEEE Conference on Computer Vision and Pattern Recognition (CVPR), 2021.

A Cross-Season Dataset for Multi-Weather SLAM in Autonomous Driving

The group of Daniel Cremers presented a novel data set covering seasonal and challenging perceptual conditions for autonomous driving [5]. Among other capabilities, it enables research on visual odometry, global place recognition, and map-based re-localization tracking. The data was collected in different scenarios and under a wide variety of weather conditions and illuminations, including day and night. This resulted in more than 350 km of recordings in nine different environments ranging from a multi-level parking garage to urban (including tunnels), countryside, and highway driving. Moreover, the team of Daniel Cremers developed self-supervised learning methods to recover dense and detailed reconstructions of the world around the car from a single car-mounted camera. [6]

New ERC Proof of Concept grant awarded to Michael Bronstein in 2020

Michael Bronstein was awarded the ERC Proof of Concept grant Hyperfoods, to explore the commercial application of graph-based deep learning methods for discovering drug-like molecules in food ingredients. The project, based on previous research of Michael Bronstein on drug repositioning, took a tasty twist through collaboration with the renowned Italian chef Bruno Barbieri, who prepared a series of recipes based on ingredients the team identified. Following an ERC Starting Grant, an ERC Consolidator Grant, and two ERC Proof of Concept Grants, Hyperfoods is Michael Bronstein's fifth grant from the European Research Council.

Figure 2, The group of Daniel Cremers scanned the Bavarian Minister-President Dr. Markus Söder with their 3D scanner. He received the print as a gift from TUM at the Bavarian High Tech Summit that took place in February 2020.

New ERC Advanced Grant SIMULACRON awarded to Daniel Cremers in 2020
Daniel Cremers started on his fifth ERC grant project, following an ERC Starting Grant, an ERC Consolidator Grant and two ERC Proof of Concept Grants. SIMULACRON is focused on inferring physical simulations of the observed world from videos. The project addresses the shortcoming that computer vision has been largely focused on recovering the 3D surface of observed objects, neglecting the underlying physical properties of the observed objects. Yet, recovering a complete physical model of an observed action should enable us to simulate this action so as to better extrapolate into the future allowing predictions of what will happen next.

Michael Bronstein received the Royal Academy of Engineering Silver Medal
for developing "pioneering methods of graph deep learning, a new class of AI algorithms allowing to perform machine learning on complex systems of relations of interactions such as molecules, biological interactomes, and social networks." ■

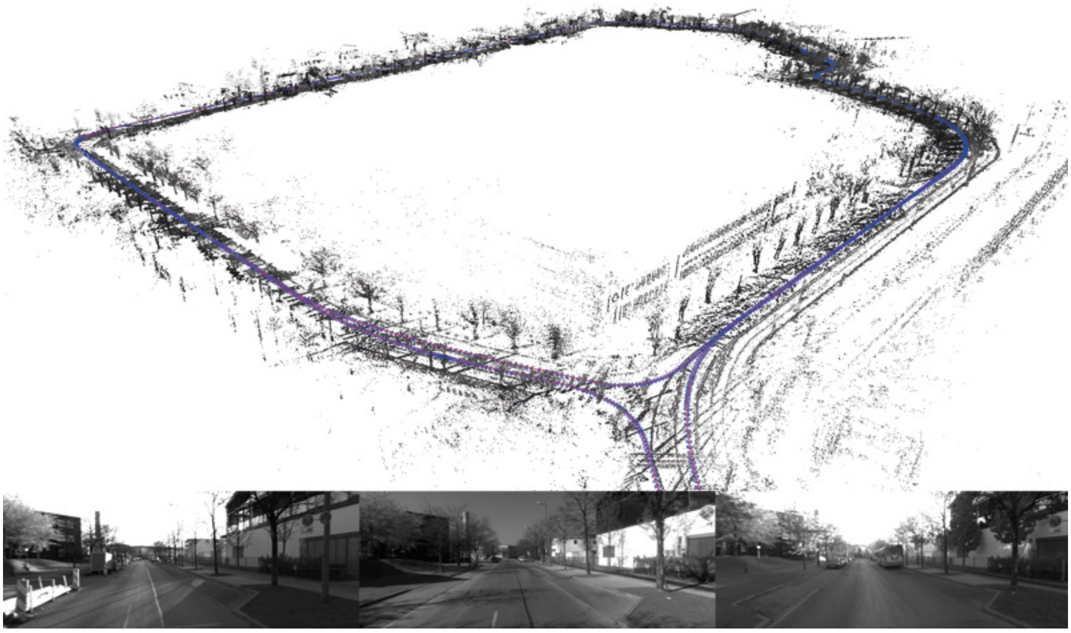

Figure 3, Example of data in the 4Seasons dataset.

Focus Group Modeling Spatial Mobility

Prof. Rolf Moeckel (TUM), Rudolf Mößbauer Tenure Track Professor | **Prof. Kelly J. Clifton (Portland University),** Alumna Hans Fischer Senior Fellow | **Dr. Ana Tsui Moreno Chou, Dr. Carlos Llorca Garcia, (TUM),** Postdoctoral Researchers | **Wei-Chieh Huang, Nico Kühnel, Alona Pukhova, Cat Silva, Qin Zhang, (TUM),** Doctoral Candidates | Host: Modeling Spatial Mobility, TUM

Prof. Rolf Moeckel

Prof. Kelly J. Clifton

Transport modeling and travel behavior research

The Focus Group Modeling Spatial Mobility (MSM) concentrates on integrated land use/transport modeling and travel behavior research. This includes developing models of land use, transportation, and related issues such as environmental impact and health. This also includes the spatial analysis of travel behavior and location choice of households and firms. The interaction between land use and transportation is of particular interest.

An integrated land use/transport modeling suite has been implemented for the Munich Metropolitan Area. The base year is 2011, and the model simulates land use and travel behavior through 2050. The study area consists of 444 municipalities with a population of 4.5 million. The study area has been delineated on the basis of commuter flows. The size of the study area was chosen because of long distances many people commute, motivated in part by the rather high cost of living in Munich. The modeling suite consists of the land use model SILO, the travel demand model MITO, and the assignment model MATSim. The former two were developed from scratch by this research group, and the latter was developed at ETH Zurich and TU Berlin. All three models are built as agent-based models that simulate individual households and persons.

In cooperation with Hans Fischer Senior Fellow Kelly Clifton from Portland State University, we further integrated the existing modeling suite with the pedestrian model MoPeD. MoPeD has been reestimated with Munich data and integrated with the above-described SILO/MITO/MATSim modeling suite. All models developed by this research group are open source under the GNU license and provided free of charge at https://github.com/msmobility. Interested users are welcome to download, use, and further develop these models. As far as legally possible, data to run these models are shared as well.

Complementing this work is the exploration of walking behaviors and the links to health outcomes using novel data sources. The emergence of longitudinal, location-based data offers the potential to understand the variability of individual activity and travel patterns. Recent studies have found that people have a large variability in daily travel behavior [1, 2]. The level of variability could be quite different when analyzed at different temporal scales. Most of the recent studies have focused on the daily or weekly level [3-5], but few have had the opportunity to observe variability at the monthly, seasonal, and annual scales due to the lack of longitudinal data. Google Location History (GLH) data, as a novel data source, can provide a rich data set in travel

[1] E. Heinen and K. Chatterjee, “The same mode again? An exploration of mode choice variability in Great Britain using the National Travel Survey”, Transportation Research Part A: Policy And Practice, vol. 78, pp. 266-282, 2015.

[2] C. Raux, T. Ma and E. Cornelis, “Variability in daily activity-travel patterns: the case of a one-week travel diary”, European Transport Research Review, vol. 8, no. 4, 2016.

[3] O. Järv, R. Ahas and F. Witlox, “Understanding monthly variability in human activity spaces: A twelve-month study using mobile phone call detail records”, Transportation Research Part C: Emerging Technologies, vol. 38, pp. 122-135, 2014.

behaviors at a fine temporal scale over a long time period.

A survey was conducted to collect information about individuals' personal characteristics, household attributes, the occurrence of major life events, and volunteers' GLH data. The research aims at investigating travel regularity and irregularity based on GLH data for a small sample of individuals (N<30). The results show that individuals tend to have a regular start time of daily activity. On a monthly basis, people expend a relatively fixed amount of time on travel, but the daily travel time budget is less fixed. In addition, individuals have a high variability in walking time. Further analysis indicates that weekly walking time is highly dependent on personal characteristics (e.g., age, occupation, car ownership), temporal attributes (e.g., day of the week, weather condition and holiday), and spatial attributes of the home location (e.g., area type, activity density). ■

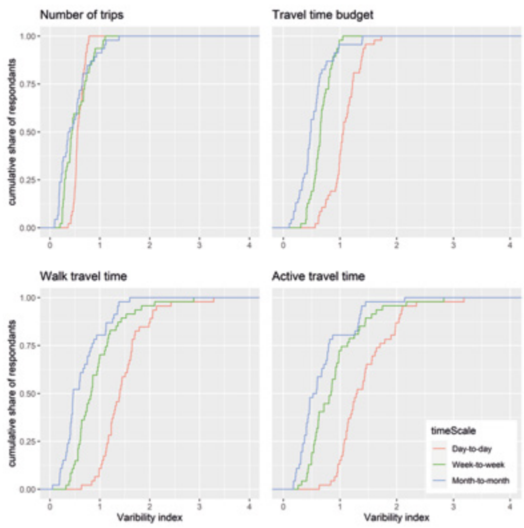

Figure 1, Variability distribution of all samples in different travel behaviors (number of trips, total travel time, walk travel time, and active walk+bike travel time) over various time periods (daily, weekly, monthly).

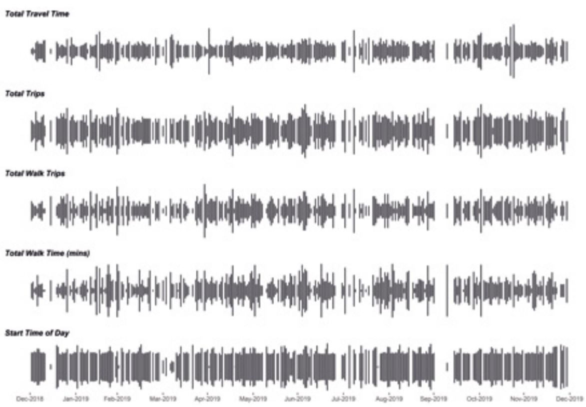

Figure 2, Individual travel "Cardiogram" – Day-to-day travel behavior based on the Google Location Data of one sample person. Each vertical line represents one day.

[4] M. González, C. Hidalgo and A. Barabási, "Understanding individual human mobility patterns", Nature, vol. 453(7196), pp. 779-782, 2008.

[5] K. Geurs, T. Thomas, M. Bijlsma and S. Douhou, "Automatic Trip and Mode Detection with Move Smarter: First Results from the Dutch Mobile Mobility Panel", Transportation Research Procedia, vol. 11, pp. 247-262, 2015.

Focus Group Multi-Messenger Astrophysics and the United Nations Open Universe Initiative

Prof. Paolo Giommi (Italian Space Agency), Alumnus Hans Fischer Senior Fellow | **Theo Glauch (TUM),** Doctoral Candidate | Host: **Prof. Elisa Resconi,** Experimental Physics with Cosmic Particles, TUM

Prof. Paolo Giommi

The connection between astrophysical neutrinos and blazars

The origin of the most energetic particles that travel our Universe is a century-old puzzle that still remains largely unsolved since their first detection in 1912 by Victor Hess, who was awarded the Nobel Prize for this discovery in 1936. Very large particle detectors have since been built to measure the flux of cosmic rays (protons and heavier nuclei), from our galaxy and beyond, with energies up to 100 million times higher than those achievable at the Large Hadron Collider at CERN.

Despite the enormous technical efforts that have been made, especially over the last few decades, many challenges remain in the identification of the sources where cosmic rays originate. This Focus Group has contributed to the global effort to understand where and how these particles are accelerated.

Cosmic rays include different types of particles and radiation, each with its own peculiarities:

- Highly energetic charged particles can only travel a limited distance before being absorbed by cosmic background radiation. In addition, they are deflected by magnetic fields and therefore lose the directional information that is necessary to connect them to their origin.
- Neutrinos can travel cosmological distances but barely interact with matter, which means that to detect them it is necessary to use extremely large detectors. Hence only few high-energy astro-physical neutrinos have been detected so far.
- Gamma rays are produced in a large variety of astrophysical processes, a large majority of which are not necessarily connected to neutrinos or charged cosmic rays.

It was only recently that the IceCube Neutrino Observatory at the South Pole, together with several ground and space telescopes, announced the detection of astrophysical neutrinos and gamma rays emanating from a source named TXS 0506+056. Our studies here at the TUM-IAS found that this object is very peculiar since it is not only a blazar, a powerful galaxy hosting a supermassive black hole and a jet of highly accelerated particles pointing toward us, but also is a special subtype — a masqueraded BL Lac — that has a very strong photon field that facilitates particle interactions.

Blazars have long been suspected to be promising sources of cosmic neutrinos, as they are thought to be capable of accelerating particles up to the highest observed energies. Our study of TXS0506+056 was very encouraging, so over the last year we applied the analysis methods that were derived to study this object to dozens of additional high-energy neutrinos detected by IceCube over a period of several years. This effort was successful as it led to the identification of several other candidates, evolving the status of our knowledge about neutrino sources from the case of a single object to that of a sample of 48 blazars, approximately 20 of which, according to our statistical study, are expected to be truly neutrino emitters.

While the case for a correlation between astrophysical neutrinos and blazars is mounting, we are only beginning to exploit the full potential of the available data. Now that we have secured a sample of neutrino candidate counterparts, we have started detailed studies of each object. We have done so by combining the increasing availability of multi-wavelength archival observations with fresh data collected by our collaborators using large optical telescopes, in an effort to identify possible specific characteristics of neutrino emitters and possibly understanding these peculiarities from a theoretical viewpoint. The first results of these activities have been published in two very recent papers. Other publications will follow in the near future.

A good part of the research carried out by this Focus Group was included in the thesis of doctoral candidate Theo Glauch, who very successfully completed his doctoral studies (summa cum laude) a few months ago. ■

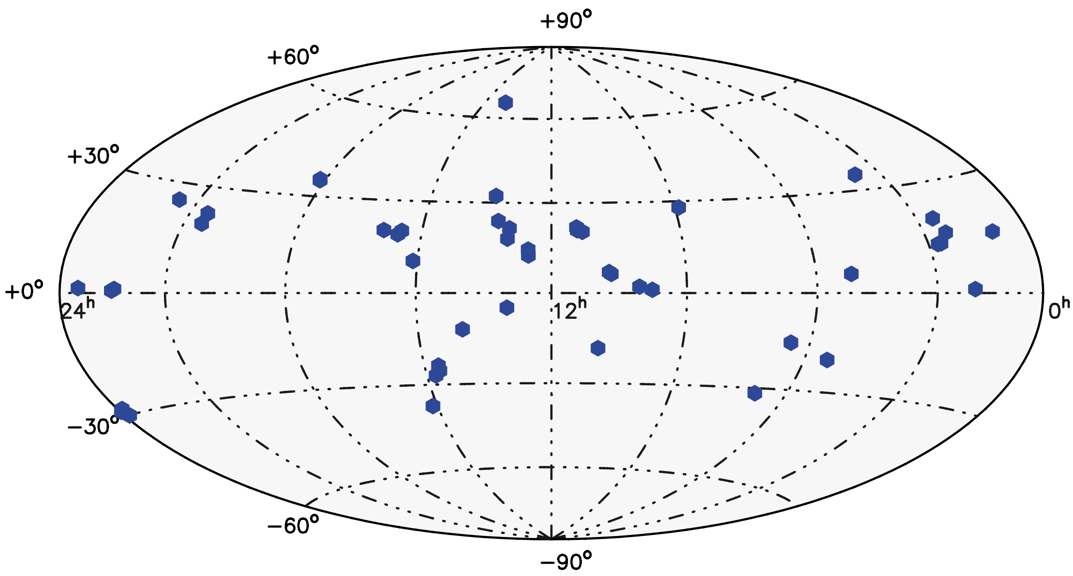

Figure 1, Sky map showing the position of the 48 candidate neutrino emitters selected by the Focus Group.

Focus Group Structural Membrane Biochemistry

Prof. Franz Hagn (TUM), Alumnus Rudolf Mößbauer Tenure Track Professor | **Dr. Inguna Goba (TUM),** Postdoctoral Researcher | **Melina Daniilidis, David Goricanec, Elisabeth Häusler, Kai Klöpfer, Kolio Raltchev, Laura Sperl, Andrea Steiner, (TUM),** Doctoral Candidates | Host: Structural Membrane Biochemistry, TUM

Prof. Franz Hagn

NMR-based structural biology of membrane proteins in a native lipid environment

The TUM-IAS Focus Group Structural Membrane Biochemistry works on the development of tools for the high-resolution structure determination of membrane proteins in a native lipid bilayer environment by nuclear magnetic resonance (NMR) spectroscopy and other structural methods. Since membrane proteins are very difficult to study with structural methods, advanced strategies are required.

