The molecular biomechanics of collagen

As we move around in the world, our body is often exposed to forces such as squeezing and stretching. This is true also at the cellular level. Mechanobiology studies how cells can sense and respond to mechanical forces. So far, research has been focused a lot on structures within cells, such as the cytoskeleton and cell adhesions. HITS group leader **Frauke Gräter** has been thoroughly investigating the mechanobiological properties of collagen, with in silico and in vitro methods. Together with colleagues from Israel and the U.S., she wants to explore the space

outside the cell, often filled with collagen, and uncover its signaling in the cell. For their proposal to the Human Frontier Science Program (HFSP), the three researchers received an HFSP Research Grant Award 2024. The project will start on 1 July 2024, with about $1.5 million USD funding for three years. "The novel idea behind this proposal is that proteins outside of the cell can also be affected by force and generate diffusible chemical signals that can reach nearby cells and influence their function", Frauke Gräter explains. In their recent observations they found that in controlled lab conditions, stretching extracellular protein collagen causes rupture of chemical bonds that release free radicals. "Our goal is to prove that this process happens also in living tissues under normal physiological forces and to study the impact of mechanoradicals on the health of the tissue and the entire organism", Alexander Dunn, a molecular biologist and expert in tissue engineering from Stanford University, USA, adds.

To this end, the researchers will use two model systems: a tendon taken from a mouse and the worm Caenorhabditis elegans. Tendons are highly collagenous tissue that connects muscles to bones and can be cultured outside of the animal for several days. C. elegans is a powerful genetic model system and its exoskeleton is made nearly entirely of collagen. "But the collagen of C. elegans has a different, still unknown structure", says Ronen Zaidel-Bar, a cell and development biologist and C. elegans expert from Tel Aviv University, Israel. The researchers will try to measure the effect of mechanoradicals on the integrity of the tissue and the well-being of the organism, including its fertility, resilience to stress, and lifespan. "Eventually, we will uncover mechanoradicals as a previously unrecognized molecular species in life that converts tension into physiological responses with implications for health, disease, and aging", Frauke Gräter resumes.

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13 July 2024, 11 am – 5 pm
Open Day at HITS
Weather, viruses and the Universe - AI for the world of tomorrow
www.h-its.org/event/open-day-at-hits-2024/

HITS

HITS researcher appointed ECMWF Fellow

Sebastian Lerch, junior research group leader at the Karlsruhe Institute of Technology (KIT) and visiting scientist in the CST group, has been appointed as a Fellow by the European Centre for Medium-Range Weather Forecasts (ECMWF), Reading/UK. The ECMWF Fellowship program

fosters links between ECMWF and individual scientists carrying out pioneering work in areas relevant to ECMWF's strategic goals. Lerch wants to advance the use of methods from artificial intelligence and machine learning for improving the accuracy and reliability of probabilistic weather forecasts on subseasonal-to-seasonal timescales.

Marie Curie Fellowship for HITS scientist

Debora Monego, PostDoc in the Molecular Biomechanics (MBM) Group at HITS, has

been awarded the Marie Skłodowska-Curie Actions Postdoctoral Fellowship (MSCA), one of the most prestigious awards for Postdocs in Europe, for her research work on the mechanochemical behavior of collagen, the main structural protein in the human body (more in section "Beyond the limits").

New employees and visiting scientists

Master student:	Paulius Greicius (MBM)
Communications:	Michael Stitz (Communications Manager)
Team assistant:	Kristin Weidner (TOS)
Visiting scientist:	Denis Kiesewetter (MBM, Heidelberg University)
HITS Journalist in Residence:	Felicitas Mokler (Germany)

HITS groups (06/2024): Astroinformatics (AIN), Computational Molecular Evolution (CME), Computational Statistics (CST), Data Mining and Uncertainty Quantification (DMQ), Machine Learning and Artificial Intelligence (MLI), Molecular Biomechanics (MBM), Molecular and Cellular Modeling (MCM), Natural Language Processing (NLP), Physics of Stellar Objects (PSO), Scientific Databases and Visualization (SDBV), Stellar Evolution Theory (SET), Theory and Observations of Stars (TOS).


HITSters

Bioinformatics tools help reveal complexity of avian evolution

Phylogenetic relationships are key to understanding the evolution of species. These relationships are typically identified by comparing, among other things, similarities in DNA or anatomical features. An international team of researchers from the "Bird 10,000 Genomes Project" (B10K), among them **Alexandros Stamatakis, Julia Haag** and **Oleksiy Kozlov** from the Computational Molecular Evolution group (CME) at HITS, have now analyzed genomes of 363 bird species by using their intergenic regions and

a plethora of computational methods. The result is a well supported tree, which however also exhibits a stunning degree of discordance.

