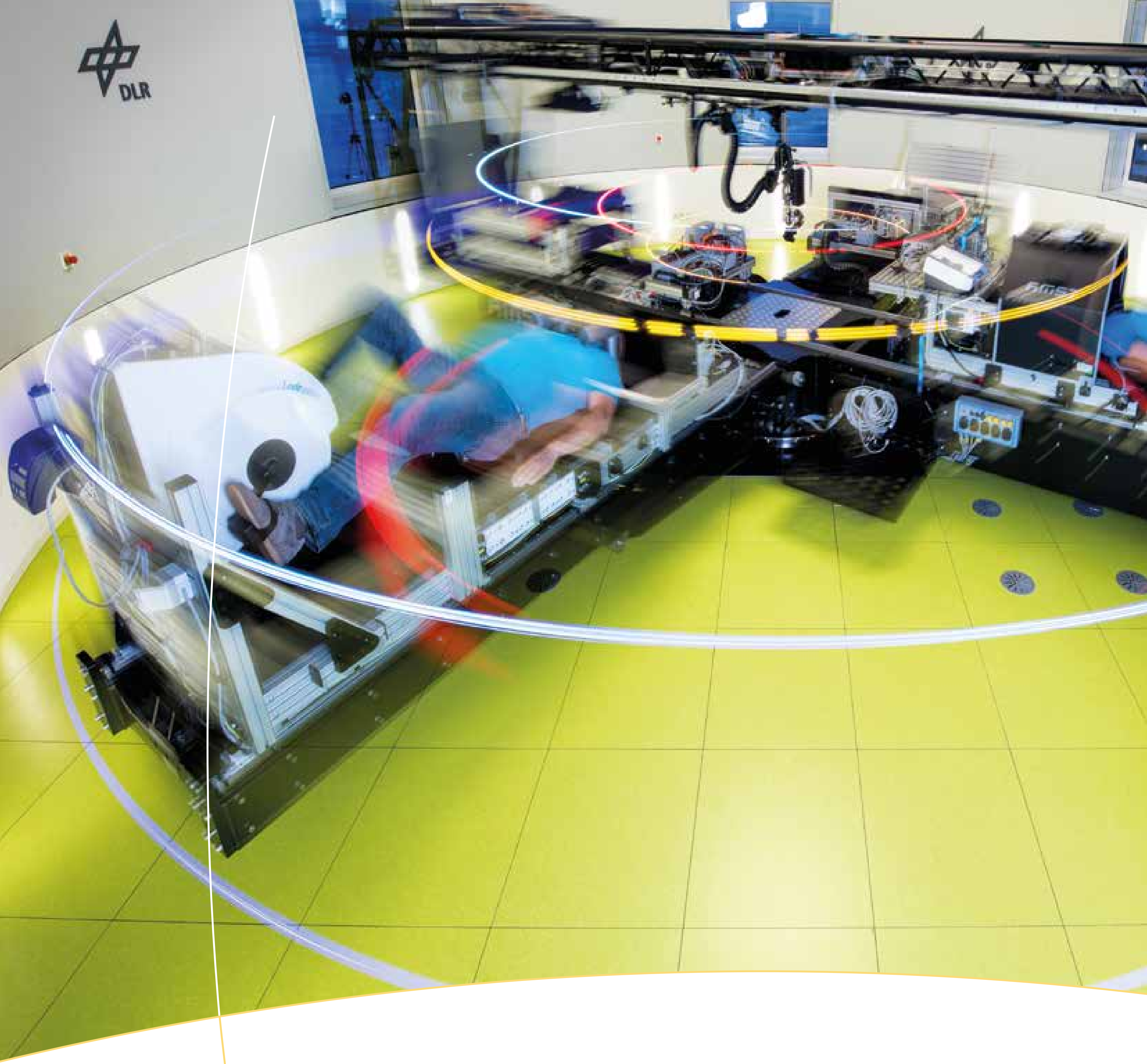


The Institute of Aerospace Medicine

Report 2017-2020

Content

I. The Institute of Aerospace Medicine

Jens Jordan, Head of the Institute of Aerospace Medicine, DLR

Ruth Hemmersbach, Acting Head of the Institute of Aerospace Medicine, DLR

The overarching institutional goal is to improve human health span in space and on Earth.

The DLR Institute of Aerospace Medicine serves as interface between biology, medicine, psychology, and advanced technologies. The Institute contributes fundamental new knowledge and innovative solutions for chances and challenges imposed by aeronautics, space, and transport on human beings.

The Institute of Aerospace Medicine develops tools to identify risks for health and psychological well-being of flying personnel including pilots and astronauts and designs individual countermeasures. Moreover, research findings and technological developments are applied to help addressing important societal needs, such as demographic change, technological transformation, and sustainability on Earth. An important aim is to create opportunities for economic developments in the rapidly evolving space and aeronautics sector in Germany. Furthermore, the research informs political decision making. To attain these goals, the Institute closely collaborates with leading national and international research institutions, agencies, and industry.

The research program, which is rooted in long-standing experience in selecting and caring for pilots, air traffic controllers, and astronauts, follows the premise that mechanistic understanding drives innovation. The biomedical and psychological research comprises field experiments under space conditions, in airplanes, or in the homes of people affected by traffic. The Institute is intimately involved in experiments on the International Space Station (ISS), on compact satellites, on sounding rockets (DLR Mapheus program), and on parabolic flights among others.

Field studies are flanked by carefully controlled experiments on Earth under highly standardized conditions. To enable this research, the Institute's research infrastructure and scientific expertise have been further strengthened and focused in recent years. In particular, the one-of-a-kind medical research facility :envihab ("environment" and "habitat") was established and now allows performing human investigations that would be difficult or impossible to conduct elsewhere. The combination of advanced human physiology profiling, state-of-the-art imaging modalities, highly standardized simulation and manipulation of environmental conditions are particula strengths of this research program. The environmental conditions covered by our research include atmosphere composition and pressure, gravitation, noise, light, radiation, nutrition, and the microbiome. The human research focuses on central nervous system and behavior, cardiovascular structure and function, bone and muscle biomechanics and metabolism. In addition, :envihab is approved for hosting and evaluation of ESA astronauts directly after their return from the International Space Station to Earth.

Systematic ground-based studies in radiation, astro- and gravitational biology are performed in the planetary and space simulation facilities and are complemented by successful investigations in space over many years. By studying responses to environmental conditions prevailing on other planets and moons on living systems, fundamental questions about limits of life and how organisms adapt to these harsh conditions are discovered. Moreover, conception and testing of life-sustaining closed biological systems, which are crucial for long-term space missions, also address important societal issues on Earth.

I.1 Structure

The Institute of Aerospace Medicine comprises seven research departments that are located in Cologne and in Hamburg. The Departments for Cardiovascular Aerospace Medicine, Sleep and Human Factors Research, Clinical Aerospace Medicine, Muscle and Bone Metabolism, Radiation Biology, and Gravitational Biology are located at the DLR campus in Cologne. The Department for Aerospace Psychology is located in proximity to Hamburg airport.

I.2 Organization chart

DLR INSTITUTE OF AEROSPACE MEDICINE — **DEPARTMENTS AND CONTACT PERSONS**

J. JORDAN | Head — **R. HEMMERSBACH** | Acting Head

Finance and Administration P. Hermann	**Cardiovascular Aerospace Medicine** J. Tank	**Sleep and Human Factors Research** D. Aeschbach	**Clinical Aerospace Medicine** C. Stern	**Muscle and Bone Metabolism** J. Rittweger	**Aerospace Psychology** P. Maschke	**Radiation Biology** C. E. Hellweg	**Gravitational Biology** R. Hemmersbach
Technical Infrastructure D. Poddig	**Advanced Functional Imaging** J. Tank	**Performance and Sleep**	**Aeromedical Center AeMC** M. Trammer	**Mechano-Physiology** U. Mittag	**Crew Performance and Transport** D. Stelling	**Astrobiology** P. Rettberg	**Gravisensorics** C. Liemersdorf
Information Technology T. Urlings	**Cardiovascular Control in Health and Disease** K. Heußer	**Noise Effects Research**	**Occupational Medicine** P. Tuschy	**Molecular Musculo-skeletal Research** C. Clemen	**Air Traffic Control** H. Eißfeldt	**Biodiagnostics** C. E. Hellweg	**Bioregeneration** J. Hauslage
Quality Management J. Aeckerlein		**Baromedicine**	**Aerospace Ophthalmology** C. Stern	**Translational Metabolism Research** D. Pesta	**Space Psychology**	**Biophysics** T. Berger	**Cellular Mechano-transduction**
Public Relations F. Wütscher		**Digital Health** M. Lindlar		**Training and Countermeasures** J. Zange		**Radiation Protection in Aviation** M. M. Meier	
Study Team M. von der Wiesche						**Aerospace Microbiology** R. Möller	
Research Relations and Development E. Mulder							

I.3 Interdisciplinary cross-sectional research topics

01.
Mechanisms by which gravity and atmospheric conditions impact human health and performance in space, in aviation, and on Earth

02.
Genome-environment interactions on sleep, performance, and cardiometabolic disease in the mobile society

03.
From molecular mechanisms to individualized risk assessment and radiation exposure prevention

04.
Human, environment, and microbiome interactions: From aerospace research towards sustainable economic management on Earth

05.
Human-human and human-machine interactions: Challenges and opportunities in the light of demographic change

An overview on contributions of the departments to cross-sectional topics is provided on pages 84-85. In the following sections, working group contributions to cross-sectional topics are indicated by colors corresponding to the graph above.

I.4 Programmatic involvement at DLR

The Institute of Aerospace Medicine is the only Life Science Institute at DLR, thus, serving as interface between humans, the environment, and DLR high-tech expertise. With its research at :envihab, an internationally unique research infrastructure, the Institute contributes to finding solutions to challenges facing human beings in space, in aeronautics, and on Earth. Human space exploration is an important element of research under space conditions. Within the DLR space program the Institute contributes to enabling long-term stays of humans in space by investigating the mechanisms affecting health and performance and developing targeted countermeasures.

As part of the Helmholtz Association, the Institute of Aerospace Medicine receives program-oriented funding. The Institute is primarily supported by the DLR space and aeronautics programs and to a lesser degree by the DLR transport program. Within the DLR priority areas aviation, space and traffic, the Institute investigates human-machine interactions from a medical and psychological perspective. We develop and implement procedures for selection, assessment, and performance of operators including astronauts, pilots, and air traffic controllers. Research on bioregeneration is crucial for space exploration and may yield novel technology for waste management applications on Earth.

Due to shortage of skilled personnel, demographic changes and internationalization, the selection of suitable personnel is also highly relevant in other professional groups. The assessment of the effects of aviation and transport on the health of the population, such as noise and atmospheric composition, are among the core tasks of the Institute. In fact, the subjective annoyance and objective physiological burden caused by noise is considered to be a major constraint on further traffic development. Of particular interest are also the effects of carbon dioxide and atmospheric oxygen concentration and pressure on human performance and health. Therefore, the Institute of Aerospace Medicine has also begun to combine data from DLR Earth observation with medical findings on Earth.

I.5 Strengths of the Institute and practical applications

The Institute of Aerospace Medicine is the interface between the life sciences of biology, medicine, and psychology and the high-tech sector of DLR. The Institute's research is conducted in close cooperation with leading national and international research institutions. The position of the DLR research campus in Cologne as international hub for aerospace medicine will be further strengthened. In 2021, German Air Force Center of Aerospace Medicine will be relocated from Fürstenfeldbruck to the DLR campus in Cologne. DLR and the German Air Force have signed a cooperation to foster scientific exchange and professional training.

Many of the psychological and medical challenges in space and aviation are also relevant to people on Earth. For example, without targeted countermeasures, space travel replicates many age-related physiological changes such as loss of muscle and bone mass, reduced cardiopulmonary fitness, and limitations in coordination and eye health. Both space and aviation can lead to disturbances of circadian rhythms and associated sleep disorders, which not only impair health but also can limit human performance and increase error rates.

The Institute’s particular strengths are the combination of advanced human physiological methods with the highly standardized simulation of environmental conditions. The research findings are directly incorporated into psychological and medical selection procedures and the medical care of flying personnel and air traffic controllers at the Institute. The aim is to maintain and promote the health and performance of human beings in space, aviation and on Earth.

The Institute of Aerospace Medicine promotes cooperation with other DLR Institutes, either existing or in the process of being founded, in order to bring socially relevant topics in the fields of environment and health, big data, Earth observation, human-machine interactions in robotics, flight guidance and space systems into biomedical applications. The programmatic integration takes place mainly in the programs Space and Aeronautics. A stronger integration in the program topics Transport and Security is being achieved.

II. Departments of the Institute of Aerospace Medicine

II.1
Cardiovascular Aerospace Medicine

Prof. Dr. med. Jens Tank (Head)

PD Dr. med. Karsten Heußer (Deputy)

Mission Goal
The Department for Cardiovascular Aerospace Medicine investigates gene-environmental influences on the human cardiovascular system. We focus on real and simulated weightlessness, atmosphere conditions, nutrition, and exercise. The major aim is to elucidate mechanisms of cardiovascular structural and functional adaptation and how these responses are integrated by the autonomic nervous system. Human space experiments are flanked by highly controlled terrestrial studies in healthy persons and in patients in close collaboration with leading university medical faculties. Combination of physiological or pharmacological challenges with high-fidelity human phenotyping and biomedical engineering is our particular strength. Moreover, we translate observations in patients with rare cardiovascular conditions and defined genetic variants to astronauts confronting spaceflight and vice versa. The ultimate goal is to improve diagnostics, cardiovascular countermeasures, and treatments in space, in aeronautics, and on Earth.

Cardiovascular Aerospace Medicine

Unique selling points of the department

- Highly controlled mechanistic studies applying high-fidelity cardiovascular phenotyping in healthy persons, in selected patient cohorts, and in astronauts
- Unique expertise and infrastructure combining PET/MRT imaging with human physiological profiling with a focus on the brain-heart axis
- International leadership in clinical autonomic research in space and on Earth

Current and future challenges

- Combine high-fidelity cardiovascular phenotyping with advanced functional and molecular imaging to study the brain-heart axis
- Translate the results into terrestrial medicine
- Establish long-lasting national and international cooperation
- Attract young physicians/scientists to the field

Cardiac function in extreme environments

Long-term spaceflight profoundly changes demands on the cardiovascular system. In weightlessness, blood volume and interstitial fluid are rapidly shifted towards the head. The response is followed by compensatory changes in blood and plasma volume, left ventricular muscle mass, cardiac geometry, and cardiac function. Moreover, atmospheric conditions on spaceships and in future habitats may differ from conditions on Earth. With upcoming ambitious goals in spaceflight and increasing mission durations the risk for pathological alterations in the cardiovascular system increases and more effective countermeasures are needed. Broader understanding cardiovascular adaptation to the harsh environmental conditions in space and how they interact with genetic predisposition may help attenuating potential health risks in space and habitats.

Mechanisms of orthostatic intolerance in astronauts and in patients

The ability to stand upright on Earth while maintaining blood pressure is an evolutionary advantage of human beings. With standing, 500-1000 ml of blood are pooled below the diaphragm and plasma volume decreases 10-20%. Failure of proper blood pressure regulation may cause profound hypotension and loss of consciousness (syncope). Post-spaceflight orthostatic intolerance poses risks for astronauts and data on cardiovascular responses to active standing on other celestial bodies is lacking. The department has long lasting expertise in passive and active orthostatic testing and is internationally acclaimed for evaluation and clinical management of patients with orthostatic dysfunction.

Cardiovascular control in health and disease

Several mechanisms interact in a complex fashion to regulate the cardiovascular system. To unravel their individual mode of operation and their concerted interaction, we apply high-fidelity cardiovascular phenotyping in healthy persons submitted to highly controlled interventions and in patients suffering from autonomic nervous system disease. Through mechanistic understanding we aim at early detection and development of targeted interventions to maintain cardiovascular performance and health in aerospace and terrestrial medicine:

- We profile cardiovascular control mechanisms through simultaneous recordings of mechanical and electrical phenomena, e.g. of the heart (impedance cardiography, electrocardiography), vessels (arterial pressure, pulse wave characteristics), lungs, and nerves (direct intraneural measurements of sympathetic nerve activity).
- We apply physiological challenges, such as head-down bedrest, head-up tilt table testing, and lower body negative pressure (LBNP), pharmacological interventions, and electrical stimuli (e.g. electrical baroreflex stimulation) to elucidate responses and adaptations of cardiovascular control systems.
- We apply these methods in healthy volunteers as well as in patients with defined disorders, including patients with orthostatic hypotension (e.g. caused by synucleinopathies: Parkinson's, Pure autonomic failure, Multiple system atrophy) or arterial hypertension. Studies in patients enable us to translate scientific findings between the clinic and cardiovascular space research and to gain mechanistic insight.

Working Groups

Cardiovascular control in health and disease
(PD Dr. med. Karsten Heußer)

- High fidelity cardiovascular phenotyping including direct measurements of muscle sympathetic nerve activity in healthy subjects and in patients with rare autonomic disorders as model for spaceflight conditions
- Inflight experiments (parabolic flights and ISS missions)
- Validation of certified non-invasive methods under extreme non-invasive
- Application and development of physiological and pharmacological methods and challenges, e.g. head-down tilt bedrest studies
- Determine the efficacy of drug therapy as well as nonmedical treatments including countermeasures and physical training
- Improving early detection of pathological changes and translation of those methods into terrestrial medicine
- Development and improvement of hard- and software
- Goal-driven combination of in-house and external methodological expertise, e.g. baroreflex activation in fMRI to further probe the brain-heart axis

Advanced functional imaging
(Prof. Dr. med. Jens Tank)

- State of the art neuroimaging methods
- Functional MRI assessment of the brainstem and hypothalamus, the centers of autonomic control
- Autonomic testing within the MRI scanner, to characterize the function and neuroplastic adaptations in response to immobilization, diseases, and life style
- Cardiac MRI under extreme environments, including hypoxic condition and immobilization
- Detection of cardiovascular deconditioning and impairment in immobilization and diseases
- Probing the brain-heart axis with brain and cardiac imaging
- Unique combinations of novel methods in the MRI setting such as lower body negative pressure during neuro imaging

- We develop and improve hard- and software which supports above mentioned methodology.
- We collaborate with other groups to combine our methods and to expand scientific capabilities.

Functional imaging of cardiovascular reflexes at the brainstem and hypothalamic level

Brainstem and hypothalamus are the two major control centers in the brain integrating incoming information from baro- and chemoreceptors and adjust efferent signals that regulate breathing, heart rate, and blood pressure. Previous studies, during and after spaceflight showed that abnormalities in the cardiovascular system during weightlessness and after landing may at least in part be due to changes in central cardiovascular regulation. However, our knowledge about these mechanisms below the cortical level is scarce in humans. Moreover, cardiovascular diseases including arterial hypertension and heart failure are often accompanied by changes in central autonomic cardiovascular control and impaired reflex mechanisms which may influence the progression of the disease or the response to therapies. To gain deeper insight in the functioning of this so-called brain-heart axis is our major research interest.

Development of effective countermeasures for space and for clinical use

Lower body negative pressure (LBNP) has been developed in the early sixties of the last century as a countermeasure for space-flight mediated deconditioning. The idea was to counteract volume shifts towards the head and to maintain cardiovascular reserve. However, currently used protocols with short-time interventions at the end of spaceflight and stationary technologies onboard the ISS yielded suboptimal results. Systems and protocols have to become more effective, mobile, and comfortable. One aim of the department is to develop and to test new LBNP concepts with applications in space and in terrestrial medicine, such as in patients with raised intracranial pressure in neurological intensive care units.

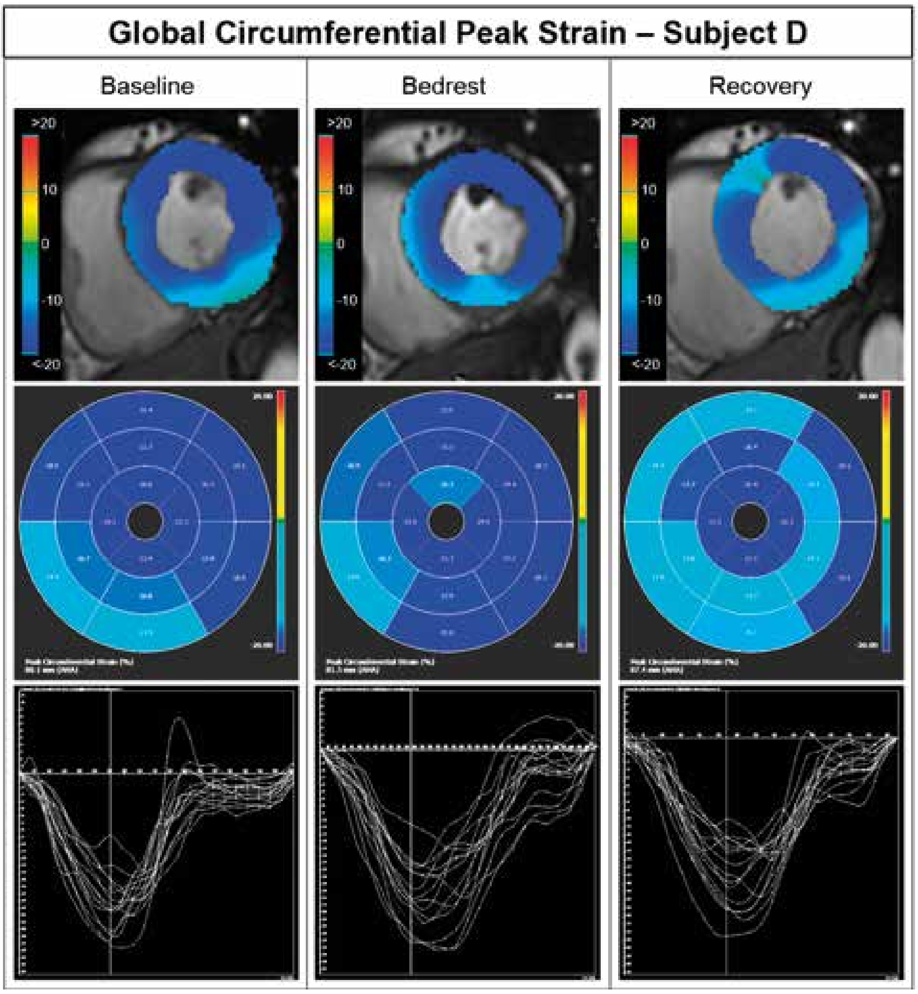
Main projects 2017-2020

Cardiac Deconditioning – From bedside to space

We examined cardiovascular adaptation to a spaceflight analog, namely -6° head-down-tilt bedrest for 60 days, within the AGBRESA study in 2019, conducted by the DLR, ESA, and NASA. We applied echocardiography and state-of-the-art cardiac MRI before, during, and after bedrest in a repeated fashion in order to quantify possible benefits of artificial gravity training.

Our results show that movement and deformation of cardiac tissue (strain, figure 1) did not change. That means, that we could not observe structural changes, which is at odds with findings of cardiac atrophy during space flight. Long-term bedrest led to functional alterations which we could not prevent by application of artificial gravity (short arm human centrifuge). Yet, we have proven normal cardiac function already on recovery day 4 after bedrest.

The findings mentioned above are challenged in real microgravity. For example, we observed that prolonged space flight is associated with substantial reductions in natriuretic peptides which respond to myocardial stretch. We currently run the Cardiovector flight experiment onboard the International Space Station since 2018 in close collaboration with the Institute for Biomedical Problems in Moscow and the University Hospital of Cologne. The major aim is to phenotype the cardiovascular and autonomic nervous system and their responses to spaceflight in cosmonauts. Examinations include hemodynamic measurements prior, after, and during the mission as well as cardiac MRI prior and after flight using exactly the same protocols as in the bedrest studies.



Typical global circumferential strain measurement in one subject of the AGBRESA study. Upper panel shows the circumferential strain overlay on a short axis plane of the left ventricle just above the papillary muscles at baseline, at the end of bedrest, and during recovery. Middle panel displays the 'American Heart Association 16 segments model' of the left ventricle with their peak strain values over time. Lower panel describes the time course of strain values in these segments over time (shown is one heart-beat, temporal resolution is 25 images per heart beat) reaching peak strain at the end of systole.

Hypoxia and myocardial regeneration (MyoCardioGen)

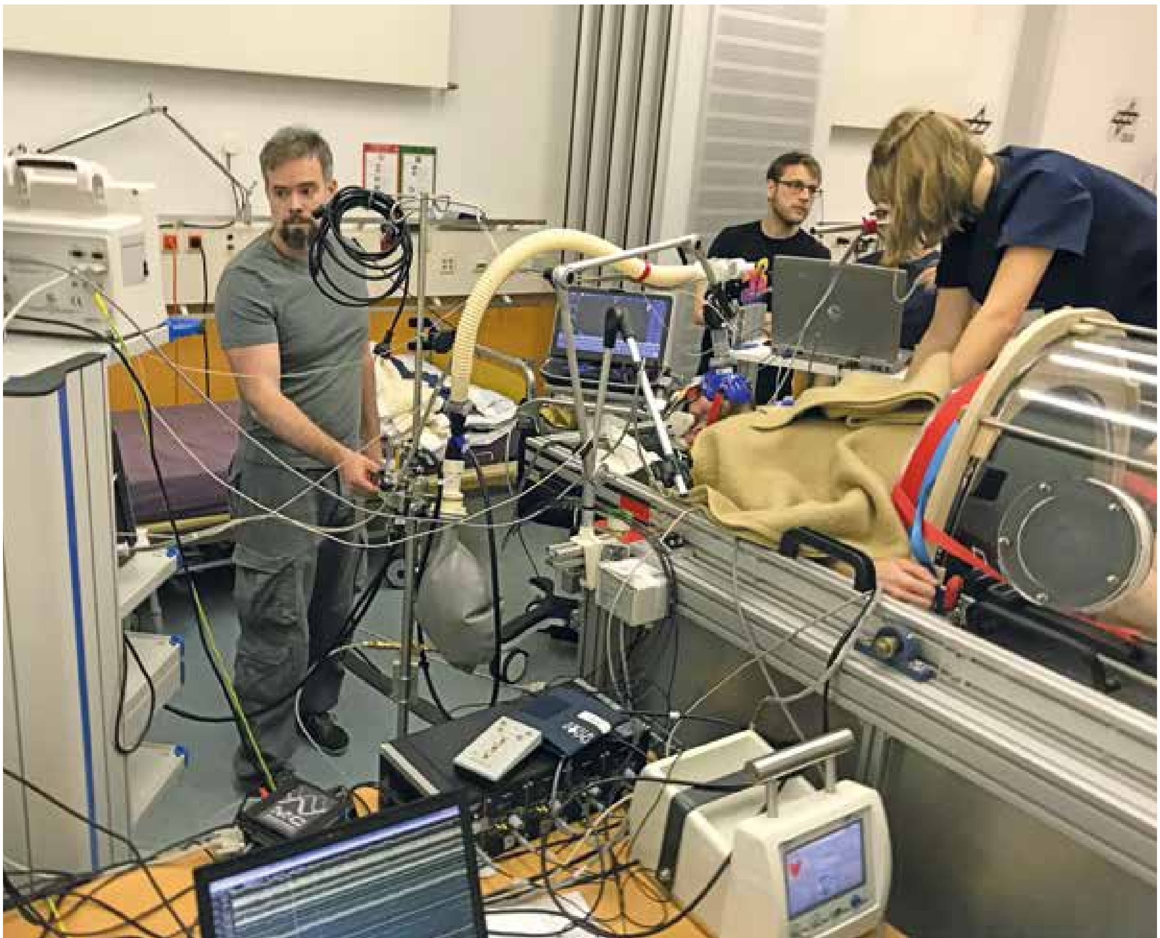
DLR in cooperation with researchers from University of Texas Southwestern (UTSW) in Dallas intends to translate findings from animal studies indicating that severe sustained hypoxia (close to Mt. Everest conditions) can improve cardiac function and induce myocardial regeneration to human beings. A proof-of-concept and safety study at DLR in Cologne was conducted in two professional mountaineers in 2018. They lived in the :envihab facility for a total of 5 weeks. Ambient oxygen concentration was decreased stepwise to a minimum of 8% (corresponding altitude 7,112 m) and was kept at a stable level of 8.5% during daytime and 8.8% during the night for the last two weeks. Subjects underwent daily physical exams, spirometry, echocardiography, cardiac MRI, brain MRI, muscle MRI, cognitive and strength testing as well as blood sampling. Both subjects tolerated severe hypoxia well. Although we could observe acute mountain sickness-like symptoms during acclimatization, they soon regressed. Cardiac function did not deteriorate in this atmosphere and physical performance, although diminished, was preserved. First results were published in Circulation in 2020.

We could prove that human research is safe and feasible in a severely hypoxic environment. This study paves the way for follow-up trials including first patients who have a history of myocardial infarction. In that approach we can test the hypothesis that hypoxia can stimulate myocardial regeneration. Next trials are planned for 2021 at DLR in close collaboration with UTSW and many other partners.

LOCAR: Probing the 'Limits of cerebral autoregulation'

Cerebral autoregulation is the ability of the cerebral vasculature to maintain adequate blood flow and oxygen delivery to the brain. The system has individual upper and lower limits. Crossing the lower limit may cause syncope and reaching the upper limit may cause brain damage. For example, staying within autoregulatory limits during surgery is crucial and reliable brain perfusion monitoring is required. Currently, mean arterial blood pressure is mainly used for monitoring but cardiac output seems to play a major role, too. To test this hypothesis we conducted an experiment to induce large blood volume shifts under controlled conditions to reach the upper and lower limits of cerebral autoregulation in healthy subjects.

