

Academia Raetica  
SWITZERLAND



9<sup>th</sup> conference  
**Graubünden forscht**

Davos Congress Centre, Hall Aspen  
November 8-9, 2024

**Abstracts**

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Friday, November 8

10:00–10:30

**Insights from ETH Studio Davos**

Chair: Barbara Haller Rupf / Academia Raetica

(Website: <https://gr-forscht.ch/abstracts?kategorie=insights-from-eth-studio#resultat>)

## **Machine learning techniques in solar jet detection**

Original abstract title: Automatic detection of solar jets using machine learning techniques

Henrik Jentgens, Rémy Moll, Michel Tào

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The Sun is the driving factor for many phenomena on Earth, such as the origin of life. Thus, understanding the characteristics of our host star is crucial for many disciplines, be it environmental science, ecology, space sciences or astrophysics. Many fields therefore rely on accurate modeling and prediction of the Sun's behavior and features. Solar features are various structures found on the surface of the Sun, ranging in size from small bursts (European country size) to large coronal mass ejections (size of a quarter of the space between Earth and the Sun).

Among these features are solar jets, transient, small-scale eruptions of plasma in the solar atmosphere.

Despite their small scale, they are numerous and thus, a few questions arise: What influence do jets have on solar wind, the stream of particles generated continuously by the solar atmosphere? Do jets influence space weather? Space weather refers to the environmental conditions in space that can affect technology and human activities in or near Earth's atmosphere.

Solar jets occur in highly dynamic and complex solar environments. Thus, they are usually detected manually by researchers based on visual analysis of satellite images.

However, recent advancements in solar imaging satellites, such as the Solar Orbiter probe, have resulted in the generation of vast amounts of high-resolution data of the Sun's atmosphere. The large data volume renders traditional manual analysis methods impractical, highlighting the need for automated detection techniques.

This work in the context of the ETH Studios program explores this challenge of solar physics through an interdisciplinary approach with machine learning. We aim to detect solar jet events from satellite image data using machine learning by utilizing the dynamics of the processes and incorporating them into different neural network architectures.

The machine learning approach of this work offers a promising solution for the automatic detection of solar jets. Our implementation shows that a more efficient survey of the data is possible without the loss of accuracy. This will enable a more thorough statistical analysis of jets and ultimately enhance our understanding of dynamic solar processes. Moreover, this method of detection is not limited to solar physics and has potential applications in other fields where dynamic features have a defining role.



Friday, November 8

10:45-11:45

**Session 1    Natural Sciences, Robotics, and Photonics**

Chairs: Britta Allgöwer / Academia Raetica, Ruzica Dacic / WSL Institute for Snow and Avalanche Research SLF

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-01-natural-sciences#resultat>)

## **Why does a snow scientist bring a saw and black ink on a field trip?**

Original abstract title: Elastic snow properties for the optimization of weak layer fracture toughness estimates

Melin Walet<sup>1</sup>, Jakob Schöttner<sup>1</sup>, Valentin Adam<sup>1,2</sup>, Florian Rheinschmidt<sup>2</sup>, Jürg Schweizer<sup>1</sup>, Philipp Rosendahl<sup>2</sup>, Philipp Weissgraeber<sup>3</sup>, Alec van Herwijnen<sup>1</sup>

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### **Introduction**

Snow avalanches come in many different types and sizes. The deadliest type of avalanche, the dry-snow slab avalanche, releases after a crack propagated through a weak layer inside the snowpack. Understanding the fracture properties of weak layers is thus essential to improve avalanche prediction. As avalanches only release on slopes steeper than 30 degrees, a crack in a weak layer is always subjected to a combination of shear and normal forces, making crack propagation a mixed-mode fracture problem. However, little is known about the mixed-mode fracture toughness of weak layers, a material property describing the resistance to crack growth under different loading conditions.

### **Methods**

To investigate the fracture toughness of weak snowpack layers, field experiments were conducted using natural snow samples containing a buried weak layer. Each experiment involved extracting a one-meter-long sample from the snowpack, ensuring the inclusion of the target weak layer. The sample was then placed in a tilting device, loaded with weights (metal rods) and tilted to the desired angle. We then used a snow saw to cut into the weak layer until reaching the critical cut length, at which point the crack propagated across the sample. The side wall of the snow samples was speckled with black dye and recorded on video.

From the recorded videos, accurate values of critical cut length were extracted. We then used digital image correlation (DIC) analysis on the video recordings to assess the displacement within the snow samples. These displacement fields served as input to derive the elastic properties of the weak layer and the overlying snow slab using a closed-form model. In a last step, the collected input parameters and the retrieved elastic properties were used to obtain a fracture toughness value and the respective mode I and mode II contribution in each test.

### **Results**

We performed over 150 experiments and obtained fracture toughness envelopes for various weak layers. Fracture toughness values were typically around 2 J/m<sup>2</sup> in mode II and 0.5 J/m<sup>2</sup> in mode I. For the experimental setup used, our results indicate that the fracture toughness was larger in mode II than in mode I in line with the behaviour observed in other materials. Furthermore, we observed that the fracture envelope expands as the weak layers strengthen over time.

### **Discussion and conclusion**

Our results provide valuable benchmark data for numerical models and much needed data on mixed-mode fracture toughness values of weak snowpack layers to improve avalanche prediction.

In the future, we will investigate the fracture properties of numerous weak layer microstructures. Since the snow microstructure most likely controls the mechanical properties, a characterization of the microstructure is essential. The connection between weak layer fracture and the microstructure of weak snowpack layers can be used to ultimately improve slab avalanche forecasting.

## **A century of rewilding**

Original abstract title: 110 years of rewilding enhances red deer density and plant diversity

Raphael S. von Büren<sup>1,2</sup>, Martin Schütz<sup>3</sup>, Christian Rixen<sup>4</sup>, Sabine Rumpf<sup>2</sup>, Sonja Wipf<sup>1</sup>

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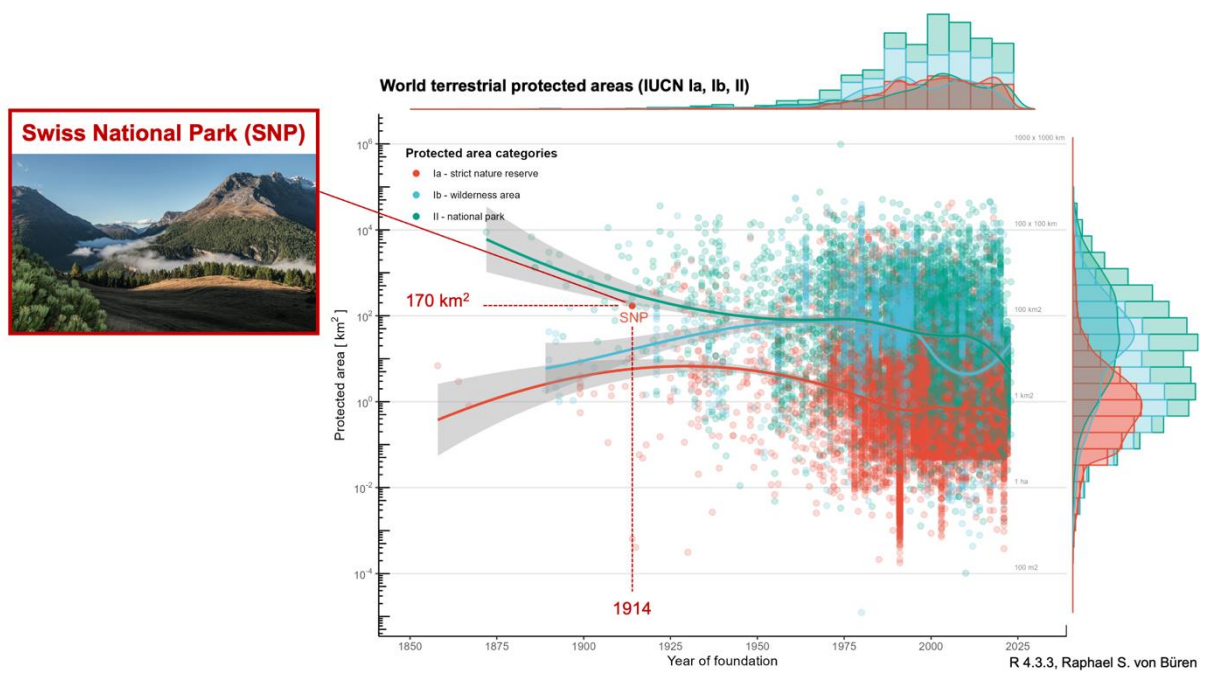
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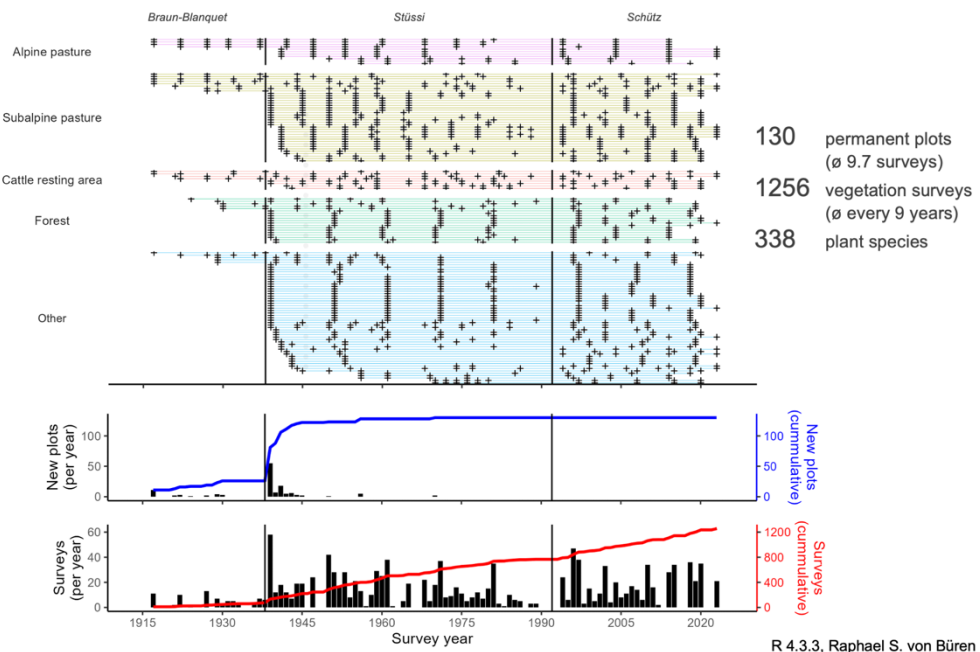
<sup>4</sup> Institute for Snow and Avalanche Research SLF, Davos, Switzerland