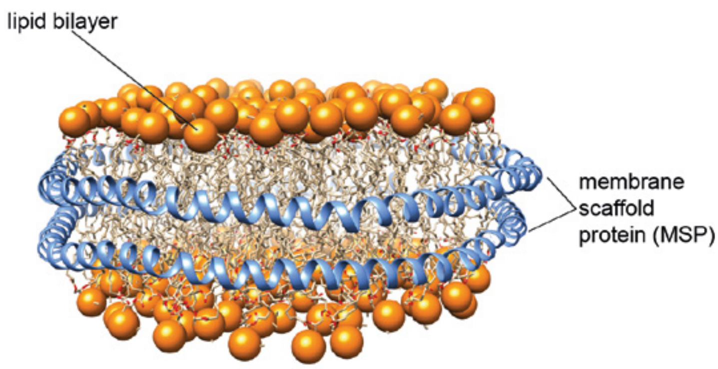

Figure 1, Structure of a lipid bilayer nanodisc. A patch of lipid bilayer membrane is surrounded by two copies of a so-called membrane scaffold protein (MSP). Highly stable and homogenous nanodiscs of various sizes have been successfully designed.

The development of native lipid bilayer mimetics is crucial to study sensitive membrane proteins and their complexes. In the last years, we were able to establish the use of so-called lipid nanodiscs for the investigation of the structure and dynamics of membrane proteins by solution-state NMR spectroscopy. Lipid nanodiscs consist of a patch of a lipid bilayer membrane encircled by two copies of a membrane scaffold protein (MSP) (Figure 1). To facilitate NMR and electron microscopy (EM) structural studies, we designed nanodiscs of different sizes, ranging from 6 to 26 nm in diameter [1]. To obtain better size homogeneity and stability of these nanoparticles, we applied protein ligation methods to produce circularized MSPs [2]. Furthermore, since sample homogeneity is essential for structural investigations, we developed a robust assay to probe and optimize the number of membrane proteins that are inserted into nanodiscs [3].

In addition to the development of lipid nanodiscs, we are dedicated to obtaining novel structural and functional insights on membrane proteins involved in signal transduction, apoptosis, and metabolite transport.

Membrane-anchored Bcl2 proteins play a major role in the regulation of apoptosis at the outer mitochondrial membrane. Pro-apoptotic members form pores or induce pore formation, leading to the release of pro-apoptotic factors. Anti-apoptotic members inhibit pore formation. We succeeded in producing these proteins in a lipid bilayer environment in high yields for structural studies by NMR [4] and were able to show that anti-apoptotic BclxL is located at the membrane surface, whereas pro-apoptotic, pore-forming members insert into the bilayer. This work will be the basis for studying these proteins and their complexes by structural methods in various states and in a lipid environment. ▸

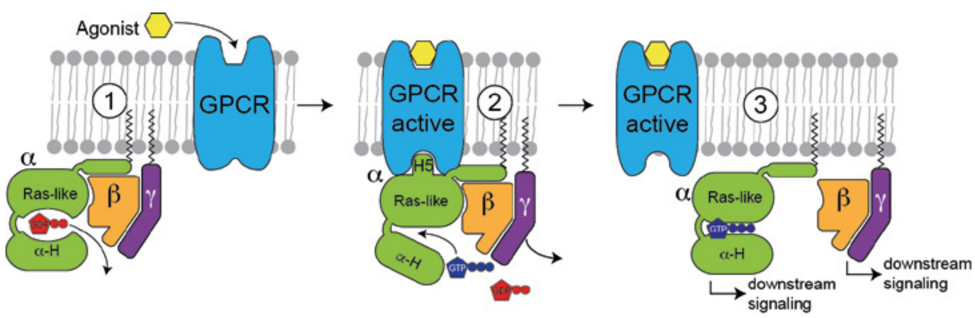

Figure 2, Structural and dynamical investigations of GPCR and G-protein activation. Using a stabilized neurotensin receptor obtained by directed evolution, we are able to investigate this system by high-resolution NMR and characterize the agonist-induced transition between the inactive and active states, as well as its impact on G-protein structure and dynamics.

[1] F. Hagn, M. Etzkorn, T. Raschle and G. Wagner, "Optimized phospholipid bilayer nanodiscs facilitate high-resolution structure determination of membrane proteins", Journal of the American Chemical Society, vol. 135, no. 5, pp. 1919-25, 2013; F. Hagn and G. Wagner, "Structure refinement and membrane positioning of selectively labeled OmpX in phospholipid nanodiscs", Journal of Biomolecular NMR, vol. 61, no.3-4, pp. 249-60, 2015; F. Hagn, M.L. Nasr and G. Wagner, "Assembly of phospholipid nanodiscs of controlled size for structural studies of membrane proteins by NMR", Nature Protocols, vol. 13, no. 1, 79-98, 2018; K. Klöpfer and F. Hagn, "Beyond detergent micelles: The advantages and applications of non-micellar and lipid-based membrane mimetics for solution-state NMR", Progress in Nuclear Magnetic Resonance Spectroscopy, vol. 114-115, pp. 271-283, 2019.

[2] M. L. Nasr et al., "Covalently circularized nanodiscs for studying membrane proteins and viral entry", Nature Methods, vol. 14, no. 1, pp. 49-52, 2017; J. Miehling, D. Goricanec and F. Hagn, "A Split-Intein-Based Method for the Efficient Production of Circularized Nanodiscs for Structural Studies of Membrane Proteins", ChemBioChem, vol. 19, no. 18, pp. 1927-1933, 2018.

[3] E. Häusler et al., "Quantifying the insertion of membrane proteins into lipid bilayer nanodiscs using a fusion protein strategy", Biochimica et Biophysica Acta – Biomembranes, vol. 1862, no. 4, pp. 183190, 2020.

[4] K. Raltchev, J. Pipercevic and F. Hagn, "Production and Structural Analysis of Membrane-Anchored Proteins in Phospholipid Nanodiscs", Chemistry, vol. 24, no. 21, pp. 5493-5499, 2018.

[5] I. Goba et al., "Probing the Conformation States of Neurotensin Receptor 1 Variants by NMR Site-Directed Methyl Labeling", ChemBioChem, vol. 22, no. 1, pp. 139-146, 2021.

[6] M. Zhang et al., "Cryo-EM structure of an activated GPCR-G protein complex in lipid nanodiscs", Nature Structural & Molecular Biology, vol. 28, no. 3, pp. 258-267, 2021.

G-protein coupled receptors (GPCRs) and their associated G-proteins (Figure 2) represent another important membrane protein class where a native environment is crucial for functionality. GPCRs are very difficult to produce, especially for NMR. Using a stabilized GPCR (neurotensin receptor) obtained by directed evolution, we were able to study this important protein by NMR [5] and cryo-EM [6], and we were able to investigate the structural transition between the inactive and active states as well as the complex with a G-protein. Using NMR, we were also able to characterize the dynamical features a G-protein required for nucleotide exchange [7]. With these ongoing experiments, we will be able to define the structural hallmarks of GPCR activation, which will be of high interest for the design of novel small molecule inhibitors.

In a very recent study, we used NMR to determine the structure and functional features of the Alzheimer disease risk factor TREM2, a receptor on microglia cells in the brain that binds to Amyloid fibers and induces its clearance by phagocytosis [8]. The transmembrane domain of TREM2 is cleaved by the intramembrane protease γ-secretase. We show that the initial γ-secretase cleavage site is located in a dynamic region of TREM2. Disease-linked mutations in this region reduce its dynamics and lead to altered processing by γ-secretase. This study contributes to a better understanding of the substrate specificity of an intramembrane protease where recognition is based on structural and dynamical features (Figure 3).

With this toolset at hand, we are going to tackle challenging membrane protein systems in the future. A particular area of interest will be pore forming proteins as well as metabolite transporters in mammals and plants that are often difficult to characterize and consequently are only poorly explored. ■

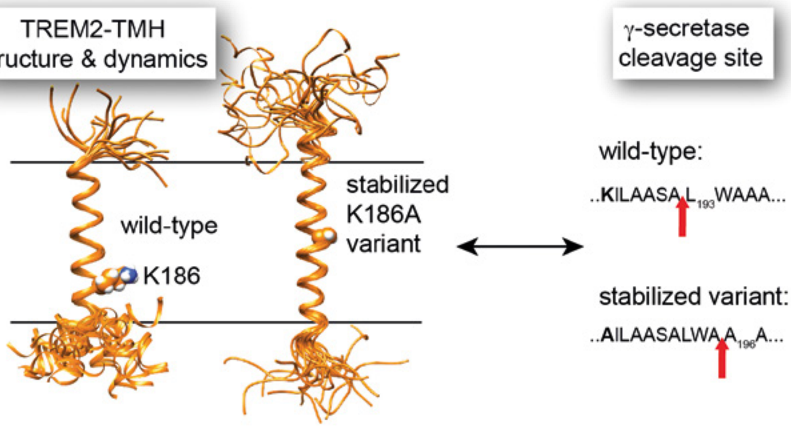

Figure 3, The TREM2 transmembrane helix (TMH) adopts a kinked structure with increased flexibility. Charge removal leads to TMH stabilization and reduced dynamics. Strikingly, these dynamical features match with the site of the initial γ-secretase cleavage event. These data suggest an unprecedented cleavage mechanism by γ-secretase where flexible TMH regions act as key determinants of substrate cleavage specificity.

[7] D. Goricanec and F. Hagn, "NMR backbone and methyl resonance assignments of an inhibitory G-alpha subunit in complex with GDP", Biomolecular NMR Assignments, vol. 13, no. 1, pp. 131-137, 2019; D. Goricanec et al., "Conformational dynamics of a G-protein alpha subunit is tightly regulated by nucleotide binding", Proceedings of the National Academy of Sciences of the United States of America, vol. 113, no. 26, pp. E3629-38, 2016; B. Zeng et al., "Structure, Function, and Dynamics of the Galpha Binding Domain of Ric-8A", Structure, vol. 27, no.7, pp. 1137-1147 e5, 2019.

[8] A. Steiner et al., "g-Secretase cleavage of the Alzheimer risk factor TREM2 is determined by its intrinsic structural dynamics", The EMBO Journal, vol. 39, no. 20, pp. e104247, 2020.

Focus Group Coding for Communications and Data Storage (COD)

Prof. Antonia Wachter-Zeh (TUM), Alumna Rudolf Mößbauer Tenure Track Professor | **Prof. Camilla Hollanti (Aalto University),** Alumna Hans Fischer Fellow | **Dr. Ragnar Freij-Hollanti, Dr. Nikita Polianskii, Dr. Sven Puchinger, (TUM),** Postdoctoral Researchers | **Haider Al Kim, Lukas Holzbaur, Hendongliang Liu, (TUM),** Doctoral Candidates | Host: Coding for Communications and Data Storage, TUM

Prof. Antonia Wachter-Zeh

Prof. Camilla Hollanti

Efficient repair and privacy in distributed storage systems

The focus of our group is on coding theory and its application in different settings.

In distributed storage, algebraic codes are used to protect the system against data loss in the event of a server failure. While this significantly reduces the storage overhead compared to the trivial solution of replicating files, one downside is that the process of recovering from a server failure must include a large number of surviving servers. To remedy this problem, tremendous attention has been directed toward the study of codes with locality, which make it possible to compensate for the likely event of a single or very few server failures while only contacting a small number of surviving nodes. The second downside to employing algebraic codes is the large amount of traffic between the servers required for the recovery of a failed server. To this end, researchers have proposed solutions that reduce this traffic. In [1] we are looking to get the best of both worlds and propose a combination of the two approaches. Here, any single server failure can be recovered from a small set of surviving nodes, while only transmitting the minimal amount of data possible.

Another major concern in today's connected world is the privacy of the users. However, it is not only the data of a given user that is subject to privacy concerns. Consider a distributed storage system offering a potentially large set of users access to a number of files such as movies, stock prices, or medical data. Unless it is an open public service, any user must be identifiable by the database. Consequently, if no additional precautions are taken, the database operator has full knowledge about the files requested by any given user. The problem of protecting the identity of the files requested by a user is referred to as private information retrieval (PIR). In [2] we introduce a new scheme based on cryptographic principles with the goal of providing privacy against an attacker (curious database) with access to all servers in the database. Another model that has received considerable attention in literature is a setting where the attacker only has access to a subset of servers in the database, which is not known to the user. Under this assumption it is possible to guarantee perfect privacy, and in [3] we investigate the best achievable rate, i.e., the minimal size of the total download required to privately obtain a file of a given size. Specifically, we consider the setting where the database employs an algebraic code (for protection against data loss) and the user is able to request specific functions of the shares of the data stored on each server. We also investigate PIR robust against adversaries, where some of the servers do not correctly serve the request but actively attempt to prevent the user from obtaining the correct file. Furthermore, we consider the case of symmetric privacy, where the database is interested in allowing the user to

[1] L. Holzbaur, S. Puchinger, E. Yaakobi and A. Wachter-Zeh, "Partial MDS codes with local regeneration", in 2020 IEEE International Symposium on Information Theory (ISIT), 2020, pp. 628-633.

[2] L. Holzbaur, R. Freij-Hollanti and C. Hollanti, "On the Capacity of Private Information Retrieval from Coded, Colluding, and Adversarial Servers", 2019 IEEE Information Theory Workshop (ITW), 2019.

[3] L. Holzbaur, C. Hollanti and A. Wachter-Zeh, "Computational Code-Based Single-Server Private Information Retrieval", in 2020 IEEE International Symposium on Information Theory (ISIT), 2020, pp. 1065-1070.

obtain the requested file but no information about any other file. This model is of practical interest in applications where, for example, the user is required to pay for each requested file.

In a classical setting, providing a user with privacy means that all potentially sensitive data or requests need to be hidden, as it is not possible to determine whether a curious database has read the information. However, in a quantum setting the rules change. A quantum system, e.g., a quantum bit (qubit), is a superposition of states that can be measured to obtain the contained information. This measurement consumes the qubit; in other words, a qubit can be measured exactly once. In a model considering attackers that are honest (i.e., need to conform to the protocol) but curious (i.e., interested in the private data or request), this can be exploited, as it is possible to guarantee that the information in a quantum system can only be obtained by destroying it.

In [4] we consider the problem of quantum PIR, in a setting similar to that of [3], but where servers respond with quantum systems. This allows for significantly increasing the communication rate and, in some cases, it is possible to enable private retrieval of a file with no communication overhead. ■

[4] M. Allaix, L. Holzbaur, T. Pllaha and C. Hollanti, “Quantum Private Information Retrieval from Coded and Colluding Servers”, IEEE Journal on Selected Areas in Information Theory, vol. 1, no. 2, pp. 599-610, 2020.

Figure 1, Illustration of a distributed storage system with locality.

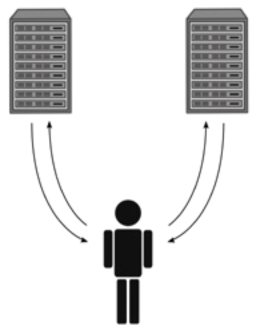

Figure 2, Illustration of PIR from multiple servers.

Focus Group Collective Quantum Dynamics

Prof. Michael Knap (TUM), Alumnus Rudolf Mößbauer Tenure Track Professor | **Dr. Alvise Bastianello (TUM),** Postdoctoral Researcher | **Annabelle Bohrdt, Johannes Feldmeier, Wilhelm Kadow, Clemens Kuhlenkamp, Alexander Schuckert, Elisabeth Wybo, Philip Zechmann, (TUM),** Doctoral Candidates | Host: Collective Quantum Dynamics, TUM

Prof. Michael Knap

Collective quantum dynamics: Teamwork of quantum particles

Matter appears in phases with distinct properties. Some materials become magnetic when they are cooled to low enough temperatures; others conduct power without dissipation – they turn into superconductors. Both of these phases are examples of collective quantum phenomena, arising due to the interactions between the electrons in a solid.

In condensed matter physics we have the luxury that we are able to write down the microscopic theory of any matter. The Hamiltonian describes the kinetic energy of electrons and ions and their mutual interactions. However, this microscopic theory is fundamentally insoluble because we are interested in its behavior for many quantum degrees of freedom. Instead of solving it, we should rather ask the question, “What are the emergent and universal properties of condensed matter?”