In 2019, we conducted a feasibility study, together with the Anesthesia Department of the University Hospital Bonn, using lower body positive pressure in combination with hypoxia to increase cardiac output and to reach the upper limit of cerebral autoregulation. We applied lower body negative pressure to approach the lower limit. Our results in five healthy subjects show, that 40 mmHg positive pressure in combination with moderate hypoxia does not shift enough blood volume towards the head to reach the upper limit. In contrast, we reached the lower limit in all subjects by applying negative pressure up to -60 mmHg. Oxygen saturation of the brain, measured by near infrared spectroscopy (NIRS), was the best predictor of presyncope or loss of consciousness. We will now apply the technology to assess mechanisms of orthostatic tolerance following simulated and real space flights.



Experimental setup for the LOCAR study

Baroreflex function and sympathetic activity with cardiac unloading: from patients with artificial hearts to astronauts

Prolonged space flight is associated with reduced cardiac loading which could negatively affect neural control mechanisms. Heart failure patients implanted with left ventricular assist devices (LVAD) served as model for cardiac unloading to test two hypotheses. First, physiology textbooks claim, that sympathetic activity is unleashed with low pulse pressure, an important stimulus for baroreceptors, such that sympathetic activity should be increased after LVAD implantation.

Second, cardiac transplantation in heart failure normalizes sympathetic neurohumoral activity. Can this be expected to occur with LVAD implantation? To test these hypotheses, we recorded sympathetic activity intraneurally in heart failure patients before and after LVAD implantation. We observed that sympathetic nerve activity did virtually not change despite markedly reduced pulse pressures and improved hemodynamics after LVAD implantation.

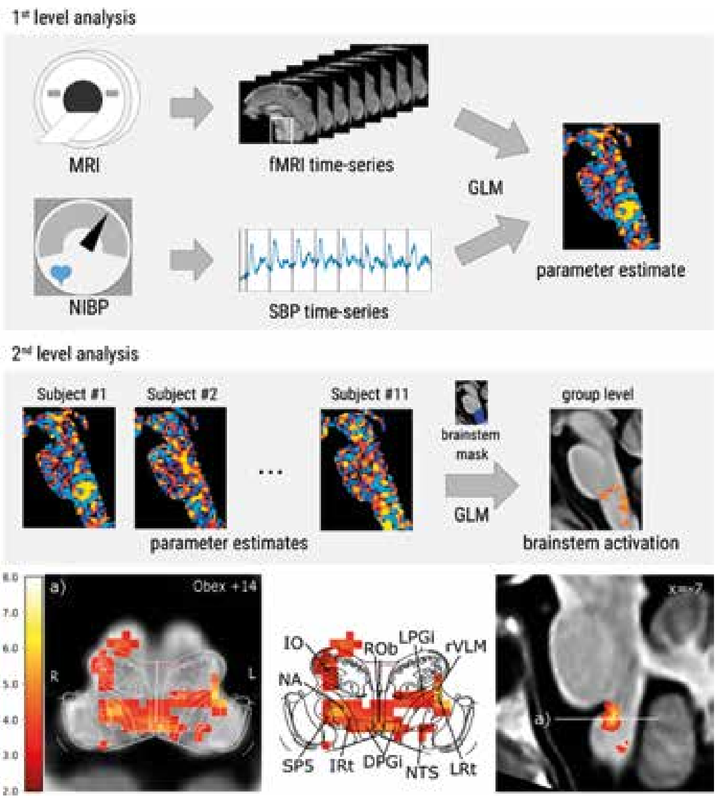
Cardiovascular reflex interactions govern adjustments to environmental challenges

Baroreflexes and chemoreflexes are engaged when gravitational loading conditions and atmosphere conditions, particularly changes in oxygen and carbon dioxide, are altered. The interaction between reflexes on cardiovascular control is important for cardiovascular control in space and in patients with cardiovascular disease. Electrical baroreflex pacers provide a unique model to study these mechanisms in human beings. The devices are implanted at the carotid artery in patients with refractory hypertension. Studies suggested that the peripheral chemoreflex is beings tonically active in hypertensive patients and may inhibit the baroreflex. To test the hypothesis that baropacing is less effective during chemoreflex activation, we compared baroreflex responses during isocapnic hypoxia (hemoglobin oxygen saturation 79%) and hyperoxia.

Unexpectedly, our results clearly showed that chemoreflex activation does not compromise electrical baroreflex activation therapy. These findings illustrate that mechanistic studies in selected patient populations are clinically meaningful as they can provide unique insight in human baroreflex physiology and reflex interactions that could not be gained otherwise.

Deciphering the neural signature of cardiovascular regulation

Brainstem and hypothalamus are primary relay stations regulating the cardiovascular system in the face of environmental challenges. We conducted a proof-of-concept study in young, healthy men. The protocol included pharmacological baroreflex testing (phenylephrine bolus technique using an automated injection pump), repeated moderate hypoxia, and alternating blocks of lower body negative pressure (LBNP) as stimuli. Hemodynamics and respiration were recorded continuously in the 3T PET/MR environment. Resting state high-resolution fMRI of the brainstem and hypothalamus was performed. In close cooperation with the research group of Prof. Beissner, Hannover Medical School (MHH), we were able to assess the human baroreflex regulation at the level of the brainstem. We identified sympathetic sites, like rostral ventrolateral medulla, Ncl. raphe obscurus, and parasympathetic sites, like Ncl. ambiguus. Three distinct parts of the hypothalamus regulate the human cardiovascular system. The subsystems are connected with the lower brainstem and with each other. Finally, we were able to show the rhythmic activity of the subsystems at the hypothalamic level in frequency bands known from heart rate and blood pressure variability. Using hypoxic stimuli we detected nuclei involved in blood pressure regulation as well as in respiration.



Based on these findings, a clinical study in patients with multiple system atrophy (MSA) was started in 2020 together with the University Clinic Cologne and the MHH to image possible connectivity changes in hypothalamic subsystems associated with orthostatic hypotension. These studies will pave the way for studies assessing whether simulated or real space conditions affect the brain-heart axis at the level of brainstem and hypothalamus.

Collaboration partners within the Institute

- Dept. of Muscle and Bone Metabolism
- Dept. of Clinical Aerospace Medicine
- Dept. of Sleep and Human Factors Research
- Dept. of Gravitational Biology
- Dept. of Radiation Biology
- Study Team

Collaboration partners within the DLR

- Institute for Software Technology, Cologne
- Institute of Material Physics in Space, Cologne

Collaboration partners in Germany

- University of Cologne (Radiology, Cardiology, Neurology, Nuclear Medicine)
- Charité-Berlin-Buch (ECRC, cardiac imaging)
- MDC-Berlin (Molecular Physiology of Somatic Sensation)
- Hannover Medical School (neurology, neuroradiology, brainstem imaging; microRNA)
- MP Institute of Biophysical Chemistry Göttingen (real time MRI)
- SpoHo-Cologne (exercise, epigenetics)
- University of Bonn (pediatric cardiology)
- University of Düsseldorf (Cardiology, Neuroanatomy)
- RWTH Aachen (Anesthesiology, Neurology)
- ITEM Fraunhofer
- Hannover, Department of Neurosurgery
- German Armed Forces Central Hospital Koblenz (Neurosurgery)
- Profil Institute for Metabolic Research GmbH

Collaboration partners worldwide

- University of Colorado (AltitudeOmics)
- Johns Hopkins University, Baltimore (hypoxia induced factors)
- Penn-State Univ., Philadelphia (Cognition & performance)
- UTSW, Dallas, Texas (DNA repair, chronobiology, imaging)
- Université Libre de Bruxelles, Belgium (wearables, AI)
- Vanderbilt Univ. Nashville, TN (biosignal analysis)
- Austrian Institute of Technology, Vienna (pulse wave analysis)
- Lomonossov University Moscow, Russia (cardiac imaging)
- IBMP (Institute of Biomedical Problems), Moscow, Russia (wearables)
- Politecnico di Milano, Italy, Biomedical Engineering Department (cardiac MRI)

Selected publications

Gerlach, D., Manuel, J., **Hoff, A., Kronsbein, H., Hoffmann, F., Heusser, K.,** Ehmke, H., Diedrich, A., **Jordan, J., Tank, J.,** Beissner, F. (2019) *Novel Approach to Elucidate Human Baroreflex Regulation at the Brainstem Level: Pharmacological Testing During fMRI.* Frontiers in Neuroscience. 2019; 13: 193.

Heusser, K., Thöne, A., Lipp, A., Menne, J., Beige, J., Reuter, H., **Hoffmann, F.,** Halbach, M., Eckert, S., Wallbach, M., Koziolek, M., Haarmann, H., Joyner, M., Paton, J.F.R., Diedrich, A., Haller, H., **Jordan, J., Tank, J.** (2020) *Efficacy of electrical baroreflex activation is independent of peripheral chemoreceptor modulation.* Hypertension. 2020; 75: 257-264.

Hoffmann, F., Limper, U., Zaha, V., Reuter, H., Zange, L., Schulz-Menger, J., Hein, M., Baldus, S., Levine, B., **Jordan, J., Tank, J.** (2020) *Evolution of pulmonary hypertension during severe sustained hypoxia.* Circulation. 2020; 141: 1504-1506.

Limper, U., Möstl, S., Tank, J., Prisk, K., **Heusser, K., Hoffmann, F.,** Goßmann, A., Migeotte, P.-F., **Gauger, P., Beck, L.E.J.,** Schlegel, H.W., Levine, B.D., **Jordan, J.** (2020) *A 20 year evolution of cardiac performance in microgravity in a male astronaut.* Clinical Autonomic Research, EPUB.

Manuel, J., Färber, N., **Gerlach, D.A., Heusser, K., Jordan, J., Tank, J.,** Beissner, F. (2020) *Deciphering the neural signature of human cardiovascular regulation.* eLife, 9 (e55316).


DLR

II.2
Sleep and Human Factors Research

Prof. Dr. sc. nat. Daniel Aeschbach (Head)

PD Dr. med. Eva-Maria Elmenhorst (Deputy)

Mission Goal
Our mission is to maintain optimal human performance, sleep, and wellbeing for operators working under the specific challenges and risks of a mobile 24-hour society. Shift work is highly prevalent in operators working in the field of aeronautics, space, and transport exposing a large number of persons to its negative short-term (cognitive decline) and long-term (health) consequences. We apply our highly advanced and controlled laboratory environment to systematically study how homeostatic and circadian processes regulate cognitive performance as well as the quality, duration, and timing of sleep and how they are impacted by disturbances like acute and chronic sleep loss or circadian misalignment. In a unique combination of molecular neuroimaging and behavioral research, we strive to uncover mechanistic pathways that help us understand why some individuals show stronger cognitive decline and negative health consequences due to sleep loss than others.

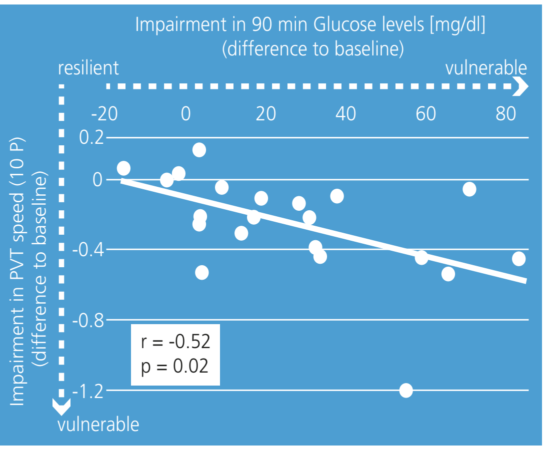
Our society's need for mobility is in conflict with local residents' need for undisturbed recreation and sleep. In order to ease this conflict, we investigate how sleep, cognitive performance, and annoyance are affected by air, rail, and road traffic noise, and share protection concepts with stakeholders. Aircrews and astronauts work and sleep under conditions of hypobaric hypoxia or hypercapnia. Thus, we have a specific interest in studying systematically in the lab or inflight how barometric and atmospheric alterations affect performance, sleep and well-being. This research includes examining aeronautic protective equipment and emergency protocols for aviation industry. Digital health expertise provides medical support for patients and research through remote applications.

Sleep and Human Factors Research

Unique selling points of the department

- Human research on sleep and circadian rhythms under highly controlled laboratory as well as ecological field conditions which translate basic research to the application of countermeasures such as noise protection or improved rosters
- Predicting individual vulnerability of cognitive performance and sleep to sleep loss based on molecular neuroimaging
- Event-related exposure response functions of traffic noise effects on sleep
- Inflight monitoring of pilots' performance/fatigue
- Baromedical fit-for-air-travel testing in diseased individuals

The department focuses on the conditions and factors impacting human performance, sleep and wellbeing in the modern mobile 24-h society. Within DLR, the research has been funded mainly by the Aeronautics program and to a lesser extent by the Space and the Transport programs. Among the factors that are studied are sleep loss, circadian disruption, workload, noise, atmospheric pressure, hypoxia, and hypercapnia. The work is aimed at understanding and ultimately improving the conditions for operators, but also for residents impacted by transport systems particularly by noise. We use highly controlled basic human sleep research in the lab as well as neuroimaging techniques directed at elucidating underlying mechanisms such as the role of the brain's adenosine system in wake-sleep regulation. In a translational/applied approach, we examine the influence of circadian, barometric, and atmospheric conditions in the operational environment in the field and the lab to assess factors such as fatigue in pilots and to derive adequate countermeasures like improved rosters and fit-for-air-travel testing in obese individuals. We also develop traffic noise protection concepts derived from ecologically valid field studies. An important new development in our work through the past funding cycle has been to better understand individual trait vulnerabilities to adverse factors, including sleep loss as well as traffic noise exposure. With respect to new methods, we successfully applied molecular neuroimaging through positron emission tomography. Moreover, we added bio-mathematical modelling of performance and sleep to our portfolio. We will continue establishing and making judicious use of new methods and technologies. Maintaining and expanding neuroimaging expertise and infrastructure as well as acquisition of a new auralization tool that will enable us to investigate noise effects on humans of aircrafts such as unmanned aerial vehicles or electric aircrafts that have yet to be built. A new initiative under DLR leadership will be important to bring together experts from various disciplines to reinvigorate noise effects research in Germany.



Correlation between impairments in the 10th percentile (10P) of psychomotor vigilance performance (PVT) speed (1/reaction time) and glucose concentrations 90 min after glucose ingestion (oral glucose tolerance test) indicating a trait resilience / vulnerability to sleep restriction (5 nights with 5 h sleep opportunity).

Main projects 2017-2020

SomnoSafe - Chronic sleep loss: From molecular neuroimaging to safety and health in space

Operators in aviation, space, and transport often work in shift work systems, which compromise the duration and quality of sleep. Cognitive performance may also decline since sleep and work is scheduled at adverse circadian times. In our study, we investigated the single and combined impact of chronic sleep restriction and acute wake extension on cerebral adenosine receptor availability, sleep, cognitive performance, and glucose metabolism in 36 healthy adults who stayed 12 days and nights at :envihab. We were especially interested whether chronic sleep loss elicited through five nights with five hours sleep opportunity each aggravates the negative effects of acute sleep loss (36 hours continuous wakefulness) despite an intermittent recovery night. Moreover, we assessed cerebral adenosine receptor availability as potential mechanistic link between sleep loss and individual vulnerability of cognitive performance and metabolic health. These research aims have direct relevance for shift workers in space and on Earth and provide guidance for individualized protection.

Sleep provides the basis for proper cognitive performance and vigilance and is, therefore, key for safe operations. In space and on Earth, operators' sleep is often disturbed and short for multiple reasons including circadian misalignment. Work environments resulting in chronic sleep loss increase risks for human errors and accidents while promoting cardio-metabolic diseases. Yet, human beings exhibit large interindividual variability in the magnitude

Working Fields

Performance and Sleep

- Effects of sleep loss, adverse work hours and workload
- Neuromolecular mechanisms conveying individual (trait) vulnerabilities
- Developing individualized countermeasures

Noise Effects Research

- Effects of transport noise on sleep, performance, annoyance, and cardiometabolic healths
- Exposure-response relationships and physiologically based noise protection concepts
- Defining vulnerable groups (e.g. children)

Baromedicine

- Effects of breathing atmosphere on sleep, circadian phase shifting, performance, and cardiometabolic disease
- Hypoxia and hypercapnia interactions guiding aircraft design
- Fit-for-air-travel testing in diseased individuals
- Human proof-of-concept studies (e.g., cardiac regeneration)
- Testing of new technologies (e.g. O2-masks)

Digital Health

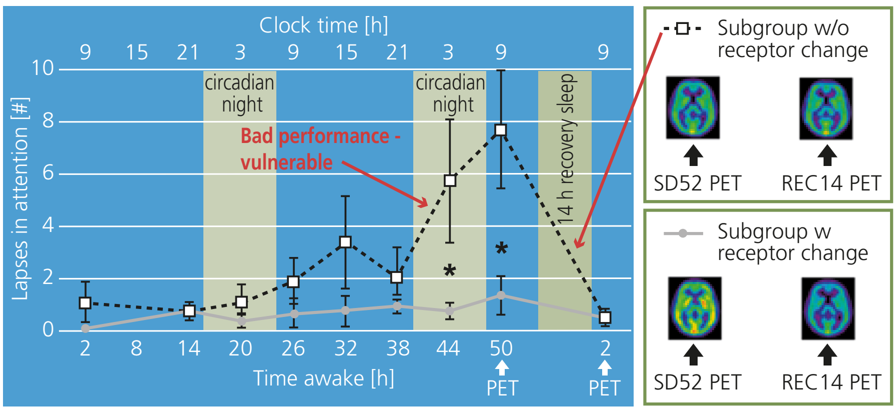
- Developing and evaluating biomedical systems and care concepts

of performance decline due to sleep loss. The brain's adenosine system plays an important role in sleep-wake regulation and appears to reflect the deep sleep need, which accumulates with increasing time awake. The adenosine system also conveys inter-individual differences to the wake promoting response to caffeine. Therefore, adenosine and adenosine receptors were promising mechanistic candidates to explain the observed trait differences.

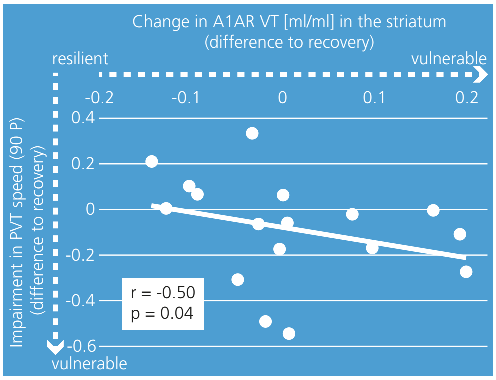
To date, we have already identified the individual changes in cerebral adenosine receptor availability in response to acute sleep deprivation. Moreover, we observed similar responses to ethanol intake. The findings suggest common mechanisms mediating individual differences in cognitive performance decline to sleep deprivation and to alcohol consumption.

In the SomnoSafe project, five sleep-restricted nights worsened cognitive performance, glucose tolerance, and insulin sensitivity. Remarkably, individuals were both either vulnerable or resilient with respect to impairments in both cognitive performance and glucose tolerance/insulin sensitivity.

Glucose tolerance/insulin sensitivity was still impaired after the following eight hour recovery sleep opportunity. Chronic sleep restriction did not alter cerebral adenosine receptor availability compared to rested conditions which is in line with the finding that compensation processes during these five nights nearly completely preserved the duration and intensity of deep sleep. However, individual changes in adenosine receptor availabilities were correlated with cognitive impairment.



Lapses in attention in a psychomotor vigilance task (PVT) during 58 h of total sleep deprivation and after 14 h of recovery sleep. Based on high or low A1AR availability change from 52 h of wakefulness to recovery (small inserts indicate average parametric receptor maps), participants were divided into two groups. Participants with small A1AR availability change were vulnerable (red arrows), participants with high A1AR availability change were resilient. An asterix represents significant differences between groups (independent t-test). [Elmenhorst et al. 2017].

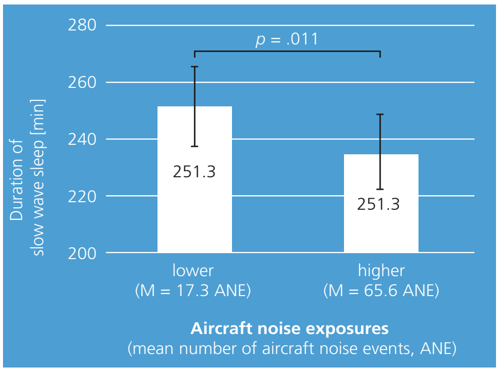


Correlation between impairments in the 90th percentile (90P) of psychomotor vigilance performance (PVT) speed (1/reaction time) and change in the distribution volume (VT) of adenosine A1 receptors (A1AR) in the striatum indicating a trait resilience/vulnerability to sleep restriction (5 nights with 5 h sleep opportunity).

One 8-h sleep opportunity after chronic sleep restriction restored cognition but reminiscent cognitive impairments unveiled in the following extended wakefulness episode. The observation indicates cumulative effects of chronic and acute sleep loss despite intermittent recovery, which need to be considered for future duty roster planning. We did not observe these cumulative effects for deep sleep, for cerebral adenosine receptor availability, or for glucose metabolism. Glucose tolerance/insulin sensitivity, on the contrary, remained at normal rested levels after acute sleep deprivation. Chronic sleep loss and acutely extended wake duration appear to activate different regulatory responses in glucose metabolism.

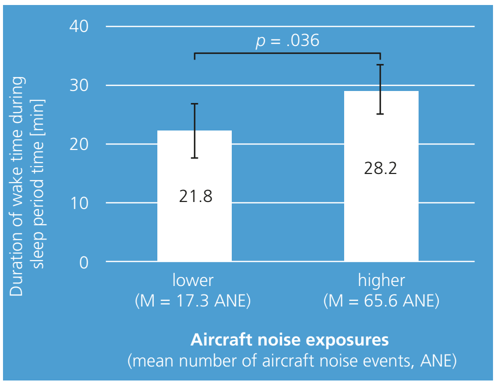
Protecting the individual from negative acute and chronic consequences of shift work will be the focus of our future work. For this purpose, we need to uncover more health aspects that share the observed trait vulnerability. Apart from the increased metabolic risk, epidemiological studies indicate that shift workers also have an increased cancer and cardiovascular risk. Thus, in future projects, we will target the immune and cardiovascular system under conditions of rest and sleep loss. Individualized shift work systems promise enhanced protection against fatigue, human error, and disease. However, to date only the individual chronotype has been identified as easily accessible biomarker. Objective sleepiness markers derived from eye, eyelid, and pupil motion as well as wake- and sleep-EEG, and personality questionnaires provide promising further candidates, which we will test for their potential to predict individual sleep loss-induced cognitive decline. We identified performance following ethanol ingestion as potentially useful readout. Moreover, studies examining caffeine as a countermeasure and its effect on the cerebral adenosine system under chronic sleep restriction are currently underway.

Effects of nocturnal aircraft noise on children



Duration of slow wave sleep (S3 and S4) in nights with lower and higher aircraft noise exposure defined by the number of aircraft noise events (ANE) per time in bed.

We investigated acute influences of nocturnal aircraft noise exposure on objective and subjective sleep quality, annoyance, and attentional performance in primary school children. The study aimed to identify the mechanisms by which noise interferes with childhood sleep and to what extent these sleep disturbances translate to subjective sleep and annoyance ratings and performance data of a computer-based attention test in the morning. We conducted a field study with 51 healthy children aged 8 to 10 years residing near Cologne/Bonn Airport representing an important German hub with a 24-h operating scheme. Children's sleep was electro-physiologically assessed with polysomnography during four consecutive nights. Simultaneously, all aircraft and background sounds were recorded close to the ear.



Duration of wake time during the sleep period time in nights with lower and higher aircraft noise exposure defined by the number of aircraft noise events (ANE) per time in bed.

Sleep disturbances represent an important adverse effect of nocturnal aircraft noise exposure. Acute disturbances include awakenings, changes in sleep depth, and sleep continuity. Children are in a sensitive developmental period and restorative sleep is vital for their physiological and cognitive development. Individuals who are exposed to high transportation noise levels from an early age may have higher risks for cardiovascular diseases in their adult life. Children generally sleep longer than adults and, thus, spend more time asleep during shoulder times of the night when (air) traffic density is high.

As a consequence, children are considered vulnerable to negative consequences of transportation noise. However, little is known about childhood sleep exposed to transportation noise and the secondary effects of these sleep disturbances, such as subjective poor sleep quality, increased noise annoyance and a reduced cognitive performance in the morning. Aircraft noise exposure affected sleep architecture. A larger number of noise events during the night was associated with reduced slow wave sleep and increased wake time during the sleep period time.

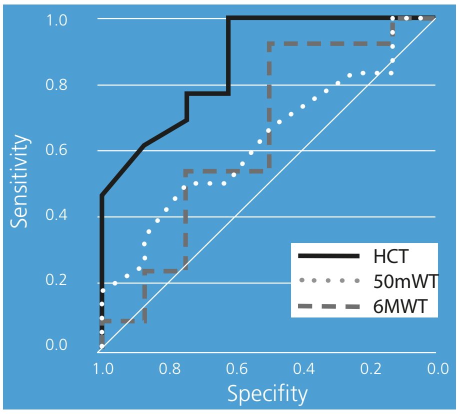
Sleep latency tended to be longer in nights with higher noise exposure, however, sleep efficiency and REM sleep duration remained unchanged. The magnitude of the change in sleep architecture resembles responses in children suffering from obstructive sleep apnea syndrome (OSAS). With regard to awakenings associated with single aircraft noise events, we observed that the probability for an awakening was influenced by both acoustical (e.g., maximum level of aircraft noise event, level of the background noise, maximum rise rate of level increase), and situational/non-acoustical factors (e.g., elapsed sleep time, sleep stage preceding the aircraft noise event, presence of worrying events in the near past or future). Comparing the resulting exposure-response curve to an established curve for adults from the same airport region revealed a higher wakeup threshold to aircraft noise events in children.

Contrasting the objective deteriorations of children's sleep, their self-rated sleep quality, fatigue, and annoyance in the morning did not differ between nights with higher and lower aircraft noise exposure. Self-assessments of sleep quality and fatigue were only partly related to the objective results. Thus, our findings underline the importance of objective measures for identifying noise-induced changes in sleep instead of using parents' or self-assessments only. Children's annoyance judgment in the morning was neither significantly related to the equivalent sound pressure level, nor to the number of aircraft noise events during the time spent in bed. Attitudes towards air traffic, noise sensitivity and coping behavior seem to be more relevant than the noise exposure itself. With regard to a potential deterioration of attentional performance we did not find an effect of the aircraft noise exposure. However, we found an association between the amount of slow-wave sleep per night and key indicators of attentional performance. This relationship suggests that nocturnal aircraft noise exposure tends to have at least an indirect effect on attention.

The current findings on the impact of aircraft noise on slow-wave sleep duration apply to a continuous nighttime noise scenario without a night flight ban between e.g. 23:00 h and 5:00 h and a moderate number of flights during the shoulder times of the night. The consequences of a night curfew for primary school children's sleep are still unexplored but of special importance as the increased air traffic during the hours before 23:00 h overlaps with the early sleep phase in which slow wave sleep is predominant. The small but recurring disturbances of slow wave sleep have been postulated as a major risk for metabolic, cognitive, and cardiovascular diseases. We therefore plan to systematically investigate the impact of different operational scenarios in future laboratory studies with special focus on the consequences of aircraft noise-induced loss of slow wave sleep. Hence, in future studies, we will expand our methodological spectrum to evaluate autonomic, cardiovascular and metabolic effects of aircraft noise exposure.

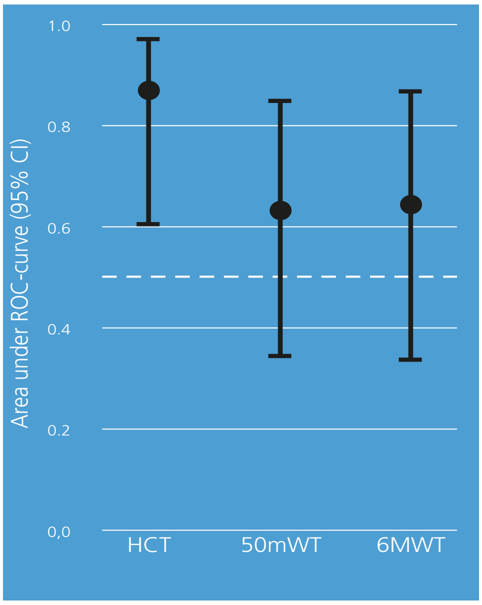
HyPaFly - Evaluation of diagnostic tests to determine fitness for air travel in obese individuals

Obesity poses a rapidly growing health challenge in modern societies and obese individuals are at increased risk of in-flight medical complications. Physicians need to evaluate their patients' ability to fly safely, but unfortunately, practitioners seeking guidance are confronted with inconclusive evidence and even contradictory advice, especially when it comes to examination methods available outside of highly specialized centers. The fact that numerous past studies did not acknowledge the diagnostic nature of fitness to air travel assessment, perpetuates the prevailing uncertainty among physicians. Aim of the HyPaFly project was to shed light upon this blind spot in the diagnostic toolbox of flight physicians. For this purpose, we studied and compared the diagnostic accuracy of three potential test methods for fitness to air travel evaluation – 50 meter of walking, six minutes of walking and normobaric hypoxic challenge testing – in 21 obese individuals (men and women, BMI > 30 kg/m²). Fitness to fly was defined as a person's ability to maintain oxygen saturation (SpO_2) greater or equal to 90% when exposed to flight conditions. Most clinical guidelines define SpO_2 < 90% as threshold for hypoxia and there is no known risk of tissue damage above this level. This reference standard was established in an altitude chamber.