### **Abstract**

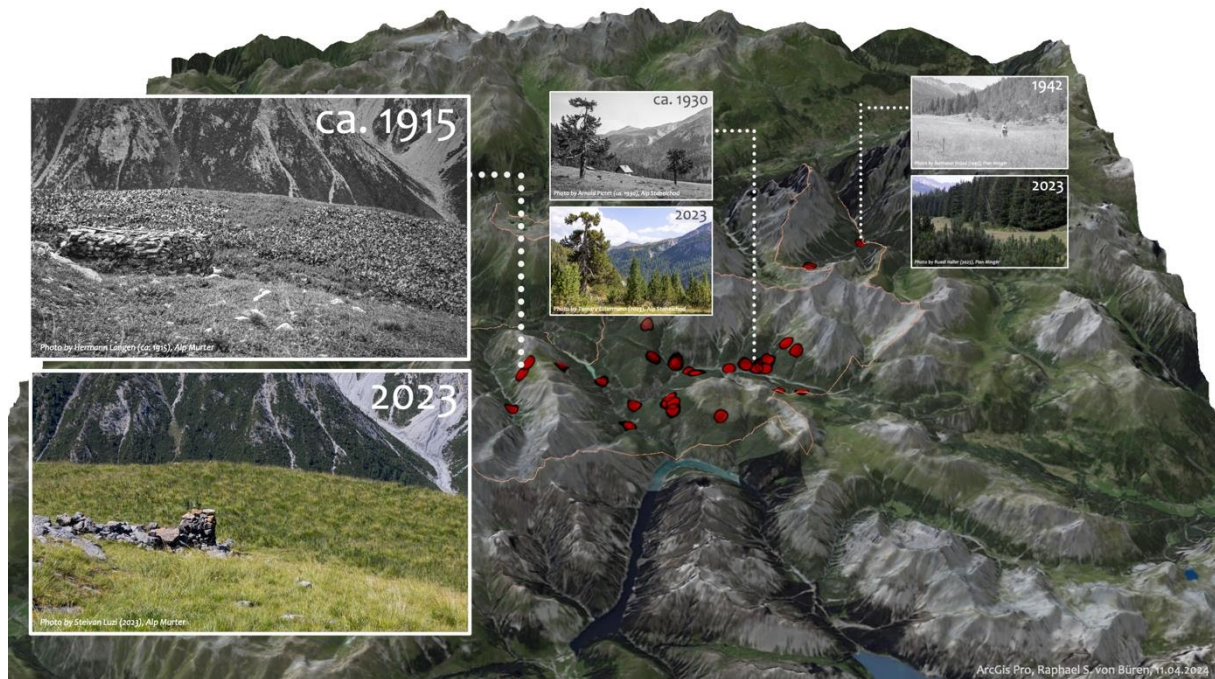
Worldwide, the rapid decline of biodiversity due to intensive land-use, overexploitation and pollution poses a critical threat to ecosystems, impacting the provision of essential ecosystem services. The United Nations decade on ecosystem restoration 2021-2030 seeks to halt the biodiversity decline. One promising restoration strategy is rewilding, which has received increasing scientific attention over the past 10 years. Rewilding aims at restoring human-dominated ecosystems into their natural state, for instance by re-establishing keystone species such as large herbivores, and habitat connectivity. It promotes trophic cascades, ecosystem services and resilience against environmental changes with the goal of halting biodiversity loss and habitat degradation. Since rewilding represents a nascent scientific concept, publications are mostly opinion papers or short-term experiments. Analyses with long-term empirical data are missing. To fill this knowledge gap, we explore a unique rewilding experiment that was initiated 110 years ago: In 1914, stringent regulations were implemented in a 170 km<sup>2</sup> mountain area in the European Alps, banning any human use such as alpine farming, hunting, mining, and forestry. This action led to the establishment of the Swiss National Park, a protected area with the highest possible level of protection (IUCN Ia), where human presence is restricted to a network of trails. As a result, the Swiss National Park is the world's second-oldest IUCN Ia protected area larger than 12 km<sup>2</sup>. To monitor the expected natural succession from grassland into secondary natural forest, permanent vegetation plots were set up in 1917 and marked with wooden posts, allowing to re-survey the plots within centimetre-precision the following years. Until today, 130 permanent plots were re-surveyed, on average every 9 years. This results in 1256 vegetation surveys, all including abundance estimations on species level, and a total of 338 observed vascular plant species. Annual observations of ungulates revealed that at the beginning of the rewilding experiment, red deer were locally extinct due to overexploitation and hunting. Only three years after, the first red deer returned to the park area and the population exponentially increased until the 1980s, with a slight decline thereafter until today. The return of this keystone species suppressed forest succession and increased plant diversity. This effect was strongest in permanent plots with highest local red deer grazing intensity, which was mainly where cow densities were highest before farming was banned (cattle resting areas). There, the rewilding strategy counteracted recent global change effects on plant communities and diversity by impeding the increase of thermophilic, nitrophilic and competitive species. Under intensive red deer grazing, the presence and abundance of non-thermophilic plant species increased because thermophilic species tend to be taller and more nutritious, hence preferably eaten by red deer. Contrary to common assumptions, our results suggest that restored biotic interactions following rewilding have the potential to overrule the effects of global change on plant communities in the long run. Moreover, our contiguous, very long-term time series allows us to explore the particularly slow vegetation shifts in mountain ecosystems that are typically dominated by clonal, long-lived plant species. Finally, our approach advances opinion-based papers with data-based analyses to quantify the effectiveness of long-term rewilding as restoration strategy.