Over the recent years it became possible to create and explore non-equilibrium states of matter using novel quantum technology. These new experimental capabilities range from pump-probe spectroscopy in the solid state to quantum computers and quantum simulators. Big open questions are: What are the universal properties of quantum matter out of equilibrium? How do they manifest in experiments? How can we classify dynamical quantum phases?

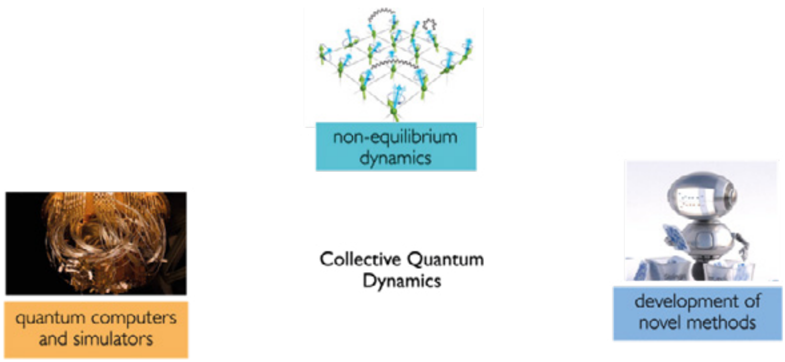

Figure 1, Overview of research activities.

Our Focus Group is working on collective quantum dynamics, which is a subfield of condensed matter theory. We are mainly interested in understanding the universal properties of non-equilibrium quantum states of matter (Figure 1). In order to elucidate the effects of strong interactions and emergent collective behavior, we develop both classical analytical and numerical methods, exploit artificial intelligence and machine learning, and develop algorithms for quantum computers. An important factor of our research is also its immediate relevance for experiments, which leads to a close collaboration with experimental groups all over the world.

Universality out of equilibrium: Emergent hydrodynamics

Understanding the fundamental mechanism of how non-equilibrium states relax toward thermal equilibrium has fascinated scientists for centuries. Ludwig Boltzmann derived his famous transport equation based on the statistical behavior of non-equilibrium states. Later, the term arrow of time was coined to describe the asymmetry of the flow of events that is rooted in the second law of thermodynamics. How macroscopic dynamics emerges from the microscopic, reversible physics is a long-standing question. A common anticipation is that effective classical hydrodynamics of a few conserved quantities emerges also at late times for complex, isolated quantum systems, as strong interactions effectively scramble quantum degrees of freedom. Over the past years, we have developed novel techniques to study the emergence of conventional diffusion in strongly interacting lattice bosons [1] and the emergence of fracton hydrodynamics in magnets with charge and dipole conservation [2]. (See Figure 2.) ▸

[1] A. Bohrdt, C. B. Mendl, M. Endres and M. Knap, “Scrambling and thermalization in a diffusive quantum many-body system”, New Journal of Physics, vol. 19, 063001, 2017.

[2] J. Feldmeier, P. Sala, G. de Tomasi, F. Pollmann and M. Knap, “Anomalous Diffusion in Dipole- and Higher-Moment Conserving Systems”, Physical Review Letters, vol. 125, 245303, 2020.

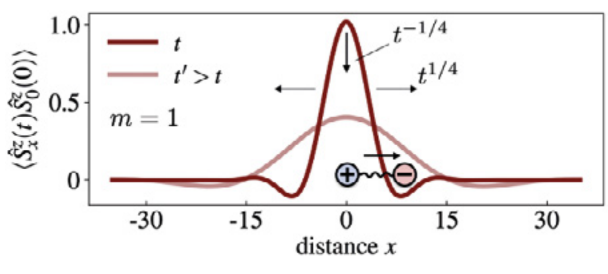

Figure 2, Fracton hydrodynamics [2].

[3] P. Bordia, H. Lüschen, S. Scherg, S. Gopalakrishnan, M. Knap, U. Schneider and I. Bloch, "Probing Slow Relaxation and Many-Body Localization in Two-Dimensional Quasi-Periodic Systems", Physical Review X 7, 041047, 2017.

[4] B. Chiaro, C. Neill, A. Bohrdt, M. Filippone et al., "Growth and preservation of entanglement in a many-body localized system", arXiv:1910.06024.

Absence of equilibration: Disordered many-body systems

Disorder has a drastic effect on transport properties. In the presence of a random potential, a system of interacting electrons can become insulating; this phenomenon is known as many-body localization. However, even beyond the vanishing transport such systems have very intriguing properties. For example, many-body localization describes an exotic phase of matter that is robust to small changes in the microscopic Hamiltonian. Moreover, fundamental concepts of statistical mechanics break down in the many-body localized phase. In a collaboration with Immanuel Bloch's group, we analyzed properties of the many-body localization transition with a quantum simulator of cold atoms [3]. With the Google quantum computing team, we have characterized the local integrals of motion of many-body localized superconducting qubits [4]. Due to the ability to create quantum superpositions of the qubits, a detailed investigation of the fundamental constituents was possible.

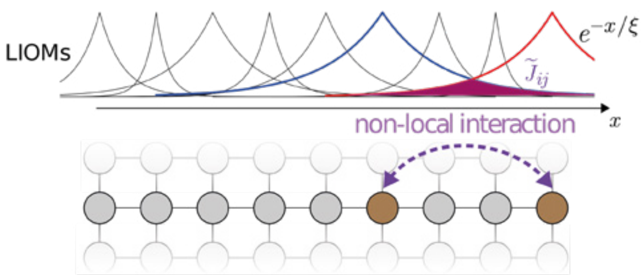

Figure 3, Effective interactions between localized integrals of motion [4].

New probes of correlated quantum states

Quantum simulators offer the opportunity to develop novel probes to study the effects of correlations in interacting many-body systems. We have pioneered the study of quantum snapshots using machine learning techniques, which has developed into an active field of research [5]. Recent developments made it possible to realize the doped Fermi-Hubbard model, which is believed to describe the essential physics of high-temperature superconductors. We have made significant steps toward gaining a deeper understanding of this model using high-end numerical techniques, semi-analytical theory, and collaborations involving cold atom experiments [6]. Our work has helped to establish a parton theory of charge carriers in the 2D Hubbard model which captures essential features in a large regime of its phase diagram. The methods we developed enable a detailed comparison of different candidate theories with experimental and numerical results. ■

[5] A. Bohrdt, C. S. Chiu, G. Ji, M. Xu, D. Greif, M. Greiner, E. Demler, F. Grusdt and M. Knap, "Classifying Snapshots of the Doped Hubbard Model with Machine Learning", Nature Physics, vol. 15, 921, 2019.

[6] C. S. Chiu, G. Ji, A. Bohrdt, M. Xu, M. Knap, E. Demler, F. Grusdt, M. Greiner and D. Greif, "String patterns in the doped Hubbard model", Science, vol. 365, issue 6450, pp. 251-256, 2019.

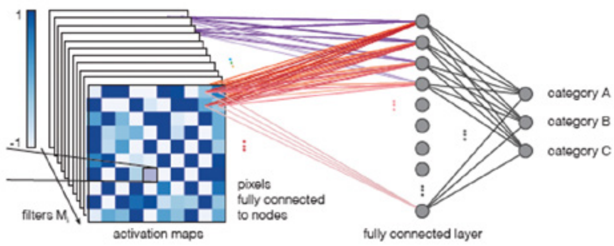

Figure 4, A neural network trained to distinguish quantum theories [5].

Focus Group Theory of Complex Quantum Systems

Prof. Robert König (TUM), Alumnus Rudolf Mößbauer Tenure Track Professor | **Dr. Lisa Hänggli, Dr. Cambyse Rouzé, (TUM),** Postdoctoral Researchers | **Margret Heinze, Alexander Kliesch, (TUM),** Doctoral Candidates | Host: Theory of Complex Quantum Systems, TUM

Prof. Robert König

From quantum communication to computation

Since 2015, the Focus Group Complex Quantum Systems has been studying to what extent quantum effects can be exploited to enhance information processing. We have made a variety of contributions to quantum information theory and the theory of quantum computation. Our work provides new fundamental physical limits to communication using quantum systems, as well as novel ways of harnessing quantum effects to enhance computation.

Our research focuses on the question of whether and how imperfect quantum devices can provide robust information-processing primitives. To this end, we have studied the design and use of error-correcting codes both for qubits as well as bosonic (infinite-dimensional) quantum systems. In addition to finding near-optimal codes for communication over so-called additive bosonic noise channels, we have shown how to render certain computational schemes for near-term quantum computing devices fault-tolerant.

Recent contributions of our Focus Group advance the state-of-the-art of our current understanding of the potential of small- to intermediate-scale quantum devices. This is becoming particularly important with the currently accelerating experimental developments in this area.

Unconditional computational quantum advantage with near-term devices

Arguably the most significant result we have found is an unconditional separation between two analogously defined quantum and classical computational models: It is the first complexity-theoretic result that provides a rigorous proof that quantum devices are superior to classical ones without relying on unproven hardness conjectures.

The result immediately raises the question of whether and how such a so-called quantum advantage can be observed in the lab. We have made progress in this direction by establishing schemes relying on noisy components (qubits and gates, respectively) only [1]. We are now seeking even simpler schemes that could be realized more easily, and more generally working toward a theory of computation with near-term quantum devices. Such devices are typically small and subject to noise. Dealing with these limitations and understanding their impact remains a major challenge.

Toward practically useful quantum algorithms

Demonstrating that quantum devices can solve certain problems more efficiently or using fewer resources than comparable clas-

[1] S. Bravyi, D. Gosset, R. König and M. Tomamichel, “Quantum advantage with noisy shallow circuits”, Nature Physics, vol. 16, pp. 1040-1045, 2020.

sical devices is important as a proof-of-principle on the road towards quantum computing. Ultimately, though, one would like to use quantum devices to tackle real-world problems of practical relevance.

Our present work is aimed at finding new ways of using quantum devices for ubiquitous problems such as combinatorial optimization. While there are some corresponding proposals, assessing their merits is often challenging in the absence of an actual device. It is therefore important to develop classical simulation tools and new analytical techniques to assess the performance of quantum algorithms. Ideally, one would like to establish performance guarantees for generic instances when comparing a quantum algorithm to the best known, or best possible, classical efficient algorithm.

In [2], we have established the first upper bounds on approximation ratios achievable by near-term realizations of the so-called quantum approximate optimization algorithm (QAOA). This is a popular proposal intended to solve combinatorial optimization problems. Unfortunately, our results demonstrate that for generic instances, the famous (classical) Goemans-Williamson algorithm outperforms the QAOA. At the same time, we proposed a modification of the quantum algorithm that overcomes its current limitations. Preliminary numerical evidence suggests that this modified algorithm (which we call the recursive quantum approximate optimization algorithm) has significant potential. Future work will seek to establish performance guarantees for such approaches. ■

[2] S. Bravyi, A. Kliesch, R. König and E. Tang, "Obstacles to State Preparation and Variational Optimization from Symmetry Protection", Physical Review Letters, 125 (26), 260505, 2020.

[3] L. Hänggli, M. Heinze and R. König, "Enhanced noise resilience of the surface-GKP code via designed bias", Physical Review A, 102, 052408, 2020.

a) **b)**

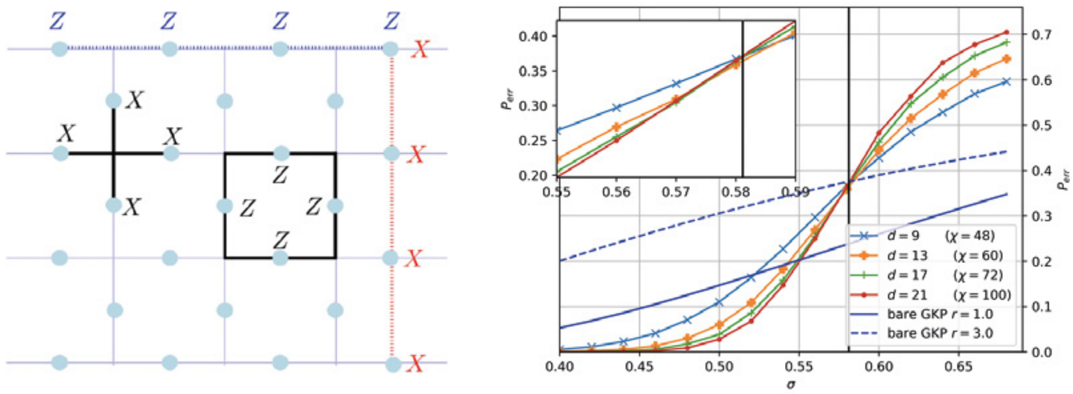

Figure 1, a) Surface-GKP-codes (where GKP stands for Gottesman, Kitaev and Preskill) encode a single logical qubit into an array of bosonic modes. **b)** Error thresholds of surface-GKP codes. Using large-scale simulations with hundreds of modes, we demonstrated in [3] that the introduction of asymmetry boosts fault-tolerance: It leads to a reduction of the logical error probability. Our construction yields bosonic codes with the best currently known error thresholds as measured by the tolerable displacement noise standard deviation.

Focus Group Synthetic Biochemistry

Prof. Kathrin Lang (TUM), Alumna Rudolf Mößbauer Tenure Track Professor | **Marko Cigler, Maximilian Fottner, Marie-Lena Jokisch, Kristina Krauskopf, Susanne Mayer, Anton Murnauer, Marie-Kristin von Wrisberg, Vera Wanka, (TUM),** Doctoral Candidates | Host: Synthetic Biochemistry, TUM

Prof. Kathrin Lang

Expanding the genetic code: novel chemistries in living systems

The Focus Group for Synthetic Biochemistry was part of the TUM-IAS family from April 2014 until April 2020, during which time I was a Rudolf Mößbauer Fellow at the TUM-IAS and appointed as a W2 Tenure Track Assistant Professor in the Department of Chemistry at TUM. In April 2020 I was tenured as a W3 Associate Professor at TUM, and since April 2021 I am Full Professor for Chemical Biology at ETH Zurich, Switzerland.

[1] K. Lang and J. W. Chin, "Cellular incorporation of unnatural amino acids and bioorthogonal labeling of proteins", Chemical Reviews, vol. 114, no. 9, pp. 4764-806, 2014.

[2] K. Krauskopf and K. Lang, "Increasing the chemical space of proteins in living cells via genetic code expansion", Current Opinion in Chemical Biology, vol. 58, pp. 112-120, 2020.

[3] J. W. Chin, "Expanding and reprogramming the genetic code", Nature, vol. 550, no. 7674, pp. 53-60, 2017.

Our lab's research interests lie in the fascinating interdisciplinary area between chemistry and biology, applying concepts from organic chemistry and protein engineering to study and manipulate biological systems. Very much in the spirit of Richard P. Feynman, who coined the saying "What I cannot create, I do not understand," we are convinced that an interdisciplinary approach between chemistry and biology is not only uniquely placed to increase our understanding of biological processes by developing tools to control biological activities, but is also indispensable for designing novel artificial biological pathways and ultimately even for engineering artificial living systems.

Our group has been especially active in developing and advancing approaches to endow biomolecules with new chemical reactivities within their physiological environment [1, 2]. In contrast to more traditional approaches of organic chemistry, our focus lies therefore not on creating ever more complex reactions in defined, laboratory settings, but on striving to discover novel reactivities that are amenable to and selective within the most complex environment: the living cell. In particular, we are interested in enabling and promoting methods to expand the genetic code by introducing artificial non-canonical amino acids (ncAAs) into proteins and in developing new in vivo chemistries to endow proteins with new chemical moieties, a combination that is ideally suited to addressing unmet challenges in studying and manipulating biological processes [2, 3].

Nature uses a limited set of 20 amino acids to synthesize proteins. In recent years it has become possible to genetically encode an expanded set of designer amino acids with tailored chemical and physical properties into proteins in bacteria and eukaryotes by reprogramming the genetic code and rewiring the translational machinery [3]. These strategies have started to have a big impact on biological studies, as they enable diverse applications including approaches for imaging and probing proteins, controlling and manipulating protein activity, and engineering and designing new protein functions and protein therapeutics.

My group has contributed over the last seven years to this exciting endeavor and has developed new tools for investigating and modulating molecular networks in living cells. We take a multidisciplinary approach and combine organic chemical, biochemical, biophysical, structural, and cell biological techniques to unravel the complex world of biology.