Receiver operating characteristic curves of HCT, 50mWT and 6MWT.
HCT = normobaric hypoxic challenge test,
50mWT = 50-meter walking test,
6MWT = six-minute walking test.

Modern society grants individuals with longer lives and a wide range of liberties, including the freedom to travel. At the same time obesity is on the rise and a common mode of travel, the airplane, is starting to pose a serious health risk for a growing number of people. Obesity affects the respiratory system in multiple ways: fat deposition impairs mechanical lung function and gas exchange, induces ventilation/perfusion mismatch and narrows the upper airways, predisposing airway occlusion. These physical austerities, in combination with the reduced atmospheric pressure in an airliner cabin, up to an altitude-equivalent of 8,000 ft (2438 m), make highly overweight individuals susceptible to adverse medical events during flight.



Point estimators and 95% confidence intervals of area under the receiver operating characteristic curve (ROC) of HCT, 50mWT and 6MWT.
HCT = normobaric hypoxic challenge test,
50mWT = 50-meter walking test,
6MWT = six-minute walking test.

This problematic interaction between obesity and air travel requires physicians to make the decision whether the person in front of them can or cannot safely travel by airplane. Often this decision is made on the basis of common clinical metrics recorded at sea level, such as SpO_2 or lung function, but an emerging consensus deems these unsuitable.

Viable alternatives for practicing physicians are sparse. The two most frequently proposed methods in scientific literature, either simulation of the corresponding hypobaric atmosphere or, as next best option, exposure to hypoxic gas, are not routinely available. Several tests have been proposed to fill this gap but while some were quickly rejected, such as a number of predictive equations, the potential of others, such as exercise or symptom based assessment, remains uncertain.

Thirteen participants of the cohort (BMI: 36 kg/m^2 ± 5 SD, age: 51 years ± 15 SD) were identified as not fit to fly, according to our reference standard; i.e. SpO_2 was ≤ 90% under flight conditions in the altitude chamber. While both walking tests were in good agreement with each other (r = -0.83), only the prediction of hypoxic challenge testing was significantly different from chance level (p = 0.008), i.e. confidence interval does not include 0.5.
These results indicate robust diagnostic accuracy of hypoxic challenge testing with regard to occurrence of in-flight hypoxia in obese individuals, while both walking tests did not separate the reference groups of fit to fly and not fit to fly individuals. The latter is worrisome. While evidence supporting actual diagnostic efficacy is sparse, these two walking tests are frequently mentioned in grey literature, such as operating manuals of air carriers, as useful means to assess fitness for air travel.

Given the demographic and public health challenges in modern mobile societies, refinement of the diagnostic instruments for pre-flight assessment is needed. A critical role in diagnostic studies, such as this one, plays the reference standard, i.e. the definition of fitness to fly. Unquestionably, a person not experiencing any negative consequences during and after air travel is fit to fly but at what point a person is no longer fit to fly is less clear — today we have no agreed way of quantifying that state-of-affairs. Up until now, most studies, including this one, used blood oxygenation under some condition as a surrogate marker for fitness to fly. However, it has been reported that oxygenation might not sufficiently predict in-flight medical symptoms and it appears, therefore, necessary to study domains beyond saturation. We plan to take this next step in a follow-up project, since it is a prerequisite to enable meaningful future research of medical pre-flight assessment.

Collaboration partners within the Institute

- Dept. of Aerospace Psychology
- Dept. of Cardiovascular Aerospace Medicine
- Study Team
- Dept. of Clinical Aerospace Medicine
- Dept. of Muscle and Bone Metabolism

Collaboration partners within the DLR

- Institute of Aerodynamics and Flow Technology
- Institute of Flight Guidance
- Institute of Flight Systems
- Institute of Air Transport and Airport Research

Collaboration partners in Germany

- Research Center Jülich
- University of Cologne
- University of Bonn
- ZEUS GmbH Germany
- Bethanien Hospital Solingen

Collaboration partners worldwide

- Harvard Medical School, USA
- UTSW Dallas, USA
- University of Pennsylvania, USA
- University of Zurich, Switzerland
- Royal Netherlands Aerospace Center, The Netherlands
- Finnish Institute of Occupational Health, Finland
- Stockholm University, Sweden
- Manchester Metropolitan University, United Kingdom
- CY Cergy Paris University, France
- Budapest University of Technology and Economics (BME), Hungary
- Environnons, France
- Anotec Engineering, Spain

Selected publications

Bartels, S., Rooney, D., Müller, U. (2018) *Assessing aircraft noise-induced annoyance around a major German airport and its predictors via telephone survey The COSMA study.* Transportation Research Part D: Transport and Environment, 59, 246-258.

Elmenhorst, E.-M., Elmenhorst, D., **Benderoth, S.,** Kroll, T., Bauer, A., **Aeschbach, D.** (2018) *Cognitive impairments by alcohol and sleep deprivation indicate trait characteristics and a potential role for adenosine A1 receptors.* Proceedings of the National Academy of Science (PNAS), 115 (31), 8009-8014.

Elmenhorst, D., **Elmenhorst, E.-M., Hennecke, E.,** Kroll, T., Matusch, A., **Aeschbach, D.,** Bauer, A. (2017) *Recovery sleep after extended wakefulness restores elevated A1 adenosine receptor availability in the human brain.* Proceedings of the National Academy of Science (PNAS), 114 (16), 4243-4248.

Rooney, D., Wittkowski, M., Bartels, S., Weidenfeld, S., Aeschbach, D. (2020) *Influence of transient pressure changes on speech intelligibility: Implications for nextgeneration train travel.* PLoS One, 15 (4), e0232024.

Rooney, D., Herkenrath, S., Priegnitz, C., **Putzke, M.,** Treml, M., **Wenzel, J., Aeschbach, D.,** Randerath, W. (2019) *Choosing an Adequate Test to Determine Fitness for Air Travel in Obese Individuals.* Chest, 156 (5), 926-932.

II.3
Clinical Aerospace Medicine

Dr. med. Claudia Stern (Head)

Dr. med. Martin Trammer (Deputy)

Mission Goal
The Department of Clinical Aerospace Medicine is responsible for medical qualification and individual health prevention strategies in aviation, spaceflight, and other occupational settings. We primarily target private and professional pilots, aircrew members, astronauts as well as personnel in the other areas of aerospace, air traffic control and transportation. Additionally, we apply our experience in medical qualification examinations supporting the Institute's departments in selecting test subjects for various clinical and physiological trials.

Our aim is to maintain flight safety as part of the flight medicine community. One key factor for flight safety is a healthy and well trained cockpit and cabin crew. One centerpiece of this process is the medical qualification examination according to national and international requirements. In addition, we care for other operators with different responsibilities and tasks contributing to flight safety including air traffic controllers, airplane technicians, mechanics, and ramp agents. Indeed, flying and non-flying tasks are equally important to maintain flight safety in aviation. We translate our findings to other occupational settings like spaceflight, terrestrial medicine, scientific research, traffic, and transportation among others. Our overall goal is to support aerospace safety and maintain the health of aerospace personnel during their working life time. To attain this goal, we closely collaborate with the Institute's research departments to foster the translation of science to applications in aerospace medicine.

Clinical Aerospace Medicine

Unique selling points of the department
Aeromedical Center (AeMC), one of five in Germany

- High altitude physiology advice and training, certification, high altitude simulation chamber
- Selection, certification and follow-up examination of all European astronauts until retirement and beyond
- Clinical data collection in astronauts returning from Space (Direct Return)
- Advising and "on-site support" during astronaut training
- In-flight advice in medical experiments and health related questions via console operation
- Leading aerospace ophthalmologist, AeMC orthoptist
- Experience in astronaut selection (e.g. "Die Astronautin")
- Occupational Health Service for DLR sites in the western region
- Engineering, bioastronautics, machine learning, and human subjects research experience

Aviation

The department is certified by the national civil aviation authority (Luftfahrt-Bundesamt) as an Aeromedical Center (AeMC). Pilots, cabin crews and air traffic controllers are medically examined and certified according to current European and national requirements. Moreover, we provide medical travel guidance and an accredited yellow fever vaccination center. The AeMC is a frequently consulted for pilot waiver procedures by the authority, as it provides specialists for ophthalmology and optometry. We train pilots, flight engineers, astronauts, and other professionals dealing with high altitude and/or low oxygen workplaces in realizing and coping with the danger of sudden incapacitation using a high altitude simulation chamber. In 2022, we will move into a new DLR building together with the German Air Force Centre of Aerospace Medicine.

Spaceflight

The second major topic is the medical certification and continuous recertification of the entire European ESA-Astronaut-Corps according to international agreed standards within the International Space Station Program. The department's mission support comprises pre-, in-, and postflight activities, as the European astronauts have returned directly to the :envihab after their Soyuz-landing in Kazakhstan, within the scope of the " direct return", since 2013. Given our strength in aerospace ophthalmology, we contributed to the discovery of eye changes in astronauts on long duration spaceflights. The finding has led to an increased emphasis on eye health with regular follow ups and participation in several scientific studies. The fact that changes in the eye may result from raised intracranial pressure is a matter of concern and intense ongoing research activities. The department has had the leading role in the psychological and medical selection process of the first German female astronaut candidate, a private initiative.

Clinical study support

The department with its clinical expertise supports human studies of the Institute, especially in the area of test subject selection and medical monitoring during experiments, as well as further cross section support. Long-term bed rest studies are challenging because of the large number of examinations and need for additional staff members to ensure medical safety of test subjects. One of the most important aspects of future NASA and ESA bed rest studies are eye changes and targeted countermeasures. Therefore, we will be highly involved in these studies in collaboration with the study team and other scientific departments. Furthermore, we will support and conduct our own experiments during the upcoming NASA

Optical Coherence Tomography examinations of the retina during bed rest studies

Optic disc edema in test subject after 30 days of head down tilt with increased CO_2 ambient air.

Working Groups

Aeromedical Center
(Dr. med. Martin Trammer):
Examination and certification of aviation personnel, certified physician for patient information due to the federal genome diagnostic act (Gendiagnostikgesetz GenDG)

Aerospace Ophthalmology
(Dr. med. Claudia Stern):
Ophthalmological research and examinations of astronauts, aviation personnel and test subjects

Occupational Health Service
(Peter Tuschy):
- Prevention and managing health of DLR staff and test subjects, medical specialist training in occupational medicine
- responsible physician for hygiene related topics
- certified physician for patient information due to the federal genome diagnostic act (Gendiagnostikgesetz GenDG)

bed rest study dealing with countermeasures against eye changes during head down tilt. The knowledge of eye changes in head down tilt leads to the terrestrial question on whether head up tilt will help patients suffering from glaucoma which we will examine in future studies.

Occupational Health Service

We serve as the occupational health service for DLR sites in the western region (approx. 3000 employees), all new DLR Institutes without an occupational health service and the residencies abroad (Brussels, Paris, Tokyo and Washington D.C.). We are certified for medical specialist training in occupational health and are responsible for all hygiene related topics. In 2021, we will perform the medical examination for the next European Astronaut Selection. Astronauts and test subjects within bed rest studies in 6°-head down tilt can develop optic disc edema. We will support future astronauts on deep space missions (e.g., Mars) with artificial intelligence to diagnose their eye changes to modify countermeasures. This method will be later on implemented in terrestrial emergency medicine and medical care in rural areas.

Main projects 2017-2020

Eye changes in simulated microgravity

- Examination of eye changes during head down tilt bed rest studies, especially in the context of globe flattening, refraction and optic disc edema to get more insight into the Spaceflight associated neuro-ocular syndrome (SANS). This syndrome describes the changes that about 70% of long-term mission astronauts suffer from during and after their missions. These changes include globe flattening, optic nerve sheath distension, optic disc edema, choroideal folds and cotton wool spots. The changes can be transient or permanent and the origin is still unclear.
- During two NASA/ESA studies with a bed rest of 30 and 60 days we reproduced for the first time optic disc edema during bed rest without pillow and in one study with an increased CO_2 level as existing on the International Space Station.
- We could also show that changes in refraction and the globe are different from those seen in astronauts. In future bed rest studies, we plan to further examine these changes to find a source for the differences and to also examine whether different countermeasures prevent eye changes in bed rest studies.

Planned head-up tilt study to reduce intraocular pressure

Artificial Intelligence and retinal diagnostics

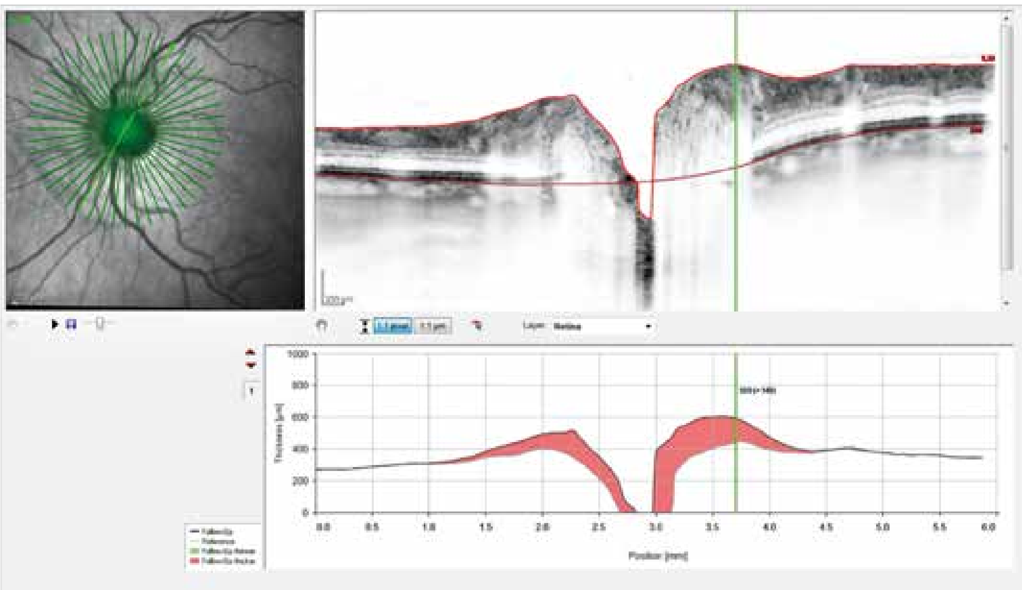
- With this project, we want to support astronauts during (long-term) missions to diagnose their retinal changes with the help of artificial intelligence, especially when communication with Earth is difficult and access to near real-time ground-based medical expertise is not possible (e.g., on the way to Mars). We already tested the applicability of machine learning applications for SANS, in using retinal optical coherence tomography (OCT) scans, collected from ongoing bed rest studies, to train and validate three custom models to predict SANS. The most accurate of these models detects SANS with 94% accuracy and serves as proof-of-concept for this project. In addition to that we performed a comparison between different fundus cameras to select the one that fit our demands best.
- The space-based testing phase of this project has been accepted for the Matthias Maurer mission. Later on, these results will be applied to terrestrial models for emergency medicine and medical care in rural areas. This project is developed in cooperation with the “Spaceship” European Astronaut Center, the University Eye Hospital Bonn, and the Helmholtz Center Munich.

Mobile fundus camera technology readiness level advancement

Mobile fundus cameras have been clinically validated and approved for routine clinical use worldwide. These cameras are lightweight, affordable, and potentially useful for spaceflight applications. To test these devices in space, their technology readiness level must first be validated in ground-based studies and microgravity parabolic flights. This project aims to provide validation that these devices can feasibly operate in ground based studies and microgravity parabolic flights, so that they can be used in future spaceflight missions.

Other activities

- Direct Returns including pre- and postflight examinations of the astronauts, who are brought back directly after their Soyuz-landing in Kazakhstan to our :envihab facility where they stay for two weeks: Thomas Pesquet (2017), Alexander Gerst (2019), Luca Parmitano (2020)
- German Female Astronaut Selection “Die Astronautin”
- Revival and execution of the refresher training “Kölner Fliegerarzttage“



Optic disc edema (increase of disc tissue in red) in Ocular Coherence Tomography (OCT)

Collaboration partners within the Institute

- Dept. of Aerospace Psychology
- Dept. of Muscle and Bone Metabolism
- Dept. of Sleep and Human Factors Research
- Dept. of Cardiovascular Aerospace Medicine
- Dept. of Gravitational Biology
- Dept. of Radiation Biology
- Study Team

Collaboration partners within the DLR

- Technology Marketing
- DLR Safety Department

Collaboration partners in Germany

- European Astronaut Center (EAC)
- Technical University Braunschweig
- University of the Armed Forces
- Luftfahrt-Bundesamt
- Bundesanstalt für Flugsicherung
- Ministry of transport and digital infrastructure
- University Eye Hospital Bonn
- University Eye Hospital Cologne
- Helmholtz Center Munich
- University Hospital Freiburg
- German airlines (Lufthansa, Eurowings, Germanwings, TUI, Condor)
- Federal (-state) Police

Collaboration partners worldwide

- All international space agencies (ESA, NASA, Roskosmos, JAXA, CSA)
- International Space University
- European Aviation Safety Agency (EASA)
- Federal Aviation Administration (FAA)
- European airlines (Star Air, Ryanair, Easyjet, Cargolux)
- Virgin Galactic, National Research Council (NRC) Canada
- United Nations Office for Outer Space Affairs

Selected publications

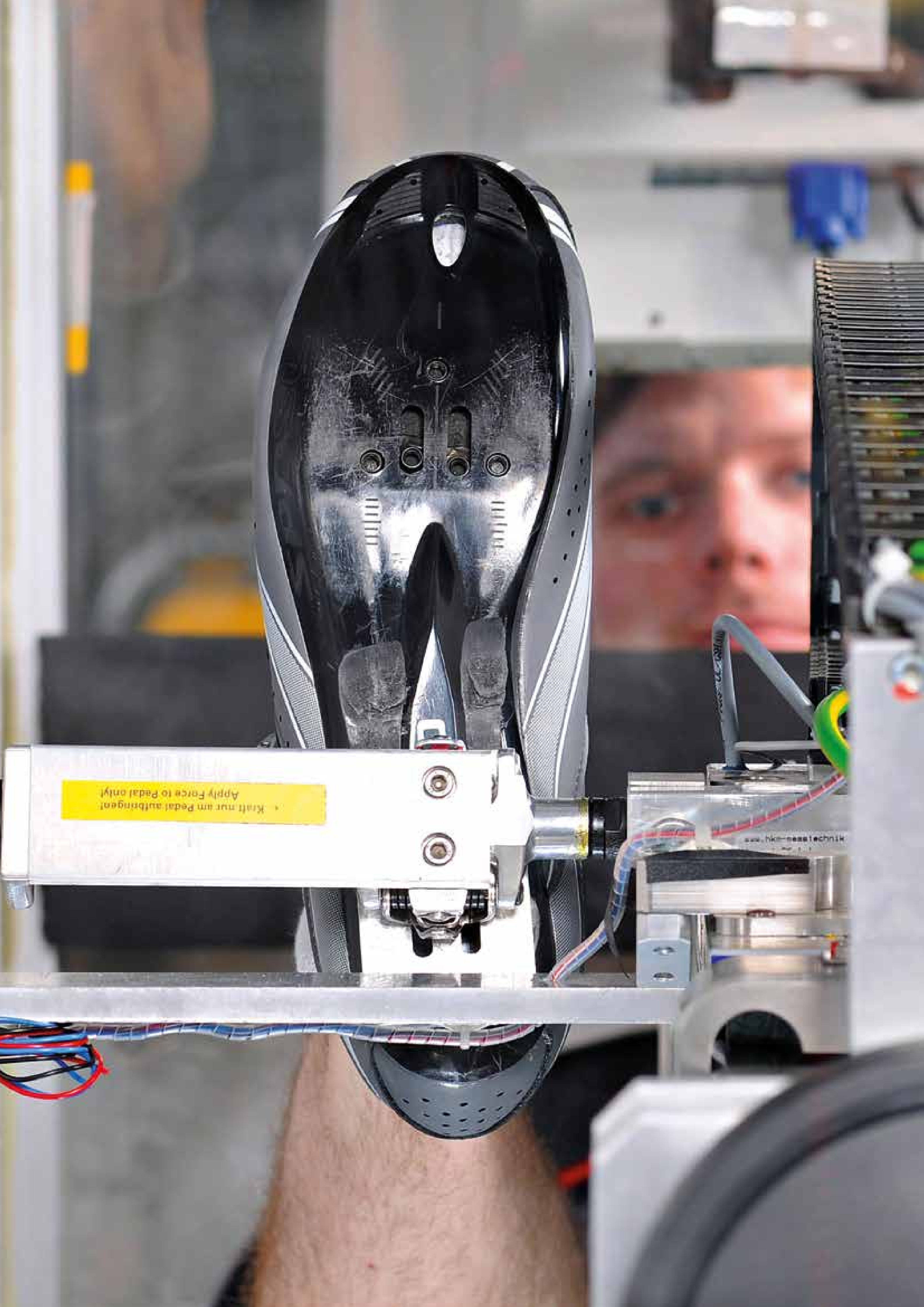
Händel, A., **Stern, C., Jordan, J.,** Dietlein, T., Enders, P., Cursiefen, C. (2020) *Augenveränderungen im All.* Der Opthalmologe, 117, 721-729.

Jordan, J., Hellweg, C.E., Mulder, E., Stern, C. (2020) *Von humanen terrestrischen Modellen zu neuen Präventionsansätzen für Augenveränderungen bei Astronauten.* Der Opthalmologe, 117, 740-745.

Laurie, S.S., Macias, B.R., Dunn, J.T., Young, M., **Stern, C.,** Lee, S.M.C., Stenger, M.B. (2019) *Optic Disc Edema after 30 Days of Strict Head-down Tilt Bed Rest.* Ophthalmology, 126 (3), 467-468.

Laurie, S.S., Lee, S.M.C., Macias, B.R., Patel, N., Young, M., **Stern, C.,** Stenger, M.B. (2019) *Optic Disc Edema and Choroidal Engorgement in Astronauts During Spaceflight and Individuals Exposed to Bed Rest.* JAMA Ophthalmology, 138 (2), 165-172.

Wostyn, P., de Winne, F., **Stern, C.,** de Deyn, P.P. (2018) *Dilated Prelaminar Paravascular Spaces as a Possible Mechanism for Optic Disc Edema in Astronauts.* Aerospace Medicine and Human Performance, 89 (12), 1089-1091.


Kraft nur am Pedal aufbringen!
Apply Force to Pedal only!

II.4
Muscle and Bone Metabolism

Prof. Dr. med. Jörn Rittweger (Head)

Prof. Dr. med. Christoph Clemen (Deputy)

Mission Goal
Humans have evolved as a species that is uniquely capable of long-lasting physical performances. Long periods of physical inactivity, conversely, lead to deconditioning, to untoward metabolic consequences, and to compromised health. The Muscle and Bone Metabolism department therefore examines the effects of physical activity, and of the lack thereof in the context of mission-related environmental conditions, such as microgravity, atmospheric challenges, nutrition, circadian disruption and radiation. Genetic predisposition and the ageing process are taken into account as well.

Our ultimate goals are the prevention and rehabilitation of immobilization-related musculoskeletal disorders. To this purpose, we aim to develop efficient measures to counteract muscle atrophy, bone atrophy and metabolic derailment in space and on Earth. We aim at these goals in a rational approach that ranges from cellular to organismic levels.

Researching the biomechanics and mechanophysiology of muscles and bones are a prerequisite to understand the physiological effects of muscle contractions and exercise. This is seconded by research into skeletal muscle's metabolism and its systemic interactions. Combining this knowledge with genetic model systems allows us to develop exercise and other countermeasures that are purpose-optimized for space and specific Earth-based applications.

Muscle and Bone Metabolism

Unique selling points of the department
We study immobilization-related problems of the musculoskeletal system from bench to bedside. This encompasses genetic, mechanic, metabolic and functional aspects in astronauts, in clinical populations and in old people.

Muscle wasting in immobilization and space

Muscles readily shrink when not used appropriately, and we demonstrated that low oxygen levels also cause muscle atrophy. Recent results suggest that gravity-dependent alterations of blood supply and tissue oxygenation can serve as explanation for limited effectiveness of exercise in bed rest and during spaceflight. Thus, exercises involving stretch-shortening cycles constitute a powerful countermeasure.

Intramuscular connective tissue

Intramuscular connective tissue integrates muscle fibers and fascicles, blood vessels, and nerves into the muscle as a whole organ. Connective tissue essentially contributes to the biomechanical properties of muscle, and its make-up depends on muscle type, physical activity, immobilization, aging and disease.

Systemic metabolic interactions in musculoskeletal disorders

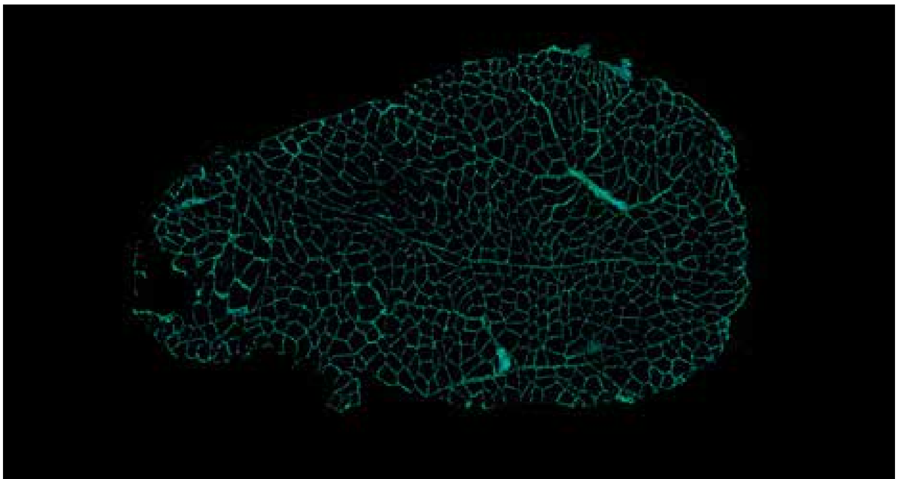
Skeletal muscle can turn into a metabolically highly active tissue at maximal exercise levels. During immobilization, however, there is a rapid derailment of the body's metabolism. Understanding the body's metabolic network, a crosstalk between muscle, liver, adipose tissue and bone, is important to define spaceflight countermeasures ensuring long-term health of astronauts.

Long-term effects of physical activity and inactivity

As astronauts for future missions to Moon and Mars will be older than on ISS, long-term health effects of spaceflight-associated inactivity deserve additional attention. Muscle wasting disorders are associated with the senile phenotype. Hence, will the biological aging process be decelerated by physical inactivity? And how will biological aging be affected by long-term spaceflight?

Countermeasure development in space

Countermeasure exercisers implemented on ISS show sufficient effectiveness to safely return astronauts to Earth, but they still experience substantial de-conditioning effects. Thus, exercisers must become more effective and less bulky for long-term space missions. We aim to contribute to the next generation of exercisers, and to transfer that knowledge for utilization on Earth.



Working Groups

Mechanophysiology
(Dr. rer. nat. Uwe Mittag)
- Biomechanical testing, biomechanical modeling, technology development, data management

Molecular Muscle and Bone Research
(Prof. Dr. med. Christoph Clemen)
- Biochemistry, genetically modified cells and organisms, cellular and animal studies

Translational Metabolism Research
(Prof. Dr. rer. nat. Dominik Pesta)
- Metabolic studies, euglycemic hyperinsulinemic clamp testing, biosample management

Training and Countermeasures
(PD Dr. rer. nat. Jochen Zange)
- Exercise training studies, musculoskeletal imaging, exercise countermeasure development

Examinations of muscles in space

The flight-experiment 'Sarcolab-3' investigates muscle breakdown in space in a holistic way, ranging from organismic functional to the level molecular biology. The experiment consists of measurements both on the ISS and on Earth before and after the flight. In-flight measurements help us to assess the time course of leg muscle wasting in space. Moreover, we also study the excitation transfer from the nerve cell to the muscle. The ground-based pre- and post-examinations also cover the biomechanics of muscle contractions, magnetic resonance imaging and muscle biopsies allow us to identify the causes of muscle weakness, i.e. why the muscles of astronauts become intrinsically weaker and which signaling pathways are responsible for the muscle changes. Sarcolab-3 uses MARES (muscle atrophy research and exercise system) developed by the European Space Agency (ESA). With MARES, complex functional examinations of the muscles in weightlessness were carried out on the ISS for the first time. Another novelty are ultrasound muscle measurements in space, with which muscle changes can be imaged.

The in-flight part of the experiment was carried out in 2016 and 2017, pre- and post-flight tests are scheduled to take place until 2021. Results from the Sarcolab pilot study, which had been performed prior to Sarcolab-3 suggest that lack of external loading forces play an important role for muscle wasting in space (Rittweger et al., 2018). Moreover, muscle biopsy proteomic data suggest that spaceflight restricts the muscle's aerobic metabolism. In addition to the loss of strength and performance, muscle breakdown also has effects on systemic inflammatory processes (Capri et al., 2019). Therefore, the current training methods on the ISS seem to be not yet entirely effective and improvements have to be made.

In 2019, we have also performed the Sarcolab-BR study, which is a replica of the Sarcolab-3 astronaut study in the setting of the experimental bed rest study AGBRESA. Data and biosample processing is currently underway. Finally, the Sarcolab's successor experiment 'MetaMuscle', which is currently implemented for ISS, will study the impact of muscle wasting in Space on long-term effects in physical functioning, in biological aging, and in cardiovascular risk indicators.