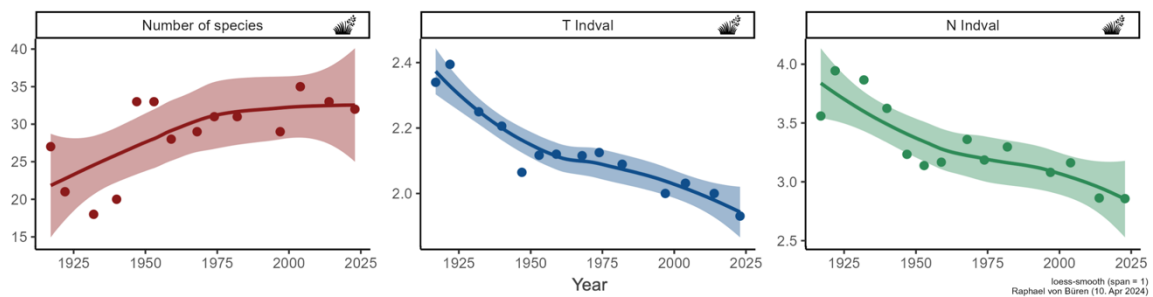
**Figure 1:** Year of foundation and size of the world's terrestrial highly protected areas (IUCN Ia, Ib, II). The Swiss National Park, indicated as SNP, is the world's second-oldest IUCN Ia protected area larger than 12 km<sup>2</sup>.



**Figure 2:** Temporal distribution of the studied permanent vegetation plots within the Swiss National Park. Crosses indicate vegetation surveys. Visualised on top of the graph are the three botanists which conducted the vegetation surveys (1917-1938 Josias Braun-Blanquet; 1939-1989 Balthasar Stüssi; 1992-today Martin Schütz).



**Figure 3:** Map with spatial distribution of the permanent vegetation plots (red points) within the Swiss National Park (orange line). Historic and recent photographs of three permanent plots. From left to right: Alp Murter, Alp Stabelchod, Plan Mingèr.



**Figure 4:** Plant community changes during 110 years of rewilding at Alp Murter, a former cattle resting area, today with high local red deer grazing. Number of plant species increased, while Landolt indicator values for temperature (T Indval) and nutrients (N Indval) decreased.

## Quantitative analysis of forest windfall damage using aerial ortho-imagery

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### Abstract

Rapid, safe, and cost-effective assessment of windfall damage after storms is essential for effective forest management and mitigation of economic impacts. This study investigates the application of drones in assessing windfall damage efficiently. Utilizing high-resolution drone ortho-imagery, we aim to enhance current damage assessment methods. Our findings suggest that automated image analysis can detect, measure and geographically locate fallen trees in aerial photographs taken by drones efficiently. Thus, our approach can rapidly and safely quantify storm damage, providing valuable data for forest management and economic impact analysis.

### Introduction

In the night of October 29 to 30, 2018, Storm Vaia caused widespread destruction across parts of Europe, including Graubünden in Switzerland. With wind speeds exceeding 180 km/h at Piz Martegnas, the storm inflicted severe damage, toppling high-voltage pylons and affecting 100 hectares of forest. The resulting damage exceeded 60,000 cubic meters of timber. While significant, such events are not unprecedented in the region's history. Forests in mountainous regions like Graubünden serve crucial protective functions against natural hazards such as avalanches and rockfalls. Post-disaster, it is vital to quickly assess the extent of forest damage to address immediate protective needs and manage timber resources. Traditionally, district foresters conduct on-site inspections to make decisions regarding storm wood clearance and temporary protective measures.

### Methodology

A collaborative project initiated by the WSL Institute for Snow and Avalanche Research SLF and developed by the Institute of Photonics and Robotics (IPR) at the University of Applied Sciences Graubünden aimed to refine damage assessment methods using aerial images. Commissioned by the Office for Forests and Natural Hazards (Amt für Wald und Naturgefahren, AWN), SLF executed several drone flights, one of them over Val Mela, an area impacted by Storm Vaia. The captured ortho aerial images provided a precise, distortion-free, vertical view with a resolution of approximately 2 cm per pixel. These high-resolution colour images facilitated the detailed analysis required for accurate damage assessment.

### Results

The University of Applied Sciences Graubünden developed software to automatically evaluate these images. The software detected, measured, and geographically localized fallen trees (Fig. 1), enabling the compilation of statistics on storm-damaged timber and its distribution. This approach allows for rapid, efficient damage analysis without the need for hazardous on-site inspections.

By recording the damage using drones, there is no need for dangerous access and manual recording by people walking in the damaged area between freshly fallen trees in a rough mountain area that is difficult to access with the potential risk of falling. The results are also available much faster. The rapid determination of the amount of storm-damaged timber also makes it possible to assess the economic impact of the supply of storm-damaged timber on the timber market – an important economic factor in Graubünden – and its influence on the price of timber at an early stage.



## Discussion

The developed software represents an early-stage technology that requires further validation. Future work will involve comparing the automated estimates of storm-damaged timber with manual measurements and actual cleared quantities. To this end, the involved Grisons institutes plan to undertake a joint research project to further refine and validate this technology.

## Conclusion

This study lays the groundwork for improving forest damage assessment post-storm events through the use of high-resolution aerial imagery and automated analysis. By enhancing the speed and safety of damage assessment, this method holds promise for future applications in forest management and economic planning.

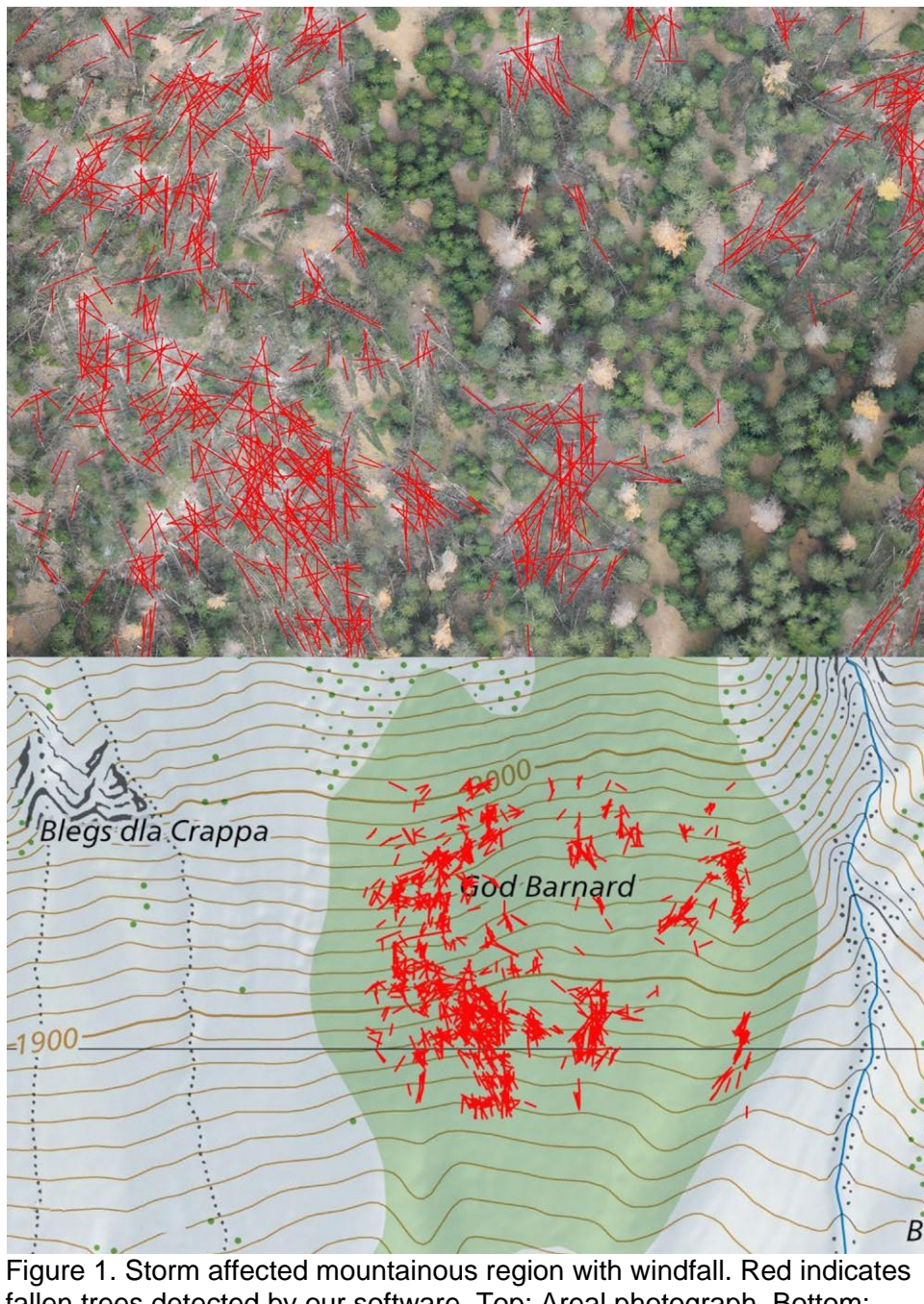


Figure 1. Storm affected mountainous region with windfall. Red indicates fallen trees detected by our software. Top: Areal photograph. Bottom: Ortho-map overlaid with fallen trees (image credit: Federal Office of Topography swisstopo).