In order to attain these results, large amounts of data are necessary to resolve discrepancies, which can be due to the diversity of species sampled, the phylogenetic method used, and the choice of genomic regions. Some of the most essential tools for processing these data were developed by the CME team together with scientists from its sister group, the Biodiversity Computing Group (BCG) at the Institute of Computer Science (ICS) of the Foundation for Research and Technology Hellas (FORTH), Heraklion, Greece.

Enabling research in evolutionary biology
"What we mainly do is to enable research in evolutionary biology via software, algorithms and model development," says Alexandros Stamatakis, who also holds an EU-funded ERA chair at FORTH. "The ParGenes software, for example, which is very central for the paper, can efficiently schedule the inference of a huge number of per-gene phylogenetic trees on distinct input gene datasets on a large compute cluster. This is classic fundamental computer science as it focuses on efficient job
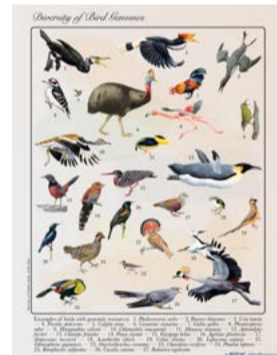
scheduling." A late addition to this paper was the Pythia difficulty prediction developed by Julia Haag. "Given an input dataset it predicts how difficult a phylogenetic inference on that dataset will be, that is, how much signal for a single tree there is in the data, using machine learning techniques," says Stamatakis. "

The tools the CME group have developed and that are being used in this paper are all open source and extremely highly cited. "In this project, we provide the basic toolbox for our fellow scientists that actually enables them to do their science," says Stamatakis. "I personally find this very gratifying."

Stiller J et al: Complexity of avian evolution revealed by family-level genomes. Nature 1 April 2024, DOI: 10.1038/s41586-024-07323-1https://www.nature.com/articles/s41586-024-07323-1
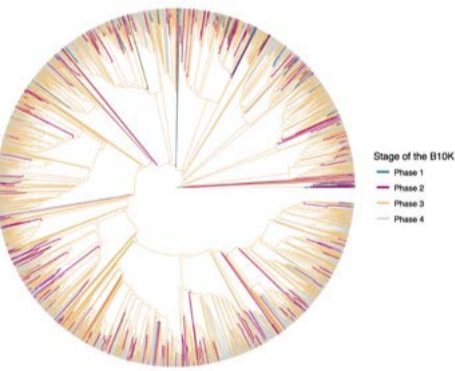
Research

Beyond the limits – Debora Monego, PostDoc, Molecular Biomechanics group (MBM)

"One of my favorite things about working at HITS is the collaborative aspect of the teams," says **Debora Monego**. She shows a simulation of a collagen molecule she is experimenting with on the computer screen at her workspace. "In our simulations, we pull the collagen fibrils to see where they break. This happens all the time in our bodies."

She was rewarded for her research work by winning the prestigious Marie Skłodowska-

Curie Actions Postdoctoral Fellowship (MSCA) (see "HITSters"). "We are very proud to have Debora as the first MSCA awardee at HITS in our group and look forward to the research ahead," says MBM group leader **Frauke Gräter**.

Born in Brazil, Debora Monego completed her PhD in chemistry at the University of Sydney, Australia. After a stay at Columbia University in New York, USA, Debora joined HITS at the beginning of 2023. Later that year, she spent two months at Harvard Medical School in Boston, USA, for a research stay, where she expanded her knowledge of bioinformatics methods.

Communicating science
Debora is keen to explain her research outside the scientific community. During a visit of the juForum congress at HITS, she told the scientists-to-be how various forces put the collagen in our bodies to the test. At the Heidelberg Science Pub, Debora elaborated to a wider public how computer simulations can help understand the reaction of proteins under high stress. Communicating

science is important to her. "In the future, I would like to combine research with teaching. My goal is to become a professor and teach the next generation of scientists."

With the MSCA Postdoctoral Fellowship, Debora Monego will now commit herself to a new project at HITS. She will focus on how collagen has adapted over the course of evolution in terms of its response to forces, particularly in the context of ageing and disease. The interdisciplinary approach combines bioinformatics, computational biophysics, and materials science and aims to show how evolution shapes protein defenses against mechanical strains.

Debora takes another look at her screen and observes the collagen fibers in her simulation. "What motivates me as a scientist is curiosity. Understanding and improving the world - that's why I became a scientist in the first place."

Beyond the limits

HITS

The Charts