Track-and-field master athletic cohort study

The beneficial effect of physical exercise for human health is undisputed. However, it is unclear which exercise categories are more beneficial, and less detrimental than others. Moreover, it is normally difficult to study life-long exercise interventions with human subjects. In this context, master athletes offer an intriguing approach to examine the interplay between fitness, health, and performance in life-long exercise. Unlike most other people, who reduce their physical activity as they age, master athletes continue participation in competitive sports, often into their 9th decade of life. They do so with a very high intrinsic motivation that is impossible to replicate in exercise intervention studies. Therefore, they constitute a 'fit and healthy' cohort that can serve as prime examples for successful aging that we can use as a comparison for our long-term studies in astronauts and bed rest participants. To this purpose, track and field athletics is particularly suitable, given the diversity of athletic specialization.

The TaFMAC study started in 2018 during the track and field Master Athletic Championships in Málaga, where data on training habits and lifestyle, on physiological fitness, and on cardiovascular health and muscle strength were collected. In 2019, World Master Athletics (WMA) decided to strategically support TaFMAC, and to accommodate testing sessions during their yearly competition events. The plan is to include 1,000 athletes in to the TaFMAC cohort, and to follow them up over one decade.

First results from the 2018 data collection campaign demonstrate that master athletes maintain a healthy body composition into very old age, and that that body composition information and vertical jump test performance jointly predict running performance very well. Moreover, we found that resting metabolism is elevated in master athletes. Next, we will be looking at health and well-being in this study.

Mouse and cell models for inherited myopathies

We established genetically modified mouse lines and derived myoblast cell lines that closely mirror essential aspects of two specific human myopathies, desminopathies and filaminopathies, and investigated important aspects of their complex molecular pathophysiology. We now elaborate open questions relevant to space flight-induced muscle deconditioning with these models, such as skeletal muscle wasting and weakness. For this, we started testing the effects of acute, strenuous and chronic, low intensity physical exercise as well as the cell and tissue-protective effects of drugs on skeletal muscle. Moreover, we are determining the effects of low oxygen levels on cultured muscle cells. This work aims to decipher disease- and muscle wasting-related pathophysiological aspects, and, in the long term, to develop therapeutic concepts for genetically determined muscle diseases and to optimize countermeasures for space flight-induced muscle deconditioning.

Examination of patients with X-linked hypophosphatemia

In 2019, we examined patients with X-linked hypophosphatemia, which is an inborn disorder characterized by excessive urinary excretion of phosphate caused by a dysregulation of reabsorption in the kidneys. The deficiency of systemic phosphate results in an insufficient mineralization of bones and the development of rickets beginning at early childhood. We compared performance, mass and energy metabolism of the hip and leg musculature of such patients with age matched healthy subjects. We found that the reductions of absolute values in mass, force and power of the patients' musculature likely result from the more immobile behavior of the patients caused by the severe impairments of the skeleton. A novel medication currently only applied to children but not officially approved for adult patients may in future also help to improve the mobility and general health state of adult patients, because a therapy combining adapted physical training with a medical reduction of phosphate excretion can stimulate muscle growth and bone mineralization.

New countermeasure exercisers for space

Future space vehicles used for long term exploration missions to Mars will provide by far less space for exercise devices as it has been available on the ISS. Moreover, recently successfully tested training modalities in bed rest studies not only include slow resistive exercise, as currently possible on the ISS, but also high intensive plyometric exercise and whole body vibration. New devices for exercise countermeasure must allow the save and efficient performance of several training modalities while being small and light weighted, resistive to high peak forces, almost energy neutral for the space craft and not transducing any mechanical impulses to the walls of the space craft. In cooperation with Space Application System (Sint-Stevens-Woluwe, Belgium) in two projects (ATHLETIC and Nex4Ex) sponsored by ESA we developed two prototypes following different concepts that potentially could fulfill the above mentioned requirements.

Collaboration partners within the Institute

- Dept. of Clinical Aerospace Medicine
- Dept. of Cardiovascular Aerospace Medicine
- Dept. of Sleep and Human Factors Research
- Dept. of Gravitational Biology
- Dept. of Radiation Biology
- Study Team

Collaboration partners within the DLR

- Institute for Software Technology
- Institute of Materials Research
- Institute of Material Physics in Space
- German Remote Sensing Data Center (DFD)

Collaboration partners in Germany

- University of Cologne
- University of Erlangen
- German Sports University of Cologne
- University of Constance
- University of Applied Sciences, Aachen
- CECAD Cologne
- University of Applied Sciences, Krefeld

Collaboration partners worldwide

- IBMP Moscow, Russia
- University of Bologna, Italy
- University of Pavia, Italy
- University of Padova, Italy
- University of Milan, Italy
- Manchester Metropolitan University, United Kingdom
- University of Graz, Austria
- University of Texas, Austin, USA
- University of Sasketchewan, Canada
- Northumbria University, UK
- Space Application Services, Belgium

Selected publications

Frings-Meuthen, P., Luchitskaya, E., **Jordan, J., Tank, J.,** Lichtinghagen, R., Smith, S.M., Heer, M. (2020) *Natriuretic Peptide Resetting in Astronauts.* Circulation, 141, 1593-1595.

Johannes, B.W., Bronnikov, S.V., Bubeev, Y., Kotrovskaya, T.I., Shastlivtseva, D.V., **Piechowski, S., Hoermann, H.-J., Rittweger, J., Jordan, J.** (2019) *Operational and Experimental Tasks, Performance, and Voice in Space.* Aerospace Medicine and Human Performance, 90, 624-631.

Parganlija, D., Nieberg, V., Sauer, M., Rittweger, J., Bloch, W., **Zange, J.** (2019) *Lower body negative pressure enhances oxygen availability in the knee extensor muscles during intense resistive exercise in supine position.* European Journal of Applied Physiology, 119, 1289-1303.

Rittweger, J., Albracht, K., Flück, M., Ruoss, S., Brocca, L., Longa, E., Moriggi, M., Seynnes, O., Di Giulio, I., Tenori, L., Vignoli, A., Capri, M., Gelfi, C., Luchinat, C., Franceschi, C., Bottinelli, R., Cerretelli, P., Narici, M. (2018) *Sarcolab pilot study into skeletal muscles adaptation to long-term spaceflight.* npj Microgravity, 4, 18.

Herrmann, H., Cabet, E., Chevalier, N.R., Moosmann, J., Schultheis, D., Haas, J., Schowalter, M., **Berwanger, C.,** Weyerer, V., Agaimy, A., Meder, B., Müller, O.J., Katus, H.A., Schlötzer-Schrehardt, U., Vicart, P., Ferreiro, A., Dittrich, S., **Clemen, C.S.,** Lilienbaum, A., Schröder, R. (In press) *Dual functional states of R406W-desmin assembly complexes cause cardiomyopathy with severe intercalated disc derangement in humans and in knock-in mice.* Circulation. These authors contributed equally to this work.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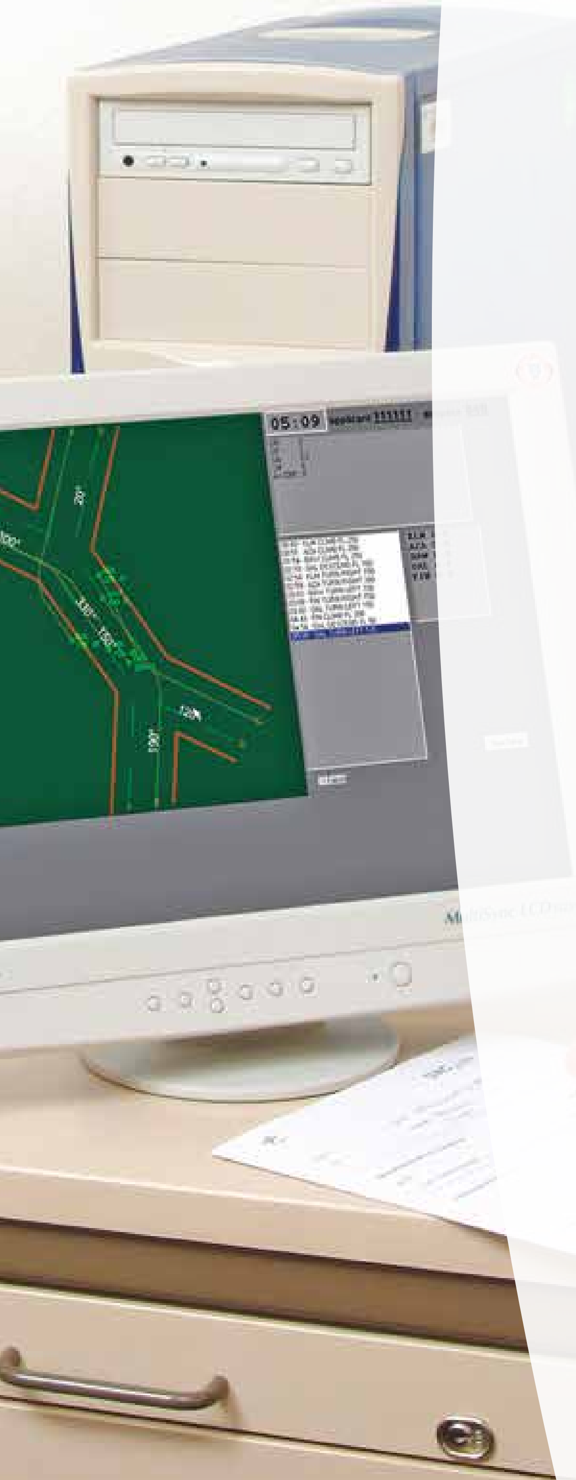
II.5
Aerospace Psychology

Dr. phil. Peter Maschke (Head)

Dr. phil. Hinnerk Eißfeldt, Prof. Dr. phil. Dirk Stelling (Deputies)



Mission Goal

Pilots, air traffic controllers, astronauts, and operators in other skilled professions are, both, an asset and a liability regarding safety in aerospace. Indeed, proper decisions together with functioning human-machine and human-human interactions enhance the reliability of technical system tenfold. Yet, operators are also responsible for the majority of aviation incidents and accidents. By developing, validating, and implementing comprehensive selection systems, the Department of Aviation and Space Psychology contributes significantly to aerospace safety. Given the importance of human factors, our work will help attaining the goals of Flightpath 2050, an 80% reduction in accidents. Our safety-related research program is of high societal value, contributes to employment security and job satisfaction of selected candidates, and supports economic development of aerospace industry by reducing training costs and minimizing errors. An additional part of our research addressed acceptance of new technologies, which is a critical barrier for economic success of novel technology.

Aerospace Psychology

Unique selling points of the department
With its long-standing expertise in human factors research and >10,000/year psychological examinations of airline pilots, air traffic controllers, and astronauts, the department of aviation and space psychology sets worldwide standards in aerospace psychology and provides a substantial contri-bu-tion to safety and economy in aviation.

The research program of our department is integrated in the DLR-research fields aeronautics, space, and transport. We are particularly strong in third party funded projects in close coop-eration with airlines, air traffic control, and space agencies.

Psychological requirements

New technologies and automation will have a strong impact on the requirements of the different operators by introducing changes within a socioeconomic framework. To increase safety and reliability of highly qualified operators in aviation including pilots, air traffic controllers, and Unmanned Aircraft Systems (UAS) operators, detailed knowledge of the different job requirements is essential. Future modifications in system design, such as remote tower control, as well as socio-economic changes (e.g. decreasing number of applicants) have to be taken into account.

Selection of aerospace operators

On the basis of job requirement profiles of pilots, air traffic controllers, and UAS-operators, selection and training methods have to meet future demands in a globalized aviation world. Particularly, leadership in UAS human factors with special regard to job requirements and selection will guarantee a competitive advantage in this fast growing aviation segment. New approaches in selection of operators could comprise eye gaze analysis or virtual reality scenarios.

Group decision making

Whereas individual decision making has been in focus of scientific research for many years, the process of team decision making is largely unknown. As safety related decisions in avia-tion are not taken by one person, team decision making is particularly relevant for aviation.

Passenger comfort and acceptance of new technologies

New cabin concepts in transport systems as well as new technologies have to be tested ac-cording to the subjective acceptance of the passengers and the general public. In addition to technological and medical advances, passenger acceptance will be crucial to restart touristic and business flight travel following the corona virus pandemic.

Drone flight for bridge inspection

Working Groups

Air Traffic Control
(Dr. phil. Hinnerk Eißfeldt)

- Job requirements of controllers and UAS operators
- Selection of air traffic controllers
- Inter team cooperation
- Eye tracking methods
- Urban air mobility
- Acceptance of aviation systems

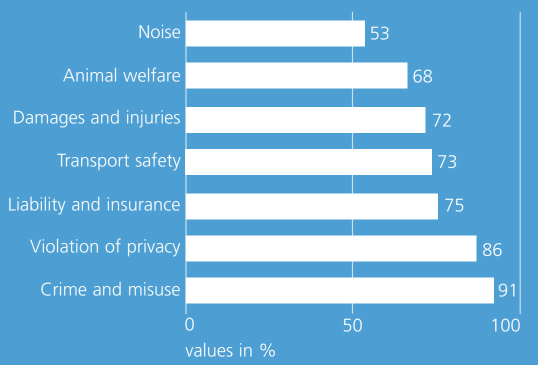
Crew Performance and Transport
(Prof. Dr. phil. Dirk Stelling)

- Selection of airline pilots
- Development and validation of diagnostic methods
- Cabin comfort
- Virtual reality
- Selection und support of bed rest candidates

Space Psychology

- Selection of astronauts
- Psychological inflight support of astronauts

Concerns about civil drones



Main projects 2017-2020

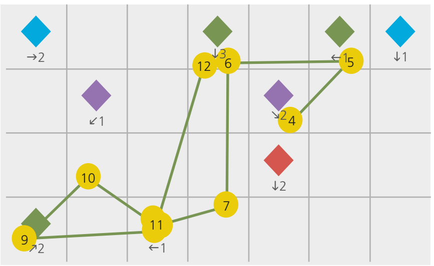
Acceptance of civil unmanned aircraft in the German population – A nationwide representative study

In recent years, the development of new technologies in the field of unmanned aerial vehicles has been steadily progressing. A large number of different applications have emerged for civil drones, such as package deliveries or the inspection of industrial facilities. With the expected increase in usage, the interest in public perception is also gaining in importance.

In 2018, a nationwide telephone survey on public acceptance of civil drones was conducted as a joint effort of the Department of Human Factors of the DLR Institute for Flight Guidance in Braunschweig and our department in Hamburg. A computer assisted telephone interview (CATI) was carried out in a standardized manner by infas (Institute for Applied Social Sciences) with the aim of reaching conclusive results representative for the German population. The study comprised 832 respondents (51. 8% male, 48.2% female) between 14 and 94 years.

Similar to comparable studies, a rather balanced pattern of acceptance was found with a slightly positive attitude towards civil drones, with 49% of the participants being rather positive, 43% rather negative, and about 8% undecided. Acceptance varies with several sociodemographic factors such as age, gender, income, and place of residence. For instance, male and younger respondents showed a higher acceptance and mentioned fewer concerns than women and older participants. General technical interests as well as knowledge about drones have also been identified as important influencing factors. Different applications such as the use of drones in civil protection, rescue missions, and research work were clearly supported by the majority of the respondents, whereas flights for advertising, leisure, and parcel delivery purposes were refused by at least half the respondents. Overall, concerns were more common among respondents with no prior experience with civil drones. Among all the areas of concerns, noise concerns best explained the attitude towards civil drones.

The results of the study will be the basis for activities to further increase the acceptance of civil drones and to reduce occurring reservations. These activities may promote successful development of new concepts for integrating unmanned aircraft systems in airspace. A useful means could include development of measures and methods to provide information to specific target groups or to elaborate reasonable regulations. Further research will focus on public perception and the possibility to reduce drone noise to foster public acceptance of civil drones in Germany. Moreover, the further development of the public perception in general, as well as a more detailed look at specific differences in the population and other possible influencing factors will be taken into account.



Eye Movement Conflict Detection Test
A single scan path is illustrated.

Can eye gaze analysis become a viable tool in selection and training?

Air traffic controllers work under high standards in a safety-critical environment. Given the high demands of the job, DLR has established a highly selective selection procedure for air traffic control candidates for job training with the German Air Navigation Service Provider DFS. Over the course of this multiple-stage process, applicants' performance on cognitive ability and work sample tests is usually assessed by performance measures, i.e., response accuracy and speed. To gain deeper insight into the cognitive processes underlying performance on visual tasks, alternative approaches such as eye tracking are required. Through eye gaze analysis, visual search activities can be assessed and quantified, including task solving strategies.

To investigate eye tracking in the selection of air traffic controllers, a new computer-based work sample test was developed. The Eye Movement Conflict Detection Test meets the requirements for eye gaze analysis and simulates conflict detection between aircraft, a key task of air traffic controllers. Results showed that gaze behavior is significantly associated with test performance and contributes relevant additional information about attentional and strategic processes of air traffic control candidates. Testing provides an objective individual performance measure during selection, making the process of visual search transparent, quantifiable, and comparable between candidates.

Further research aims at integrating eye tracking to the existing selection process. Moreover, eye movements will be assessed as indicator for psychological test performance in different cognitive ability and work sample tests. In this context, general decision criteria based on eye movements must be established. Technical advances in eye tracking technology will improve gaze analysis and facilitate applications in not only selection but also training, in which performance needs to be assessed over longer periods. Overall, eye tracking has substantial potential as a tool in diverse domains, including selection and training of air traffic controllers and other aviation operators.

Control room resource management training for subway operators - application of COCO project's outcomes

Control center operations are highly demanding in terms of the collaboration required for monitoring and decision making in teams. In a joint effort, several institutions, led by the DLR, investigated psychological requirements for monitoring systems and for collaborative decision-making among teams in control centers (COCO). Within the COCO project, we specifically asked how recent changes for control room staff such as automation, digitization, and system wide information sharing change the nature of collaboration among staff. Moreover, we asked whether new or different skills would be required and how these skills could be developed by training. The COCO project commenced with the identification of the psychological requirements for control room operators. A key outcome was that teamwork in control rooms is particularly important in case of system failures, emergency situations, unforeseeable events (from outside of the system), and dynamic situations within the system. Subsequently, an initial control room resource management training was developed within the COCO project and tested in a prototype with a group of operators of the Galileo Control Center. The final training procedure consists of theoretical units, discussions, and exercises on communication and teamwork, team dynamics, hazards and risks, and decision

Subway control center of the Hamburger Hochbahn AG

making in dynamic situations. Additionally, the training involves methods to improve transfer of training content into practice. The final control room resource management was validated in seven trainings with a total of 79 operators of the subway control center of the Hamburger Hochbahn AG. Acceptance of the training was high, with about 90 percent of the 77 participants rating the training positive. When asked three months after completed training, whether or not the majority of the individuals would still recommend the training to colleagues. In conclusion, the theoretical knowledge about collaborative work gained from the COCO project can be successfully applied to develop training procedures to specifically address requirements in collaborative work environments such as control rooms

Depiction of the Control Center Task Environment (ConCenT)

Collaboration among and between teams in aviation

Multi-team systems are a dominant organization form in aviation. In such highly dynamic work environments, where short-term team members work together in a very interdependent manner under time pressure, existing goal conflicts may create mistrust, which in turn has the potential to hinder the successful collaboration. The project ITC (Inter Team Collaboration) aims to provide system engineers with human-factors tools and concepts that enable systemic access to the social side of socio-technical systems. Collaborative work processes across organizational boundaries are investigated in order to develop guidelines on how to build up a more flexible and resilient multi-team system for the dynamic aviation environment. As ITC is an interdisciplinary project involving both laboratory and applied research, several DLR departments of the Institute for Aerospace Medicine and the Institute of Flight Guidance are involved. An experimental study is prepared to investigate the impact of conflicting goals on communication and collaboration. A simulation of a Control Center Task Environment is used, which was developed and validated in order to investigate selected requirements for control room operators under controlled conditions. Measurements of performance, perceived trust communication data and gaze data are collected and will be analyzed to examine different coordination and communication patterns at a team level. The study will provide answers to the questions of how to design, measure, evaluate and enhance the collaborative work processes of multi-team systems in aviation. As part of the ITC project and in addition to this experimental study, large-scale simulations with experienced operators will take place to investigate and validate the elaborated methods. From that, implications for appropriate interventions in operational work environments can be derived in order to improve the collaborative processes in multi-team systems and thus to further ensure safe and efficient coordination processes in future aviation.

Impact of artificial outside view on passenger comfort

Virtual reality has gained popularity in the entertainment industry and various professional contexts, such as healthcare, rehabilitation, and aviation. Due to the vast technological advances in the last decades, the opportunities to develop applications allowing to experience and interact with immersive virtual environments have increased substantially. Despite its wider dissemination and improved technology, many virtuality users of VR still complain about symptoms of cybersickness during and after an exposure to virtual environments, including nausea, disorientation and headache. Cybersickness can be ameliorated to some extent by adjusting characteristics of the VR application and the hardware system but large inter-individual differences in the susceptibility to cybersickness remain. The Department of Aerospace Psychology investigates which factors contribute to the development of cybersickness and how it influences performance and the subjective perception of well-being.We tested conditions leading to cybersickness on a bicycle simulator and in the cabin module of the Air Vehicle Simulator in cooperation with the Institute of Flight Systems.

In addition to a strong dependence on the properties of the employed hardware, it was observed that factors of the individual motion sickness susceptibility contribute to the development of cybersickness. Large inter-individual differences were found which can be attributed to a large extent on different levels of anxiety, the tendency to catastrophize negative body sensations and body awareness.

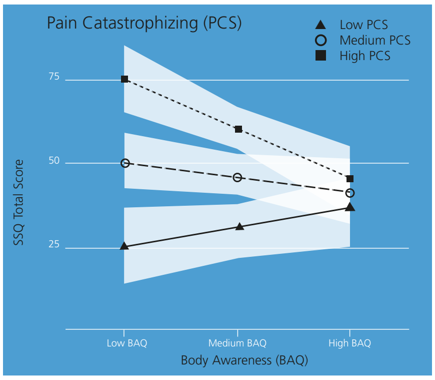
Cybersickness is a syndrome that is extremely unpleasant and greatly impedes the use of new, immersive technologies. As symptoms of cybersickness can linger for a prolonged period of time after termination of the exposure, manufacturers of VR equipment recommend refraining from driving or using machines until symptoms cease. The good news, however, is that cybersickness only has a minimal effect on cognitive performance, which means that even after the experience of cybersickness, affected persons still have a high level of cognitive capability.

Passenger comfort in the Next Generation Train

To strengthen its popularity for the passengers, railways have to provide an attractive environment reliably and comfortably transporting passengers while using as little energy as possible and ensuring rail-based mobility as integral part of the overall mobility system. One important aspect determining the attractiveness of rail journeys is the thermal comfort that is provided in a passenger rail car. In a multi-disciplinary team of psychologists, engineers, and physicists, we are addressing this topic in the fields of Human Factors, Transport, and Energy as part of the DLR project Next Generation Train (NGT).

So far we focused on passengers thermal comfort provided by different ventilation systems. We assessed comfort sensations in low-momentum ventilation techniques such as Cabin Displacement ventilation, Ceiling-integrated, or Hatrack-integrated low-momentum ventilation and their combination as a hybrid concept. We also assessed personalized comfort zones providing individual micro-climates for passengers. In addition to improving comfort, the approach may reduce energy utilization through more targeted air conditioning.

Bicycle simulator



Interaction of catastrophizing and body awareness on cybersickness magnitude.

Collaboration partners within the Institute

- Dept. of Clinical Aerospace Medicine
- Dept. of Sleep and Human Factors Research
- Study Team

Collaboration partners within the DLR

- Institute of Flight Guidance
- Institute of Flight Systems
- Institute of Aerodynamics and Flow Technology
- Institute of System Architectures in Aeronautics

Collaboration partners in Germany

- Lufthansa
- Deutsche Flugsicherung
- CityLine
- ADAC
- Industrie Design Studio
- University of Lübeck
- University of Dresden
- Technical University of Hamburg
- University of Hamburg
- German national police
- Luftfahrtbundesamt
- German Armed Forces

Collaboration partners worldwide

- Austrian Airlines
- Turkish Airlines
- Royal Jordanian Airlines
- Swiss Airlines
- Swiss Army
- Luxair
- European Space Agency

Selected publications

Bruder, C., Hasse, C. (2019) *Differences between experts and novices in the monitoring of automated systems.* International Journal of Industrial Ergonomics, 72, 1-11.

Eißfeldt, H., Vogelpohl, V., Stolz, M., Papenfuß, A., Biella, M., Belz, J., Kügler, D. (2020) *The acceptance of civil drones in Germany.* CEAS Aeronautical Journal, 11, 665-676.

Hermes, M., Albers, F., Böhnke, J.R., **Huelmann, G., Maier, J., Stelling, D.** (2019) *Measurement and structural invariance of cognitive ability tests after computer-based training.* Computers in Human Behavior, 93, 370-378.

Maier, J., Zierke, O., Hörmann, H.-J., Windemut, I. (2016/2017) *Subjectivity of Lighting Perception and Comfort: The Role of Preferences and Expectations.* Environment and Behavior, 49, 1105-1127.

Mittelstaedt, J., Wacker, J., **Stelling, D.** (2019) *Emotional and Cognitive Modulation of Cybersickness: The Role of Pain Catastrophizing and Body Awareness.* Human Factors, 61 (2), 322-336.

II.6
Radiation Biology

PD Dr. med. vet. Christine E. Hellweg (Head)

Dr. rer. nat. Petra Rettberg (Deputy)

Mission Goal
The Radiation Biology department conducts biophysical and cell biological research to elucidate mechanisms of cell damage and repair following radiation exposure. The goal is to improve individual risk prediction for space missions, in aeronautics, and on Earth. Radiation exposure can initiate and promote carcinogenesis and cause cell death, cellular senescence, and genetic defects, or even acute radiation sickness. Therefore, cosmic radiation remains a major limiting factor for long-term space missions and an important occupational health issue at aviation altitudes.

Our findings are applied to improve radiation protection in aviation and spaceflight. Moreover, we closely collaborate with leading medical partners to translate our findings from space radiobiological research to advance the knowledge of aging-associated diseases and oncologic radiotherapy. Another focus of our department is microbiology which in addition to providing cell models for radiation biology research is applied to elucidate biotic and abiotic factors limiting microbiological life and adaptation to extreme conditions. We apply this knowledge to develop novel approaches to limit spread of infectious agents, to investigate the human microbiome, and to support the search for extraterrestrial life and habitable environments on other celestial bodies.

Radiation Biology

Unique selling points of the department

- Lead of international ISS radiation dosimetry, phantom measurements for exploration missions and radiation modelling, and partner in dosimetry on Moon and Mars and beyond combined with assessment of space radiation effects and radiosensitivity
- Microbial life in space, on Earth, and on other celestial bodies and the interactions of microorganisms with environmental factors and higher organisms such as plants and humans

The department contributes to DLR's long-term goals to support astronauts' presence in space, to explore our solar system, to search for extraterrestrial life, and to examine the air transport system in its entirety. The work is based on long-standing expertise in radiation dosimetry and modeling, space and heavy ion accelerator experiments, hardware development, and field and mechanistic lab studies. The unique radiation fields at aviation altitudes and in different space mission scenarios are characterized using active and passive dosimetry as well as modeling to derive radiation exposure. New dosimeters are developed, tested, and operated in low Earth orbit, during Moon missions, and at aviation altitudes. The knowledge about the radiation fields and the astronaut's exposure is a prerequisite for radiation protection guidelines and development of suitable countermeasures. This challenging task requires investigating biological effects of space radiation (especially heavy ions) and other environmental stressors (e.g. hypoxia) on different test systems at the cellular and molecular level and in target organs, such as the brain. Depth-dependent dose distribution measurements and a better understanding of the cellular radiation response are also vital to improving cancer radiotherapy. Human studies offer opportunities to study the variability in individual radiation sensitivity and changes in the microbiome under space-relevant conditions. The investigations into the microbial world encompass detection and characterization of microbes present in different (extreme) environments, their adaptation mechanisms, interactions with non-living and living environment, and the development of new methods for decontamination with applications for both planetary protection and daily life.

Main projects 2017-2020

Space Radiation Dosimetry from low Earth orbit to Mars

The RAMIS radiation detector flying on the DLR Eu:CROPIS mission

Long-term exposure to space radiation may predispose to cancer due to long-term steady flux of galactic cosmic rays (GCR). Acute radiation sickness can occur during a Solar Particle Event (SPE). While the International Space Station (ISS) is somewhat protected against radiation by the Earth magnetic field, humans travelling in deep space are unprotected. For human exploration, the main questions to solve are: "How much radiation would one receive?", "What is the associated radiation risk?" and "What are the best ways to determine radiation load and gain more information about the risks?"

To solve these issues, we develop radiation detectors for highly complex radiation fields: The Tissue Equivalent Proportional counter (TEPC) for the ESA Active Dosimeter experiment was onboard the ISS in 2016-2017. Furthermore, we built the RAMIS silicon detector telescope currently flying onboard the DLR Eu:CROPIS Mission and the M-42 radiation detector which will be part of the upcoming Matroshka AstroRad Radiation Experiment (MARE) (https://www.dlr.de/me/mare).

For MARE, we built upon the heritage from the ISS MATROSHKA experiments and developed a research payload which will for the first time measure the radiation load in female phantoms flying to the Moon with the NASA Artemis I mission in 2021. Moreover, we foster international collaboration onboard the ISS with the DOSIS 3D project since 2012 providing the area monitoring capabilities in the European Columbus Laboratory and as ESA contractors with the European Crew Personal Dosimeter (EuCPD) as personal dosimeter for all European astronauts. Finally, in international collaborations, we are involved in studies using instruments on the Mars (MSL-RAD), in the lunar orbit (CRaTER), and on the surface of the Moon (LND).

The MARE experiment with HELGA and ZOHAR in the NASA Orion spacecraft for the Artemis I mission.