## Ground-based solar radiation measurements and the study of atmospheric aerosols

Original abstract title: Aerosol optical depth ground-based measurement and measurement-modelling advancements

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Group Leader: Julian Groebner<sup>1</sup>

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Aerosols are an important constituent in the study of atmosphere. They affect the Earth's energy budget by interacting with radiation, affecting also the solar radiation exposure at the surface [Wild 2012]. They also play a crucial role in cloud formation and properties [Fan et al. 2016]. Interactions between aerosols and clouds are important for radiative forcing attribution, climate modelling and weather forecasts [Rosenfeld et al. 2014, Glotfelty et al. 2019]. Finally, aerosols are one of the most important air pollutants [WHO 2013].

Aerosols are a heterogeneous mixture of non-gaseous particles. To study their effects on climate we need to quantify several properties of the aerosol column. One way to achieve this is the use of solar radiation measurements from ground-based instruments (which can also serve as reference for satellite instruments).

One of the most important parameters regarding aerosols is the Aerosol Optical Depth (AOD), which describes the aerosol column effect on solar radiation extinction [WMO 2003]. The AOD is observed through Sun photometers. Sun photometers are instruments that measure the direct solar irradiance reaching the ground at specific wavelengths. To retrieve the AOD through the solar irradiance, we require the solar irradiance at the top of the Earth's atmosphere (calibration constant) and the effect of gases. Several networks of different Sun photometers are used worldwide to measure the AOD.

There are other properties defining the optical and microphysical properties of aerosols like the single scattering albedo (SSA), the effective radius ( $R_{\text{eff}}$ ), the total volume concentration ( $C_v$ ). SSA shows the balance between radiation absorption and scattering from aerosols,  $R_{\text{eff}}$  is the weighted average of their radius,  $C_v$  their volume per atmospheric air unit. These properties can be retrieved using different components of the solar radiation, the AOD and additional information like the gas absorption.

This thesis aims to contribute to the assessment of the differences between different instruments and methodologies for aerosol properties' retrievals, the homogenisation of sun photometric networks and the improvement of the aerosol monitoring. It includes four objectives:

- The first objective was about the consistency between the AOD and its long-term trends between two different co-located sun photometers in Davos during 2007-2019 (one belonging to the Global Atmospheric Watch-Precision Filter Radiometer or GAW-PFR network and another to AErosol RObotic NETwork or AERONET). The study includes the effect of factors such as the trend analysis method and the temporal resolution [Karanikolas et al. 2022]. Most differences were within the corresponding uncertainties.



- The second objective was an assessment of the differences between the networks GAW-PFR and SKYNET and the effect of the different calibration methods that the two networks are using. The GAW-PFR network uses the Langley Plot method (LP) in high altitude locations [Kazadzis et al. 2018]. The SKYNET instruments (Prede POM sky radiometers) are calibrated ‘on site’ with the Improved Langley Plot method (ILP) [Nakajima et al. 2020]. For the investigation we used measurements from co-located instruments in Davos and Rome during campaigns of 2017-2021 [Karanikolas et al. 2024]. The results showed a systematic lower POM AOD, which can be attributed to modelling required for the ILP calibration method.
- The third objective is about the retrieval of aerosol size properties and concentration using only AOD observations through an aerosol model called GRASP [Torres et al. 2017]. Preliminary results suggest higher accuracy at small aerosols (fine mode) and concentration retrievals.
- The fourth objective aims to the retrieval of spectral SSA. This is accomplished using the Precision Spectroradiometer, which can measure the global and direct solar irradiance simultaneously at 1024 wavelengths between 300 and 1020 nm.

Aerosols remain one of the most important sources of uncertainties in climate science [IPCC 2021] and weather forecasting [Huang & Ding 2021]. An improved aerosol monitoring can be beneficial to the study of major global issues like climate change and air pollution.

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Friday, November 8

10:45-12:00

## **Session 2    Medicine and Life Sciences**

Chairs: Mirjam Schenk / CK-CARE Christine Kühne-Center for Allergy Research and Education, Willem Van de Veen / Swiss Institute of Allergy and Asthma Research (SIAF)

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-02-medicine-life-sciences#resultat>)

## **An allergic twin is different from a healthy one, right?**

Original abstract title: Allergy discordant twins do not exhibit differences in gene expression in naïve and memory B cells

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**Background:** Allergies are a worldwide present affliction of dysregulated type 2 IgE-mediated immune responses against certain 'harmless' proteins from the environment. At the centre of allergic diseases stand B cells and their regulatory mechanisms. The regulation of allergen specific B cells in allergies, determines if an individual has an allergic or tolerant response to foreign antigens. The general agreement is, therefore, that in healthy and allergic individuals the B cell regulation is different. This means there should also be significant differences in B cell gene expression that would give insight to the underlying process of allergic dysregulation. This project aims to characterize B cells of allergic individuals on a transcriptomic level and investigate the differences of their gene expression in comparison to their healthy twins. The goal is to discover allergy relevant differential gene expression patterns and pathways between allergy discordant twins.

**Methodology:** We used bio banked PBMCs from 16 monozygotic twin pairs that are either allergy concordant or discordant. They were mainly allergic to pollen (birch and timothy grass) and/or house dust mites, while not undergoing any immunotreatment. We separated the switched and unswitched B cells (going forward correspondingly referred to as memory and naïve B cells) from the individual donors with FACS and performed RNA extraction. The extracted RNA was depleted from ribosomal RNA, reverse transcribed, libraries generated and sent for 100bp single-end RNA sequencing using the Illumina Novaseq 6000 platform.

**Results:** The unbiased clustering, without long non-coding RNA, indicates the grouping of the data points is determined by memory vs naïve B cells, twin pairs, and then by concordance status. Allergies had little to no weight for the clustering algorithm. PCA analysis of the top 300 significant genes show no clustering by health status as well. We further compared the healthy vs allergic donors of the discordant twin pairs gene expression analysis. Using a log fold change >0.5 as a base, we discovered that the FDR stayed above 0.99 until we reached a p-value threshold of <0.00001. This strongly indicates that any differences are purely random variation and not differently regulated B cell pathways across the whole B cell population.

The PCA analysis from discordant twins gives the same results with no clustering determined by allergy status of the donors.

**Conclusion:** We found no conclusive evidence that the underlying cause for allergies is a general dysregulation of B cells. In allergy discordant twin pairs, neither memory nor naïve B cells show overarching differences between healthy or allergic donors. Comparing the B cells between healthy and allergic twin pairs showed that the expression patterns are not as distinct as expected. What differences there are, are more likely contributed by differences between twin pairs than in allergy status. These results are counterintuitive to the perceived picture of allergies. Rather than a systemic difference in immune regulation, we propose that the effects are limited to the allergen specific B cells. As such we hypothesize that only allergen specific cells differ in their gene expression between allergic and healthy individuals. These effects most likely are overshadowed by overall variability due to how rare specific B cells are.

## **Characterising 'sugared' proteins with mass spectrometry**

Original abstract title: A novel framework for deep glycoproteome characterisation with data-independent acquisition (DIA) proteomics

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## **Protein glycosylation and its function**

Protein modifications are chemical changes proteins undergo during (co-translational) or after (post-translational) their synthesis. These modifications play critical roles in the regulation of protein function, localization, stability, and interactions, and consequently in fundamental biological processes. Glycosylation is one of the most prevalent but complex forms of protein modifications. It involved the covalent attachment of sugar moieties (glycans) to serine/threonine (O-linked) or asparagine (N-linked) residues. The glycosylation process is non-templated and encompasses co-translational modifications (specifically in N-glycosylation) and post-translational modifications (in both N- and O-glycosylation) regulated by key enzymes including glycosyltransferases (GTFs), oligosaccharyltransferases (OSTs) and glycosidases. The intricate interplay among these enzymes fine-tunes glycan structures and modulates the protein folding, stability, distribution, and cell-cell interactions, thereby regulating glycoprotein functionality within cells. Aberrations in protein glycosylation are increasingly recognized as contributing factors in the pathogenesis of various diseases, including infection, inflammation, and cancers. Many studies aiming at biomarker discovery have reported dysregulation of glycosyltransferases, and linking alterations in glycosylation to immune response against tumour cells, treatment resistance and survival.