In my time as a Rudolf Mößbauer Fellow at the TUM-IAS and Professor at TUM, I have developed a vigorous research program to expand the genetic code and endow proteins with new functionalities in living cells. To expand the chemical space and functional repertoire of proteins within living cells, we have developed and applied rational and evolutionary approaches aimed at engineering components of the protein translational machinery that enable the site-specific incorporation of custom-designed ncAAs acids into proteins in living cells. By equipping proteins with functionalities beyond the ones provided by the 20 natural amino acids, we have contributed to three main research areas: ▸

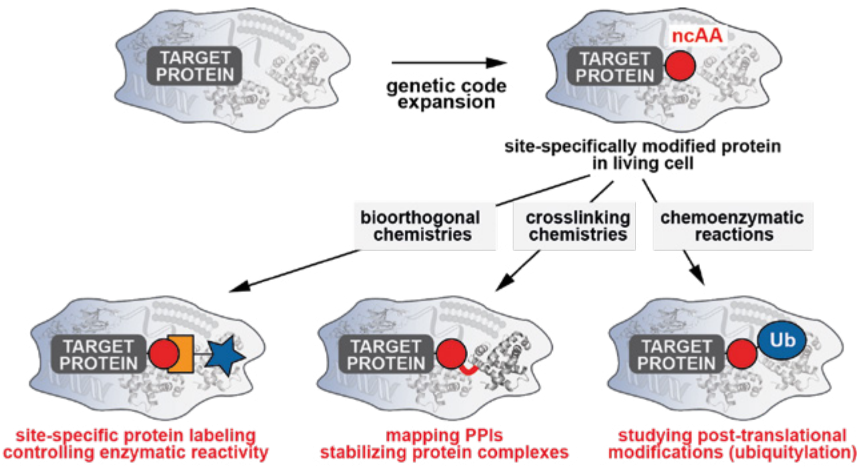

Figure 1, Genetic code expansion approaches allow the site-specific introduction of non-canonical amino acids (ncAAs) into proteins in living cells. Introduction of bioorthogonal moieties allows the site-specific labeling of proteins within their physiological environment with biophysical probes. Alternatively, incorporation of ncAAs bearing crosslinking groups makes it possible to study protein-protein interactions (PPIs) and to stabilize transient protein complexes. Finally, ncAA-modified proteins make it possible to access complex post-translational modifications (e.g., ubiquitylation) via engineered chemoenzymatic reactions.

1

Bioorthogonal chemistries for studying and controlling protein activity: We have developed approaches to site-specifically endow proteins with ncAAs bearing bioorthogonal handles that allow the selective and rapid functionalization of proteins within living cells under physiological conditions. This has enabled us not only to image and probe proteins in vivo with various biophysical probes, but also to control and manipulate their enzymatic activity within their physiological environment [1] [4–11].

2

Chemical tools to validate and manipulate protein-protein interactions: A second research line in our lab involves development of crosslinking chemistries to study and validate protein-protein interactions (PPIs). PPIs are central to many biological processes. A considerable challenge, however, consists in understanding and deciphering when and how proteins interact, and this can be particularly difficult when interactions are weak and transient. In recent years we have developed approaches to site-specifically install ncAAs that upon a certain trigger (proximity or light) form covalent interactions with proteins in their vicinity. This allows us to covalently trap PPIs and thereby identify novel interactors, and to stabilize low-affinity and transient protein complexes to pioneer their structural elucidations [12–15].

[4] K. Lang and J. W. Chin, “Bioorthogonal reactions for labeling proteins”, ACS Chemical Biology, vol. 9, no. 1, pp. 16-20, 2014.

[5] K. Lang et al., “Genetic Encoding of bicyclononynes and trans-cyclooctenes for site-specific protein labeling in vitro and in live mammalian cells via rapid fluorogenic Diels-Alder reactions”, Journal of the American Chemical Society, vol. 134, no. 25, pp. 10317-10320, 2012.

[6] K. Lang et al., “Genetically encoded norbornene directs site-specific cellular protein labelling via a rapid bioorthogonal reaction”, Nature Chemistry, vol. 4, no. 4, pp. 298-304, 2012.

[7] T. S. Elliott et al., “Proteome labeling and protein identification in specific tissues and at specific developmental stages in an animal”, Nature Biotechnology, vol. 32, no. 5, pp. 465-72, 2014.

[8] C. Uttamapinant et al., “Genetic code expansion enables live-cell and super-resolution imaging of site-specifically labeled cellular proteins”, Journal of the American Chemical Society, vol.137, no. 14, pp. 4602-4605, 2015.

[9] Y. H. Tsai, S. Essig, J. R. James, K. Lang and J. W. Chin, “Selective, rapid and optically switchable regulation of protein function in live mammalian cells”, Nature Chemistry, vol. 7, pp. 554-561, 2015.

[10] S. Mayer, S. and K. Lang, “Tetrazines in Inverse-Electron-Demand Diels–Alder Cycloadditions and Their Use in Biology”, Synthesis, vol. 49, no. 4, pp. 830-848, 2017.

3

Novel tools to generate and study post-translational modifications: In a third research line we are pioneering approaches in which site-specifically introduced ncAAs serve as a platform for tailored, chemoenzymatic reactions to site-specifically ubiquitylate target proteins both in vitro and in vivo [16]. Ubiquitylation represents a post-translational modification that controls almost every process in eukaryotic cells and has as such attracted considerable interest and promise as a therapeutic target. We have very recently been awarded an ERC Consolidator Grant to further develop an interdisciplinary chemical and synthetic biology platform that will provide unique insight into ubiquitylation and will lay the foundation for identifying new drug targets within the ubiquitin system.

Looking ahead to the future, our aims lie in understanding mechanisms of complex biological processes such as ubiquitylation through the application of synthetic molecules with tailored functions and properties. In particular, we plan to extend approaches for endowing proteins with new chemical moieties and thereby re-engineering and designing new protein functions. This will open up many possibilities for synthetic biology, drug design, biomaterials, and gene therapy. ■

[11] S. V. Mayer, A. Murnauer, M. K. von Wrisberg, M. L. Jokisch and K. Lang, "Photo-Induced and Rapid Labeling of Tetrazine-Bearing Proteins via Cyclopropenone-Caged Bicyclononynes", Angewandte Chemie International Edition in English, vol. 58, no. 44, pp. 15876-15882, 2019.

[12] T. A. Nguyen, M. Cigler and K. Lang, "Expanding the Genetic Code to Study Protein-Protein Interactions", Angewandte Chemie International Edition in English, vol. 57, no. 44, pp. 14350-14361, 2018.

[13] M. Cigler et al., "Proximity-Triggered Covalent Stabilization of Low-Affinity Protein Complexes In Vitro and In Vivo", Angewandte Chemie International Edition in English, vol. 56, no. 49, pp. 15737-15741, 2017.

[14] S. Tremel et al., "Structural basis for VPS34 kinase activation by Rab1 and Rab5 on membranes", Nature Communications, vol. 12, no. 1, 1564, 2021.

[15] J. Du et al., "Rab1-AMPylation by Legionella DrrA is allosterically activated by Rab1", Nature Communications, vol. 12, no. 1, 460, 2021.

[16] M. Fottner et al., "Site-specific ubiquitylation and SUMOylation using genetic-code expansion and sortase", Nature Chemical Biology, vol. 15, no. 3, pp. 276-284, 2019.

Focus Group Neuromorphic Computing

Prof. Hai (Helen) Li (Duke University), Alumna Hans Fischer Fellow | **Shuhang Zhang (TUM),** Doctoral Candidate | Host: **Prof. Ulf Schlichtmann,** Electronic Design Automation, TUM

Prof. Hai (Helen) Li

Toward reliable and efficient neuromorphic computing

Neuromorphic computing aims to utilize very large-scale integration (VLSI) systems to mimic biological architectures, thus achieving cognitive functionalities and self-learning abilities. In the past decades, neuromorphic computing was mainly conducted at the software level, especially with neural networks.

Figure 1 shows the basic structure of a neural network. The nodes represent neurons, and connections represent the relations between neurons in different layers. In a neural network, the output of a neuron is a function of the inputs and the connection weights. However, the traditional computing architecture (Von Neumann architecture) cannot support neural networks efficiently because of the processing time mismatch between CPU and memory. This phenomenon is also known as the “memory wall.” Therefore, to improve the performance of neuromorphic computing, the hardware should also be carefully reshaped.
With traditional CMOS technology, it is hard to overcome the problem, but the invention of memristor technology allows us to fundamentally change the computing platform, because memristors can be used as both processing and memory units. Also, the scalability and power-efficiency of memristors make them a promising candidate for high computing

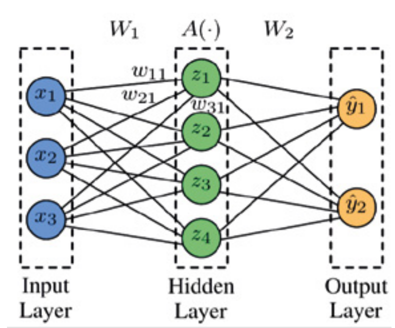

Figure 1, Basic structure of a neural network.

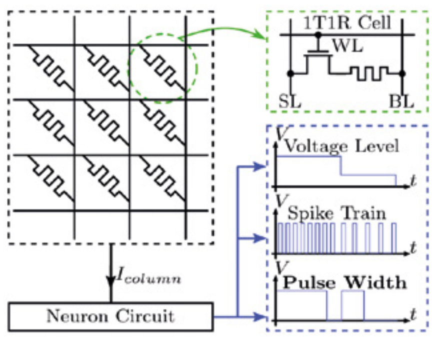

Figure 2, RRAM crossbar and various types of neuron formats.

density and efficiency. As shown in Figure 2, memristors sit on the crosspoints of horizontal wordlines and vertical bitlines in a crossbar structure, representing the synapses between neurons. These memristors (synapses) are programmed into different conductances to represent different neuron connections. The neuron circuits receive activations delivered by these memristors and generate voltage signals transferred to the next layer. In this way, neural networks are implemented with memristor technology.

We have been exploring memristor-based neural network accelerators in a bottom-up approach. First, we have focused on the reliability problem of memristor devices and proposed a software and hardware co-optimization framework. Furthermore, to improve the efficiency of signal transfer, we have designed a new neuron circuit. Finally, we have demonstrated a novel architecture based on the connection information within crossbars, which can significantly improve performance.

Like traditional CMOS devices, memristors also suffer from common reliability problems, such as aging and thermal issues. Aging affects the lifetime of manufactured devices, and the thermal issue causes unexpected results and accelerates the aging process. Therefore, we propose an effective optimization framework that counters both aging and thermal problems at both software and hardware levels. During the software training phase, we include the aging and thermal information in the cost function to average aging and thermal effects. Afterwards, we utilize a row-column swapping method to further balance the aging and thermal issues.

In neuromorphic computing, neuron circuit design is also important, and this affects computing efficiency. In the traditional neuron designs shown in Figure 2, they receive the activation from memristors, and then they generate voltage levels or spikes to the following neurons. In these formats, the transferring latency is large and requires additional processing units, leading to extra area requirements and power consumption. We have proposed a novel neuron design we call the "time neuron." Upon receiving activation, the time neuron encodes it into a variable-width pulse, which then can be directly transferred to the following neurons.

Furthermore, we have also proposed a novel computing mechanism, which is based on the connections of different data instead of the current information within crossbars, as shown in Figure 3. After writing data into crossbars, the calculation results have already been embedded in these crossbars. We then just need to read them out. In this way, we can avoid the complex computing phase used by the traditional approaches. Besides, this connection-based design can form a larger equivalent crossbar without changing the output current range, which avoids the re-design of neuron circuits.

In conclusion, we have studied neuromorphic computing intensively at different levels. Our results can improve practical applications in the real world. We hope that they will also inspire other researchers to generate new ideas. Currently, we plan to continue to explore in two different directions. The first direction is the software training algorithm for neural networks. To fully benefit from the proposed connection-based design, a specifically designed software training algorithm is necessary. The other direction for future research is applying our proposed methods and algorithms on real devices to examine their efficiency in the real world. ■

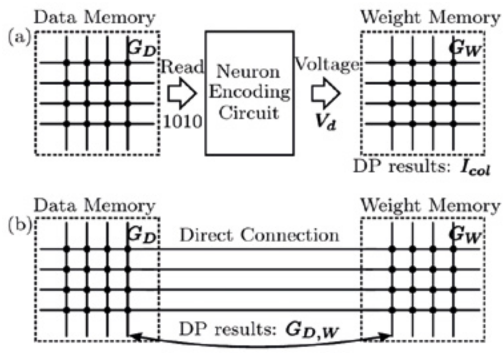

Figure 3, (a) Current-based and (b) connection-based computing frameworks.

Focus Group Improving Breast Cancer Care Through Cognitive and Physcial Interventions Leveraging Advanced Technolgies

Prof. Nina A. Mayr (University of Washington), Alumna Anna Boyksen Fellow | Host: Prof. Stephanie E. Combs, Radiation Oncology, TUM

Prof. Nina A. Mayr

Heart protection from toxicity and enhanced wellbeing in breast cancer therapy

Heart toxicity challenge in breast cancer therapy

In patients with breast cancer, the most common cancer in women, radiation therapy to the breast or chest is frequently needed to control the tumor and improve the chance of survival. Despite advances radiation therapy for breast cancer, there are two challenges: 1. Cardiac injury from scattered radiation to the heart that can result in long-term morbidity and mortality in breast cancer survivors [1, 2], and 2. Patients' cognitive distress and anxiety that often interfere with their ability to tolerate novel heart-protecting radiation therapy techniques aimed at reducing the radiation dose to the heart. The aim of the Focus Group is to develop and test innovative approaches to alleviate both these challenges.

Advanced radiation delivery technologies and the human factor

Respiratory motion management is the most promising such advanced technique for heart-protecting radiation therapy in breast cancer. By delivering radiation therapy in a highly targeted/focused technique and during an extended controlled deep inspiration breath hold (DIBH), greater physical separation between the radiation target (breast, chest wall) and the heart can be achieved. With greater distance of the heart from the target, the radiation dose spillage to the heart is reduced, and this dose reduction holds the promise to achieve better cardiac health in breast cancer survivors. DIBH requires the patient to perform a precisely timed and sustained voluntary breath hold for each daily radiation treatment in the three- to four-week course of treatment. However, the DIBH procedure is often poorly tolerated and poorly performed by patients, resulting in variable success; and clinical protocols of DIBH vary widely.

Patients who undergo radiation therapy for breast cancer generally experience significant cognitive distress and anxiety, augmented by the added burden of recovery from preceding surgery and chemotherapy. This is aggravated by the repetitive stringent treatment procedures demanded by advanced radiation techniques and the confining, threatening therapy equipment, which frequently intensifies patients' anxiety and leaves them unprepared and unable to cooperate with the treatment.

"High-tech and gentle-touch"

Our Focus Group has been investigating a new approach combining the novel heart-protecting (heart-sparing) radiation therapy technologies and techniques with targeted preparatory training and anxiety-reducing cognitive interventions that leverage physical conditioning for DIBH while promoting anxiety and stress reduction through rap-

[1] S. C. Darby, M. Ewertz, P. McGale, A. M. Bennet, U. Blom-Goldman, D. Brønnum, C. Correa, D. Cutter, G. Gagliardi, B. Gigante et al., "Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer", New England Journal of Medicine, vol. 368, no. 11, pp. 987-998, 2013.

[2] V. A. van den Bogaard, B. D. Ta, A. van der Schaaf, A. B. Bouma, A. M. , Middag, E. J. Bantema-Joppe, L. V. van Dijk, F. B. van Dijk-Peters, L. A. Marteij, G. Hl. de Bock et al., "Validation and Modification of a Prediction Model for Acute Cardiac Events in Patients With Breast Cancer Treated With Radiotherapy Based on Three-Dimensional Dose Distributions to Cardiac Substructures", Journal of Clinical Oncology, vol. 35, no. 11, pp. 1171-1178, 2017.

port, reframing, and relaxation techniques. We leverage this combined advanced technology ("high-tech") and integrative health ("gentle-touch") approach to improve patients' skill and compliance with radiation therapy procedures in DIBH, and to improve physical and emotional well-being, both and in the short term by alleviating physical and cognitive distress during cancer therapy, and in the long term by reducing therapy-induced cardiac toxicities.

DIBH training and cognitive interventions

Leveraging and synergizing the leading-edge technical advancements in breast cancer at TUM Radiation Oncology, embedded in the Comprehensive Cancer Center (CCC-M and RHCCC), the EU clinical trial environment, Molecular Cardiac Imaging, and Molecular Biology, the Focus Group has been working to apply novel patient-directed cognitive and training interventions in combination with the further developed advanced DIBH radiation therapy technologies and techniques to derive a cohesive integrated strategy for DIBH and heart dose optimization.

The TUM Radiation Oncology Team (Stephanie Combs, Jan Wilkens, Daniel Habermehl, Franz Pfeiffer, Markus Oechsner, Fridtjof Nüsslin, Kai Borm), is focused on understanding underlying mechanisms of radiation-induced cardiac toxicities and unraveling the relevance of dose to different heart structures [3-6]. The Focus Group's work builds on the TUM faculty's investigations aimed at understanding which heart sub-structures are the most critical targets for dose reduction to prevent cardiac toxicities [3].