Working Groups

Biophysics (Dr. techn. Thomas Berger)
- Space radiation dosimetry and modeling from ISS to Moon and Mars

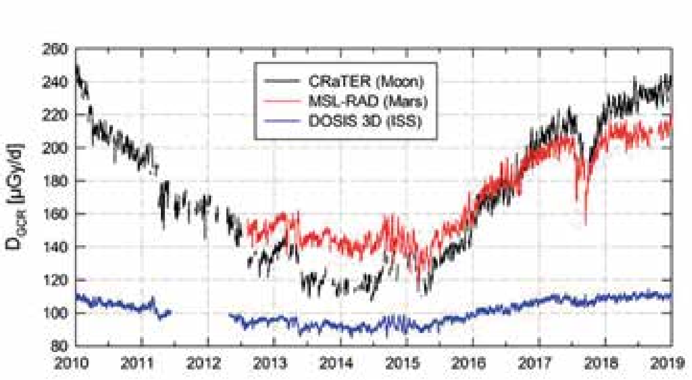
Radiation Protection in Aviation (Dr. phil. nat. Matthias M. Meier)
- Radiation effects in the atmosphere
- Development of products and services for the aviation industry and the society

Biodiagnostics (PD Dr. med. vet. Christine E. Hellweg)
- Molecular mechanisms of space radiation effects in CNS and other target organs, modifiers of radiation response and radiosensitivity

Aerospace Microbiology (Prof. Dr. rer. nat. Ralf Möller)
- Radiation response of microorganisms
- Human microbiome research, biofilm formation, antimicrobial materials and decontamination approaches

Astrobiology (Dr. rer. nat. Petra Rettberg)
- Life in extreme environments and microbiome of confined habitats

We also focus on simulations of radiation environments, having developed a new model for the GCR environment (the Matthiä/DLR model) and being the responsible partner for the joint evaluation and testing of radiation transport codes for the simulation of the radiation environment on Mars. Together, the data will enable us to measure, to model, and to calculate radiation exposure and to determine risks faced by humans leaving low Earth orbit on future exploration missions.



The variation of the galactic cosmic ray dose (2010- 2019) measured with instruments onboard the ISS, in lunar orbit and on the surface of Mars

New legal radiation protection regulations in aviation – focus on space weather

The Radiation Protection in Aviation Group has offered scientific services for airlines since radiation protection regulations became legally binding in Germany in 2001. We developed the computer program Professional AviatioN DOse CAlculator (PANDOCA) based on an atmospheric radiation model for dose assessment of aircrew registered in Germany. Furthermore, measuring techniques have been established as standards for quality assurance.

New legal requirements have to be implemented by the airline industry by the end of 2020 necessitating adaptation of existing and development of new products and services. For example, ICRP recommendations concerning radiation and tissue weighting factors for calculation of the effective dose had to be implemented into PANDOCA. An analysis of the consequences for the accrued flight doses showed corresponding decreases in dose rates of about 30 % during solar minimum conditions, which are going to prevail for the coming years.

New legal requirement obliges airline companies to appoint radiation protection officers with a requisite qualification in radiation protection in aviation. The Radiation Biology Department is among the few providers of such courses in Germany.

Furthermore, the amended German Radiation Protection Act stipulates a new dose limit for the equivalent dose in the uterus of female flight attendants of childbearing age, which poses new challenges and opportunities for further services, such as early space weather radiation alerts to support airlines in their efforts to limit occupational and passengers’ radiation exposure.

Space radiation as show-stopper for long-term space missions: biological heavy charged particle effects

Given the chronic low-dose whole-body exposure to galactic cosmic rays (GCR), astronauts are at risk for late radiation effects such as cancer or eye lens opacities (cataracts). Furthermore, central nervous system effects including cognitive deficits and neurological damage (“space brain”) are a matter of concern. The high biological effectiveness of high-linear-energy-transfer GCR is generally ascribed to different patterns of cellular energy deposition compared to low-linear-energy-transfer radiation on Earth (such as X-rays), resulting in complex and difficult to repair DNA damage.

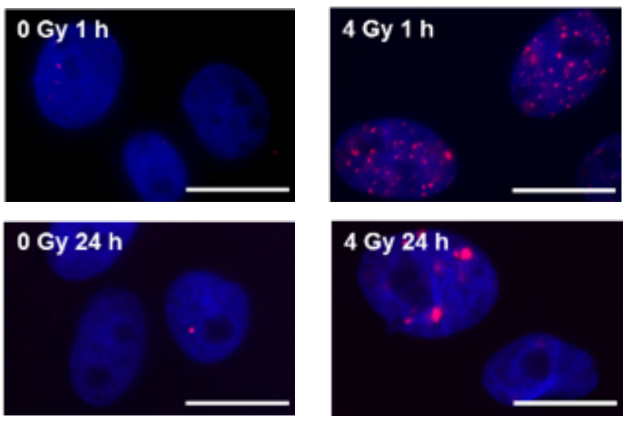
Therefore, we studied cellular responses to high-energy particles beyond the classical DNA damage response focussing on pro-inflammatory pathways, tissue-specific responses, and degenerative effects, in main target organs or susceptible cells, such as the eye lens and neurons. High-energy particles were much more efficient in activating the pro-inflammatory transcription factor Nuclear Factor κB (NF-κB) in human cells compared to X-rays. The phenomenon was especially interesting as NF-κB can also promote cell survival. Yet, the killing effect of high-energy particles was higher compared to X-rays. Knock-down experiments revealed that NF-κB supports survival after X-ray exposure, but not after exposure to high-energy particles. Indeed, NF-κB activation did not confer cells which were exposed to high-energy particles a survival advantage, but allowed them to scream loader “I am damaged” by cyto- and chemokine expression compared to X-ray irradiated cells.

The finding may be important for cell-cell communication among hit as well as non-hit cells (bystander effect). As the bystander effect is highly important in cases of low-dose exposures and single particle hits as relevant during space missions, the role of NF-κB in this process was investigated and the factor was indeed involved in amplification and transmission of the bystander signal. These experiments with epithelial cells and fibroblasts have clearly shown the pro-in- flammatory potential of ionizing radiation, especially high-energy particles, in directly hit cells and in bystander cells.

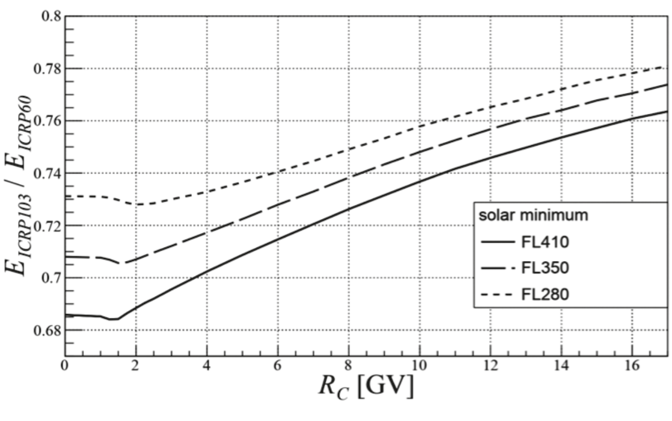
In a unique organ such as the eye lens, other organ-specific mechanisms might contribute to the detrimental effects of radiation. These mechanisms were examined in isolated pig eye lenses and lens epithelial cells. Repair of X-ray-induced DNA damage was impaired in lens epithelial cells as well as whole lenses. More damage persisted at the equatorial region (differentiation zone) of the eye lens, which could possibly initiate lens opacification. DNA repair impairment and cell-cycle disturbances indicate the vulnerability and sensitivity of lens epithelial cells to- wards ionizing radiation. In future studies, the interaction of different paths towards lens opacification, e.g. residual DNA damage and calcium deposits will be addressed, and exposure of pig eye lenses to natural GCR on the ISS could provide insight into the low-dose effects.

Currently, the methods established for DNA damage and repair detection in cell and organ cultures are adapted to be used in human blood lymphocytes in order apply them to determine inter-individual differences of DNA repair capacity under different environmental conditions and at different ages in cooperation with CECAD Cologne.

Furthermore, the recently started investigation of radiation effects in primary neuronal cells will be continued in order to determine how effective complex DNA damage is repaired, and how it contributes to degenerative effects and inflammatory responses in the brain. The significance of the findings concerning heavy-ion-induced NF-κB activation for carbon tumor therapy will be determined using tumor cell lines.



Immunofluorescence staining of γH2AX (pink foci) in porcine lens epithelial cells. Cells were fixed with 3.5 % formaldehyde 1 h and 24 h after X-ray exposure. Fluorescent antibody staining for γH2AX is given by pink foci whereas the blue stain of the cell nuclei is due to DAPI stain. Scale bar represents 20 µm.



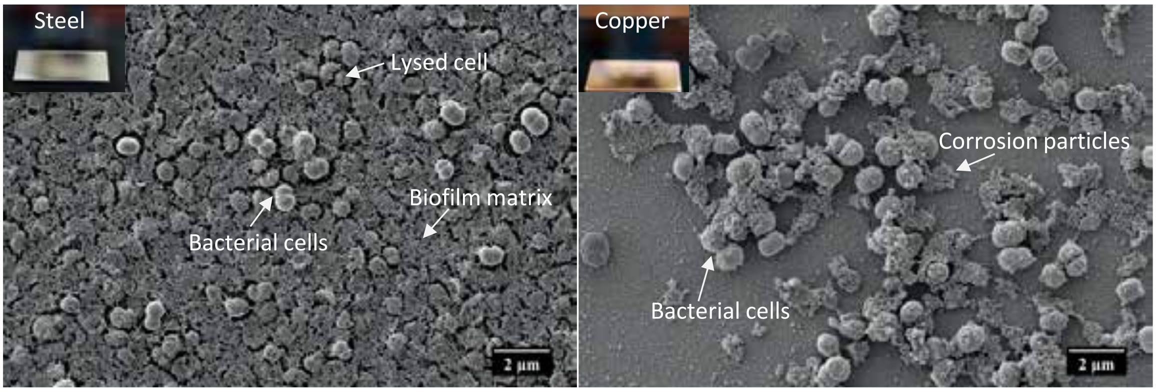
Ratio of the effective dose rates after the recommendations by ICRP103 and ICRP60 at different altitudes during solar minimum conditions in dependence on the effective geomagnetic cut-off rigidity RC, a parameter used for the quantification of the shielding effect of the Earth’s magnetic field.

Innovative approaches to counter microbial threats – insights from the BIOFILMS spaceflight experiment

Microorganisms are ubiquitous and will accompany all human space missions. The microbial populations in these man-made environments mainly come from the crew (skin, upper respiratory tract, mouth, and gastrointestinal tract). Environmental microorganisms are also present. The human and habitat microflora is further shaped both in diversity and mass by the unique combination of environmental factors aboard the ISS. A main concern regarding crew health is activation of opportunistic pathogens in space, as the immune system of the astronauts can be affected by high working pressure, confinement, defined diet, and restricted hygienic practices, microgravity and radiation. Therefore regular microbial monitoring, efficient and reliable disinfection and decontamination strategies are needed for future spaceflight as well as under current pandemic conditions.

The Coronavirus SARS-CoV-2 outbreak highlights the importance of innovative methods to contain the spread of pathogens. Besides droplets and aerosols, a frequent transmission path, pathogenic microorganisms may be transmitted via contact surfaces. One approach to prevent microorganism surface attachment and transmission is the use of antimicrobial surfaces. The antimicrobial agent (such as silver, copper and their alloys) inhibits or reduces the ability of microorganisms to grow on the surface of a material and to form biofilms. Antimicrobial surfaces can be used in several environments, where strict hygiene standards are inevitable such as in intensive care units, quarantine units, nurseries, or other health care settings, for pharmaceutical and industrial purposes and human spaceflight.

Microbial biofilms can damage equipment through polymer deterioration, metal corrosion, and bio-fouling. Surface-associated biofilms were abundant on the Mir Space Station and continue to be a challenge on the ISS. The health and safety hazards linked to biofilms are particular concerning in the setting of compromised immune function during spaceflight. The BIOFILMS project will investigate the effect of microgravity on bacterial biofilm formation on non-inhibiting surfaces, such as steel, and on antimicrobial, laser-nanostructured metal surfaces onboard the ISS in ESA's Columbus laboratory. For the project, a set of human-associated and space-relevant bacterial strains were selected. One of the selected strains was previously isolated aboard ISS and belongs to the genera *Staphylococcus sp*. as surrogate pathogenic staphylococcal strains. The BIOFILMS project will help understanding the effectiveness of antimicrobial surfaces in space.



Biofilm formation of *Staphylococcus capitis* on non-inhibitory steel (left) and the absence of a biofilm on copper (right).

Furthermore, different types of surface sterilization and decontamination approaches are highly relevant in various technological fields including food packaging and preservation, air sanitation, production of (disposable) materials and laboratory consumables, pharmaceutical industry, and spaceflight missions. Here, atmospheric pressure plasmas for biomedical applications have gained increasing interest in the last years and have been employed for bacterial inactivation, tissue sterilization and to promote wound healing. These plasma processes appear to be reliable, non-toxic, and user-friendly alternatives to conventional sterilization methods and have been successfully employed for microbial decontamination. Due to the recent demand of novel and improved disinfection and sterilization methods, the aerospace microbiology research group aims to address the utilization of cold atmospheric plasma as novel aerospace-qualified decontamination strategy.

Microbial sampling in the ISS by the astronaut Jack Farmer (© NASA/ESA).

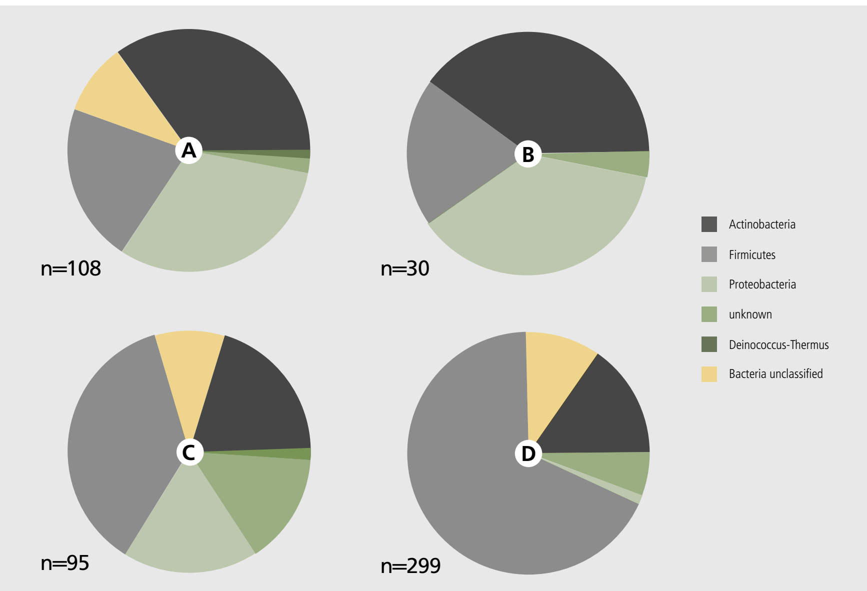
Microorganisms with versatile metabolic pathways, high adaptability and pronounced resistance – challenges and applications in space

Microorganisms, the first form of life on Earth, are integral environmental components. Microorganisms inhabit almost all places on Earth, even environments which are considered extreme from an anthropogenic point of view. Multicellular organisms have co-evolved with their specific microbiome. Most of the microorganisms are not harmful for them, only a few are pathogenic for humans, animals, or plants, others are obligatory symbionts. We investigate the adaptability and resistance of microorganisms, their interaction with biotic and abiotic factors, and the underlying metabolic processes. The aim is (i) to achieve a better understanding of limits of life on Earth to support the search for life in our solar system and to develop suitable planetary protection measures, (ii) to explore the use of microorganisms for biotechnological applications in space such as biomining, (iii) to characterize the human and plant microbiome in confined habitats and bioregenerative life support systems to ensure the safe space travel of humans to the Moon and to Mars.

The subsurface oceans of the moons Europa and Enceladus in the outer solar system are identified as habitable based on today's knowledge about the moons and about microbial Earth life in extreme cold and salty environments. The existing knowledge gaps were identified in the project Planetary Protection for the Outer Solar System (PPOSS) and are the basis of ongoing research activities with extremophilic microorganisms from the three domains of life. We investigate their resistance in our Planetary and Space Simulation Facilities, during balloon flights, in Antarctica, and on the ISS (experiments IceCold and MEXEM).

The influence of different gravity levels on microbe-mineral interactions was investigated in the project BioRock. Cultures from three bacterial species (*Sphingomonas desiccabilis, Bacillus subtilis, Cupriavidus metallidurans*) were exposed to microgravity and simulated Mars and Earth gravity in the presence of basalt in the ESA facility KUBIK on the ISS. The growth, bioleaching capability with respect to rare Earth elements (REE) and biofilm formation were investigated afterwards on ground. Microgravity and Mars gravity had no effect on the final biomass of the bacteria. One bacterial species, *Sphingomonas dessicabilis,* produced biofilms on the basalt surface and was found to have leached higher concentrations of REEs than the abiotic control samples in all gravity conditions. Thus, microgravity has a limited effect on bacterial cell growth and bioproduction can be performed at low gravity, e.g. for *in situ* resource utilization (ISRU) on the Moon and on Mars.
Microorganisms in confined space habitats such as the ISS are unavoidable. The microbial diversity, distribution, functional capacity and resistance profile of the ISS microbiome was characterized by a combination of cultivation-independent and-dependent analyses (project EXTREMOPHILES). ISS microbial communities exhibited fluctuations, although a core microbiome persisted over time and locations. The genomic and physiological features selected by ISS conditions do not appear to be directly relevant to human health. Yet, adaptation in biofilm formation and surface interactions were observed.

In future space habitats, plants will be cultivated in confined greenhouses. The microbiome of a mobile greenhouse test facility in Antarctica was investigated in the DLR-coordinated EDEN-ISS project over nine months. Clear differences between microbiomes of plants grown in the confined EDEN-ISS greenhouse and of grocery plants used as controls were observed with respect to abundance and biodiversity. The bioburden of the greenhouse surfaces increased over time despite regular cleaning activities, but never exceeded critical values concerning pathogens.



Distribution of bacterial phyla. A: produce, B: EDEN ISS plants, C: liquid nutrient samples, D: surface samples (Fahrion et al., 2020)

Collaboration partners within the Institute

- Dept. of Gravitational Biology
- Dept. of Cardiovascular Aerospace Medicine
- Dept. of Muscle & Bone Metabolism
- Study Team

Collaboration partners within the DLR

- Institute for Planetary Research, Berlin
- Institute of Materials Physics in Space, Cologne & Oberpfaffenhofen
- Institute of Space Systems, Bremen
- Institute of Materials Research, Cologne
- Institute of Composite Structures and Adaptive Systems, Braunschweig
- Institute of System Architectures in Aeronautics, Hamburg

Collaboration partners in Germany (selection of 5 from 26)

- Christian Albrechts Universität zu Kiel (CAU)
- Technical University Munich (TUM)
- Universität des Saarlands Homburg
- University of Cologne
- Robert-Koch-Institut (RKI), Berlin

Collaboration partners worldwide (selection of 5 from 56)

- Centre d'Étude de l'énergie Nucléaire/Belgian Nuclear Research Center, SCK•CEN, Mol, Belgium
- European Space Agency (ESA)
- Massachusetts Institute of Technology (MIT), USA
- Medical University Graz, Austria
- National Aeronautics and Space Administration (NASA), USA

Selected publications

Cortesão, M., de Haas, A., Unterbusch, R., Fujimori, A., Schütze, T., Meyer, V., **Moeller, R.** (2020) *Aspergillus niger Spores Are Highly Resistant to Space Radiation.* Frontiers in Microbiology, 11, 560.

Hellweg, C.E., Spitta, L., Koch, K., Chishti, A.A., Henschenmacher, B., Diegeler, S., Konda, B., Feles, S., Schmitz, C., Berger, T., Baumstark-Khan, C. (2018) *The Role of the Nuclear Factor κB Pathway in the Cellular Response to Low and High Linear Energy Transfer Radiation.* International Journal of Molecular Sciences, 19 (8), 2220.

Meier, M., Matthiä, D. (2019) *Dose assessment of aircrew: the impact of the weighting factors according to ICRP 103.* Journal of Radiological Protection, 39 (4), 698-706.

Mora, M., Wink, L., Kögler, I., Mahnert, A., **Rettberg, P.,** Schwendner, P., Demets, R., Cockell, C., Alekhova, T., Klingl, A., Krause, R., Zolotariof, A., Alexandrova, A., Moissl-Eichinger, C. (2019) *Space Station conditions are selective but do not alter microbial characteristics relevant to human health.* Nature Communications 10, 3990.

Zhang, S., Wimmer-Schweingruber, R.F., Yu, J., Wang, C., Fu, Q., Zou, Y., Sun, Y., Wang, C., Hou, D., Böttcher, S.I., Burmeister, S., Seimetz, L., Schuster, B., Knierim, V., Shen, G., Yuan, B., Lohf, H., Guo, J., Xu, Z., Freiherr von Forstner, J.L., Kulkarni, S.R., Xu, H., Xue, C., Li, J., Zhang, Z., Zhang, H., **Berger, T., Matthiä, D., Hellweg, C.E.,** Hou, X., Cao, J., Chang, Z., Zhang, B., Chen, Y., Geng, H., Quan, Z. (2020) *First measurements of the radiation dose on the lunar surface.* Science Advances 6, eaaz1334.

II.7
Gravitational Biology

PD Dr. rer. nat. Ruth Hemmersbach (Head)

Dr. rer. nat. Christian Liemersdorf (Deputy)

Mission Goal
Life evolved in terrestrial gravity, which is the only environmental factor that has remained constant for billions of years. The lack of gravity during space travel poses health challenges to astronauts while providing unique insight in the fundamental mechanisms of gravity- and mechano-sensing. Indeed, biological systems perceive gravity directly and indirectly through mechanosensitive structures and pathways. The main scope of the Gravitational Biology Department is to better understand the impact of gravity on biological systems. Moreover, we assess implications of altered gravity on technology development. Our goal is to elucidate molecular mechanisms of gravity perception and resulting biological responses ranging from single cells to human beings. We apply the acquired mechanistic knowledge to develop and refine countermeasures for space travel. Moreover, we translate findings on cellular mechano-sensing to terrestrial medicine in collaboration with medical departments in the Institute and elsewhere. Another main focus is to improve closed biological life-support systems, which are a prerequisite for long-term human space missions. With our innovative DLR C.R.O.P.® (Combined Regenerative Organic food Production) technology we aim at optimizing waste recycling for food production. The technology is applicable for stations on Moon and Mars, but also for sustainable agricultural systems on Earth.
Our Gravitational Biology research builds the basis for long-term human space exploration, guides human health research, and contributes to sustainable economic development on Earth.

Gravitational Biology

Unique selling points of the department

- Custom-design of centrifuges and microgravity simulators to create altered gravity conditions combined with e.g. live-cell imaging or biochemical (Omics) analyses and proof-of-concept under real microgravity conditions in space
- Long-standing expertise in human centrifugation. Support of sophisticated physiological research, centrifuge training, and technology development including virtual reality on the :envihab Short Arm Human Centrifuge
- In-house developed C.R.O.P.®-filter technology as innovative purely biological concept for waste recycling including degradation of excreted medications

The research topics of the Gravitational Biology Department range from micro- and hypergravity science in cells and in human beings to biological life support systems. Basis of our research are in-house developed ground-based simulation facilities mimicking weightlessness conditions for cells, small plants, and animals. We validate these approaches through bioassays and corresponding experiments on real microgravity platforms. Hypergravity studies including high-end microscopy and human training programs, and annual access to real microgravity via the DLR Mapheus rocket program complement our research. Highlights in our research are the identification of gravity-triggered pathways and gene expression patterns in different cellular systems.

Our main focus is the interaction of gravity with the cellular cytoskeleton, specific intracellular signal transduction chains, and mechanosensitive ion channels in the cell membrane. Our aim is to delineate fundamental mechanisms of gravity-/mechano-sensing (e.g. resulting in cellular migration, proliferation, regeneration, and aging). The challenge for the future is translating our results from space to medical applications on Earth.

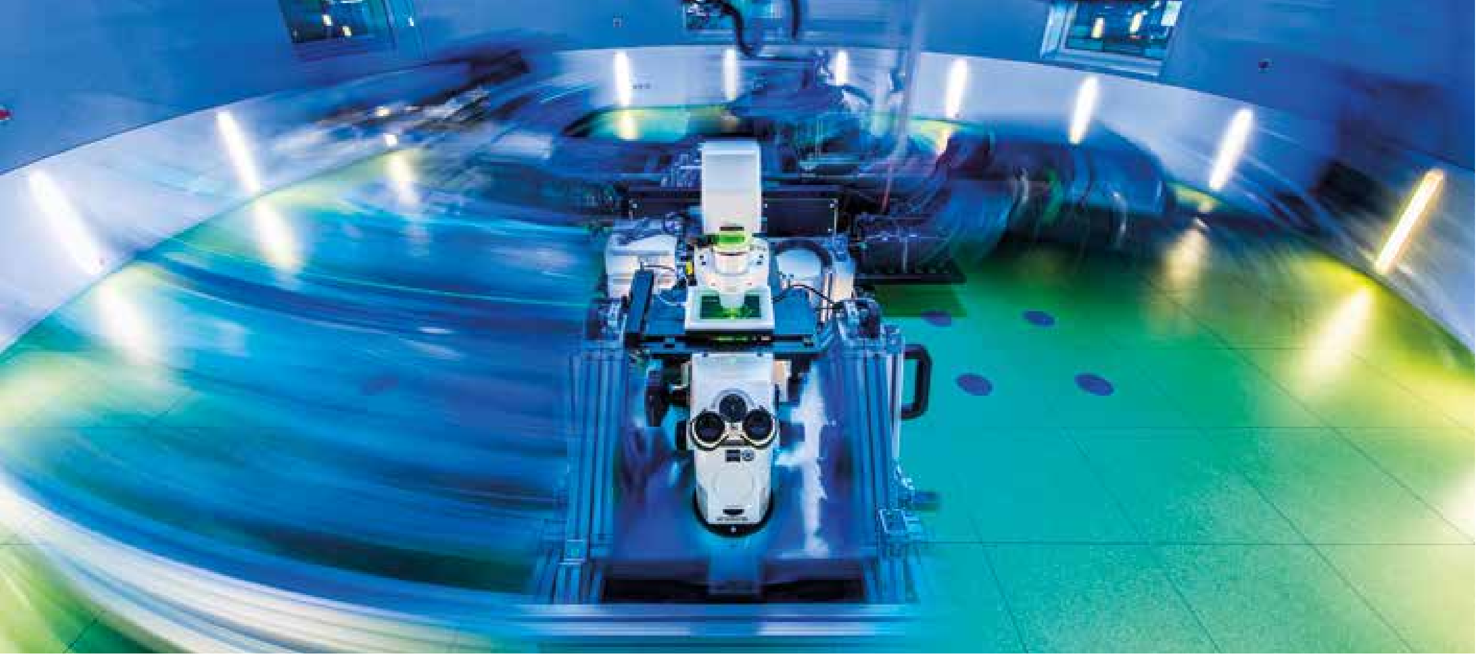
In bioregeneration research, we successfully developed an effective biofiltration system for nitrogen-rich organic wastes. The challenges for the next years are the design of a space-qualified prototype and its testing under real conditions, and the removal of pharmacological residues by the system. At the same time the C.R.O.P.®-filter technology will be further adapted for terrestrial applications. Our knowledge will contribute to design a life support infrastructure which enables healthy living during long-term missions in space and on foreign celestial bodies.

Main projects 2017-2020

DLR Mapheus sounding rocket missions: biological experiments within 6 min of microgravity

The DLR Mapheus rocket program permits unique and direct access for material and life science experiments in real microgravity. The rockets are launched by DLR MORABA from ESA Esrange in Kiruna, Sweden. From 2017 to 2019, we successfully participated in three flight campaigns with 11 individual experiments, which contributed to the understanding of mechanisms of gravity perception and sensitivity of biological processes. Furthermore, we developed and constructed scientific payloads for chemical sample fixation, online kinetics analysis based on luminescence assays, and microscopy of various model systems including membranes, plants, yeast, protists, stem cells, and neuronal cells. We delivered the proof of concept that our versatile experiment units can be implemented for life science experiments under space conditions. Moreover, the experiments yielded essential information for the design of future experiments under long-term microgravity conditions on the ISS and other platforms.

The sounding rocket modules for MemEx (top) and CellFix (bottom) integrated into the rocket shell structure.



Working Groups

Gravisensorics
(Dr. rer. nat. Christian Liemersdorf)

- Identification of gravity-sensitive responses of individual cell types that model various behavioral and physiological deconditioning phenotypes in humans (membranes, neurons, astroglia, skeletal muscle cells, immune cells and cardiomyocytes)
- Verification of ground-based studies in hypergravity/simulated microgravity in simulated weightlessness in real microgravity using various platforms including DLR Mapheus sounding rockets, drop-tower, parabolic aircraft flights, and the Biolab on ISS
- Evaluation of artificial gravity achieved through short arm centrifugation alone or in combination with physical training or virtual reality applications as potential countermeasure for health issues during space travel

Bioregeneration
(Dr. rer. nat. Jens Hauslage)

- Analysis of biogenic waste degradation by microbial trickle filters, optimization of the filters to generate maximal efficiency in producing plant nutrients
- Conversion of the set-up to applications in space with the goal to reclaim water while generating fertilizers for space travel and terrestrial agriculture (slurry)

The experiment MemEx in collaboration with the University of Hohenheim addressed biophysical alterations of cell membranes in microgravity. We studied fluidity and incorporation of substances such as lidocaine in artificial lipid vesicles membranes. We applied photomultiplier techniques in combination with open source microcontrollers (ARDUINO). Microgravity-induced changes in fluorescence anisotropy suggested increased fluidity of the lipid-bilayer membrane. The capacity to integrate hydrophobic molecules was decreased. These results indicate that microgravity might affect lipid membrane function and interaction with pharmacological agents through a hitherto unknown mechanism. The finding could have relevance for drug therapy during human space exploration.