## **Protein glycosylation in lymphoma**

Lymphoma is a clinically heterogeneous cancer with deep molecular profiling achieved by omics studies like genomics, transcriptomics and proteomics. Several glycoproteomics studies have evidenced the clustering of differentiation glycoproteins in lymphoma prognosis. Unique glycoprotein biomarkers were also identified in classifying the lymphoma subtypes. Nevertheless, these studies solely uncovered the peptides' glycosylation sites or the overall released glycans. In our pilot study in lymphoma proteomics, we have revealed alterations in glycosylation machinery in different immunoglobulin heavy variable (IGHV) mutational status, indicating the potential change of glycosylation. A comprehensive and precise profile of intact glycopeptides in lymphoma is thus necessary to gain mechanistic insight.

## **Lymphoma glycoproteomics profiling with liquid chromatography coupled mass spectrometry (LS-MS)**

Liquid chromatography coupled mass spectrometry has emerged as a powerful analytical tool for characterization of glycoproteome. In contrast to the proteomics study, profiling of glycoproteomics on the intact glycopeptides' level encounters challenges including poor ionisation, structural complexity and low stoichiometry of individual glycopeptide forms due to the inherent heterogeneity. Recent advancements of MS instruments (scanning speed, resolution and fragmentation technology), sample preparation (enrichment of glycopeptides from regular peptides) and database searching tools (robust identification of complex modifications) have shed light on the deep and comprehensive characterization of glycoproteomics. To facilitate our knowledge in lymphoma, we are establishing and optimising an in-house sample preparation and data-dependent acquisition (DDA)-based MS measurement pipeline for deep lymphoma glycoproteomics profiling. Such glycoproteome mapping could lead to the clustering of potential subtypes, identification of biomarkers and thus therapeutic targets, and a deeper understanding of mechanisms in lymphoma pathogenesis.

## **Sprint-Interval-Training under hypoxia in persons with Multiple Sclerosis: A feasibility study**

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### **Background**

High-intensity interval training modalities are time-effective and have positive effects on various MS symptoms like walking impairment, fatigue and MS-related performance impediments (cardiorespiratory fitness). Exercise under hypoxic conditions induces comparable training effects to exercise performed under normoxic conditions with the required workloads being significantly lower to achieve these effects. Lower workloads under hypoxic conditions are beneficial for persons with multiple sclerosis (pwMS) especially when fatigue or reduced mobility prevents pwMS from exercising with higher workloads. This study investigates the feasibility of a sprint interval training (SIT) on a cycle ergometer under hypoxic conditions in pwMS.

### **Methods**

Ten pwMS (Relapsing-Remitting phenotype) participated in seven SIT sessions (3 per week) under normobaric hypoxia, equivalent to an altitude of 3000 m above mean sea level. All training sessions took place in addition to the standard rehabilitative care during a three-week inpatient stay at the Valens clinic, Valens, Switzerland. SIT was performed on a cycle ergometer while participants wore masks that covered mouth and nose, connected to the hypoxic generator via tubes. Heart rate (measured via Bluetooth chest belt) and oxygen saturation (SpO<sub>2</sub>; measured via an ear clip non-invasive fibre optic pulse oximeter) were constantly monitored during the sessions. SIT sessions consisted of 3 min warm-up followed by three series of five sprints à 10 s (with maximal possible revolutions per minute, rpm) with an active rest of at least 30 s between the sprints and 3 min between the series and ended with 3 min cool-down. Warm-up, active rest and cool down were performed with 20-50 Watts (60-80 rpm). When SpO<sub>2</sub> decreased during or after a sprint below 90%, active rest was prolonged until oxygen saturation was ≥ 90%.

Primary outcomes were feasibility of the study protocol (>70% of participants completing >70% of planned sessions) and data collection (>70% of complete data sets), and acceptability of the intervention from the participants' perspective (measured via semi-structured interviews). Secondary outcomes were Peak Power Output (PPO) of a graded exercise test (Watts, Watts/kg), 10 Meter Walk Test (10MWT), Two Minute Walk Test (2MWT), Six Minute Walk Test (6MWT), Timed Up and GoTest (TUG) and Patient Reported Outcomes Measurement Information System Questionnaire mental and physical score (PROMIS mental/physical) at baseline (T<sub>0</sub>) and discharge after three weeks (T<sub>1</sub>). Wilcoxon's signed rank test was conducted to analyse the changes between T<sub>0</sub> and T<sub>1</sub> in these parameters. Semi-structured interviews (conducted at T<sub>1</sub>) covered perceptions of participants' physical reactions to SIT, their attitude and motivation towards SIT and the procedures of the SIT sessions.

### **Results**

The study protocol was feasible with 80% of the recruited participants completing 79% of the planned series within the scheduled sessions. 88% of the data collection was successfully achieved. Results of the interviews show a high acceptability and motivation of the participants towards SIT, all participants would participate in a SIT again. Wilcoxon's signed rank tests revealed significant improvements from  $T_0$  to  $T_1$  in the following outcomes: a significant increase in PPO ( $p=0.046$ ), 2MWT ( $p=0.008$ ), 6MWT ( $p=0.005$ ), PROMIS mental ( $p=0.042$ ), PROMIS physical ( $p=0.042$ ) and a significant decrease in TUG ( $p=0.048$ ).

### **Conclusion**

SIT under hypoxia in persons with MS on a cycle ergometer is feasible, accepted and positively evaluated by the participants, and improving patient-reported and health-related outcomes.

### **Keywords**

Endurance training, hypoxia; Multiple Sclerosis; PROMS, high-intensity

## **Low-level laser therapy in patients with head and neck tumour undergoing radio- or radiochemotherapy**

Original abstract title: Effect of low-level laser therapy in patients with head and neck carcinoma undergoing radio- or radiochemotherapy with regard to therapy-associated side effects: A retrospective study

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### **Goals**

Studies showed that mucositis, the most common side effect of radiotherapy or radiochemotherapy for head and neck tumors, can be treated with a low level laser. [1] This is a retrospective study to examine the hypothesis that the short-wavelength light has a beneficial effect on the mucosa in the oral region.

### **Material and Methods**

113 patients were divided into two groups based on whether they were treated with radiotherapy or radiochemotherapy. Within this groups, an intervention group which has been treated with a laser, either from *Raditec Medical AG*, *Bellikon* or *THOR Photomedicine Ltd* and a control group were defined. The study examined the following parameters: degree of mucositis, weight progression, pain and analgetic medication.

### **Results**

The statistical analysis proved that there were no significant differences between the groups, with one exception (the irradiation dose from THOR Photomedicine Ltd compared to the control group), in terms of age, noxious agents, irradiation dose and tumour stages, which allowed the groups to be compared.

The results have shown significantly ( $p < 0.05$ ) lower mucositis scores at the beginning (1,97) and at the end of the therapy (1,92) in the radiochemotherapy intervention group compared to the control group at the beginning (2,71) and at the end (2,43). The highest degree of mucositis reached also the significance level, 2,67 in the intervention group and 3,14 in the control group. The weight loss in the follow-up was also significantly less in the intervention group (6%) compared to the control group (11%).

In the radiotherapy group the values did not reach the significance level, but a tendency towards an improved outcome is clearly evident.

### **Conclusion**

In conclusion, low-level laser therapy is strongly advocated in patients who have received radiochemotherapy in the head and neck region. To further validate the results, a larger, prospective double-blinded study should be performed.



## Spatial Transcriptomics to study Fracture Healing in Mouse Models

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**Introduction:** Mouse models have become essential tools in studying bone healing and the underlying mechanisms of impaired healing and fracture non-union. These models replicate the clinical condition where fractured bones fail to heal properly, providing a controlled environment to investigate factors that contribute to healing impairments. Researchers utilize these models to test new treatments and understand the molecular and cellular processes involved in bone repair. In this context, we apply spatial transcriptomics – a cutting-edge technique that enables the visualization and spatial quantification of gene expression. By combining this technique with non-union mouse models, we gain a comprehensive understanding of the spatial and temporal dynamics of gene expression during bone healing.

Furthermore, the application of spatial transcriptomics extends to the evaluation of (calcium phosphate) bone graft substitutes, which are commonly used to promote bone regeneration. These substitutes provide a scaffold that supports new bone growth, and spatial transcriptomics can help elucidate the interactions between the graft materials and the host tissue at a molecular level.