Investigations at the University of Washington, Seattle, are exploring novel strategies to improve DIBH procedure performance by patients through coached patient self-training interventions [7, 8]. The team developed an in-advance coaching and preparatory home practice regimen that improved patients' ability to perform DIBH and further reduced the dose to the heart (maximal cardiac dose: 13.1 Gy), compared to patients who performed DIBH without coaching (19.4 Gy, p=0.004) [8]. The Focus Group's work also builds on the Alumna Fellow's prior investigations at Ohio State University demonstrating that advanced rapport, reframing, and relaxation techniques, applied before medical procedures, enhanced patients' comfort with distressing medical imaging procedures [10, 11]. The Focus Group has been developing applications of both the targeted training and the anxiety-reducing cognitive interventions to augment the heart-dose reducing effectiveness of DIBH.

Clinical trial development

The existing clinical trial entitled GATing at TUM (GATTUM), currently open to accrual at TUM Radiation Oncology, provides an outstanding platform for implementing and testing the effect of the training and cognitive interventions. The trial employs image-guided targeted radiation therapy and collects precise chest wall motion tracking, respiratory monitoring, and imaging data in DIBH radiation therapy to establish DIBH quality performance metrics. Imaging and radiomics analyses will ultimately provide data to guide dose optimization and dose reduction strategies for critical normal tissue organ sparing of the heart and adjacent organs.

The Focus Group is implementing the developed training modules at TUM and within GATTUM. The cognitive rapport, reframing, and relaxation techniques, which have to date been applied in imaging and interventional procedures but not in radiation oncology, are being adapted to the specific needs of breast cancer patients and to the physical and cognitive demands and process of DIBH. These techniques are integrated with targeted respiratory training to enhance each patient's physical DIBH capability and tolerance. Script development for the ▸

[3] M. N. Duma, A. C. Herr, K. J. Borm, K. R. Trott, M. Molls, M. Oechsner and S. E. Combs, "Tangential Field Radiotherapy for Breast Cancer-The Dose to the Heart and Heart Subvolumes: What Structures Must Be Contoured in Future Clinical Trials?", Frontiers in Oncology, 7:130, 2017.

[4] M. N. Duma, M. Molls and K. R. Trott, "From heart to heart for breast cancer patients – cardiovascular toxicities in breast cancer radiotherapy", Strahlentherapie und Onkologie, 190:5-7, 2014.

[5] M. A. Shevtsov, B. P. Nikolaev, V. A. Ryzhov, L. Y. Yakovleva, A. V. Dobrodumov, Y. Y. Marchenko, B. A. Margulis, E. Pitkin, A. L. Mikhrina, I. V. Guzhova and G. Multhoff, "Detection of experimental myocardium infarction in rats by MRI using heat shock protein 70 conjugated superparamagnetic iron oxide nanoparticle", Nanomedicine, vol. 12, no. 3, pp. 611-621, 2016.

[6] W. Sievert, K. R. Trott, O. Azimzadeh, S. Tapio, H. Zitzelsberger and G. Multhoff, "Late proliferating and inflammatory effects on murine microvascular heart and lung endothelial cells after irradiation", Radiotherapy & Oncology, vol. 117, no. 2, pp. 376-381, 2015.

[7] A. Kalet, A. Kim, N. Cao, D. Hippe, L. Fang, L. Young, J. Meyer and N. A. Mayr, "Impact of breath hold coaching and home practice on surface-tracked deep inspiratory breath-hold (DIBH) radiotherapy in patients with left-sided breast cancer", (abst), AAPM: The American Asso-

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[10] A. Norbash, K. Yucel, W. Yuh, G. Doros, A. Ajam, E. Lang, S. Pauker and N. A. Mayr, “Effect of team training on improving MRI study completion rates and no-show rates”, Journal of Magnetic Resonance Imaging, vol. 44, no. 4, pp. 1040-1047, 2016.

[11] E. V. Lang, W. T. Yuh, A. Ajam, R. Kelly, L. Macadam, R. Potts and N. A. Mayr, “Understanding patient satisfaction ratings for radiology services”, American Journal of Roentgenology, vol. 201, no. 6, pp. 1190-1195, 2013.

integrative health rapport, reframing, and relaxation techniques continue to evolve, and team training in the educational and cognitive techniques is planned. Oncologic quality-of-life survey tools have been adapted to the specific needs of breast cancer, DIBH, and radiation therapy.

Studies and projects in 2020

While the Covid-19 pandemic prevented us from interacting in person in 2020 due to restrictions, remote collaborations have flourished.

The randomized clinical trial proposal “Respiratory Training and Relaxation Techniques to Improve Adjuvant Radiation Therapy in DIBH in Breast Cancer” (PI: Stephanie Combs) was submitted to the Deutsche Krebshilfe and has received favorable preliminary reviews.
We undertook a major effort in 2020 at the University of Washington, with major collaboration by TUM faculty, to assemble a 13-article, two-issue Special Edition of the journal TMRI entitled “Human Touch for High-Tech Imaging and Imaging-guided Procedures: Integrative Medicine Strategies for Patient-Centered Nonpharmacologic Approaches” (Guest Editors: Nina A. Mayr, William T.C. Yuh) [12, 13]. The diverse multi-institutional and multi-disciplinary teams laid out a broad spectrum of integrative medicine and technology-based approaches in radiation oncology, imaging and other complex medical procedures for reducing patient anxiety to improve patient cooperation, quality of care and safety. Breast cancer was a major focus area in this effort [14].

Additional study of the preparatory training regimen in 2020 showed that the targeted training program not only reduced cardiac radiation dose through patients’ ability to perform an extended (i.e., “deeper”) DIBH, but also stably sustained the extended DIBH throughout treatment, particularly in challenging patients with pre-existing cardio-pulmonary disease [9].
New collaborative projects between the University of Washington, TUM (Stephanie Combs, Kai Borm), and the University of Colorado (Alexandra Chadderdon, Psy D) to systematically evaluate patient anxiety in the radiation oncology environment are ongoing and will further inform the Focus Group’s program, the trial, and future strategies.

Future directions

These projects and rich collaborations between TUM, the TUM-IAS, the Alumna Anna Boyksen Fellow, and the new collaborating institution (University of Colorado) are ongoing. Upon completion, this work will have established a breast cancer-specific advanced-technology and integrative-health approach and will have helped to determine whether the anxiety-reducing cognitive interventions we developed, combined with targeted DIBH training, can improve procedure performance, reduce heart dose, and improve cognitive and physical symptoms of anxiety and stress in patients receiving radiation therapy for left breast cancer. ■

[12] N. A. Mayr, W. T. C. Yuh, M. A. Oztek and X. V. Nguyen, "Human Touch for High-Tech Imaging and Imaging-Guided Procedures: Integrative Medicine Strategies for Patient-Centered Nonpharmacologic Approaches: Part 1: Challenges for High-Tech Imaging and Procedures: How Can Integrative Medicine Impact Quality and Operations?", Topics in Magnetic Resonance Imaging, vol. 29, no. 3, pp. 123-124, 2020.

[13] W. T. C. Yuh. N. A. Mayr, M. A. Oztek and X. V. Nguyen, "Human Touch for High-Tech Imaging and Imaging-Guided Procedures Integrative Medicine Strategies for Patient-Centered Nonpharmacologic Approaches: Part 2: Overcoming Anxiety in Imaging and Invasive Procedures: What can Physics, Technology, and Integrative Medicine Do for Us?", Topics in Magnetic Resonance Imaging, vol. 29, no. 4, pp. 165-166, 2020.

[14] N. A. Mayr, K. Borm, A. Kalet, L. S. Wootton, A. L. Chadderdon, S. E. Combs, W. Wang, N. Cao, S. S. Lo, G. A. Sandison and J. Meyer, "Reducing Cardiac Radiation Dose from Breast Cancer Radiation Therapy with Breath Hold Training and Cognitive Behavioral Therapy", Topics in Magnetic Resonance Imaging, vol. 29, no. 3, pp. 135-148, 2020.

Focus Group Visual Computing

Prof. Matthias Nießner (TUM), Alumnus Rudolf Mößbauer Tenure Track Professor | **Prof. Leonidas Guibas (Stanford University), Prof. Luisa Verdoliva (University Federico II of Naples),** Hans Fischer Senior Fellows | **Prof. Angel X. Chang (Simon Fraser University),** Hans Fischer Fellow | **Dr. Justus Thies (TUM)**, Postdoctoral Researcher | **Shivangi Aneja, Armen Avetisyan, Dave Zhenyu Cheng, Manuel Dahnert, Ji Jou, Andreas Rössler, (TUM),** Doctoral Candidates | Host: Visual Computing, TUM

Prof. Matthias Nießner

Prof. Leonidas Guibas

Prof. Luisa Verdoliva

Prof. Angel X. Chang

Toward photorealistic reconstruction

We in the Visual Computing Focus Group are research enthusiasts pushing the state of the art at the intersection of computer vision, graphics, and machine learning. Our research mission is to obtain high-quality digital models of the real world, which include detailed geometry, surface texture, and material in both static and dynamic environments.

In our research, we heavily exploit the capabilities of RGB-D and range sensing devices that are now widely available. However, we ultimately aim to achieve both 3D and 4D recordings from monocular sensors – essentially, we want to record holograms with a simple webcam or mobile phone. We further employ our reconstructed models for specific use cases, such as video editing, immersive AR/VR, semantic scene understanding, and many others. Aside from traditional convex and non-convex optimization techniques, we see great potential in modern artificial intelligence, mainly deep learning, in order to achieve these goals. The relevance of the research ranges across several areas that are impacted by 3D digitization and semantic scene understanding. These include applications ranging from entertainment and communication to medicine and autonomous robotics. However, the primary goal is to replace videos and images with the interactive but photorealistic 3D content of the future – i.e., holograms, which we believe will impact the full range of aforementioned industries.

Current work in the Visual Computing lab focuses on two major topics: 3D scene reconstruction (algorithms to capture, reconstruct, and understand 3D environments), and photorealistic image synthesis from these reconstructed and acquired 3D representations. In addition, we put heavy emphasis on ethical implications by investigating new forensics methods to automatically detect forged image and video manipulations.

For synthesizing realistic images, we start with traditional 3D representations of a scene and a virtual camera, and we use rendering techniques such as rasterization or ray tracing to generate a 2D image. Such input 3D content is largely created through manual effort by expert artists, for example, for movie productions. However, a very recent research direction is now synthesis using neural 3D representations. These offer a potential alternative to traditional, explicit 3D reconstruction and tracking. In particular, generative neural networks such as GANs or auto-regressive techniques can now generate quite convincing images. However, the problem becomes significantly more challenging when the goal is to synthesize a consistent recording from a captured 3D scene, or to make consistent edits in a video stream. Here, the problem statement is particularly challenging due to the need to learn an underlying representation, which can facilitate viewpoint consistency and seamless animation of dynamic elements. A core idea of our line of research is to incorporate 3D knowledge directly in the neural network architectures in a fully differentiable fashion. This not only simplifies the learning process – 3D transformations are hard to learn as a series of 2D convolutions, for example – but it also provides stable anchor points for conditioning generative models. The same idea can be used for 3D scene reconstructions of static scenes. In DeepVoxels, a series of 2D images is lifted to a volumetric grid of 3D features from which novel viewpoints can be synthesized. In contrast to conventional 2D convolutional networks, this approach learns a new scene representation that generates images that are both photorealistic and temporally coherent.

With the ability to synthesize and edit images and videos, we must also consider societal implications, particularly since videos are often considered as credible and especially with the recent focus on media and fabricated news. As researchers, we have a sincere commitment to contributing to society as a whole, both in educating the public on ►

Figure 1, Matthias Nießner, Justus Thies, and Andreas Rössler presenting and discussing the research of the Focus Group Visual Computing to the German federal government (in photo: Chancellor Merkel and Vice-Chancellor Olaf Scholz) in Meseberg (near Berlin); Digitalgipfel 2019.

[1] J. Thies, M. Zollhöfer, M. Stamminger, C. Theobalt and M. Nießner, “Face2Face: Real-time Face Capture and Reenactment of RGB Videos”, CACM, Vol. 62 No. 1, pp. 96-104, 2019.

[2] A. Rössler, D. Cozzolino, L. Verdoliva, C. Riess, J. Thies and M. Nießner, “FaceForensics++: Learning to Detect Manipulated Facial Images”, 2019 IEEE/CVF International Conference on Computer Vision (ICCV), 2019, pp. 1-11.

[3] J. Thies, M. Zollhöfer and M. Nießner, “Deferred Neural Rendering: Image Synthesis using Neural Textures”, ACM Transactions on Graphics, vol. 38, no. 4, 2019.

[4] J. Hou, A. Dai and M. Nießner, “3D-SIS: 3D Semantic Instance Segmentation of RGB-D Scans”, 2019 IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR), 2019, pp. 4416-4425.

[5] A. Avetisyan, M. Dahnert, A. Dai, M. Savva, A. X. Chang and M. Nießner, “Scan2CAD: Learning CAD Model Alignment in RGB-D Scans”, 2019 IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR), 2019, pp. 2609-2618.

[6] G. Gafni, J. Thies, M. Zollhoefer and M. Nießner, “ Dynamic Neural Radiance Fields for Monocular 4D Facial Avatar Reconstruction”, to be presented at the IEEE Conference on Computer Vision and Pattern Recognition 2021 (CVPR2021), virtual conference, June 19-25, 2021.

[7] A. Dai, Y. Siddiqui, J. Thies, J. Valentin and M. Nießner, "SPSG Self-Supervised Photometric Scene Generation from RGB-D Scans", to be presented at the IEEE Conference on Computer Vision and Pattern Recognition 2021 (CVPR2021), virtual conference, June 19-25, 2021.

[8] J. Hou, B. Graham, M. Nießner and S. Xie, "Exploring Data-Efficient 3D Scene Understanding with Contrastive Scene Contexts", to be presented at the IEEE Conference on Computer Vision and Pattern Recognition 2021 (CVPR2021), virtual conference, June 19-25, 2021.

[9] A. Božič, P. Palafox, M. Zollhöfer, J. Thies, A. Dai and M. Nießner, "Neural Deformation Graphs for Globally-consistent Non-rigid Reconstruction", to be presented at the IEEE Conference on Computer Vision and Pattern Recognition 2021 (CVPR2021), virtual conference, June 19-25, 2021.

the possibilities of artificial synthesis and in developing automated approaches to detect image and video manipulations. In our FaceForensics work, we examine the synthesis of manipulation approaches, on the basis of the example of Face2Face manipulations: Can humans easily spot fakes? What about supervised learning methods that are trained to detect faces? In FaceForensics++, our work now covers Face2Face, FaceSwap, and the recently very popular DeepFake technique, introducing a new data set and benchmark with manipulations of over 500,000 source images from Youtube videos, and over 1.5 million synthesized output manipulations from these state-of-the-art editing techniques. It turns that 143 participants of a user study were only able to correctly classify 61% in a 50:50 test split of real and fake images; this is only 11% better than random chance. These experiments are pressing for an automated solution. To this end, FaceForensics++ introduces a new learning-based detection method that exploits domain-specific knowledge of the face domain by combining face tracking input with a convolutional neural classifier. The resulting approach yields a classification accuracy of 86.69% on the same benchmark – far beyond human performance. Detecting manipulated imagery becomes significantly more challenging when dealing with unknown manipulation techniques.

Following up on these important steps in the research community, our long-term goal is to obtain a perfect digital replica of the real world – ideally, from single photos or short RGB video sequences. To this end, we need to generalize capture and synthesis to fully dynamic and arbitrary real-world settings. At the same time, we will investigate the shortcomings of existing synthesis methods by developing automated detection methods. This will not only help to improve synthesis, but also open up a discussion about the social impact of artificially created imagery. ■

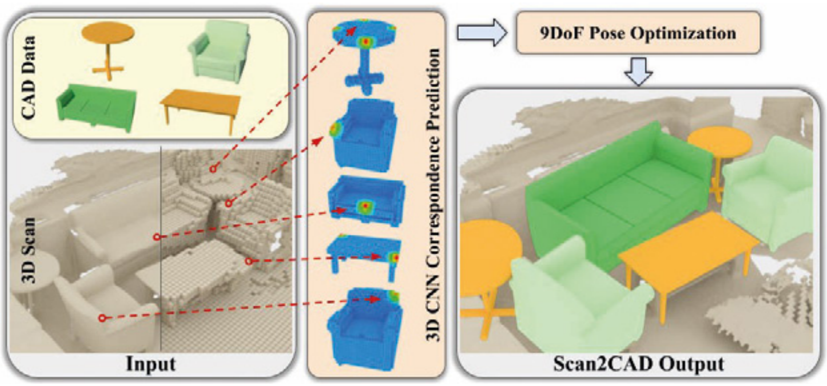

Figure 2, Scan2CAD takes as input an RGB-D scan and a set of 3D CAD models (left). We then propose a novel 3D CNNapproach to predict heatmap correspondences between the scan and the CAD models (middle). From these predictions, we formulate an energy minimization to find optimal 9 DoF object poses for CAD model alignment to the scan (right).