We constructed the CellFix module to study influences of altered gravity on the physiology of single cells. Murine primary cortical astrocytes, the most prevalent glial cell type in the mammalian brain, were successfully flown and fixed inflight, as revealed by intact cell morphology. Detailed proteomic analysis, which is an important step to understand cellular dynamics under altered gravity conditions, is currently under investigation.

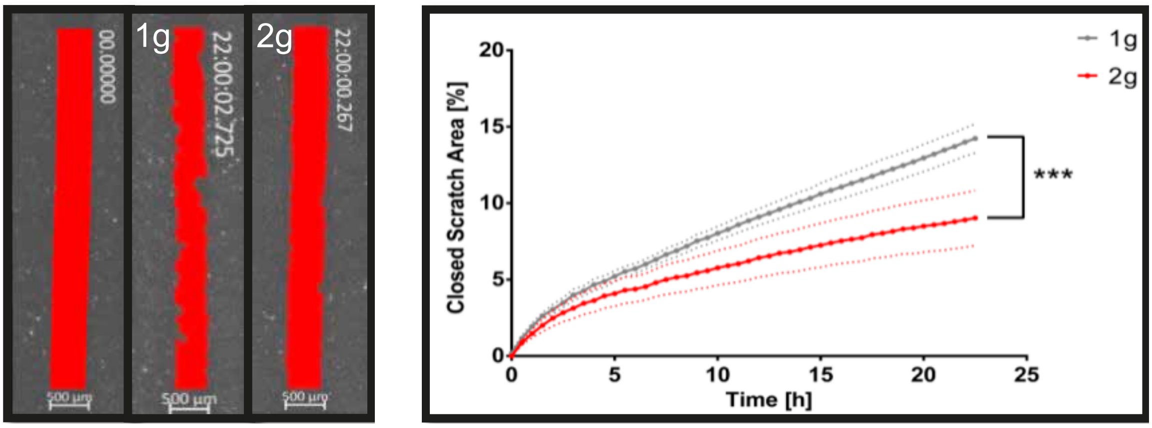
We study plants, as essential part of future life support systems, in microgravity to learn about their adaptations and culture requirements in microgravity. In our in-house-developed ARABIDOMICS hardware (in collaboration with the University of Frankfurt), *Arabidopsis thaliana* seedlings were exposed to hypergravity during launch and subsequently microgravity during the free-fall period of the rocket flight. Seedlings were chemically fixed inflight at defined time points and RNA and phytohormones were subsequently analyzed in the laboratory. We observed changes in phytohormone content including jasmonate, auxin, and several cytokines in response to hypergravity and microgravity, indicating them as molecular targets of gravity.

NeuroSpace: Gravity as a tool to identify molecular mechanisms in cellular mechano-sensing

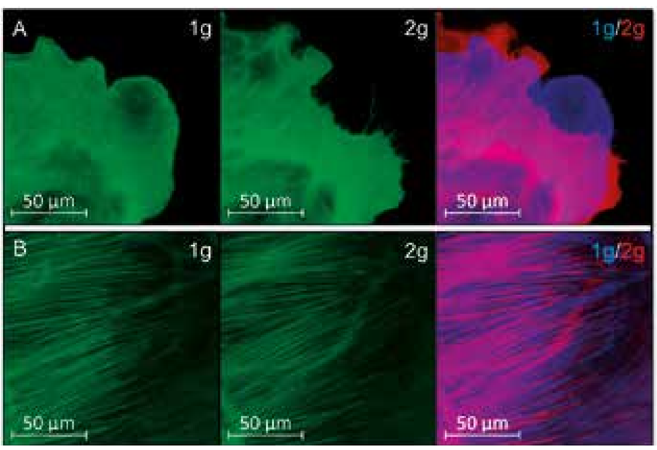
When external mechanical stimuli act on (neuronal) cells, the cytoskeleton is the most drastically affected molecular target translating the signal to molecular responses, altered gene expression, and structural rearrangements. We are particularly interested how gravity alters growth, differentiation, migration, activity, cytokine secretion and gene expression of, both, neurons and astroglial cells. The underlying pathways may have relevance for human space travel and terrestrial medicine alike. Indeed, altered cellular mechano-transduction pathways, such as mutations in the gene encoding the PIEZO-2 channel, are associated with severe neurodevelopmental abnormalities. Further, alterations in microtubule and actin cytoskeletal components are among the prevalent molecular targets of neurodegenerative disorders including Parkinson´s and Alzheimer´s disease. Based on a better mechanistic understanding, we aim to identify potential molecular targets for countermeasures or therapeutic interventions fostering neural regeneration. These interventions could be physical, such as increased gravitational loading also in combination with radiation (in collaboration with the Radiation Biology Department) and/or pharmacological approaches.

We apply hypergravity as model for increased mechanical loading, which causes remodeling of the neuronal cytoskeleton. Remarkably, hypergravity in a physiologically tolerable range of 2g elicits a cell-type specific response in neurons and astroglial cells. Astrocyte spreading and migration are approximately 40% diminished without disturbing cell growth (proliferation) or induction of apoptosis. On the other hand, neuronal growth, sprouting and elongation is augmented by approximately 20% through hypergravity. We hypothesize that the induced changes in the glial and neuronal cytoskeleton will aid to neuronal regeneration and could provide a target for neuroregenerative treatments. Cultivation of neuronal cells on microelectrode arrays (MEA) and adaptation to ground-based simulated as well as real micro- and hypergravity platforms will allow us to measure the impact of gravity, e.g. in combination with pharmacological stimulation, on synaptic transmission at the single neuron level and how it gets transformed into synchronous activity at the network level.

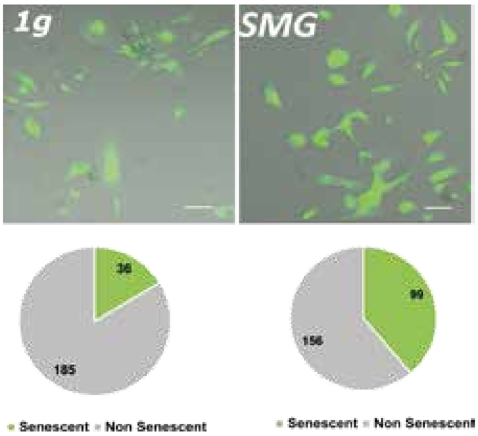
Facing the fact that neurodegeneration is a major health issue on Earth with implications for aeronautics and spaceflight, there is an unmet need for therapeutic approaches enhancing synaptic plasticity. Our promising experiments in collaboration with the group of Prof. El Sheikh at TH Cologne show that new and highly effective ketamine derivatives exhibit an increased pro-neuroplastic effect on cultured neurons with reduced cytotoxicity compared with the parent compound. Currently, we test their effects on synaptic plasticity of primary murine embryonic hippocampal neurons as functional and electrophysiologically active neuronal networks *in vitro* in combination with altered gravitational load. Our ultimate goal is to enhance synaptic plasticity and counterbalance the loss of synaptic contacts induced by microgravity as well as neurodegenerative disease.



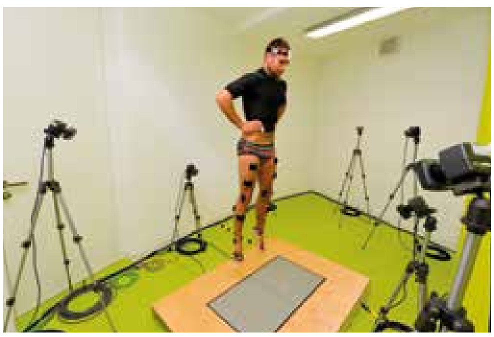
Astrocytic migration rate was diminished upon exposure to 2g hypergravity as seen by wound healing assays on a custom-designed DLR incubator-centrifuge as well as live by means of a centrifuge microscope.



LifeAct-GFP expressing neuronal cells showed fluorescently labelled actin filaments that re-arranged in a highly dynamic manner under 1g control and 2g hypergravity conditions inducing changes in cytoskeletal structures like lamelipodia and filopodia, which are mediating for cell migration.



Significant increase of senescence in hiPSCs derived cardiomyocytes by exposure to simulated microgravity (SMG) compared to the 1g control; scale bar 20 µm (A. Acharya)



Participant´s jumping position during continuous or variable centrifugation on the short arm human centrifuge and vertically against terrestrial gravity.

Human cardiac muscle cells show aging-related phenotypes induced by microgravity

Mechanical cardiac over-loading, be it through increased blood pressure, obesity, or cardiac remodeling following myocardial infarction, promotes myocardial hypertrophy and fibrosis. Conversely, cardiac unloading predisposes to cardiac deconditioning. In collaboration with the group of Prof. A. Sachinidis, University of Cologne, we apply altered gravity to human cardiomyocytes as a cellular heart-related model to elucidate the underlying molecular mechanisms within cardiac muscles exposed to microgravity. Moreover, microgravity seemed to impact cardiomyocyte aging and metabolism. Thus, the development of effective countermeasures against cellular aging of heart muscle cells is necessary for both human patients on Earth as well as long-duration space exploration missions.

We exposed human cardiomyocytes (hCMs) from human induced pluripotent stem cells (hiPSCs) to simulated microgravity applying custom-designed clinostats. The transcriptome and proteome analyses revealed gene expression changes within several pathways. Most importantly, senescence, indicating cellular ageing, was induced and associated with metabolic alterations, such as an increase in the formation of reactive oxygen species (ROS) and a decrease in energy production (ATP). Our findings suggest that reduced mechanical loading modeled through simulated microgravity may promote cardiomyocyte aging. Furthermore, different gravitational conditions can alter contractile activities of cardiomyocytes. Whether these changes are caused by chromosomal conformational changes, muscle fiber architectural changes, or metabolic programming will be demonstrated in future experiments in combination with real spaceflight conditions. Thereafter, we will probe countermeasures against the aging phenotype of human heart cells and tissue, e.g. employing hypergravity combined with pharmacological small molecule interventions, for potential applications in terrestrial medicine as well as during long-term spaceflights.

Artificial gravity to prevent spaceflight-induced deconditioning

Prolonged stays in microgravity without effective countermeasures for spaceflight-induced deconditioning pose safety risks. Despite successful maintaining astronaut´s performance for mission durations of 4-6 months, current ISS training does not counter physical deconditioning completely, likely due to lack of gravity. Artificial gravity could provide a multi-system countermeasure mitigating most of the effects of weightlessness. Our department develops and evaluates unique devices and training protocols for interdisciplinary investigations under increased mechanical loading ranging from cells to human beings.

Artificial gravity could help restoring body fluid distribution to the upright and seated position on Earth and protect astronauts from the negative effects of head-ward fluid shifts in weightlessness. During the 60-days AGBRESA (Artificial Gravity Bed Rest Study) study at the :envihab research facility, we were responsible for centrifuge interventions with support of the study team. The primary objective of the study was to compare the protective effects of daily 30 minutes passive centrifugation with +2Gz at the feet and +1Gz at the center of body mass. The study compared a control group with two artificial gravity groups, each with 8 subjects. One artificial gravity group was submitted to continuous 30 minutes centrifugation and one to interval centrifugation for 6 x 5 minutes. Artificial gravity was well tolerated with no serious adverse events and <1% run termination due to pre-syncope. Despite relatively high spin rates, daily motion sickness scores were low, but significantly higher in continuous centrifugation group across.

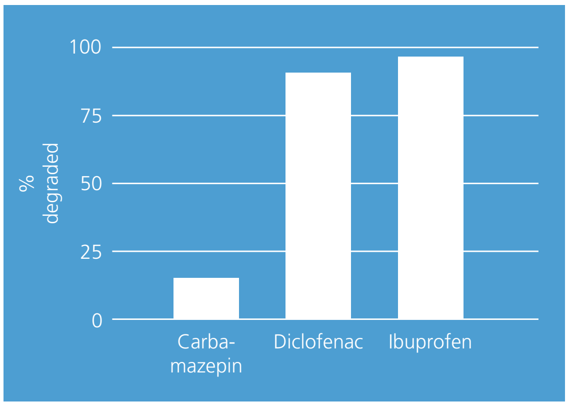
At the end of their 60-day bed rest in December 2019, the subjects had completed 54,000 laps on the centrifuge in a total of 1,800 minutes. Recent studies showed that a combination of artificial gravity with exercises is feasible and well tolerated. We tested plyometric training; here jumping exercises (like reactive jumps or countermovement jumps) with 15 male subjects (JUMP study) in collaboration with the University of Konstanz and the German Sports University in Cologne in the frame of the second National Centrifuge Program funded by the DLR Space Administration. Subjects performed a combination of jumping exercise during centrifugation at different gravity loads (+0.5-1.5Gz) that involved major muscle groups of the lower body and provide high load peaks on the bones. We showed that jumping exercises in the supine position can be used for training on a short arm centrifuge. While head movements markedly differed, motion sickness scores were only modestly increased with jumping on the short arm centrifuge compared with vertical jumps. Serum cartilage oligomeric matrix proteins concentrations were increased by all types of impact loading but less when jumping on the centrifuge. Thus, plyometric exercises during centrifugation were well tolerated, but adaptation takes time to achieve an equivalent mechanical load and performance as on Earth. As a next step, we will evaluate the tolerability and performance of resistance training, rowing and treadmill running during centrifugation.

C.R.O.P.® (Combined Regenerative Organic food Production)

The DLR project C.R.O.P.® focuses on nutrient recycling from biological wastes with microbial filters. Recently, we divided the research program into three areas of interest: C.R.O.P.®space, C.R.O.P.®medic and C.R.O.P.®agrar. C.R.O.P.®space includes research questions concerning Bioregenerative Life Support Systems for space and planetary habitation. Over the past years we developed and tested an aqueous fixed-bed biofiltration system applicable to convert human urine and toilet flushing water into plant-available fertilizer. The fertilizer can be used for crop plants in modern soilless cultivation systems, thus closing elementary loops in space and reducing supply costs. A miniaturized C.R.O.P.®-system coupled with a tomato greenhouse was integrated into the spin-controlled compact satellite Eu:CROPIS. The goal was testing its functionality under simulated lunar and Martian gravity levels achieved through rotation of the satellite at different speeds. The satellite was successfully launched in 2019; however, due to technological problems we did not receive the results from the life support systems, but our Radiation Biology Department is the first to gain long-term radiation data at 600 km altitude and thus under the conditions humans will experience during interplanetary missions. The future activities in C.R.O.P.®space will focus on building a space-qualified biological life support system including the C.R.O.P. ®-technology in collaboration with the DLR Institute of Space Systems. Closing material loops is also a necessary prerequisite to develop sustainable agricultural practice on Earth with minimized consumption of finite resources like artificial fertilizers and reduced leakage of pollutants. Therefore, C.R.O.P.®agrar aims at adapting the C.R.O.P.®-biofilter for the processing of cattle and pig slurry with the objective of developing a marketable system for agricultural purposes. The application of processed slurry protects the groundwater and reduces the release of ammonia into the atmosphere, which is known as a source for eutrophication of natural landscapes and fine dust pollution. C.R.O.P.®medic links both application areas mentioned above by addressing the fate of pharmaceutical residues in the C.R.O.P.®-filters. When animal and human feces are recycled, remains of medication are a key factor concerning application safety. It must be ensured that no pharmaceutically active substances are ingested with the food produced with the C.R.O.P.®-fertilizer.

Pharmaceutical residues are at least partially degraded by microorganisms in the soil or in wastewater treatment facilities. In case of a crew member using medication during a long-term space mission, the concentration of pharmaceutical residues in the urine collected for recycling will be considerably higher than in municipal wastewater due to the limited water buffer available for dilution. We simulated the situation of one of three crew members being sick and needing treatment in our laboratory. The concentrations of three drugs licensed for space missions (carbamazepine, ibuprofen, diclofenac) in the collected urine were calculated. Then three C.R.O.P.®-filters were fed for ten days with urine containing the calculated quantities of the three drugs.

Diclofenac and ibuprofen are effectively degraded in the aerobic process. Carbamazepine appears more stable but data imply that degradation starts after an adaptation period longer than the experiment. An influence of drug presence on fertilizer production could not be detected. Next experiments will focus on enhancing carbamazepine degradation and evaluating the degradation of more drug types and the influence of their presence on the fertilizer production process.



Percentages of the parental drugs degraded in C.R.O.P.®-filters during fertilizer production from urine. Metabolites not shown.

Collaboration partners within the Institute

- Dept. of Radiation Biology
- Study Team
- Dept. of Cardiovascular Aerospace Medicine
- Dept. of Muscle and Bone Metabolism
- Dept. of Clinical Aerospace Medicine
- Dept. of Sleep and Human Factors Research

Collaboration partners within the DLR

- Institute of Materials Physics in Space (Mapheus)
- RY Bremen (EU:CROPIS, C.R.O.P.®)
- Institute of Materials Research (Hydrogels)
- Mobile Rocket Base MORABA (Space Operations and Astronaut Training)
- Microgravity User Support Center (Space Operations and Astronaut Training, BIOLAB, FLUMIAS)
- DLR Technology Marketing
- European Astronaut Center (SpaceShip EAC, C.R.O.P.® Bioreactor, Training, Centrifuge, VR)

Collaboration partners in Germany

- Tiermed. Hochschule Hannover
- University of Bonn
- University of Cologne
- University of Hohenheim
- University of Magdeburg
- University of Erlangen
- Philipps University Marburg
- University of Frankfurt
- Charité Berlin
- University Witten/Herdecke
- LMU Munich
- TU Munich
- Leibniz Institute of Vegetable and Ornamental Crops (IGZ) Großbeeren
- WFP Innovation Accelerator
- HU Berlin
- Bauhaus-Universität Weimar
- FH Aachen
- OHB Bremen
- TH Cologne
- DZNE Deutsches Zentrum für Neurodegenerative Erkrankungen in der Helmholtz Gemeinschaft
- GSI Helmholtz Zentrum für Schwerionenforschung
- Hochschule Ruhr-West
- Hochschule Bonn-Rhein Sieg
- University of Konstanz
- German Sports University Cologne

Collaboration partners worldwide

- Universitätsklinik Zürich, Switzerland
- King´s College London, UK
- University of Pennsylvania, USA
- Manchester Metropolitan University, UK
- University College London, UK
- CAS Wuhan, China
- European Astronaut Center (SpaceShip EAC, Lunar Habitat, SpaceShip EAC, C.R.O.P.® Bioreactor, Training, Centrifuge, VR)
- European Space Agency (Spin Your Thesis, Ground-based Facility Program)
- ISU Strasbourg, France
- NASA Ames, USA
- University of Aarhus, Denmark
- Karolinska, University of Stockholm, Sweden
- University of Sao Paulo, IPEN, Brasilia
- University of Luzern, Switzerland
- La Trobe University, Melbourne, Autralia
- University of Texas Medical School in Houston, USA

Selected publications

Acharya, A., **Brungs, S., Lichterfeld,** Y., Hescheler, J., **Hemmersbach, R.,** Boeuf, H., Sachinidis, A. (2019) *Parabolic Flight-Induced Acute Hypergravity and Microgravity Modulate the Beating Contractile Rate of Human Cardiomyocytes.* Cells, 8, 352.

Bornemann, G., Waßer, K., Hauslage, J. (2018) T*he influence of nitrogen concentration and precipitation on fertilizer production from urine using a trickling filter.* Life Sciences in Space Research, 18, 12-20.

Frett, T., Green, D.A., **Mulder, E., Noppe, A., Arz, M., Pustowalow, W., Petrat, G.,** Tegtbur, U., **Jordan, J.** (2020) *Tolerability of daily intermittent or continuous short-arm centrifugation during 60-day 6o head down bed rest (AGBRESA study).* PLOS ONE 15 (9), e0239228.

Hauslage, J., Cevik, V., **Hemmersbach, R.** (2017) *Pyrocystis noctiluca represents an excellent bioassay for shear forces induced in ground-based microgravity simulators (clinostat and random positioning machine).* npj Microgravity, 3, 12.

Kohn, F.P., **Hauslage, J.,** Hanke, W. (2017) *Membrane Fluidity Changes. A Basic Mechanism of Interaction of Gravity with Cells?* Microgravity Science and Technology, 29, 337-342.

II.8
Study Team

Dr. rer. nat. Melanie von der Wiesche (Head)

Alexandra Noppe (Deputy)

Mission Goal
The major objective of DLR´s research facility :envihab is to explore the effects of different environmental conditions on human beings in long-term studies (e.g. at varying pressure or atmosphere conditions) and the development of appropriate countermeasures and life support systems for long-term space missions, for aeronautics, and for patients on Earth. To guarantee a consistent high quality of all different types of human studies the Institute uses a functional, interdivisional working group, the Study Team. This Team is an essential unit of the Central Management of the Institute of Aerospace Medicine. Here, internal and external human studies are centrally coordinated. With more than 11 years of experience the Study Team plans, prepares and implements various biomedical as well as clinical studies. The overall aim is to ensure rigorous standardization and high quality of the study-management, with all relevant laws and regulations being adhered to, at the same time providing the required medical care and monitoring. The main focus is on complex, highly standardized in-patient studies, e.g., head-down-tilt bed-rest studies (lasting several months) as well as clinical studies. Additionally the Study Team plans and realizes ambulant studies, focused on tests with the Short Arm Human Centrifuge (SAHC) at :envihab inducing artificial gravity.

Study Team

Main features of the Working Group

- Application procedure (ethical protocol, insurance of subjects)
- Management of subject-recruitment
- Management of highly standardized nutrition
- Project-Management
- Preparation of study documents such as protocol, case report forms, and informed consent documents
- On-site management, with GCP-trained key personnel
- Comprehensive internal reporting and communication to ensure high quality
- Central Management for scheduling studies in :envihab
- General counselling

The Study Team supports internal and external scientists and research groups in managing biomedical and clinical studies and projects at the Institute of Aerospace Medicine. We support all tasks or work packages from conception to preparation and on-site-management of various studies. Our main focus lies on complex, highly standardized in-patient and out-patient studies with >12 years experience in isolation studies, head-down-tilt bed rest studies (lasting several months), and drug trials.

The Study Team is is also involved in planning and realization of ambulatory studies, with special focus on tests with a Short Arm Human Centrifuge (SAHC) inducing artificial gravity. In this field the team coordinates internal studies as well as ESA Ground-based Facility studies and the National Centrifuge Program of DLR Space Administration. For all studies and projects within the Institute, the overall scheduling and assignment of the research facilities is organized by the Study Team.

Since 2014, the Team is responsible for hosting all ESA-Astronauts immediately after returning back to Earth from their missions on the ISS. Astronauts are accommodated in :envihab for at least two weeks. These "events", which are always associated with a high level of media interest, have been staged for many years in close cooperation with the space agency ESA. The collaboration has also resulted in our involvement in the design of the Lunar Habitat, which will be realized on the DLR campus in Cologne. Another exciting challenge will be the selection of astronauts, which will be supported by the Institute in 2021.

Study team with following staff:

- one Leader (Manager and Scientist)
- three Project Managers (one of them Scientist and Deputy Leader)
- two Study Nurses
- one Physician
- two Nutritionists
- one Diet Assistant
- one Project Assistant (with nutrition background)

VaPER-Study: Daily on-site Meeting in :envihab

Main projects 2017-2020

Bed rest studies at :envihab in cooperation with ESA and NASA

Bed rest studies are a well-established model for the multiple physiological changes experienced by astronauts during spaceflight. Weightlessness reduces mechanical loading of muscles, bones, and the vestibular system. Moreover, weightlessness leads to a continuous head-ward fluid redistribution. Bed rest studies are, therefore, a valuable tool both for investigating the underlying mechanisms and for testing potential countermeasures. Further, the results obtained in these studies can be transferred to medical applications on Earth. In 2018, the VaPER study was an international collaboration with NASA and the first study to investigate bed rest under increased ambient CO_2 conditions. The study focused on investigating the development of the Spaceflight Associated Neuro-ocular Syndrome (SANS, formerly visual impairment and intracranial pressure, or VIIP syndrome).

In 2019, the AGBRESA study was conducted, a joint project between NASA, ESA, and DLR. The primary aim of this randomized controlled study was to test the influence of artificial gravity (AG) on the :envihab short arm human centrifuge (SAHC) during 60 days of head-down tilt (HDT) on the physiology of 24 healthy subjects in two campaigns. Starting in 2021 with the first of six campaigns, another bed rest study with NASA is now planned and prepared, the SANS CM study. The aim of the study is to understand the development of SANS and to explore possible countermeasures (CM).

Since 2017 bedrest studies at DLR are carried out according to the `Guidelines for Standardization of Bed Rest Studies in the Spaceflight Context´. Highly important responsibilities within the governance of these studies - like medical care, recruitment of test subjects, standardized nutrition and subject coordination (means accommodation of test subjects and coordination of the daily routine) - are generally covered by the Study Team. Furthermore, the team contributes to the implementation of many other international science projects at the :envihab, DLR.

Tools to achieve nutritional standardization

- Education of the test subjects (information sessions, interviews, ward rounds)
- Metabolic kitchen (individually adjusted menu plans, exact weighing, trained kitchen staff)
- Documentation and evaluation of daily nutrient intake and body weight
- interdisciplinary networking (nutritionists, medical doctors, PIs, Subject coordination)

Standardized nutrition in bed rest studies

Many space agencies (and in some cases even individual investigator teams) around the world are involved in organizing bed rest studies. However, the conditions under which these studies are performed are quite diverse. Differences lie, for example, in the duration of studies, angle of the bed (6° tilt or horizontal), sunlight exposure, sleep/wake cycles, nutritional standards and control. The state-of-affairs complicates drawing overall conclusions and comparing results on countermeasure effectiveness between studies. To achieve better standardization of such studies, an International Academy of Astronauts (IAA) study group was initiated, including members from most of the entities that are actively pursuing this type of activity.

To avoid any impact of irregular nutrient supply adequate nutrient intake levels are defined. These recommended values should be regarded either as an adequate range, if a range is mentioned, or as a minimum intake level as a guideline for each study if no other nutritional constraints or nutritional countermeasures from specific proposals are required. Nutrient guidelines control over 30 nutrients throughout the study. For some of these nutrients (vitamins and elements) these recommended intakes should be achieved on an average per week. For all other nutrients the recommended intake should be achieved every day. In case of specific nutrient requirements from the PIs, the levels/ranges of the specific experiments shall replace the mentioned ones.

Effects of hypercaloric nutrition on orthostatic tolerance (HyNu-OT)

Orthostatic intolerance and especially syncope are common problems that affect all age groups and more than half of the astronauts after landing. The understanding of the pathophysiology is still incomplete and up to now, no pharmacological therapies with proven efficacy exist. Studies have demonstrated that changes in energy balance may cause significant changes of the cardiovascular sympathetic activity. A hypercaloric dietetic intervention increases cardiovascular sympathetic activity and might decrease the disposition to vasovagal syncope.

Object of this internal interdisciplinary study is to investigate changes in orthostatic tolerance after an increased caloric intake for four days. 20 healthy subjects will participate this year 2020 in two study-phases in a cross-over design (hypercaloric vs. normocaloric). Both phases follow precisely the same study protocol concerning the experiments, daily schedule and standardized nutrition. Only the nutritional energy intake will be 25 % higher in one phase.

The study is conducted in close cooperation with several departments of our Institute. For example, the cardiovascular aerospace department will contribute orthostatic testing (tilt table combined with lower body negative pressure), brainstem and hypothalamus functional magnetic resonance imaging with oral glucose loading, and plasma volume measurements. We will be in charge of body composition assessment, collection of anthropometric data, and resting metabolic rate measurements throughout the study. Nutritionists of the study team created four different menus which will be individually adjusted for each test subject. Besides the above mentioned experiments, the study team contributes the overall organization, coordination and implementation of the HyNu-OT study.

Resting metabolic rate measurement (RMR) in AGBRESA bedrest study

Artificial Gravity: Ambulant studies in the frame of the 2nd National Centrifuge Program (NZP2)

To improve the effectiveness of artificial gravity as a countermeasure, the DLR Space Agency established a scientific program called the National Centrifuge Program (NZP). The Study Team is responsible for the overall coordination of the selected projects of the external national scientists. The planning and implementation of each study was always worked out together with the SAHC-Experts of the department Gravitational Biology. In 2016/2017 and 2018 three projects were conducted in the context of the current 2nd NZP.

Investigation of Self-Orientation under Varying Gravity States (SelfOG, Hochschule Bonn-Rhein-Sieg)

In this study the aim was to identify a threshold of the influence of gravity for perceptual upright. This helps to understand what happens with the self-orientation during different g-levels. Therefore 16 participants were tested while lying on the centrifuge. 24 logarithmically spaced g-levels between 0.04 and 0.5g were applied. The perceptual upright was measured with the OCHART (Oriented Character Recognition Test). First results indicate that a gravitational field of at least 0.15g is necessary to provide effective orientation information for the perception of upright, which is close to the gravitational force found on the Moon of 0.17g. For whole body linear acceleration, the vestibular threshold is around 0.1m/s².