Refined spatial transcriptomics workflows based on transcriptomic probe transfer, such as the Visium CytAssist from 10x Genomics, promise to enhance these protocols by allowing researchers to pre-select tissue sections for more targeted analysis. However, the use of formalin-fixed paraffin-embedded (FFPE) musculoskeletal sections has posed challenges including tissue detachment during processing and a decline in RNA quality, which can affect the accuracy and reliability of the transcriptomic data obtained from these samples. Here we test the applicability of CytAssist on musculoskeletal tissues using conventional as well as hydrogel-coated histology slides. Subsequently, we investigate differences in data quality between sections on both slide types and assess differentially expressed genes (DEGs) between unions and non-unions.

**Methods:** Histological sections (n=8) used for spatial transcriptomics (Visium CytAssist FFPE; 10x Genomics, n=4 on glass slides, n=4 on hydrogel-coated slides) were obtained from a fracture healing study in female 20-week-old C57BL/6J mice receiving either a femur osteotomy (0.7mm) or a segmental defect (2.4mm) (license 22/2022, Grisons CH). Musculoskeletal sections were placed on glass and hydrogel-coated slides, H&E stained, imaged, destained and decrosslinked according to CytAssist protocol with different decrosslinking temperature and section thickness. Sequence alignment was performed using SpaceRanger. Differential gene expression was performed using DESeq2 (Seurat) followed by Gene-Set-Enrichment-Analysis (GSEA) of Gene Ontology (ClusterProfiler). Group comparison of quality measures was done using a Welch's t-test. Results are given as mean±standard deviation.

**Results:** In contrast to conventional glass slides, sections on hydrogel-coated slides stayed intact at high decrosslinking temperatures. Section thickness did not influence tissue detachment. We therefore sequenced 5µm sections using glass slides (n=4, decrosslinking temperature=70°C) and hydrogel-coated slides (n=4, decrosslinking temperature=95°C). Mean counts and genes per spot, were significantly ~10x higher for sections on hydrogel slides (counts: 4697±1796, genes: 2389±1170) compared to glass slides (counts: 463±415, genes: 250±223). Direct comparison of a non-union and union section showed a total of 564 DEGs.

**Conclusions:** Optimized spatial transcriptomics workflows based on transcriptomic probe transfer enable for improved read depth in musculoskeletal tissue enabling the characterization of molecular features discriminating non-union and union bone fractures. Within a recently launched SNSF Sinergia project (SLIHI4BONE)I, this method will allow to map gene expression to investigate how calcium phosphate bone graft substitutes can improve bone healing. By mapping gene expression patterns around the application site, researchers can gain insights into how these materials influence bone healing processes, aiming to optimized composition of bone graft substitutes and improving clinical outcomes.

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Friday, November 8

13:00-14:00

**Session 3a Medicine and Life Sciences**

Chairs: Katja Bärenfaller / Swiss Institute of Allergy and Asthma Research (SIAF) /  
University of Zurich, Esther Wehrle / AO Research Institute Davos

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-03a-medicine-life-sciences#resultat>)

## **Sex bias in intervertebral disc degeneration (IDD) and osteoarthritis (OA) research**

Original abstract title: Under-reporting of biological sex in preclinical research on intervertebral disc degeneration and osteoarthritis

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### **Introduction**

Intervertebral disc degeneration (IDD) and osteoarthritis (OA) are major causes of chronic pain and disability affecting the spine and joints. To date, long-lasting and effective treatments for them are lacking. Preclinical studies, investigating new treatments for IDD and OA, include cell and gene therapy, tissue engineering, and use of growth factors and small molecules. Elucidation of molecular mechanisms involved in these processes is crucial for the development of new treatments. Biological sex is a significant risk factor for both IDD and OA, which disproportionately and significantly more often affect women rather than men—probably because of the diversity related to hormonal and genetic differences. However, sex of cell donors or animals is often under-reported in preclinical studies, affecting the reproducibility and translational potential of research findings.

### **Methods**

This study examined the reporting of biological sex in preclinical research articles related to IDD and OA published in high-impact journals in 2022. Articles included were sourced from very high-ranked journals (Q1 and Q2) in orthopaedics, rheumatology, and cell and tissue engineering categories. The inclusion criteria for articles comprised those that reported original preclinical studies involving the use of cells (*in vitro*), alive animals (*in vivo*) or tissue explants/organs from an organism in an external environment (*ex vivo*). We extracted data on whether the sex of the samples was reported, included in the analysis, and if the journals had requirements for sex reporting.

### **Results**

Of the 193 articles analysed, 73.6% were on OA and 26.4% on IDD. Of the study types, 61.9% reported the sex of the samples, but only 3.4% included sex as a variable in the analysis. Sex was reported more in *in vivo* studies than in *in vitro* or *ex vivo* studies: 57.4% versus 32.4% and 10.2%, respectively. Most journals (60.9%) required sex reporting through guidelines such as ARRIVE (Animal Research: Reporting of In Vivo Experiments), but only a few mentioned the SAGER (The Sex and Gender Equity in Research) guidelines specifically for sex and gender reporting. Additionally, we found misuse of the terms “sex” and “gender” in 7 articles, indicating a need for better understanding and training on these concepts.

### **Discussion**

We identified four main concerns: low reporting of sample sex, predominance of male samples, lack of analysis considering sex differences, and reliance on external guidelines by journals. These issues can obscure important sex differences in disease mechanisms and hinder the development of effective treatments. Accordingly, setting tight guidelines on the reporting of sex by journals with advanced editorial standards should be done. Policy that promotes sex reporting in preclinical research has to be encouraged and underpinned by all funding agencies that are publicly funded.

### **Conclusion**

The results show that a substantial number of pre-clinical research reported on IDD and OA under-reported biological sex. This is a contributor to its unsatisfactory translation to clinic trials and replication issues. Lessening sex bias within pre-clinical research is not only crucial for the sake of patients but also leads to an improvement in the quality and reproducibility of the research findings.

Abstract conference “Graubünden forscht 2024”

**Acknowledgements**

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## **How flexible are neutrophils to opposing signaling in atopic dermatitis?**

Original abstract title: Understanding the impact of Opposing Signals on Human Neutrophils in Atopic Dermatitis

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Atopic dermatitis (AD) is a chronic inflammatory skin disease with a heterogeneous clinical phenotype, affecting up to 20% of children and 3% of adults worldwide. Characterized by barrier dysfunction, persistent Th2 inflammation and skin dysbiosis due to *Staphylococcus aureus* overgrowth. Despite the overgrowth of pathogenic bacteria, skin lesions exhibit a conspicuous absence of neutrophils, potentially attributed to IL-4/13-induced suppression of neutrophil functions. Dupilumab is a game changer therapy this monoclonal antibody inhibits IL-4 and IL-13 signaling by binding to the alpha subunit of the IL-4 receptor. However, concerns persist regarding its long-term effects and symptom recurrence upon cessation.

This study addresses a knowledge gap in neutrophil adaptation to an allergic environment, we investigate neutrophil adaptation to anti-bacterial response in a type 2 immune response dominated context such as AD by doing transcriptional and epigenomic profiling along with comprehensive analysis of neutrophil functionality (netosis, phagocytosis, ROS-production, bactericidal activity, chemotaxis). Preliminary data showed that upon in-vitro stimulation with IL-4, IFN-gamma or their combination, IL-4 induces STAT-6 phosphorylation and defective neutrophil response, while IFN-gamma induces STAT-1 phosphorylation and partially restores IL-4-induced dysfunction.

Building upon in-vitro stimulation insights, then we will aim for a comprehensive analysis of neutrophil functionality, open chromatin profiles, histone modifications, DNA methylation, and gene expression in healthy individuals and AD patients treated with Dupilumab. This analysis will create an atlas of active and repressed enhancers and promoters, clarifying their dysfunction during AD and advancing clinical strategies.