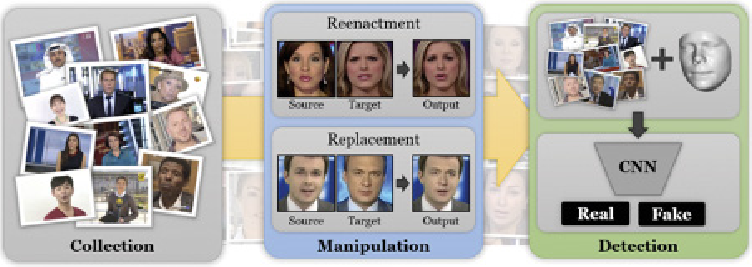

Figure 3, FaceForensics is a database of facial forgeries that enables researchers to train deep-learning-based approaches in a supervised fashion. The database contains manipulations created with three state-of-the-art methods, namely, Face2Face, FaceSwap, and DeepFakes.

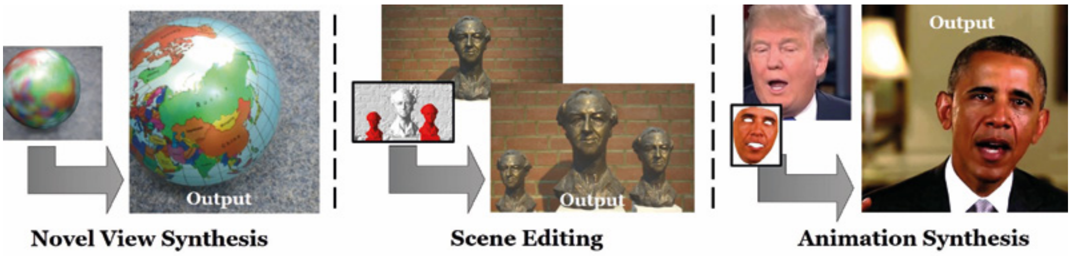

Figure 4, The modern computer graphics pipeline can synthesize images at remarkable visual quality; however, it requires well-defined, high-quality 3D content as input. In this work, we explore the use of imperfect 3D content, for instance, obtained from photometric reconstructions with noisy and incomplete surface geometry, while still aiming to produce photorealistic (re-)renderings. To address this challenging problem, we introduce Deferred Neural Rendering, a new paradigm for image synthesis that combines the traditional graphics pipeline with learnable components. Specifically, we propose Neural Textures, which are learned feature maps that are trained as part of the scene capture process. Similar to traditional textures, neural textures are stored as maps on top of 3D mesh proxies; however, the high-dimensional feature maps contain significantly more information, which can be interpreted by our new deferred neural rendering pipeline.

Focus Group Subcellular Dynamics in Neurons

Prof. Maya Schuldiner (Weizmann Institute of Science), Alumna Hans Fischer Senior Fellow | **Prof. Melike Lakadamyali (University of Pennsylvania),** Alumna Hans Fischer Fellow | **Caroline Fecher, Antoneta Gavoci, Natalia Marahori, (TUM),** Doctoral Candidates | Host: **Prof. Thomas Misgeld,** Neuronal Cell Biology, TUM

Prof. Maya Schuldiner

Prof. Melike Lakadamyali

How long-distance travel ends and diversity emerges

The last years have taught us many things – and the last one especially, has made us aware that you cannot take long-distance interactions for granted and that diversity is greatly underappreciated. Both long-distance interactions and diversity are key to the mission of the TUM-IAS – and also happen to be at the core of the questions that the TUM-IAS Focus Group Subcellular Dynamics in Neurons has addressed over the past few years.

Composed of one super-resolution microscopy expert and cell biologist (Melike Lakadamyali), one systems biologist and geneticist (Maya Schuldiner), and one neuroscientist (Thomas Misgeld), this Focus Group set out to explore how nerve cells regulate the life of their functional compartments, called organelles ("small organs").

Imagine a nerve cell: Its metabolic center is a small cell body, perhaps 50 micrometers in diameter, that has some shorter processes (a few hundred micrometers – called dendrites) and one really long one (up to many centimeters long – the axon), studded with small communication centers, called synapses. Each of these parts of a neuron represents a specific compartment with a specialized function and correspondingly specialized metabolic and energy demands. Nerve cells – like almost all cells – derive most of their energy from a set of organelles called mitochondria, that can exist in a dynamic network or as a set of rather discrete bean-shaped structures. In order to ensure the right number of functional mitochondria in all its compartments, the nerve cell entirely depends on long-distance transport of organelles (likely often lasting days or even weeks), but also utilizes a complex system of local biogenesis, anchorage, and degradation. Beyond the trope of mitochondria as the "power house" of cells, these fascinating organelles do many more things than provide energy – they are involved in numerous biosynthetic pathways, contribute to regulating ionic balances in cells, and can even initiate and regulate cell death (arguing that from a cell's perspective, mitochondria can turn quickly from energy provider to "hazardous goods"). So how does a single organelle fulfill so many tasks? And how is this regulated to match the specific needs of the different parts of a nerve cell? How is mitochondrial homeostasis ("mitostasis") – i.e., the right number of mitochondria at the right place – ensured in neurons?

The Focus Group Subcellular Dynamics in Neurons has worked on these questions over the past few years in a two-pronged approach. To address the question of mitochondrial distribution, we took advantage of Melike Lakadamyali's unique expertise in using fluorescent dyes that can switch their

[1] C. Fecher, L. Trovò, S. A. Müller, N. Snaidero, J. Wettmarshausen, S. Heink, O. Ortiz, I. Wagner, R. Kühn, J. Hartmann, R.M. Karl, A. Konnerth, T. Korn, W. Wurst, D. Merkler, S.F. Lichtenthaler, F. Perocchi and T. Misgeld, "Cell type-specific profiling of brain mitochondria reveals functional and molecular diversity", Nature Neuroscience, vol. 22, pp. 1731-1742, 2019.

[2] M. Wang, T. Kleele, Y. Xiao, G. Plucinska, P. Avramopoulos, S. Engelhardt, M.H. Schwab, M. Kneussel, T. Czopka, D. L. Sherman, P. J. Brophy, T. Misgeld and M.S. Brill, "Completion of neuronal remodeling prompts myelination along developing motor axon branches", Journal of Cell Biology, vol. 220, no. 4, pp. e201911114, 2021.

color when exposed to a brief flash of ultraviolet light. This makes it possible to label a small subset of mitochondria anywhere in a nerve cell (Figure 1) and follow their further fate (provided one has access to the right microscopes and model organisms, as Thomas Misgeld's lab provided). Such an optical "pulse chase" experiment has allowed us to do precise accounting of the flow of mitochondria through a nerve cell's processes. What we discovered is that instead of shipping "spent" mitochondria all the way back from the distant synapses, a nerve cell contains many local degradation sites in synapses, where the cell disposes of a substantial fraction of mitochondria. Moreover, we were able to identify the degradation process as molecularly different from the previously described degradation pathways – an exciting finding, as many of the genes involved are mutated in forms of neurodegeneration, but questions such as how they play together and where they exert their action are not well understood. So while this part of our work revealed that long-distance travel is not always necessary (at least for disposal of cellular junk), another part of our work emphasized the prevailing importance of mitochondrial diversity.

Maya Schuldiner, as a systems-level biologist and geneticist working on organelle biology in yeast, brought a new perspective to the Misgeld lab: Why look at one thing, if there are methods to look at many? So deviating from the Misgeld lab's traditional approach of pushing the frontier of resolution, we turned toward developing systematic tools to characterize how different mitochondria are in different contexts. Obviously such diversity can exist in shape, in molecular composition, and in function, but also in neighborhood ►

[3] N.A. Marahori, M. Schifferer, B. Plomer, T. Kleele, P. Avramopoulos, S. Hannan, S. Engelhardt, M. Lakadamyali, M.S. Brill and T. Misgeld, "A retrograde transit filter that removes synaptic mitochondria," in preparation.

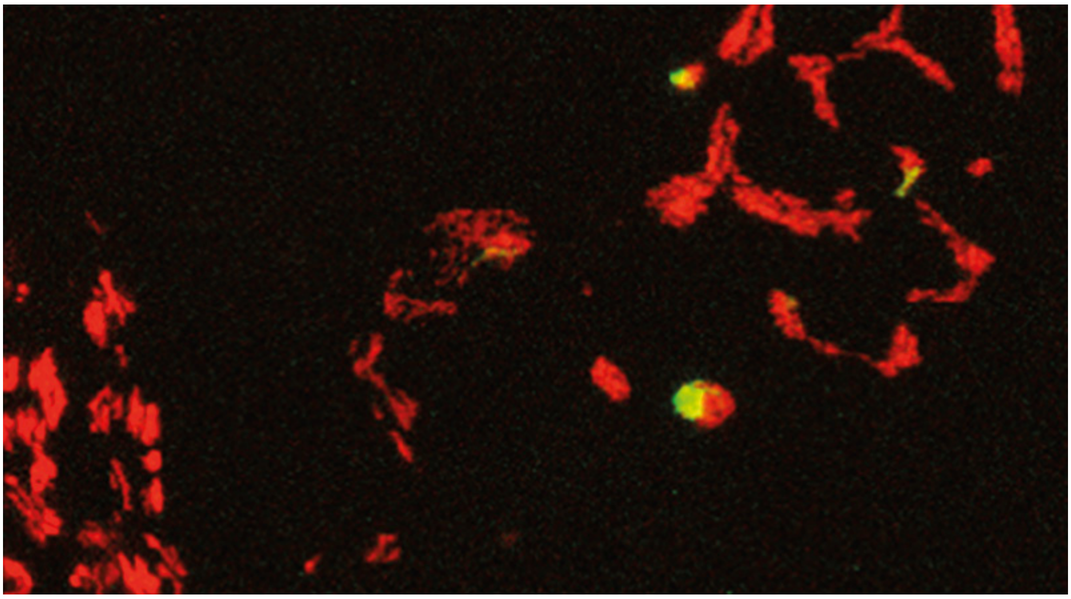

Figure 1, Nerve-muscle synapse in a mouse, where all mitochondria are labeled in red, but some mitochondria have been selectively "photo-labeled" to follow their fate.

relationships, as many organellar functions are not performed by soloists, but by smal ensembles of different organelles that are joined by so-called “organellar contact sites” (Figure 2). So on the basis of this inspiration, we developed a new and systematic approach to study mitochondrial diversity. In a large consortial effort involving several TUM research groups, we generated a new mouse line that allows us to “tag” mitochondria in any cell type we choose. Using a purification approach that depends on miniature magnetic particles to fish the tagged mitochondria out of tissue homogenates, we can to now determine the molecular composition and functional capacities of cell type- or disease-stage specific mitochondria. We are currently expanding this approach to investigate the differences of mitochondria within cells – where especially in neurons structural changes are well appreciated (e.g., between dendrites and axon), but functional differences are largely elusive.

The Focus Group and its members’ efforts led to a number of distinctions over the course of the Fellowships: Maya Schuldiner became a full professor at the Weizmann Institute of Science in 2019; in the same year, she received her third ERC Grant. In 2020,

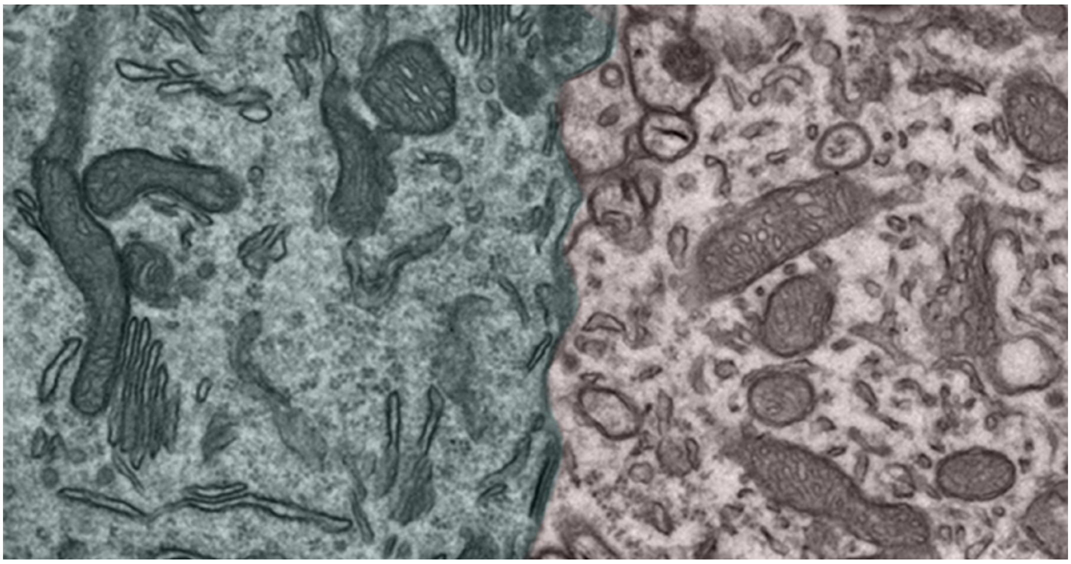

Figure 2, Electron microscopic analysis of mitochondria in a neuron (left) and a glial cell of the cerebellum, stressing the different morphologies and organelle contacts.

she was elected to be a member of the German National Academy of Sciences Leopoldina. Thomas Misgeld received TUM's Heinz Maier-Leibniz medal in 2018. In 2018, the Munich Cluster of Systems Neurology was renewed under Thomas Misgeld's co-speakership (with Maya Schuldiner and Melike Lakadamyali named as Cluster-affiliated TUM-IAS-Fellows of the first funding period). In 2018/19, the MSc "Biomedical Neuroscience" was funded by the Elite Network Bavaria with Thomas Misgeld as a speaker – the program has greatly benefited from teaching input by lecturers at the Weizmann Institute of Science and the University of Pennsylvania, especially during the Covid-19 pandemic. In summary, the TUM-IAS Focus Group Subcellular Dynamics in Neurons has been able to substantially advance the understanding of how a neuron's mitochondria regulate their mitochondrial homeostasis and how mitochondrial diversity is created in the nervous system. This work laid the foundation for numerous future collaborative efforts between the Misgeld lab at TUM and the Fellows' labs and their home institutions. ■

Focus Group Artificial Electronic Skin

Prof. Takao Someya (University of Tokyo), Alumnus Hans Fischer Senior Fellow | Host: **Prof. Gordon Cheng,** Cognitive Systems, TUM

Prof. Takao Someya

Skin-inspired mechanically flexible and stretchable electronic system

The Focus Group on Artificial Electronic Skin, led by Takao Someya and Gordon Cheng, aimed at the development of a novel paradigm that could lead to important advances in robotics and also enhance the quality of life. The potential impact of artificial electronic skin is enormous, as it is applicable across multiple domains including building safer robots, healthcare monitoring, entertainment, and wearable technologies to enhance our way of life.

This research pursues the creation of an artificial electronic skin that imitates the properties of human skin using innovative fabrication techniques of printed electronics. The concept is being used to develop a network of fully printed unit-cells integrating printed sensors and specific integrated circuitry in order to mimic the human skin's sense of touch. A large number of sensor-cells will be connected to a cell-network that determines touch information across large areas and transmits it in a manner comparable to the human nervous system. One or more cells can be connected to a processing system to interpret the sensor information and support other perception channels of a humanoid. Printed electronics technology offers inherent advantages for the development of an artificial skin: Mechanically flexible and even stretchable materials of large size can be utilized as a substrate for recently developed inks of electronic materials. These possess interesting properties, such high conductivity, high dielectric permittivity, and tunable work functions. One of the main challenges has been the integration of these sensors on large-scale area while fulfilling mechanical requirements such as stretchability and flexibility similar to that of human skin. A similar architecture may be applied on prostheses as well as for health and fitness monitoring.