Recommended Adequate Nutrient Intake Levels to be achieved

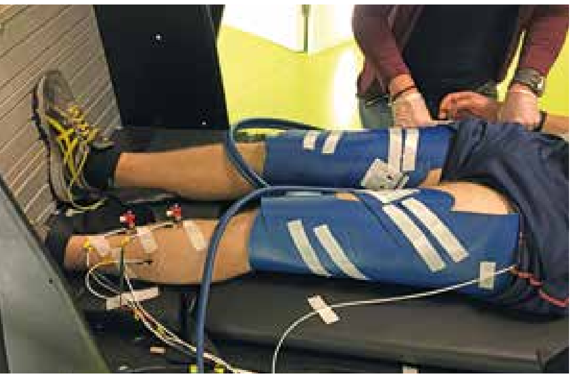
Nutrient	Adequate intake
Energy & Macronutrients	
Energy (total energy expenditure, TEE)	**WHO equation for Basal Metabolic Rate (BMR) or measured by indirect calorimetry x 1.1 (bed rest) or x 1.4 (ambulatory)**
Total fat (%TEE)	≤ 30
Protein g/kgBW/d	1.2
Carbohydrates (%TEE)	50-60
Total Fibre (g/d)	≥25
Saturated fatty acids (%TEE)	≤ 10
Monounsaturated fatty acid (%TEE)	≥ 10
Polyunsaturated fatty acids (%TEE)	≥ 7
Electrolytes and Water	
Sodium (g/d)	3.5 - 4.5
Chloride (g/d)	6.0 – 7.5
Potassium (g/d)	3.5 - 5.0
Calcium (mg/d)	1000-1200
Water (ml/kgBW/d)	35 - 50
Vitamins	
Biotin (µg/d)	30
Pantothenic Acid (mg/d)	5
Folate (µg/d)	400
Niacin (mg/d)	20
Riboflavin (mg/d)	1.5
Thiamin (mg/d)	1.5
Vitamin B6 (mg/d)	2
Vitamin B12 (mg/d)	2
Vitamin K (µg/d)	80
Vitamin D (ug/d)	5
Vitamin A (µg/d)	1000
Vitamin C (mg/d)	100
Vitamin E (mg/d)	15
Elements	
Copper (µg/d)	1500-3000
Fluoride (mg/d)	1,5-4
Iodine (µg/d)	200
Iron (mg/d)	Male: 10 | Female: 18
Magnesium (mg/d)	300
Manganese (mg/d)	2-5
Phosphorus (mg/d)	700-1500
Selenium (µg/d)	70
Zinc (mg/d)	12-15

Overview of recommended adequate nutrient intake levels to avoid any impact of irregular nutrient supply of subjects in bed rest studies (VaPER and AGBRESA)

Test Subject on centrifuge during JUMP-Study

Reactive jump training under hypergravity - comparability of movement and effects on the metabolism of articular cartilage (JUMP, University of Konstanz and DSHS Köln)

A second study was performed in cooperation with the University of Konstanz and the German Sports University Cologne. Long-term stay in weightlessness leads to extensive physiological deconditioning processes (including cardiovascular, muscle mass and bone density, cartilage mass). Therefore maintaining physical fitness for future space missions is critical. In a cross-over design we tested a special training with reactive jumps on a sledge system mounted on a short-arm human centrifuge (SAHC) and compared the effects of jumps in vertical position and on the SJS (Sledge Jump System). The SJS was successfully used as countermeasure in a recent long-term bed rest study RSL. We hypothesized an increase in cartilage metabolism after reactive jumps under hypergravity compared to control conditions. 15 male healthy subjects between the age of 20 and 35 were examined. Our results indicate that jumps on the SAHC under hypergravity lead to lower ground reaction forces but no significant increase of motion sickness due to Coriolis Forces.



Subject on the centrifuge with cooling pads during CoolSpin-Study

External cooling as a stabilizing cardiovascular countermeasure in hypergravity (CoolSpin, University Charité Berlin)

A third study was performed in collaboration with the Charité Berlin. Orthostatic dysfunction is observed in astronauts after prolonged stay in weightlessness or in subjects after mid- or long-term bed rest studies. Development of countermeasures to avoid orthostatic dysfunction after spaceflight is mandatory. Artificial gravity generated by centrifugation is a promising multi-system countermeasure that could help to maintain physical fitness of crewmembers even on long-term missions. Previous experiments have shown that the control of peripheral body temperatures due to their role in thermoregulation plays an important role in cardiovascular regulation. The influence of thermoregulation on orthostatic reactions and g-force induced loss of consciousness (GLOC) could therefore not only be used in predicting these events, but also for their prevention. The central objective of this project was therefore to use the findings to develop an efficient method to prevent and control gravitation-induced circulatory reactions and to provide astronauts an effective tool against unfortunate orthostatic responses after long periods in space. 18 healthy male participants were involved in this cross-over designed study which was conducted on the SAHC. Their thighs were cooled with cooling pads during the centrifuge run on one study day, on the other study day they performed the same centrifuge protocol without cooling. The results show that cooling seems to be a promising countermeasure to face orthostatic intolerance, but further investigation is necessary.

The Study Team coordinates the implementation of the studies of the national centrifuge programs and was also responsible for the scientific lead in two campaigns.

Internal training and updates

The legal framework and ethical regulations provide guidance in order to assure safety and high quality in human investigations and have to be rigorously followed. The Study Team is responsible for the implementation of all necessary trainings and updates.
Therefore, all employees who are involved in human studies are regularly trained and certified in accordance to Good Clinical Practice (GCP) in cooperation with the center for clinical trials (ZKS) of the University of Cologne. Another challenge was the introduction of the new General Data Protection Regulation (DSGVO) in May 2018. The Study Team coordinates the conversion of all relevant systems and the commission of a data protection officer. Standardization of central processes, formation of networks and coordination of study-relevant content between the individual departments is an important part of the quality assurance of this Institute.

Basic Life Support Training for study staff at :envihab

Collaboration partners within the Institute

- Dept. of Cardiovascular Aerospace Medicine
- Dept. of Muscle and Bone Metabolism
- Dept. of Clinical Aerospace Medicine
- Dept. of Sleep and Human Factors Research
- Dept. of Radiation Biology
- Dept. of Gravitational Biology
- Dept. of Aerospace Psychology

Collaboration partners within the DLR

- Space Administration
- Institute of Materials Physics in Space
- Health Management

Collaboration partners in Germany

- European Astronaut Center (Direct Return)
- Hochschule Bonn-Rhein-Sieg
- Charité Berlin
- German Sports University Cologne
- Zentrum für Klinische Studien Cologne
- Universitätsklinikum Cologne
- University of Bonn

Collaboration partners worldwide

- ESA/EAC
- NASA, USA
- York University, Canada
- University of Pennsylvania, USA
- University of Oregon, USA

Selected publications

Casini, A.E.M., Mittler, P., Cowley, A., Schlüter, L., Faber, M., Fischer, B., **von der Wiesche, M.,** Maurer, M. (2020) *Lunar analogue facilities development at EAC: status of the LUNA project.* Journal of Space Safety Engineering. EPUB.

Frett, T., Green, D.A., **Mulder, E., Noppe, A., Arz, M., Pustowalow, W., Petrat, G.,** Tegtbur, U., **Jordan, J**. (2020) *Tolerability of daily intermittent or continuous short-arm centrifugation during 60-day 6o head down bed rest (AGBRESA study).* PLOS ONE 15 (9), e0239228.

Frett, T., Green, D.A., **Arz, M., Noppe, A., Petrat, G.,** Kramer, A., Kümmel, J., Tegtbur, U., **Jordan, J.** (2020) *Motion sickness symptoms during jumping exercise on a short-arm centrifuge.* PLoS One, 15 (6), e0234361.

Lecheler, L., Paulke, F., Sonnow, L., Limper, U., Schwarz, D., Jansen, S., **Tank, J.**, Klussman, J.P., **Jordan, J.** (accepted) *Gravity and Mastoid effusion.* American Journal of Medicine

Noppe, A., von der Wiesche, M., Paulke, F., Mulder, E. (2018) *VaPER-Study: Strict adherence of -6°-Head Down Tilt Bed Rest An Improvement to the Ground-Based Microgravity Analogue?* 39th ISGP Meeting & ESA Life Sciences Meeting, 18.-22. Jun. 2018, Noordwijk, Netherlands.

III. Outlook: Future challenges and strategic measures

The Institute of Aerospace Medicine will adapt to dynamic changes in space and in aeronautics. Human space programs will shift from research on the ISS to space exploration towards the Moon and beyond. Commercial entities will offer recreational suborbital flights. Space technology, such as Earth observation and robotics, will create fascinating and important opportunities for human health applications. In aeronautics, economic development will increasingly be balanced with environmental protection, acceptability, and sustainability concerns. The ongoing Corona-virus crisis is a stark reminder that mobility can promote infectious spread. Finally, the strength of DLR in advanced technologies including data science, digitalization, and artificial intelligence can be fed into biomedical applications. The Institute will derive biomedical and psychological knowledge and solutions to address these challenges, contribute to the solution of important societal issues, and foster economic development in Germany.

A key strategy to attain these goals is to continue building scientific expertise and research infrastructure with a focus on interdisciplinarity, translation between aerospace and terrestrial applications, and national and international collaboration with academia, agencies, and industry. The recently established DLR and University of Texas Southwestern Alliance is a prime example of this strategy. An important challenge will be access to best junior scientists for years to come. Therefore, structured career programs, mentoring, and internationalization will be further expanded.

Future Missions

Biomedical and psychological research in space will be adapted to the rapidly evolving space programs. The Institute will contribute an important radiation biology experiment, female anthropomorphic phantoms equipped with sophisticated radiation detectors, to NASA's Artemis 1 mission to the Moon.

Expertise in high-end human research is a particular strength of the Institute. Ground-based human studies in collaboration with NASA and ESA at :envihab will address unresolved medical challenges of long-duration space missions, such as the spaceflight-associated neuro-ocular syndrome. These approaches will also serve as human models musculoskeletal, metabolic, and cardiovascular diseases, which will be contributed to research networks on aging in the region. Simulated environmental conditions, such as atmosphere or noise, combined with high-fidelity human phenotyping will guide development of future air vehicles and air traffic. Such studies require cross-validation in field studies. Moreover, in ongoing collaboration, the research expertise and infrastructure will be applied to elucidate mechanisms of disease and drug mechanisms of action with academic partners and with industry.

Research on human-human and human-machine interactions in the face of rapid changes of technology and demographic change will be an important research area. In addition to the obvious relevance for aeronautics and space, the research has applications to other societal areas. The human research program will be flanked by translational research projects conducted at the cellular level with a focus on core areas of expertise in radiation, gravitational, and astrobiology. The rich biomedical research environment in the region provides access to methodologies that are not available on the campus, such as facilities for omics techniques and animal models. Conception and testing of life-sustaining closed biological systems, which are crucial for long-term space missions, may also address important societal issues on Earth. With all this the Institute is set up for a future which will enable safe human space exploration and at the same time contribute to the related questions for Earth according to the overarching goal to improve human health span in space and on Earth.

IV. Major research facilities

:envihab

8 separate modules, 6 laboratories			
Size: ca. 5,400 m^2 (101 m x 53 m)	Research area: ca. 3,500 m^2	Air-conditioning in core area: 17–30°C, ±1°C	adjustable, 2.5°C/h temperature adaptable, 40–60% relative humidity adjustable

Modules and laboratories in :envihab

Module	Technical facts	Application
M1: DLR Short Arm Human Centrifuge (SAHC)	• Max. radial acceleration of 6 g at outer perimeter • Radius: 380 cm • Max. loading capacity: 800 kg • Max. onset rate: 0.2 g/s • Number and type of nacelles: 4 multifunctional gondolas • Radius of nacelles adaptable within 200 cm (also during centrifugation) • Centrifugation and examination of 4 test subjects simultaneously • Subject height 150 cm to max. 210 cm • Standard monitoring of vital signs: ECG, blood pressure, heart rate, arterial oxygenation, spirometry, electromyography, eye movement Standard training on e.g. vibration platform and ergonomic sledge jump system • Dynamics of movement can be monitored by a motion capture system and two triaxial power measuring platforms • Ultrasound examination while spinning by robot-guided system to study the effects on heart and vessels • Virtual Reality plattform • Swing-out plattforms for microscopes and hardware (life sciences, material physics)	The SAHC at the :envihab research facility is a custom-designed research unit and the only one of its kind in the world, offering enhanced possibilities for researching the effects of altered gravity on the human body, especially as a countermeasure to the health risks (deterioration of bone and muscle structure, cardiovascular weakness, dizziness, stuffy heads, motion sickness, inner ear disturbances, comprised immune systems, back pain) that occur in microgravity conditions. What makes this DLR facility special is the possibility of investigating the effects of different gravity levels by using variable radii, combined with the option of conducting various training as well as online-measurement options. Human studies on the SAHC can be supplemented by cellular studies by combination with the Hyperscope microscope, allowing live cell imaging during centrifugation.
M2: Baro-Lab/Prevention and Rehabilitation Lab	• Size: 110 m^2, dividable into 8 units • Ambient pressure can be reduced to min. 300 mbar (9,100 m) • Reduction of oxygen fraction at normal pressure to min. 8 % (equivalent to 7,500 m); enrichment with carbon dioxide up to 3 % • Individual control of temperature and humidity • Man-rated pressure lock	Module 2 offers the possibility of conducting long-term medical studies with test persons at reduced pressure and different atmospheric conditions. Large experimental setups as well as subsystems of aircraft can be incorporated. Scenarios related to aviation, spaceflight and mountaineering can be simulated. Movable walls enable customization to different study designs: examination of groups (e.g. in a cabin) as well as individual persons (e.g. to assess altitude adaption, sleep and circadian rhythm). Main topics are the cardiovascular system and the musculoskeletal system as well as the influences of different atmospheric conditions on the human physiology.

Modules and laboratories in :envihab

Module	Technical facts	Application
M2: Physiology Lab/Prevention and Rehabilitation Lab	• 7 labs can be freely configured, total area 200 m^2 • Decrease of oxygen down to 8 % in 5 h (25,000 ft) • Enrichment with carbon dioxide up to 3 %, change per hour 1 % • Temperature and humidity independently adjustable	In the Physiology lab we focus on experimental scenarios to solve health problems on Earth (consequences of bedriddenness, osteoporosis, muscle loss or diseases of the cardiovascular system) and develop countermeasures. Tilt testing and/or the application of lower body negative pressure (LBNP) are methodological approaches used to provide orthostatic stress. Treadmill with integrated ground reaction force plates or an isokinetic dynamometer are used for gait analysis as well as for systemic and/or localized muscle performance testing during and following simulated or real weightlessness. The module also includes a lab to simulate gait in weightlessness and performance diagnostics with spiroergometry as well as non-invasive diagnostics of the cardiovascular system.
M3: Living and Simulation Area	• 12 individual rooms and a living room, total area 364 m^2 • Reduction of oxygen to min. 8 % in 5 h (25,000 ft) • Enrichment with carbon dioxide up to 3 % • Control of light intensity in each room in the range of 3 and 1,000 lux • Blood sampling during sleep • Temperature and humidity independently adjustable • Kitchen for metabolic nutrition • Blood and Urin Lab • Foot distance to PET-MRI, pressure chamber and Short Arm Human Centrifuge - easily connected to all :envihab research facilities	The module offers optimal conditions for investigations of various aspects of aerospace medicine: Here we conduct long-term studies under strictly controlled environmental conditions: • Immobilization studies (e.g. bed-rest studies to examine bone and muscle physiology) • Research on the effects of hypoxia (e. g. during sleep). • Studies on sleep deprivation or disorder, shiftwork and irregular working hours • Studies on the impact of ambient light as a countermeasure against performance decrements and disruption of the circadian rhythm • Isolation studies • Clinical studies based on application of drugs • Continuous assessment of rhythm of hormones or metabolic products (constant routine) via porthole

Modules and laboratories in :envihab

Module	Technical facts	Application
M4: **PET-MRI**	• Siemens Biograph mMR; whole body 3 Tesla MRI with integrated PET • Combination of PET (positron emission tomography) and MRI (magnetic resonance imaging), both systems can be used simultaneously • State of the art neuro and cardiac imaging • functional imaging of the autonomic nervous system • MR-compatible thigh- and calf ergometer • Special MRI procedures: sodium imaging, phosphorus spectroscopy, perfusion and diffusion measurement and functional imaging (fMRI) • PET nuclide: 18F fluoride	Physiological changes due to various factors such as bed rest, low head position, hypoxia, sleep deprivation or long-duration space mission can be investigated in our PET MRI. The immediate vicinity of the bed station allows examinations of test subjects during or after interventions. This knowledge can be transferred to physical stress to which humans are exposed under unfavorable conditions, even on Earth. The PET scanner is used to quantify the spatial distribution of tracer substances to record metabolic processes in the brain, muscle and heart.
M5: **Psychology Lab**	• Two separated areas, connected by a passage, total area 258 m^2 • One area specially soundproofed (130 m^2) • Isolation and privacy conditions for up to 6 test subjects in parallel • Temperature and humidity independently adjustable	Psychological methods and tests in space travel and aviation as well as questions concerning working in unusual conditions can be investigated. Here we study the effects of factors like sensory deprivation, reaction to close quarters and limited social contact, homesickness as well as psychological effects of living in extreme space conditions. Different environmental conditions can be simulated, such as: • isolated research stations (Antarctica, Neumeyer Station) or working areas (offshore platforms) • stations on Moon or Mars • simulation of entire expeditions to prepare planned missions In this module, ESA Astronauts are hosted immediately after their return from ISS.
M6: **Biology Lab**	• Five laboratory rooms • Experiment preparation room • ISO class 8 clean room • Genetic laboratory safety level 1 • Professional microbiological lab equipment (e.g. microscopes, PCR and PFGE, documentation system) as well as the design of the module	The main microbiological research topics in this facility include life in extreme environments, studies on the efficiency of bioburden reduction and decontamination technologies and microbiological aspects of bioregenerative life support systems. The biology laboratory is used for the preparation and evaluation of astrobiological space experiments, bioburden and biodiversity analysis of spacecraft and clean rooms and microbiome analyses of confined habitats. The close proximity of this module to the medical core area is crucial to facilitating investigations on the microbial diversity and its adaptions with respect to the inhabited closed areas.

Further research facilities and laboratories

Facility/lab	Technical facts	Application
BARO-LAB II TITAN Pressure Chamber/Hypobaric Chamber	• Ambient pressure range between min. 0.01 bar (absolute pressure) and 1 bar • Variable gas composition, e.g. substitution of inert-gas components or enrichment of O_2 or CO_2 fraction • Rapid pressure changes of up to 0.5 bar/s • Seats for 6 test subjects • Chamber: length 2.80 m, diameter 2 m • airlock: length of 0.8 m, diameter of 1.50 m • Seats for 6 test subjects Temperature range 15–35°C • 20–80 % relative humidity (adjustable)	The baromedical laboratory II consists of a pressure chamber complex and a separate vacuum chamber for the simulation of changed pressure and atmospheric conditions as well as closed atmospheric circuits. The effects of extreme pressure conditions and changed atmospheric composition on humans are investigated. This is relevant for the stay in aircraft and spacecraft as well as for mountaineering (oxygen deficiency, decompression, pressure equalization etc.). With the ability to generate rapid pressure changes we also can simulate emergency scenarios in aerospace and to investigate pressure profiles that occur in everyday situations. An example of this is the ride on a high-speed train. Conditions such as sudden pressure drops or changes and oxygen deficiency are simulated and enable pilots and astronauts to practice emergency situations as they might occur in everyday life. Sudden changes in pressure conditions can affect not only the aerospace industry, but also traffic, high-speed trains or work at extreme altitudes.
ESA Short Arm Human Centrifuge (2020: return to ESA)	Radius: 2.8 m Max. radial acceleration of 4.5 g at outer perimeter Max. onset rate: 0.365 g/s Min. onset rate: 0.06 g/s Number and type of nacelles: 2 lying, 2 sitting gondolas Radius of nacelles adaptable within 40 cm Angle adjustment of each nacelle: -12° to 75° centrifugation and examination of 2 test subjects simultaneously Subject height 150 cm to max. 190 cm Max. loading capacity: 550 kg Standard monitoring of vital signs: ECG, blood pressure, heart rate, oxygen saturation Audio and visual monitoring Measurable human physiological and medical parameters: continuous blood pressure, ECG, spirometry, electromyography, eye movement etc.	provided by ESA Test subject can be exposed to different accelerations; in the supine position this can be up to five times of the gravitational acceleration Development of effective countermeasures for neuromuscular and skeletal changes of astronauts. Orthostatic and neurovestibular tolerance tests of pilots, astronauts and other relevant occupational groups. Medical basic research, e. g. in the field of bone structure and amyotrophia. Research on neurovestibular and cardiovascular questions.

Further research facilities and laboratories

Facility/lab	Technical facts	Application
Micro-G Lab: Mimicking space conditions on Earth	**2D clinostats** – simulation of functional weightlessness • 2D Pipette-Clinostat – exposure of e.g. cell suspensions • 2D Slide Flask Clinostat – exposure of e.g. adherent cells • 2D Fluorescent Clinostat Microscope – live-cell imaging • 2D Submersed Clinostat – exposure of aquatic biosystems • 2D Photomultiplier Clinostat – measurement of online kinetics of cellular activities • 2 D Window Clinostat – irradiation with X-rays or heavy ions during clinorotation **Random Positioning Machine** to randomize the influence of gravity (different modes of operation and speed rates) **Centrifuges:** 1–10 g; controlled environmental conditions; hardware for cultivation and video observation of biosamples • MuSIC – Multi-Sample Incubator Centrifuge • Hyperscope – Centrifuge microscope – for live cell imaging under hyper-g • Cell Biology Labs	The Micro-G Lab provides a unique portfolio of custom-built ground-based facilities to perform experiments with small biological systems under simulated microgravity (functional weightlessness) or hypergravity conditions. Gravity cannot be switched off on Earth, but its direction can be randomized. Different methods are in use aiming to achieve this situation. We are convinced by the 2 D clinostat principle as a validated simulation approach. Here, a test system is located on a horizontal rotation axis, perpendicular to the direction of the gravity vector, and constantly and rapidly rotated, assuming that the exposed system can no longer detect the direction of the gravity vector and its sedimentation is prevented. On the other hand, hypergravity, i.e. the impact of increased gravitational stimulation and simulated launch conditions of space vehicles can be tested in the Multi-Sample Incubator Centrifuge and the Hyperscope facilities. Data acquired on the ground are validated with experiments in real microgravity (drop tower, parabolic flights, sounding rockets – Mapheus, TEXUS, MAXUS, BION satellite).
Planetary and Space Simulation Facility PSI	• 93 m^2 technical simulation and exposure lab, genetic laboratory S1, biohazard laboratory S2 • 7 vacuum recipients, 5 with temperature controlled cold plates/shrouds, 5 with rotary vane pumps, 3 with additional ion getter pumps • Pirani cold cathode pressure measurement systems • 3 solar simulators, Deuterium, Mercury, Xenon lamps • double monochromator UV spectroradiometer with calibration UV lamp • X-ray tube with CO_2 and N_2 supply • 3 cryostats, thermistors, feed-back control systems • Crane, red light • Biosafety cabinet and CO_2 incubator • anaerobic workbench in adjacent microbiology laboratories	In this facility the environmental parameters of space and of other planets can be simulated, individually and in selected combinations. Biological and chemical samples are exposed and analyzed for research in the area of astro biology, radiation biology and environmental microbiology. For the preparation of spaceflight experiments this facility is used to determine the optimal parameters, to test newly developed space hardware and to perform the "Mission Ground Reference Test" (MGR) under simulated space conditions, by parallel exposure of samples to simulated space parameters according to flight data received e.g. by telemetry.
Test center for the psychological selection of pilots and air traffic controllers	110 test seats in several different test rooms	In this center we test the abilities, skills and personality traits of pilots and air traffic controllers with which we ensure a high standard of operators' performance. The main benefit is a high standard in air safety. Airlines and ATC-organizations benefit from economic advantages due to well selected staff. We conduct international applicable assessment tests. At the DLR test centers worldwide we carry out up to 10,000 psychological qualification tests per year.

V. Scientific activities

V.1 Teaching activities

2019		
Name	University	Subject
Aeschbach, Daniel	Harvard Medical School	Sleep Medicine
Anken, Ralf	Universität Hohenheim	Zoologie
Baumstark-Kahn, Christa	Lufthansa	Fachkundekurs für Strahlenschutzbeauftragte
Berger, Thomas/Hellweg, Christine	ISU Strasbourg	Master of Space Studie (MSS)
Berger, Thomas/Hellweg, Christine	Universität Bonn	Strahlenschutzkurs
Elmenhorst, Eva Maria	RWTH Aachen	Flug/Reisemedizin
Elmenhorst, Eva Maria	RWTH Aachen	Raumfahrtmedizin
Elmenhorst, Eva Maria	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Frings-Meuthen, Petra	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Goerke, Panja	Leuphana Universität, Lüneburg	Differentielle Psychologie
Goerke, Panja	Fachhochschule Wedel	Communication and Social Skills
Hauslage, Jens	ISU Strasbourg	Gravitational Biology
Hauslage, Jens	ISU Strasbourg	Biological Life Support Systems
Hauslage, Jens	Tiermedizinische Hochschule Hannover	Gravitationsbiologie
Hauslage, Jens	Universidade de São Paulo	Gravitational Biology/Biological Life Support Systems
Hellweg, Christine	FU Berlin	Pathologie
Hellweg, Christine	FU Berlin	Immunologie
Hellweg, Christine	Universität Bonn	Radiopharmaziekurs
Hellweg, Christine	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Hemmersbach, Ruth	Universität Bonn	Zoologie/Gravitationsbiologie
Heusser, Karsten	Universität Köln	Weltraumphysiologie
Heusser, Karsten	RWTH Aachen	Physiologie
Herzog, Merle	Universität Hamburg	Psychologische Diagnostik
Hörmann, Hans-Jürgen	Technische Universität München	Luftfahrtpsychologie
Jordan, Jens	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Kölzer, Anna	Fachhochschule Wedel	Communication and Social Skills
Liemersdorf, Christian	University of Bonn	Molecular Genetics, Neurobiology
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Med. Businessystem
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Biomed. Informatik
Marggraf-Micheel, Claudia	Fachhochschule Wedel	Communication Skills
Meier, Matthias	Joint Space Weather Summer Camp	Radiation Protection in Aviation
Meier, Matthias	Lufthansa	Fachkundekurs für Strahlenschutzbeauftragte
Mittelstädt, Justin	Universität Hamburg	Psychologische Diagnostik
Mulder, Edwin	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Oubaid, Viktor	Medical School Hamburg	Differentielle Psychologie & Persönlichkeitsforschung
Pustowalow, Willi	Hochschule Bonn-Rhein-Sieg	Informatik
Rettberg, Petra	ESA	Planetary Protection Course Lecture
Rettberg, Petra	ESA	Planetary Protection Course practical laboratory course
Rittweger, Jörn	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Rittweger, Jörn	Universität Köln	Medizin (Spezielle Pädiatrie)
Schennetten, Kai	Lufthansa	Fachkundekurs für Strahlenschutzbeauftragte

V.1 Teaching activities

2019

Name	University	Subject
Schudlik, Kevin	International School of Management	Organisationspsychologie
Schulze Kissing, Dirk	HS Fresenius	Allgemeine Psychologie
Stelling, Dirk	HS Fresenius	Differentielle Psychologie (SS)
Stelling, Dirk	HS Fresenius	Differentielle Psychologie (WS)
Stelling, Dirk	HS Fresenius	Experimentelles Praktikum
Stern, Claudia	Technische Universität Braunschweig	Luft- und Raumfahrtmedizin
Stern, Claudia	Universität der Bundeswehr	Raumfahrtmedizin
Stern, Claudia	ISU Strasbourg	Master of Space Studies (MSS)
Stern, Claudia	ISU Space Studies Program	Space Ophthalmology
Stern, Claudia	European School of Aviation Medicine	Basic Course Ophthalmology I
Stern, Claudia	European School of Aviation Medicine	Advanced Course Ophthalmology II
Stern, Claudia	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Tank, Jens	Medizinische Hochschule Hannover	Propädeutik
Zange, Jochen	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Zange, Jochen	Universität Köln	Medizin (Research Track)
Zinn, Frank	Universität Hamburg	Psychologische Diagnostik

2018

Name	University	Subject
Aeschbach, Daniel	Harvard Medical School	Sleep Medicine
Anken, Ralf	Universität Hohenheim	Zoologie
Berger, Thomas/Hellweg, Christine	ISU Strasbourg	Master of Space Studies (MSS)
Berger, Thomas/Hellweg, Christine	Universität Bonn	Strahlenschutzkurs
Elmenhorst, Eva Maria	RWTH Aachen	Flug/Reisemedizin
Elmenhorst, Eva Maria	RWTH Aachen	Raumfahrtmedizin
Elmenhorst, Eva Maria	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Frings-Meuthen, Petra	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Hauslage, Jens	ISU Strasbourg	Gravitational Biology Part I and II
Hauslage, Jens	ISU Strasbourg	Student Elective – Biological Life Support Systems Course
Hellweg, Christine	FU Berlin	Pathologie
Hellweg, Christine	FU Berlin	Immunologie
Hellweg, Christine	Universität Bonn	Radiopharmaziekurs
Hellweg, Christine	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Hemmersbach, Ruth	Universität Bonn	Zoologie/Gravitationsbiologie
Jordan, Jens	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Liemersdorf, Christian	University of Bonn	Molecular Genetics, Neurobiology
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Med. Businessystem
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Biomed. Informatik
Mittelstädt, Justin	Universität Hamburg	Psychologische Diagnostik: Psychologische Gutachten