## **Strategies for Flow Cytometric Profiling of BCR Immunoglobulin Heavy Chain Isotypes: Comparing Fc Receptor Blocking Agents**

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B cells can express B cell receptors (BCR) with different immunoglobulin heavy chain isotypes, such as IgM, IgD, IgG, IgA, and IgE each of which plays a unique role in the immune response. Understanding these roles is crucial for research into immune system function and diseases. B cells expressing different BCRs can be studied using flow cytometry, a technique for analyzing cell characteristics, widely used in immunology to assess cell populations and functions. Different BCRs can be labeled using fluorophore-conjugated antibodies targeting individual immunoglobulin heavy chain isotypes. In flow cytometry, researchers often use Fc receptor (FcR) blocking agents to prevent non-specific binding of antibodies to Fc receptors on cell surfaces. FcRs are proteins found on various immune cells, including B cells, natural killer cells, macrophages, and dendritic cells. Blocking these receptors ensures that the antibodies used in the assay bind specifically to their intended target rather than to FcRs on the cells. FcR blocking agents often contain human immunoglobulins, and can, therefore, interfere with the accuracy of detecting BCR heavy chain isotypes on B cells. This study evaluates the impact of FcR blocking agents on the detection of BCR heavy chain isotypes (IgM, IgD, IgA1-2, and IgG1-4).

We collected blood samples from four healthy volunteers and isolated peripheral blood mononuclear cells (PBMCs) from these samples. The PBMCs were then treated with five different FcR blocking agents: normal mouse serum, human AB serum, and three commercially available anti-human FcR blocking agents. To assess the impact of washing on detection accuracy, we divided the samples into two groups: one was washed after treatment with the blocking agents, and the other was not.

The use of normal mouse serum did not affect the detection of any BCR isotypes, making it a reliable choice for flow cytometry. However, the three commercially available anti-human FcR blocking agents negatively impacted the detection of IgG1-4+ B cells. Human AB serum interfered with the detection of multiple BCR isotypes, including IgM+, IgA1-2+, and IgG1-4+ B cells. Washing the cells before staining partially restored the detection of IgG isotypes, and washing after treatment with human AB serum completely restored the detection of IgA1-2+ B cells. Despite the benefits of washing, we observed that it led to increased background signals and reduced the overall effectiveness of the FcR blocking agents.

Therefore, our study suggests that normal mouse serum is the most reliable FcR blocking agent for detecting various BCR heavy chain isotypes expressed by B cells. It eliminates the need for washing steps, thereby simplifying the process and maintaining accurate detection. These findings provide practical solutions to the challenges associated with using FcR blocking agents in flow cytometry panels for B cell analysis, enhancing the accuracy and reliability of B cell immunology studies.

## **B cells expressing histamine receptor 1 or 2**

Original abstract title: The role of differential expression of HR1 and HR2 on B cell subsets

Minglin Yang<sup>1</sup>, Laura Buergi<sup>1</sup>, Juan Felipe Lopez Crespo<sup>1</sup>, Stephan R Schneider<sup>1</sup>, Dilara Sahin<sup>2</sup>, Huseyn Babayev<sup>1</sup>, Pattaporn Satitsuksanoa<sup>1</sup>, Anja Heider<sup>1</sup>, Lili Shi<sup>1</sup>, Anders Funch<sup>1</sup>, Willem van de Veen<sup>1</sup>, Onur Boyman<sup>2</sup>, Cezmi A. Akdis<sup>1</sup>, Mubeccel Akdis<sup>1</sup>

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### **Background**

Histamine is a vasoactive amine involved in numerous human physiological and pathological processes including allergic diseases. Four histamine receptors (HR1, HR2, HR3, HR4) regulate various actions of histamine. According to earlier studies, HR1 and HR2 are predominantly expressed in T helper 1 (Th1) and Th2 cells, respectively. HR1 is a Ca<sup>++</sup> flux-inducing activating receptor, and HR2 is an adenylyl cyclase-stimulating suppressive receptor. HR1 promotes Th1-type responses, but Th1 and Th2-type responses are suppressed by HR2. Additionally, histamine affects the antibody production of B cells. HR1 signalling contributes to T-cell-independent humoral immune responses, while HR1 and HR2 play a role in T-cell-dependent humoral responses. Our group recently demonstrated that the mRNA expression of HR1 and HR2 on B cell clones is mutually exclusive. The differential expression of HR1 and HR2 on B cells characterize two distinct B cell subsets with pro-inflammatory and suppressive properties.

### **Methods**

HR1/HR2 Plasmid transfection was carried out in Human embryonic kidney 293 (HEK293) cells following the Lipofectamine 3000 guide. Peripheral blood mononuclear cells (PBMCs) were isolated from healthy in-house donors using Biocoll. The cells were stimulated with stimuli, and subjected to flow cytometry after 0, 24 and 48h.

### **Results**

By HRs plasmid transfection to HEK293, we confirmed the exclusive expression pattern of HR1 and HR2 on primary B cells from human PBMCs with FACS. CpG showed a tendency to promote HR1 expression, and BCR tended to inhibit HR1 expression. HR2 expression on human B cells can be induced by stimulation with IL-10 and inhibited by BCR with IL-4 after 48 hours. Stimulation with IL-10 for 48 hours increased the percentage of HR double-positive B cells.

### **Conclusion**

These data provide essential contributions to a better understanding of the role of histamine in B cell regulation and its roles in immune tolerance.



Friday, November 8

14:10-14:50

**Session 3b Medicine and Life Sciences**

Chairs: Katja Bärenfaller / Swiss Institute of Allergy and Asthma Research (SIAF) /  
University of Zurich, Esther Wehrle / AO Research Institute Davos

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-03a-medicine-life-sciences#resultat>)

## The effect of L-phenylalanine on CD4+ T cell activity

Original abstract title: Immunomodulation of CD4+ T cell activity by essential amino acid L-phenylalanine

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## Background

T cell metabolism and reprogramming post cellular activation influence their proliferation, differentiation, function, and memory formation. This phenomenon has been extensively evaluated in the context of cancer and diabetes but knowledge gaps pertaining to T cell metabolic reprogramming in type 2 inflammation and allergy still exist. Hence, we aimed to study memory CD4+ T effector (Teff) and regulatory (Treg) cell metabolism in allergy to improve our understanding of metabolic mechanisms and their role in facilitating the allergy phenotype.

## Methods

In our analysis, we employed several techniques for the *ex vivo* and *in vitro* assessment of multiple CD4+ T cell populations to study their metabolism. Memory CD4+ Teff and Treg cells were sorted from allergic patients and healthy controls using fluorescence-activated cell sorting (FACS) and subjected to untargeted metabolomics by UHPLC-QToF mass spectrometry. Subsequently, to assess and characterize CD4+ T cell or T cell subset energy metabolism, proliferation, phenotype, and functionality under the influence of L-Phenylalanine we used Seahorse extracellular acidification rate assays (Seahorse), qRT-PCR, flow cytometry, Single Cell ENergetic metabolism by profiling Translation inhibition (SCENITH), CFSE based proliferation, siRNA based knockdown experiments, and carried out analysis of previously published transcriptomics datasets comparing T cells between allergic patients and healthy controls.

## Results

In healthy subjects, memory CD4+ Teff cells could be completely differentiated from memory Treg cells based on their metabolomes although their composition showed high similarity in terms of metabolite classes. Overrepresentation analysis of metabolomics data emphasized amino acid metabolism in both cell types including L-phenylalanine (Phe) metabolism. Considering this observation and very limited number of studies evaluating the effect of Phe

on CD4<sup>+</sup> T cell metabolism, we decided to focus on this amino acid and study its effect on CD4<sup>+</sup> T, Th2 and Treg cells. In *in vitro* studies, we observed that supplemented Phe enhanced memory CD4<sup>+</sup> T cell glycolysis while limiting their oxidative phosphorylation. Furthermore, Phe limited memory CD4<sup>+</sup> T cell proliferation by an interleukin-4-induced-1 oxidase (IL4I1)-dependent mechanism which was confirmed by siRNA knockdown studies. Not only were observations replicated in Th2 cells, but we also observed Phe, at high doses, significantly limited the transcription of activation markers, type 2 cytokines, and key metabolic enzymes such as *mTOR*, *CD69*, *BACH2*, *BATF*, *IL-4*, *IL-5*, *IL-13*, *PKM2*, *PFKFB3*, and *IDH2* in *in vitro* differentiated Th2 cells. Additionally, supplementation of Phe limited the expression of CD161, a documented pathogenic Th2a cell marker. Finally, we also observed increased levels of Phe in the sera of severe allergic patients combined with reduced intracellular levels in memory CD4<sup>+</sup> Teff cells and reduced expression of key Phe transporter, LAT1, in severe allergic patients.

## Conclusion

In summary, these data collectively suggest Phe plays a critical role in preventing the development of pathogenic Th2a cells which could be potentially exploited for the development of therapy in the context of allergy.