As an artificial skin, we have developed porous nanomesh-type elastic conductors that can be directly attached on human skin. The conductors consist of nanofibers and nanowires (NFs/NWs) using interfacial hydrogen bonding. We simultaneously achieve high conductivity (9190 S cm−1), high stretchability (310%), and good durability (82% resistance increase after 1000 cycles of deformation at 70% tensile strain). The direct contact between the silver NWs enables the high conductivity. The synergistic effect of the layer-by-layer structure and good adhesion between the silver NWs and the polyurethane NFs enables good mechanical properties. Furthermore, without any adhesive gel or tape, the conductors can be utilized as breathable strain sensors for precise joint motion monitoring, and as breathable sensing electrodes for continuous electrophysiological signal recording. In addition, we have developed a highly durable nanofiber-reinforced metal-elastomer composite for monitoring biological information over a long period of time without any discomfort. It is made from metal fillers, an elastomeric binder matrix, and electrospun polyvinylidene fluoride (PVDF) nanofibers for enhancing both cyclic stability and conductivity. The introduction of PVDF nanofibers enhances the toughness and suppresses crack growth by providing a fiber reinforcing effect. It is found that the conductivity of a nanofiber-reinforced elastic conductor is four times greater than that of the pristine material because the silver-rich layer is self-assembled on the top surface by a filtering effect. As a result, a stretchable electrode made from nanofiber-reinforced elastic conductors and wrinkled structures has both excellent cyclic durability and high conductivity and is stretchable up to 800%. The cyclic degradation ($\Delta R/R0$) remains at 0.56 after 5000 stretching cycles (50% strain), whereas initial conductivity and sheet resistance are 9903 S/cm and 0.047 Ω/sq, respectively. By utilizing a highly conductive and durable elastic conductor for sensor electrodes and wiring, we were able to demonstrate a skin-tight multimodal physiological sensing suit. Continuous long-term monitoring of electrocardiogram, electromyogram, and motions during weight-lifting exercises have been successfully demonstrated without significant degradation of signal quality.

Furthermore, we have succeeded in the development of nanomesh sensors that monitor finger pressure without sensory interference. Indeed, the manipulation of the finger can be monitored without disturbing the human sensation, even though our nanomesh-based pressure sensor is directly attached to the highly sensitive fingertip. It has been scientifically and quantitatively proven that the sensor-applied finger does not exhibit any statistically significant difference compared to the bare finger, even though the attachment of a super-thin (2-μm-thick) polymeric film results in a 26% increase in the grip force. The complete elimination of sensory interference has been realized by the simultaneous achievement of extreme mechanical durability (against friction/shearing force over 100 kilopascals) while keeping the sensor sufficiently soft and thin. ■

In close collaboration with Dr. Sae Franklin (TUM).

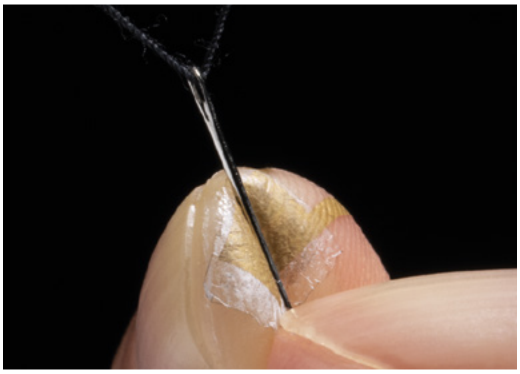

Figure 1, Robust fingertip sensor. The polyurethane and gold sensor can resist shear forces and rubbing.

Figure 2, Sensitive fingertips. The sensor is much thinner than human hair and does not affect sensitivity.

Focus Group Embedded Systems and Internet of Things

Prof. Sebastian Steinhorst (TUM), Alumnus Rudolf Mößbauer Tenure Track Professor | **Ege Korkan, Jan Lauinger, Laurin Prenzel, Emanuel Regnath, Philipp Weiss, (TUM),** Doctoral Candidates | **Dr. Mohammad Hamad, Dr. Luxi Zhao, (TUM),** Postdoctoral Researchers | Host: Embedded Systems and Internet of Things, TUM

Prof. Sebastian Steinhorst

Future-proofing the Internet of Things

The Focus Group Embedded Systems and Internet of Things was founded in November 2016 when Sebastian Steinhorst joined TUM as a Rudolf Mößbauer Tenure Track Assistant Professor and became a Fellow of the TUM-IAS. He received tenure in January 2020 and became an Alumnus Fellow.

[1] E. Regnath and S. Steinhorst, "AMSA: Adaptive Merkle Signature Architecture", 2020 Design, Automation & Test in Europe Conference & Exhibition (DATE), 2020, pp. 1532-1537.

[2] J. Lauinger, J. Ernstberger, E. Regnath, M. Hamad and S. Steinhorst. "A-PoA: Anonymous Proof of Authorization for Decentralized Identity Management", presented at the IEEE International Conference on Blockchain and Cryptocurrency (ICBC 2021), Sydney, May 3-6, 2021.

[3] P. Weiss, A. Weichslgartner, F. Reimann and S. Steinhorst, "Fail-Operational Automotive Software Design Using Agent-Based Graceful Degradation", 2020 Design, Automation & Test in Europe Conference & Exhibition (DATE), 2020, pp. 1169-1174.

The overarching research goal of our Focus Group is to enable resilient, efficient, interoperable, safe and secure system architectures for the Internet of Things (IoT).

In the past years, we have looked into decentralization methodologies for large-scale IoT environments, which cover a wide range of future applications in areas including the smart home, energy grids, and efficient traffic management. Within this domain, our research was focused on distributed consensus, blockchain-based data verification, and authentication schemes to achieve security. Our latest research regarding authentication schemes was investigating hash-based signatures (HBS), which are promising candidates to enhance IoT security in the fore-

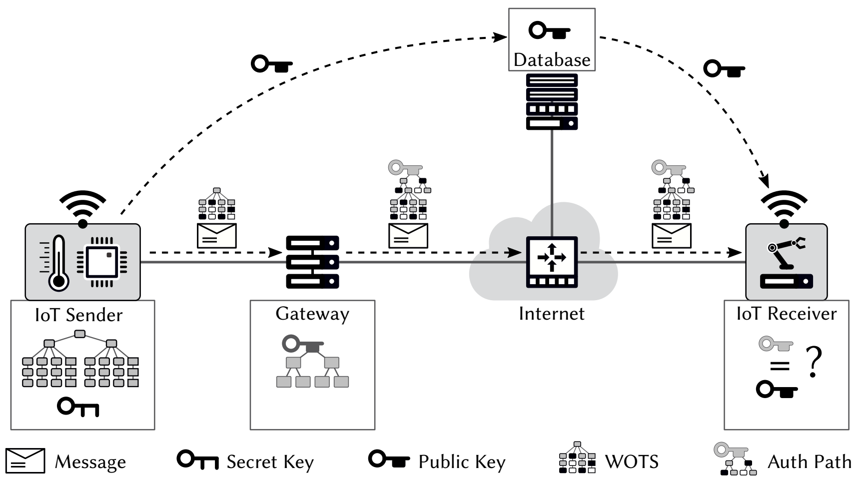

Figure 1, Reducing signature size for the sender. An IoT sender creates several Winternitz One-Time Signatures (WOTS) from a private key and offloads the non-sensitive authentication path – which connects the WOTS to the public key – to a gateway. Afterwards, the IoT sender only needs to recreate the WOTS to sign a message, and when it is sent, the gateway will append the missing authentication path to complete the signature.

seeable future. HBS are resistant against quantum computers, use fast integer math, are well understood, and produce small public keys. However, HBS can only sign a limited amount of messages and produce – like most quantum-resistant schemes – large signatures of several kilobytes. In [1], we proposed improvements that lower the size of the signature by 17.3% for the sender without sacrificing security or performance compared to related approaches. Figure 1 illustrates one of the ideas, which utilizes the gateway architecture that appears in many IoT scenarios.
From another perspective, within the EU H2020 project nIoVe, we developed an authentication protocol in the context of decentralized identity management. More specifically, the focus lies on anonymous and self-sovereign credential management based on group signatures. To issue anonymous credentials, credential issuers must reference a credential schema (defines attributes of the credential) and register a credential definition (contains public keys of a group signature scheme and revocation mechanism) on a distributed ledger. To solve the problem of undefined schema access control, our protocol, called Anonymous Proof of Authorization (A-PoA), enables root authorities to authorize credential-issuing authorities to access credential schemas. This allows credential issuers to prove legitimate authority and to issue credentials based the schema of the root authority while remaining anonymous [2].

Considering the trend toward connected and automated driving, an important application domain for IoT is automotive. Fail-operational behavior of safety-critical software for autonomous driving is essential, as no driver will be available anymore as a backup solution. Here, we have developed a methodology using agent-based graceful degradation to efficiently redistribute system resources at runtime [3]. In a failure scenario, safety-critical tasks are restarted on other available hardware resources, while, in return, non-critical tasks are shut down. To achieve system predictability, we have published an approach to analytically derive the worst-case failover time at runtime [4]. Additionally, in the domain of automotive security, we have proposed SPPS, a secure policy-based Pub/Sub model for V2C communication, which allows encryption and control of access to messages published by vehicles [5].

With our BMBF-funded cooperation project ReMiX, we are applying our expertise in IoT system architecture decentralization to improve the resilience of mixed-criticality industrial measurement and control systems. A major goal is the self-organization of hierarchical multi-agent systems through dynamic reconfiguration. This allows decentralized systems to react to unexpected events, such as failures, and recover their system performance as illustrated in Figure 2. The decentralized aspects can be realized through consensus algorithms, to allow the synchronization between agents without relying on a central server [6].

Our activity in the industrial IoT context is further extended with our involvement in the standardization activities in the World Wide Web Consortium (W3C), which aim to tackle the interoperability problem arising from an ever-increasing diversity of devices in industrial environments, as well as smart homes and cities. After contributing to the core of the W3C Thing Description standard, we have developed simple but powerful extensions that allow more complex devices to be described and to be simulated. With our recent contributions, we are enabling systematic ways to build systems by analyzing the timing behavior of Things [7] and to describe such systems to allow better inspection and verification [8]. ■

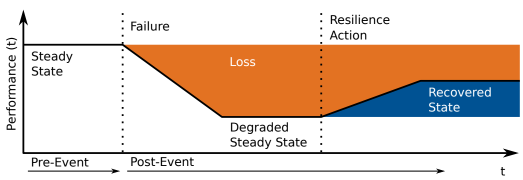

Figure 2, Resilience is a post-event mechanism to recover system performance after an unexpected event. We see resilience as a major contributor to autonomy in IoT, since many disturbances cannot be known in advance.

[4] P. Weiss, S. Elsabbahy, A. Weichslgartner and S. Steinhorst, "Worst-Case Failover Timing Analysis of Distributed Fail-Operational Automotive Applications", presented at the Conference on Design, Automation and Test in Europe (DATE 2021), virtual conference and exhibition, February 1-5, 2021.

[5] M. Hamad, E. Regnath, J. Lauinger, V. Prevelakis and S. Steinhorst, "SPPS: Secure Policy-based Publish/Subscribe System for V2C Communication", presented at the Conference on Design, Automation and Test in Europe (DATE 2021), virtual conference and exhibition, February 1-5, 2021.

[6] L. Prenzel and S. Steinhorst, "Decentralized Autonomous Architecture for Resilient Cyber-Physical Production Systems", presented at the Conference on Design, Automation and Test in Europe (DATE 2021), virtual conference and exhibition, February 1-5, 2021.

[7] V. E. Schlott, E. Korkan, S. Kaebisch and S. Steinhorst, "W-ADE: Timing Performance Benchmarking in Web of Things". In, Web Engineering, ICWE 2020, M. Bielikova, T. Mikkonen and C. Pautasso, Eds., Lecture Notes in Computer Science, vol. 12128, Cham, Germany: Springer, pp. 70-86, 2020.

[8] A. Kast, E. Korkan, S. Käbisch and S. Steinhorst, "Web of Things System Description for Representation of Mashups", 2020 International Conference on Omni-layer Intelligent Systems (COINS), 2020, pp. 1-8.

IESP e.V. Institute for Earth System Preservation

An international expert network

The IESP is a unique network of scientists, politicians, administrators, and entrepreneurs who have joined forces to provide sustainable, future-oriented solutions to the Earth System crises that challenge us humans in the Anthropocene. Caused by a toxic mixture of excess emission of greenhouse gases and the resulting global warming and climate change, the elimination of biodiversity and ecosystems to satisfy human desires, pollution of the atmosphere, water, and soil, and mismanagement of businesses, countries, and ecosystems, these crises increase social division and threaten international peace.

The network specializes in policy advice. It utilizes inter- and transdisciplinary workshops and symposia based on the concept of the Dahlem Conferences® to rally decision-makers in environmental science, humanities, industry, politics, and administration for out-of-the-box exchanges focused on specific environmental problems. From its very beginning, the network has been successful in advising and inspiring politics and political administration with new concepts and ideas through pointed, solution-oriented memoranda. These originate from the IESP's holistic participatory approach, which engages a multitude of stakeholders, through all generations, in problem-solving dialogues.

In 2002, the IESP began to evolve as the Institute of Advanced Studies on Sustainability (IoS), a sub-institute of the European Academy of Sciences and Arts (EASA). It's mission: to root environmental sciences and technology in the academy's canon. Following the workshop "The Art of Dealing Wisely with the Planet Earth" in 2008, IoS established the International Expert Group on the Preservation of the Functionality of the Earth System and published its first memorandum, known as the "Zugspitze Declaration." Since then, the IESP and the TUM Institute for Advanced Study have been collaborating, for example on events, publications, Fellowships, and research projects. In October 2020, IESP chairperson and TUM Emeritus of Excellence Prof. Klaus Mainzer was elected as the new president of the EASA.

Another chairperson of the IESP, TUM Professor for Urban Water Systems Engineering and TUM-IAS host Prof. Dr. Jörg E. Drewes, was appointed a new member of the German Advisory Council on Global Change (WBGU). The WBGU is an independent scientific advisory body of the German federal government, advising policy makers in matters regarding global environmental changes. In addition, Prof. Drewes and several others affiliated with the IESP, such as former TUM-IAS Carl von Linde Senior Fellow Prof. Dr. Annette Menzel and TUM Prof. Dr. Markus Disse have been appointed to a scientific advisory board of the Bavarian State Council on sustaining the free state's water future.

The recently deceased Nobel Prize winner Paul Crutzen, who was among the creators of the IESP, advocated for engineering solutions to solve the Anthropocene's – mostly anthropogenic – threats to the Earth System. As some of the planetary boundaries sustaining life have already been trespassed, humanity is running out of time. One major problem is excess nitrogen in water and soil. In 2017, to help avoid a penalty from the EU's then still pending case against Germany for underachieving in fulfilling the requirements of the EC Water Framework Directive (WFD), the IESP

secured funding from the Bavarian State Ministry for the Environment and Consumer Protection for an event-based research project called "Agriculture-Water Management-Climate Change. New Perspectives for Agriculture and the Environment." The recent years' dryness gives this project a new urgency.

The ongoing project's main goal is to preserve the systemic self-regulatory forces of nature (here, water and soil) and maintain both their effectiveness and efficiency in the long-term. In addition, it is imperative to resolve conflicts of use between different human stakeholders in agriculture and water management, since these disturb natural processes, which in turn affect social well-being. The protection goals and practical solutions that both enable sustainable agriculture and support achievement of the UN Sustainable Development Goals while feeding a growing world population, which have already been defined for decades, must be implemented. The IESP stands ready to continue and to facilitate the necessary dialogue. ■

IESP
International Expert Group on
Earth System Preservation

Where do the TUM-IAS Fellows come from?