2018

Name	University	Subject
Mittelstädt, Justin	Universität Hamburg	Psychologische Diagnostik: Praktische Übungen zu diagnostischen Verfahren
Mulder, Edwin	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Pecena, Yvonne	ISU Strasbourg	MSSP&SSP Lecture, Space Psychology
Rittweger, Jörn	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Rittweger, Jörn	Universität Köln	Medizin (Spezielle Pädiatrie)
Stern, Claudia	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Stern, Claudia	Technische Universität Braunschweig	Luft- und Raumfahrtmedizin
Stern, Claudia	Universität der Bundeswehr	Raumfahrtmedizin
Stern, Claudia	ISU Strasbourg	Master of Space Studies (MSS)
Stern, Claudia	European School of Aviation Medicine	Basic Course Ophthalmology I
Stern, Claudia	European School of Aviation Medicine	Advanced Course Ophthalmology II
Stern, Claudia	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Tank, Jens	Medizinische Hochschule Hannover	Propädeutik
Zange, Jochen	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Zange, Jochen	Universität Köln	Medizin (Research Track)

2017

Name	University	Subject
Aeschbach, Daniel	Harvard Medical School	Sleep Medicine
Anken, Ralf	Universität Hohenheim	Zoologie
Baumstark-Khan, Christa	Hochschule Bonn-Rhein-Sieg	Strahlenbiologie
Berger, Thomas	Hochschule Bonn-Rhein-Sieg	Strahlenbiologie
Berger, Thomas	ISU Strasbourg	Radiation Physics & Biology
Elmenhorst, Eva-Maria	RWTH Aachen	Flug- und Reisemedizin
Elmenhorst, Eva-Maria	RWTH Aachen	Raumfahrtmedizin
Hauslage, Jens	ISU Strasbourg	Gravitationsbiologie
Goerke, Panja	FH Wedel	Communication Skills Group
Goerke, Panja	Universität Lüneburg	Vertiefungsseminar differentielle Psychologie
Goerke, Panja	FH Wedel	Communication Skills Group
Hemmersbach, Ruth	Universität Bonn	Zoologie/Gravitationsbiologie
Hellweg, Christine	Hochschule Bonn-Rhein-Sieg	Strahlenbiologie
Hellweg, Christine	FU Berlin	Pathologie
Hellweg, Christine	FU Berlin	Immunologie
Hellweg, Christine	ISU Strasbourg	Radiation Physics & Biology
Hellweg, Christine	Universität Bonn	Strahlenbiologie
Hellweg, Christine	Universität Köln	Weltraumphysiologie
Keye-Ehing, Doris	Universität Ulm	Angewandte Diagnostik in Luft- und Raumfahrt
Kölzer, Anna-Magdalena	FH Wedel	Communication Skills Group
Liemersdorf, Christian	University of Bonn	Molecular Genetics, Neurobiology
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Medizinische Informations-Systeme
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Medizinische Businesssysteme
Lindlar, Markus	Hochschule Bonn-Rhein-Sieg	Health Telematics
Maier, Julia	ISM Hamburg	Einführung i. d. empirische Sozialforschung
Maschke, Peter	TU Hamburg Harburg	Faktor Mensch i. d. Luft- u. Seefahrt
Melcher, Wiebke	Leuphana-Universität Lüneburg	Einführung in die Psychologie

V.1 Teaching activities

2017		
Name	University	Subject
Melcher, Wiebke	Leuphana-Universität Lüneburg	Übung Interferenzstatistik II
Melcher, Wiebke	Leuphana-Universität Lüneburg	Computergesteuerte Datenanalyse
Mittelstädt, Justin	Universität Hamburg	Praktische Übungen zu diagnostischen Verfahren
Mittelstädt, Justin	Universität Hamburg	Psychodiagnostische Testverfahren
Pecena, Yvonne	ISU Strasbourg	Cognitive and personality testing
Pecena, Yvonne	ISU Cork	Space Psychology
Rettberg, Petra	ESA	Planetary Protection Course Lecture
Rettberg, Petra	ESA	Planetary Protection Course practical laboratory course
Rittweger, Jörn/Jordan, Jens	Universität Köln	Humanmedizin
Stelling, Dirk	Hochschule Fresenius Hamburg	Differentielle Psychologie
Stern, Claudia	TU Braunschweig	Luft- und Raumfahrtmedizin
Stern, Claudia	Technische Universität Braunschweig	Luft- und Raumfahrtmedizin
Stern, Claudia	Universität der Bundeswehr	Raumfahrtmedizin
Stern, Claudia	ISU Strasbourg	Master of Space Studies (MSS)
Stern, Claudia	European School of Aviation Medicine	Basic Course Ophthalmology I
Stern, Claudia	European School of Aviation Medicine	Advanced Course Ophthalmology II
Stern, Claudia	Universität Köln	Medizin (Wahlpflichtblock Weltraumphysiologie)
Tank, Jens	Medizinische Hochschule Hannover	Propädeutik
Zange, Jochen	Universität Köln	Physiologie
Zinn, Frank	Universität Köln	Diagnostik interaktiver Kompetenzen

V.2 Graduations

2019			
Supervised Doctoral Students	Space	Aviation	Traffic
Medizinische Hochschule Hannover	5		
Manchester Metropolitan University	1		
Ruhr-Universität Bochum	1		
ISU Strasbourg	1		
RWTH Aachen	2	1	
Universität Bonn	4		
Universität Hamburg	1		
Universität Duisburg-Essen	1		
Universität Göttingen	2		
Universität Köln	10		
SpoHo Köln	3		
Universität Leiden		1	1
Universität des Saarlandes	1		
Delft University of Technology		1	
Universität Salzburg		1	
TU Darmstadt	1	1	1
FH Aachen	1		1
Universität Regensburg	1		
Universität Erlangen	1		

2019		
Doctorates	Space	Aviation
Universität Erlangen	1	
Universität Hamburg		1
Technische Universität Dresden		1
Leuphana Universität Lüneburg		1
Skoltech Moskau	1	
Universität des Saarlandes	1	
Universität Bonn		1
RWTH Aachen	1	

2019		
Bachelor Degrees	Space	Aviation
Hochschule Bonn-Rhein-Sieg		1
Universität Bonn	4	
European University of Applied Sciences Rhein/Erft	1	
University of Applied Sciences Remagen	1	
FH Aachen	1	
Universität Leipzig		1

V.2 Graduations

2019

Diploma Theses/Master Degrees	Space	Aviation	Traffic
FH Aachen	1		
Universität Ulm	1		
Universität Bochum	1		
TH Köln	1		
Universität Gießen	1		
Fernuniversität Hagen	1		
RWTH Aachen		1	
Universität Bonn	1		
Universität Köln			1
HAW Hamburg		1	

2018

Supervised Doctoral Students	Space	Aviation	Traffic
FH Aachen	1	1	
Manchester Metropolitan University	1		
Medizinische Hochschule Hannover	2		
RWTH Aachen	2		
Sporthochschule Köln	2		
TU Darmstadt	1		
Universität Bonn	1		
Universität Düsseldorf	1		
Universität Essen	2		
Universität Göttingen	2		
Universität Heidelberg	4		
Universität Köln	2		
Universität Leiden		1	1
Universität Saarland	1		
Uni Regensburg	1		
Universität Zürich		1	

2018

Doctorates	Space	Avitation
Universität Erlangen	1	
Universität Hamburg	1	

2018

Bachelor Degrees	Space	Avitation
Hochschule Emden-Leer	1	
Hochschule Bonn-Rhein-Sieg	4	
Universität Bonn	2	

2018

Diploma Theses/Master Degrees	Space	Avitation
TU Darmstadt	1	
Universität Stuttgart	1	
Universität Hamburg		1
TH Regensburg	1	
RWTH Aachen		1
Universität Leiden		1

V.2 Graduations

2017

Supervised Doctoral Students	Space	Aviation	Traffic
RWTH Aachen	1		1
Universität Bayreuth	2		
FU Berlin		1	
Universität Bonn	1		
Universität Bremen	2		
Sporthochschule Cologne	4		
Universität Cologne	3		
TU Darmstadt	1		
Universität Dresden		2	
Universität Duisburg-Essen	2		
Universität Erlangen-Nuremberg	2		
Universität Göttingen	2		
Universität Hamburg		3	
Universität Hannover	1		
Universität Heidelberg	3		
Universität Konstanz	1		
King's College London, Great Britain	1		
Universität Lüneburg		1	
Universität Magdeburg	1		
Universität Münster	1		
Universität Saarland, Homburg	2		

2017

Doctorates	Space
Universität Cologne	2
Universität Eindhoven, Netherlands	1
King’s College London, Great Britain	1
Universität Münster	1

2017

Bachelor Degrees	Space
Hochschule Bonn-Rhein-Sieg	1
Universität Cologne	1
Universität Emden-Leer	1
Universität Magdeburg	1
Universität Osnabrück	1

2017

Diploma Theses/Master Degrees	Space	Aviation	Traffic
FH Aachen	1		
Universität Bamberg		1	
Universität Bonn		1	
TU Dresden		1	
Universität Stuttgart	1		
Universität Stuttgart-Hohenheim	1		
Universität Kiel		1	
King's College London, Great Britain	1		
Universität Stockholm, Schweden	1		

V.3 Scientific exchange

In 2018, the Institute established the DLR UTSW Alliance to foster scientific exchange and training opportunities with University of Texas Southwestern in Dallas, an internationally leading biomedical research institution (Nature index rank 22 in 2018). This collaboration will be further expanded.

2020	4 guest scientists, 1 assignment to UTSW
2019	5 guest scientist
2018	3 guest schientists, 3 assignments of staff members to: University of Pennsylvania, USA, University of Gothenburg, Sweden, University of Copenhagen, Denmark

V.4 Awards

2019

- Yannick Lichterfeld: Travel grant, 26th Assembly of the European Low Gravity Research Association, Granada, Spain, September 24–27, 2019
- Yannick Lichterfeld: Travel Grant, 57. Jahrestagung der Deutschen Gesellschaft für Luft- und Raumfahrtmedizin, Schönhagen, 24–26 October, 2019
- Kendrick Solano: Travel grant, 26th Assembly of the European Low Gravity Research Association, Granada, Spain, September 24–27, 2019
- Kendrick Solano: Member of the Month (10/2019) of the Student European Low Gravity Research Association
- Willi Pustowalow: Student Award 2019 der Konferenz für Angewandte Automatisierungstechnik in Lehre und Entwicklung in der Kategorie beste Bachelor-Arbeit
- Katja Gayraud: Werner-Straub-Preis der TU Dresden
- Eva-Maria Elmenhorst: Albrecht-Ludwig-Berblinger Preis der Deutschen Gesellschaft für Luft- und Raumfahrtmedizin
- Matthias Meier: NASA Group Achievement Award
- Stella Koch: 1st prize – Student contest "Space Factor", 19th EANA Astrobiology Conference, Orléans, France, September 3–6, 2019
- Marta Cortesão: EANA 2019 Poster Award, 19th EANA Astrobiology Conference, Orléans, France, September 3–6, 2019
- Darius Gerlach: Deutsche Hochdruckliga e.V. DHL®: Reisestipendium und Einladung zu den " Best of …" Sessions
- Katharina Siems: Honorable Mention, Art Competition, American Society for Gravitational and Space Research (ASGSR), November 20–23, Denver, USA, 2019
- Katharina Siems: 1st Prize for startup idea, German Biotechnology Conference, Würzburg, April 9–10, 2019
- Luisa Becher: 2nd Prize for startup idea, German Biotechnology Conference, Würzburg, April 9–10, 2019

2018

- Marta Cortesão: Grant – PhD, grant for the Biofilms 8 Conference in Aarhus, Denmark, from May 27–29, 2018
- Marta Cortesão: Travel Grant, DAAD, für Feldforschung am Jet Propulsion Laboratory, Pasadena,USA, July 02–31, 2018
- Marta Cortesão: 2nd prize – Student contest "Space Factor", EANA 2018, Berlin, Germany, September 24–28, 2018
- Marta Cortesão: Women in Aerospace-Europe grant – WIA-E 2018
- Marta Cortesão: DGE Messreiseförderung, Messreise: Robert Koch-Institut, Berlin, Topic: " How does simulated microgravity affect the micromorphology and colony structure of the fungus Aspergillus niger?", April 1st–Mai 24, 2019
- Timo Frett: 1. Posterpreis "Verträglichkeit von reaktiven Sprüngen auf einer Kurzarmhumanzentrifuge", 56. Wissenschaftliche Jahrestagung der DGLRM
- Felix Fuchs: FEMS YSMG grant – registration fees for the 8th European Spores Conference in Royal Holloway, University of London
- Felix Fuchs: Grant – PhD, grant for the Biofilms 8 Conference in Aarhus, Denmark, from May 27–29, 2018
- Darius Gerlach: Travel grant, 29th International Symposium On The Autonomic Nervous System, Arbeitsgemeinschaft Autonomes Nervensystem
- Darius Gerlach: FMS/Penaz Wesseling travel Fellowship Award for "Functional brainstem imaging reveals brainstem nuclei governing human baroreflex function" at the 29th International Symposium On The Autonomic Nervous System
- Darius Gerlach: Deutsche Hochdruckliga e.V. DHL®: Reisestipendium und Einladung zu den "Best of …" Sessions
- Hendrik Kronsbein: 1. Preis "Trainee Poster Competition" der American Autonomic Society, 29th International Symposium On The Autonomic Nervous System
- Markus Rohde: Förderpreis Elektrotechnik H-BRS 2018, Bachelorarbeit: "Abschätzung der Gefährdung durch terrestrische Gammastrahlenblitze auf kommerziellen Flugreisen"
- Katharina Siems: Early career award (young microbiologist), EANA 2018, Berlin, Germany, September 24–28, 2018

2017

- Christian Liemersdorf, Timo Frett: ELGRA Research Prize 2017 für Live-cell Imaging of Neuronal Activity Changes under Altered Gravity
- Denise Lange: Travel Grant der Nordrhein-Westfälischen Gesellschaft für Schlafmedizin
- Denise Lange: Promotionsstipendium der Studienstiftung des Deutschen Volkes
- Dajana Parganlija: Best Talk Award, Tagung Junge Physiologen
- Karina Marshall Bowman: Nominierung Forbes 30 under 30 Science and Healthcare
- Felix Fuchs: VAAM-Jahrestagung 2017 gemeinsam mit DGHM

Cross-sectional and issues, related projects and studies of the Institute

	Muscle and Bone Metabolism	Sleep and Human Factors Research	Cardiovascular Aerospace Medicine	Radiation Biology
01. Mechanisms by which gravity and atmospheric conditions impact human health and performance in space, aviation and on Earth	**AGBRESA** **MAFS-18** **ReLSiP** **Sarcolab-3** **Sarcolab-BR** **SOLEUS MOLO** **VibEMod** **ViSSC**	**ATLAs** **HyPaFly**	**AGBRESA** **AO-2019-ISS-PP_039** **Cardiovector-2** **ChemoBar** **Direct Return** **HypoFon** **LOCAR** **MyoCardioGen** **VaPER**	**AGBRESA** **Effects of Neutron Radiation on Medical Devices** **EvaLyRad for MyoCardioGen** **FSE** **Hypoxia & Radiation** **New European Radiation Protection Standards in Aviation (Space Weather)** **Radiation in Commercial Aircraft** **UV Radiation effects in the atmosphere**
02. Genome-environment interactions regarding sleep, performance, and cardiometabolic disorders in the mobile society	**AGBRESA** **Mouse and cell models for inherited myopathies** **MuXLiH**	**AGBRESA** **CoCo** **HEMS FTL** **MIDAS** **PET Kaffee** **SomnoSafe** **UBA Infraschall** **VEU**	**AGBRESA** **EDS-fMRT** **Empa-MSNA** **HyNu-OT** **MSA-fMRT** **NN1965-4485** **NVC-fMRT** **Spiomi**	**AGBRESA**
03. From molecular mechanisms to individualised risk assessment and radiation exposure prevention	**AGBRESA**	**AGBRESA**	**AGBRESA**	**AGBRESA** **Development of products and services for the aviation industry and the society** **DOSIS 3D** **Effects of Neutron Radiation on Medical Devices** **ESA Active Dosimeter System** **ESA Active Dosimeter System on Artemis I** **EvaLyRad** **Hypoxia & Radiation** **IceCold** **LND** **LUX-in-Space** **M-42 (Eu:CROPIS, Mapheus 7/8)** **MARE** **MASE** **MEXEM** **MicroHeavy** **MSL-RAD** **MOMEDOS** **NEURON** **NeuroSpace** **New European Radiation Protection Standards in Aviation (Space Weather)** **NF-KB & Radiation** **PPOSS** **Radiation effects in the atmosphere** **RAMIS** **RIBE** **UV Radiation in Commercial Aircraft**
04. Human, environment and microbiome interaction: From aerospace research towards sustainable economic management on Earth	**AGBRESA**	**AGBRESA**	**AGBRESA**	**AGBRESA** **Development of products and services for the aviation industry and the society** **BAL-S** **BIOFILMS** **BioRock** **EDEN-ISS** **EURO-CARES** **EXTREMOPHILES** **IceCold** **MASE** **MEXEM** **MOMEDOS** **New European Radiation Protection Plasma-Decon** **PPOSS** **PP-VERI** **Skin & gut microbiome** **Standards in Aviation (Space Weather)**
05. Human-human and human-machine interactions: Challenges and opportunities in the light of demographic change	**AGBRESA**	**AGBRESA** **CoCo** **ITC**	**AGBRESA**	**AGBRESA** **BAL-S** **BIOLFILMS** **Effects of Neutron Radiation on Medical Devices** **Plasma-Decon**

	Gravitational Biology	Aviation and Space Psychology	Clinical Aerospace Medicine	Study Team
	AGBRESA **GraviPlax** **Ground-based Facilities Programme** - Arabidopsis - Cardiomyocytes - CounterG - Homeostasis - Hydrogels - IMMUN03D-SHAPE - Ketamines - MicroHeavy - NEMUCO - RiboSeq - T-cells - Thrombocytes **Mapheus 7/8:** - AstroProteomics - MemEx **National Centrifuge-Program:** - CoolSpin study - JUMP study - PUG-3 study **NeuroSpace** **TRN VY**	**AGBRESA** **VaPER**	**AGBRESA** **VaPER**	**AGBRESA** **Direct return of ESA-Astronauts after ISS-Missions** **National Centrifuge-Program:** - JUMP - COOL SPIN - PUG-3 **HypoFon** **MyoCardioGen** **VaPER**
	AGBRESA **Cardiomyocytes** **GravityGym National Centrifuge-Program:** - CoolSpin study - JUMP study - PUG-3 study **Mapheus 7/8** **NeuroSpace** **TRN HVY**	**AGBRESA**	**AGBRESA**	**AGBRESA** **CoCo** **Gravity Gym** **HyNu-OT** **National Centrifuge-Program:** - JUMP - COOL SPIN - PUG-3 **PET-Kaffee** **TRN-HVY**
	AGBRESA **NeuroSpace**	**AGBRESA**	**AGBRESA**	**AGBRESA**
	AGBRESA **C.R.O.P.®** **Eu:CROPIS**	**AGBRESA**	**AGBRESA**	**AGBRESA** **C.R.O.P ®**
	AGBRESA **ASYSTED II**	**AGBRESA** **City ATM** **EPOV** **ITC** **NGT** **NICo** **SIR** **UAM Acceptance** **UAV/WTF** **ValiS**	**Aeromedical center** for national civil aviation authorities **Direct return** of ESA-Astronauts after ISS-Missions DLR **Fliegerarzttage** **Medical selection** of first German female astronaut candidate **VaPER** **AGBRESA**	**AGBRESA** **CoCo** **Direct return** of ESA-Astronauts after ISS-Missions **ITC** **Medical selection** of first German female astronaut candidate **VaPER**

List of abbreviations and explanations

A

AGBRESA: 60 days ESA-NASA-DLR bed rest study with short arm human centrifuge (SAHC)
AO-2019-ISS-PP_039: Cardiovascular Magnetic Resonanc (cMR): Assessment of impact of spaceflight duration on cardiac deconditioning
AstroProteomics: G-related changes in neuronal cells demonstrated on the proteomics level
Arabidopsis: Changes in calcium signaling in plants due to exposure to altered gravity (collaboration University of Marburg)
ASYSTED II: Advanced System for Teleguided Diagnosis II – Remote ultrasound diagnostics for remote areas. Product development with DLR-Technology marketing in collaboration with German Bundeswehr and Scotty Group Austria
ATLAs: Interaction effects of hypoxia and atmospheric carbon dioxide on healthy adults in the aircraft environment (DLR project "Advanced technology long-range aircraft-concepts")

B

BAL-S: Bioinspired Antimicrobial Laquer in Space, antimicrobial peptides immobilised on different surfaces
BIOFILMS: Biofilm inhibition on flight equipment and on board the ISS using microbiologically lethal metal surfaces
BioRock: ISS experiment, biofilm formation and biomining in space

C

Cardiomyocytes: Effect of simulated microgravity and hypergravity on the senescence of human cardiomyocytes (collaboration University of Cologne)
Cardiovector-2: Individual adaptation of central arterial hemodynamics during long term space flight
ChemoBar: Peripheral chemoreflex/arterial baroreflex interaction in patients with electrical carotid sinus stimulation
City ATM: City Air Traffic Management (drone pilots in urban areas
CoCo: Effect of fatigue on eye tracking and performance (DLR Project "Collaborative operations in control rooms")
CoolSpin study: External cooling as a stabilizing cardiovascular countermeasure in hypergravity
CounterG: Hypergravity as a potential countermeasure against gene expression changes in different human blood cells in microgravity (collaboration LMU Munich)
C.R.O.P.® Combined Regenerative Organic food Production. Biofilter technology developed by DLR for degradation and modification of nitrogen rich wastewaters in closed systems and in the agricultural sector towards a fertilizer solution for plant nutrition. Degradation of xenobiotica and medication residuals in wastewater.

D

DOSIS 3D: Dose Distribution Inside the ISS 3D

E

EDEN-ISS: Ground Demonstration of Plant Cultivation Technologies for Safe Food Production in Space
EDS-fMRT: Mechanisms of Orthostatic Intolerance in patients with Ehlers-Danlos-Syndrome assessed by high fidelity phenotyping- a substudy of the ProANS trial
Empa-MSNA: Effects on blood pressure and central sympathetic nerve traffic by SGLT2-inhibition with empagliflozin compared to hydrochlorothiazide in patients with type 2 diabetes
EPOV: Enhanced Passenger outside View
ESA Active Dosimeter System: First active crew personal dosimeter system onboard the ISS
ESA Active Dosimeter System on Artemis I: Active dosimeter system in the frame of the NASA Artemis I mission
Eu:CROPIS: Euglena: Combined Regenerative food Production in space. Spin rotated satellite with lunar and Martian gravity to investigate the impact of reduced gravity on biological life support systems in long-term experiments in space.
EURO-CARES: European Curation of Astromaterials Returned from Exploration of Space, definition of the sample receiving and analysis facility for extraterrestrial material
EvaLyRad: Development of an *ex vivo* assay for determination of individual radiosensitivity
Extremophiles: ISS experiment, determination and characterization of the ISS microbiome

F

FSE: Fume und Smell Events

G

GraviPlax: Investigating the impact of gravity on the evolution of the bauplan from simple to complex with a special focus of the polarization of cells and the adaptation towards a bilateral symmetric body (collaboration TiHo Hannover)
GravityGym: Tolerability and physiological response to the performance of exercises during short-arm centrifugation (SAHC) as potential countermeasures for long-term space flight

H

HEMS-FTL: Investigation of the effects of two duty schedules on fatigue and sleep in pilots in German helicopter emergency medical services
Homeostasis: Force-induced protein homeostasis - exploring its gravity-dependent regulation and its potential for pharmacological modulation to counteract muscle loss during space flights (collaboration University of Bonn)
Hydrogels: Development of 3D scaffolds for neuronal cultures in novel hydrogels (collaboration DLR-WF)
HyNu-OT: Effects of hypercaloric nutrition on orthostatic tolerance
HyPaFly: Choosing an adequate test to determine fitness for air travel in obese patients
HypoFon: Midterm moderate hypoxia and its effects on sleep, pulmonary blood flow, hemorheology, and physical performance in patients with Fontan-circulation
Hypoxia & Radiation: Radiosensitivity (X-rays/carbon ions) of lung carcinoma cells under hypoxic conditions

I

IMMUNO3D-SHAPE: Immune system adaptation to space conditions in novel 3D spheroid bone marrow model (collaboration University of Frankfurt)
IceCold: Investigating cold adapted microorganisms as model organisms for a Europa ocean environment in CubeSat-based hardware, ISS experiment
ITC: Inter Team Collaboration

J

JUMP: Reactive jump training under hypergravitation - comparability of movement and effects on the metabolism of articular cartilage

K

Ketamines: Adaptation of neuronal plasticity by novel Ketamine-derivatives under altered gravity conditions (collaboration TH Cologne)

L

LND: Measurement of the radiation environment on the Moon's surface
LOCAR: Determination of the upper and lower limit of cerebral autoregulation in different age groups and in patients with autonomic failure - a feasibility study
LUX-in-Space: Kinetics of enzymatic repair reactions after irradiation under microgravity by use of a rapid bioluminescence-based bacterial genotoxicity assay, ISS experiment

M

M-42: Radiation detector system for fast and easy radiation measurements
MAFS-18: Master Athletic Field Study 2018
Mapheus 7/8: DLR sounding rocket campaigns
MARE: MARE experiment onboard the NASA Artemis I mission
MASE: Mars Analogues for Space Exploration, isolation and characterisation of microorganisms from extreme environments on Earth
MemEx: Membrane experiment to investigate the membrane fluidity in microgravity
MEXEM: Mars Exposed Extremophiles Mixture, ISS experiment, investigation of the resistance of microorganisms from extreme environments on Earth to Martian environmental conditions
MicroHeavy: Simulating space conditions by simultaneous application of microgravity and ionizing radiation on formation, development and aging of human brain organoids (collaboration GSI Darmstadt)
MIDAS: Effects of nighttime aircraft noise on sleep and annoyance of school children
MOLO: Mechanics and loading forces associated with Movement in simulated Low gravity
MOMEDOS: Molecular mechanisms of *Deinococcus radiodurans* survivability in space, ground control of an ISS experiment
Mouse and cell models for inherited myopathies
MSA-fMRT: Pathophysiology of neurogenic orthostatic hypotension in patients with Multiple System Atrophy – a functional MRI study
MSL-RAD: Measurement of the radiation environment on the surface of Mars
MuXLiH: Muscle fatigability and X-Linked Hypophosphatemia
MyoCardioGen: Myocardial Regeneration by Hypoxia in Humans

N

NEMUCO: Neuro-Muscular Co-Culture – a biological model for changes in human performance due to weightlessness in space (collaboration Charité Berlin)
NEURON: Mechanisms of heavy ion-induced damage in primary neuronal cells
Neuro Space: Induction of neuronal regeneration mechanisms by altered gravity and radiation conditions
NF-κB & Radiation: Role of NF-κB in the cellular response to space-relevant radiation qualities
NGT: Next Generation Train
NICo: Next Generation Intelligent Cockpit
NN1965-4485: Efficacy and safety of NNC0268-0965 versus insulin glargine in subjects with type 2 diabetes mellitus
NVC-fMRT: Neurovascular compression at the brainstem level assessed by advanced functional MRI

P

PET-Kaffee: Does habitual daily coffee intake ensure optimal cognitive performance in the face of chronic sleep restriction?
Plasma-Decon: Application of cold atmospheric plasma for the decontamination of space hardware
PPOSS: Planetary Protection of Outer Solar System, identification of knowledge gaps and scientific roadmap for the exploration of Europa and Enceladus
PP-VERI: Bioburden and Biodiversity Agency-Level Planetary Protection Verification Assays
PUG 3: Perception of Upright and investigation of self-orientation under differing Gravity States created by a Centrifuge

R

RAMIS: Measurement of the radiation field onboard the DLR Eu:CROPIS Satellite
ReLSiP: Assessment of Reflex Latencies during Sinusoidal Perturbation
RIBE: Radiation-Induced Bystander Effects
RiboSeq: Reprogramming of translation in plants in reaction to microgravity (collaboration University of Frankfurt)

S

Sarcolab-3: Myotendinous and neuromomuscular adaptation to long-term spaceflight
Sarcolab-BR: (Bed Rest) AGBRESA
SIR: Simulator Instructor Research
SOLEUS: Sensory Orthotic Lower-Leg Exerciser for Use in Space Integrated Countermeasures with Biofeedback and Actuators
SomnoSafe: Chronic sleep loss: From molecular neuroimaging to safety and health in space
Spiomi: Acute and two-week effects of Spiolto Respimat in hyperinflated COPD subjects

T

T-cells: Impact of microgravity on immune cell gene expression (collaboration Karolinska, University of Stockholm, Sweden)
Thrombocytes: Impact of altered gravity conditions on the human hemostatic system (collaboration University Witten/Herdecke)
TRN-HVY: Tolerability, biomechanics and neuromuscular activation of combined exercise performance during centrifugal-induced gravity

U

UAM Acceptance: Acceptance of unmanned systems
UAV/WTF: Unmanned aerial vehicle/ Wehrtechnische Forschung
UBA-Infraschall: Effects of infrasound immisions

V

ValiS: Validitätsstudie DFS
VaPER: 30-days NASA Bed rest study under 0.5% CO_2
VEU: Exposure-response relationship of the awakening probability due to nocturnal road traffic noise in suburban residents
VibEMod: Whole Body Vibration & Elastic Modulus In Musculature
ViSSC: Vibration-induced Stretch-Shortening Cycles

About DLR

DLR is the Federal Republic of Germany's research centre for aeronautics and space. We conduct research and development activities in the fields of aeronautics, space, energy, transport, security and digitalisation. The DLR Space Administration plans and implements the national space programme on behalf of the federal government. Two DLR project management agencies oversee funding programmes and support knowledge transfer.

Climate, mobility and technology are changing globally. DLR uses the expertise of its 47 research institutes and facilities to develop solutions to these challenges. Our 9000 employees share a mission – to explore Earth and space and develop technologies for a sustainable future. In doing so, DLR contributes to strengthening Germany's position as a prime location for research and industry.

Imprint

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