USA

Prof. Nina A. Mayr
University of Washington

Prof. Kelly Clifton
Portland State University

Prof. Leonidas Guibas
Stanford University

Prof. Leila Takayama
University of California

Dr. Sani Nassif
Radyalis LLC

Prof. Thaddeus Stappenbeck
Cleveland Clinic

Prof. Henrik Selin
Boston University

Prof. Noelle Eckley Selin
Prof. Kathleen Thelen
Massachusetts Institute of Technology

Dr. Lothar Hennighausen
National Institute of Diabetes and Digestive and Kidney Diseases (NIH / NIDDK)

Prof. Hai (Helen) Li
Duke University

Prof. Natalia Shustova
University of South Carolina

Prof. Robert J. Schmitz
University of Georgia

Canada

Dr. Angel X. Chang
Simon Fraser University

Brasil

Prof. Gustavo Goldman
University of São Paulo

Argentina

Prof. Marta C. Antonelli
Universidad de Buenos Aires

England

Dr. Michael Bronstein
Dr. Luca Magri
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Prof. Laura Herz
University of Oxford

Prof. Krasimira Tsaneva-Atanasova
University of Exeter

Ireland

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Trinity College Dublin

Germany

Prof. Daniel Cremers
Prof. Bernhard Küster
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Dr. Filippo Maglia
BMW Group

Rudolf Mößbauer Fellows at TUM

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Prof. Jia Chen
Prof. David Egger
Prof. Matthias J. Feige
Prof. Franz Hagn
Prof. Angelika Harbauer
Prof. Reinhard Heckel
Prof. Frank Johannes
Prof. Michael Knap
Prof. Robert König
Prof. Susanne Kossatz
Prof. Laura Leal-Taixé
Prof. Christian Mendl
Prof. Rolf Moeckel
Prof. Kai Müller
Prof. Frank Ortmann
Prof. Menno Poot
Prof. Ruben Portugues
Prof. Franz Schilling
Prof. Kathrin Schumann
Prof. Antonia Wachter-Zeh
Technical University of Munich

Switzerland

Dr. Mirko Bothien
ZHAW Zurich University of Applied Sciences

Prof. Eleni Chatzi
Dr. Barbara Solenthaler
ETH Zurich

Dr. Michael Bronstein
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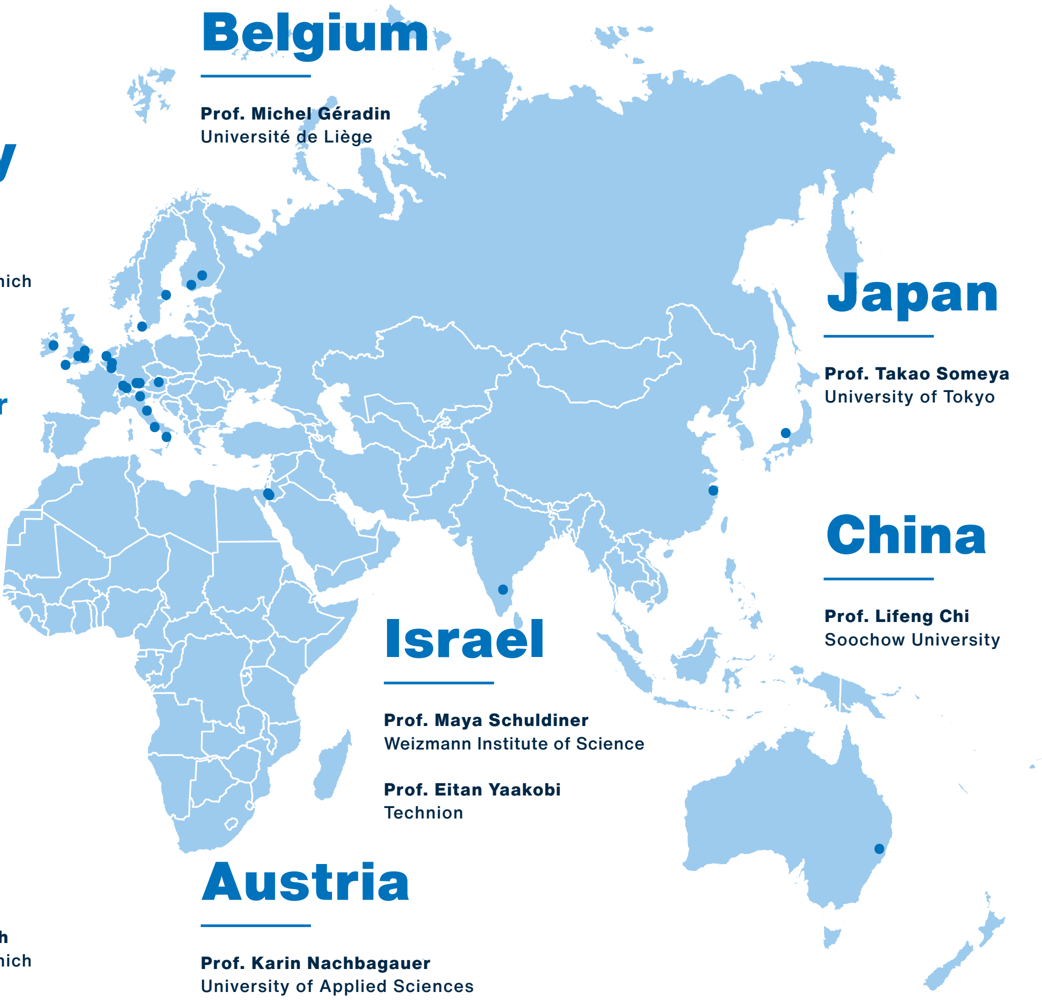
Denmark

Prof. Ib Chorkendorff
Technical University of Denmark

Netherlands

Dr. Christian Bick
Free University of Amsterdam

Prof. Ron Heeren
Maastricht University



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Université de Liège

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Weizmann Institute of Science

Prof. Eitan Yaakobi
Technion

Austria

Prof. Karin Nachbagauer
University of Applied Sciences Upper Austria

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Prof. Giuseppe Savaré
Bocconi University

Dr. Sara Lucatello
INAF Osservatorio Atronomico di Padova

Prof. Paolo Giommi
Italian Space Agency

Prof. Luisa Verdoliva
University Federico II of Naples

Finland

Prof. Camilla Hollanti
Aalto University

Sweden

Prof. Meike Schalk
KTH Royal Institute of Technology

Japan

Prof. Takao Someya
University of Tokyo

China

Prof. Lifeng Chi
Soochow University

Australia

Prof. Susan Park
University of Sydney

India

Prof. Shobhana Narasimhan
Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR)

Facts and Figures

TUM-IAS was established as a flagship of TUM's institutional strategy to promote top-level research in the Excellence Initiative of the German federal and state governments. TUM was not only successful in both rounds of this nationwide competition (2006 and 2012) but even secured the title "University of Excellence" for the third time under the new program Excellence Strategy that has evolved from the Excellence Initiative in 2019. After having played a central part in the first two rounds TUM-IAS became established as a permanent institution of TUM which is financing TUM-IAS out of the general TUM budget. The Institute has also contributed to the proposal of the Excellence Strategy and is therefore receiving funding for its new initiatives. In addition, TUM-IAS is collaborating with the Cluster of Excellence e-conversion financing a TUM-IAS@e-conversion Hans Fischer Senior Fellowship. In 2020, the first Fellow was appointed in this program.

Moreover, TUM-IAS continues to receiving further third-party funding.

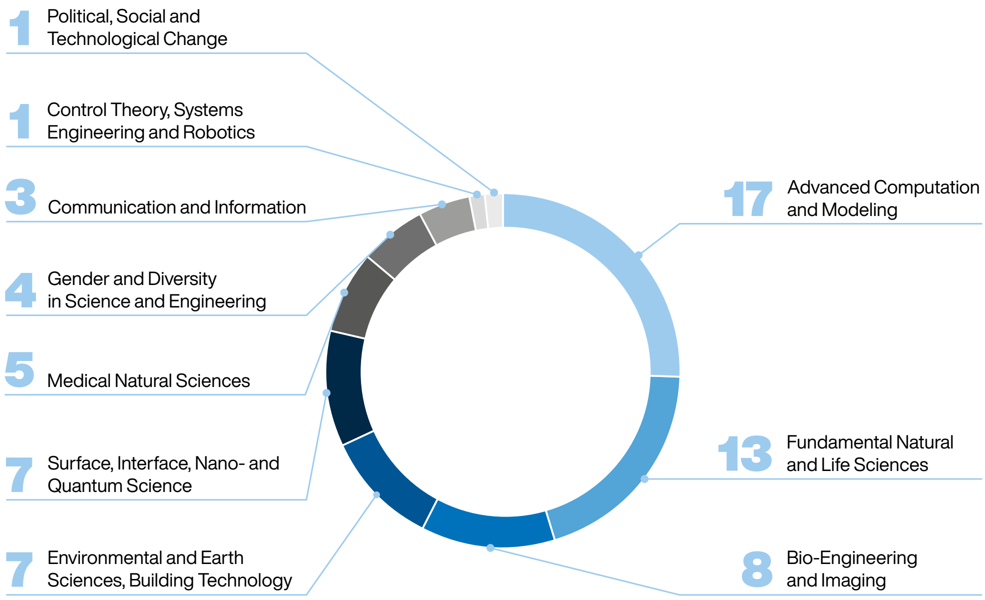
TÜV Süd Foundation

In 2015, the TÜV Süd Foundation and TUM agreed on introducing a "Hans Fischer Senior Fellowship awarded by the TÜV Süd Foundation". By funding this Fellowship, the TÜV Süd Foundation aims to support the exchange of internationally renowned scientists as well as sustainable projects in groundbreaking research fields. So far, two Fellows were appointed under this scheme.

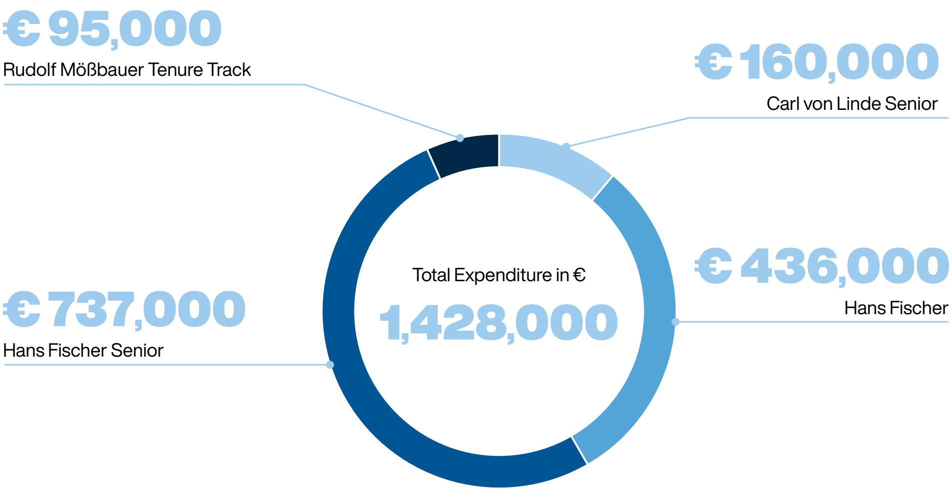
Siemens AG

The Siemens AG provides funding for six Hans Fischer (Senior) Fellowships with over two million euros. The research focus is on the fields of "Simulation and Digital Twin" and "Future of Autonomous Systems/Robotics." Four Fellows of this program have taken up their work in 2019 and 2020. Two more were appointed in 2021. ■

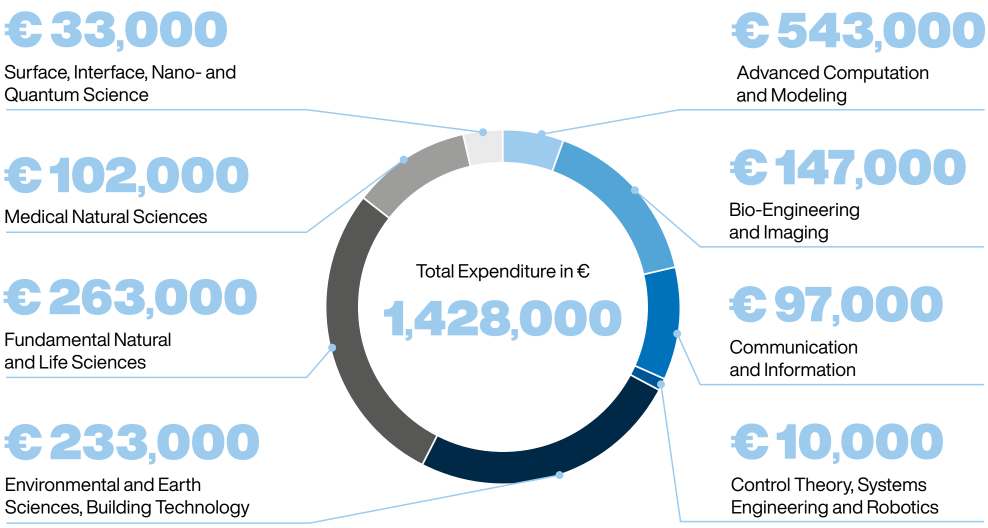
Fellow Distribution according to TUM-IAS Research Areas in 2020



Expenditure per Fellowship Category in 2020



Expenditure per Research Area in 2020



Board of Trustees

(status: May 2021)

The Board of Trustees is formed by a group of international advisors from academia, research support organizations, and industry. It advises the director on general scientific, organizational, and technical issues. The Board also defines the general strategy and standards of the Institute.

Members

Advisory Council

(status: May 2021)

The TUM-IAS Advisory Council is composed by TUM faculty, representing the different research areas of the university and this Institute. One of its prime functions is advising on the suitability and ranking of Fellow nominations the Institute receives for its various Fellowship programs. In addition, the Council advises on the scientific and technological course of the Institute, on the basis of an assessment of the potential and needs of the university. The Advisory Council meets regularly, typically three times a year.

Members

Prof. Martin Bichler, Decision Sciences & Systems

Prof. Hendrik Dietz, Biomolecular Nanotechnology

Prof. Laura Fabbietti, Experimental Physics: Dense and Strange Hadronic Matter

Prof. Hubert Gasteiger, Technical Electrochemistry

Prof. Florian Holzapfel, Flight System Dynamics

Prof. Michael Krautblatter, Landslide Research

Prof. Thomas Misgeld, Neuronal Cell Biology

Prof. Frank Petzold, Architectural Informatics

Prof. Claudia Peus, Research and Science Management/ Senior Vice President for Talent Management and Diversity

Prof. Ulf Schlichtmann, Electronic Design Automation

Prof. Chris-Carolin Schön, Plant Breeding

Prof. Miranda Schreurs, Environmental and Climate Policy

Prof. Stephan A. Sieber, Organic Chemistry II

Prof. Simone Warzel, Global Analysis

After two terms of office, the membership of **Prof. Dirk Busch, Prof. Ulrich Heiz, Prof. Katharina Krischer, Prof. Sabine Maasen, Prof. Gerhard Rempe, Prof. Daniel Straub and Prof. Barbara Wohlmuth** has ended in 2020. We would like to express our sincerest thanks for being able to rely on their experience and insight during the evaluation of our Fellowship proposals and the selection of our new Fellows for so many years.

TUM-IAS Management Office

(status: May 2021)

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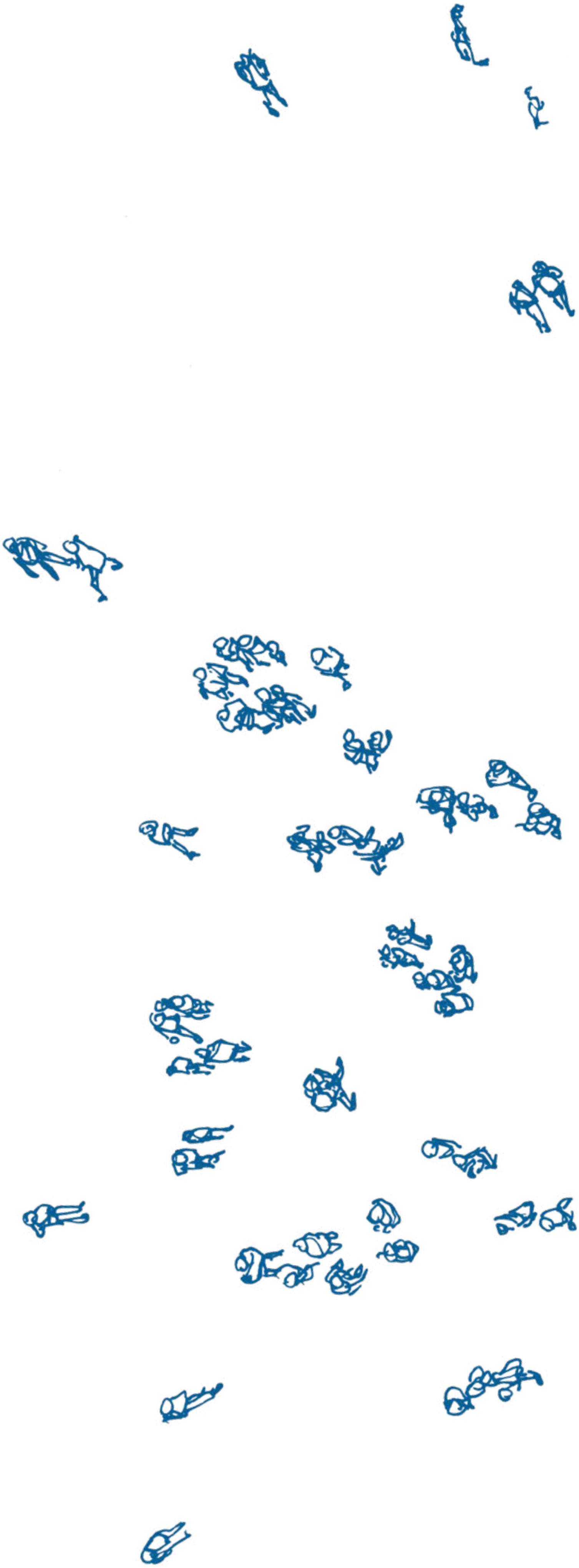

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