## **The gut microbiome metabolite heals the skin and gut epithelial barrier and shows anti-inflammatory effects**

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The gut microbiota protects the gastrointestinal system's homeostasis by producing antimicrobial substances, vitamins, and metabolites, strengthening the gut epithelial barrier, inhibiting opportunistic pathogen colonization, and regulating the immune system. In addition, the gut microbiome has prominent roles in skin epithelial homeostasis (gut-skin axis), which can be seen in inflammatory skin diseases such as atopic dermatitis. We identified a gut microbiome metabolite, (here named compound X) which improves gut epithelial barrier development speed and integrity as demonstrated in gut-on-a-chip 3D cultures. The surface application of 0.25, 1- and 4-mM doses of compound X significantly increases the gut epithelial barrier integrity compared to control by almost 2 times up to 800 ohm x cm<sup>2</sup> during the gut development phase of the gut epithelial barrier. The transcriptomic analysis shows that it upregulates gene expression associated with xenobiotics metabolism, ion transport, water transport, glucose transport, and amino acid transport pathways. It increases the tight junction protein claudin-1 gene expression. It shows an anti-inflammatory activity, as demonstrated with decreased chemokines (CXCL-5,10 and 11, CCL-20,23 and 25, CSF-1 and MCP-1) and IL-1a levels in culture medium detected by proximity extension assay. Untargeted proteomics analysis revealed that 4 mM compound X upregulates glycolysis, tricarboxylic acid cycle, and oxidative phosphorylation and downregulates lipid metabolism pathways-related proteins. Next, we assessed its effect on skin epithelial barrier integrity with an ex vivo skin tissue model. Treatment of systemic circulation-relevant doses of compound X (0.25,1 and 4 uM) alone rescued the surfactant, cocoyl methyl glucamide-induced skin epithelial barrier damage within 24 hours. In addition, it reversed the inflammation caused by cocoyl methyl glucamide demonstrated by decreased IL-18, CSF-1, PRDX-3 and PD-L1 protein levels. In conclusion, our data highlights compound X, a gut microbiome metabolite, as a promising agent for preventing, rescuing, and treating gut and skin epithelial barrier impairment.

## Decellularized Extracellular Matrix-Based Hydrogel Enhances Chondrocyte Redifferentiation *In Vitro* and *Ex Vivo*

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**Introduction:** In cartilage tissue engineering, a major challenge is that chondrocytes (cartilage cells) tend to lose their specific functions when grown on flat surfaces, making it difficult for them to form proper cartilage tissue. To address this, we developed a new type of hydrogel made from a special derivative of hyaluronic acid, which is a natural substance found in the body, and particles from decellularized extracellular matrix (dECM), which are derived from cartilage but have had all cells removed. This hydrogel aims to help maintain the chondrocyte's natural characteristics over time.

**Methods:** We prepared dECM particles by milling bovine cartilage (cow cartilage), treating it to remove DNA, and then grinding it into fine particles. These particles were mixed with chondrocytes and a special hyaluronic acid-based hydrogel, which was then solidified using enzymes and light, similar to how certain types of glue harden under specific conditions (Fig1).

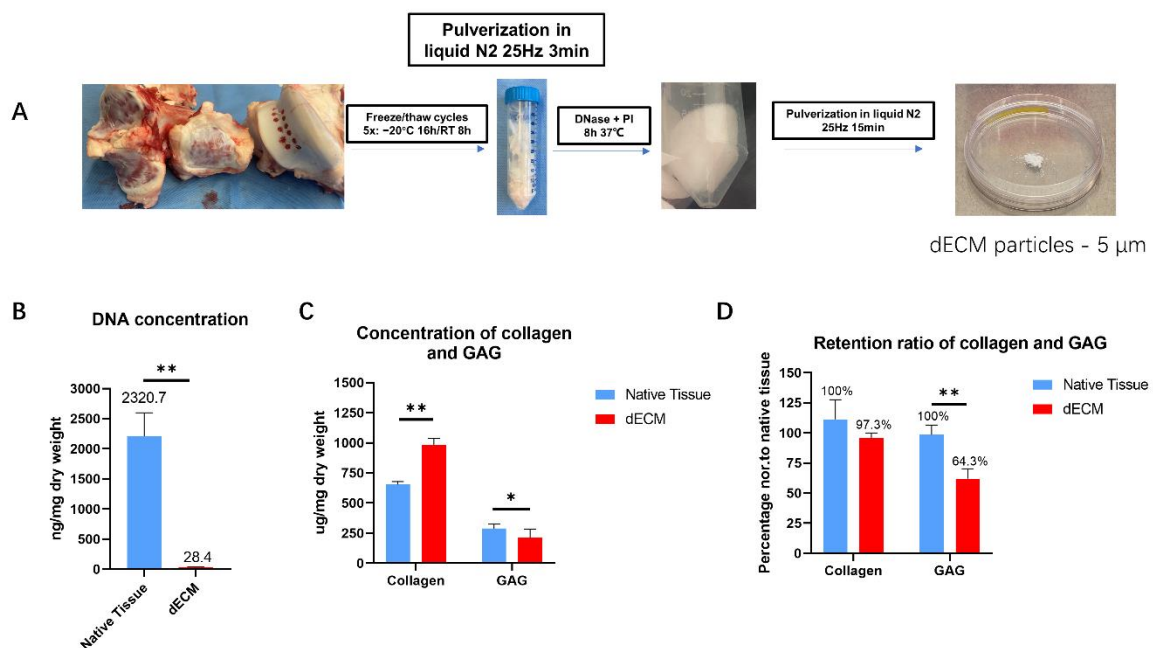


Fig. 1. (A) Macroscopic views of the production of dECM particles. (B) The DNA concentration, (C) Collagen and GAG concentration, and (D) retention ratio of collagen and GAG - (concentration x dECM yield dry weight) / (concentration x native tissue dry weight). Mean  $\pm$  SD, n = 9, \* p < 0.05, \*\* p < 0.01.

For the *in vitro* experiments, different concentrations (6, 12 and 20%) of dECM particles were tested to reveal the optimal composition to maintain chondrocytes phenotype. For the *ex vivo* experiments, we created a cartilage defect in bovine osteochondral tissue samples and implanted the hydrogel-cell mixture inside these defects (Fig2).

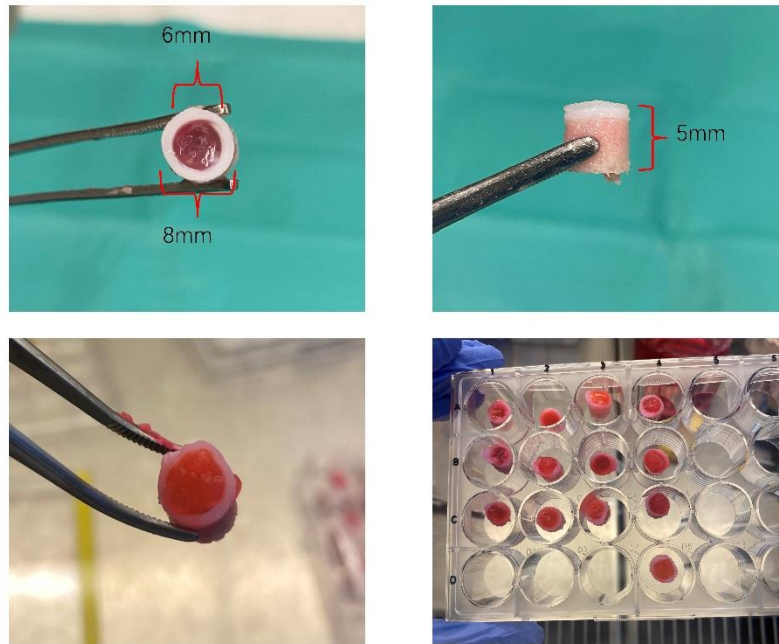


Fig. 2. a cartilage defect was created on osteochondral explants (8 mm diameter, 5 mm height) using 6 mm biopsy punch.

The samples were cultured for 21 days, after which we analyzed the cell behavior, tissue structure, and hydrogel stability.

**Results:** The dECM particles retained a high percentage of important cartilage components like proteoglycans (64.3%) and collagen (97.3%), with most DNA removed (98.8%). Proteoglycans and collagen are crucial for maintaining the structure and function of cartilage. In the *in vitro* study, dECM particles upregulated the expression levels of important cartilage markers (ACAN, COL2, and SOX9) up to day 14, which are indicators of healthy cartilage formation. The group of 20% dECM particles showed the highest level of cartilage markers expression, which was selected for the following *ex vivo* study. After 21 days, the newly formed cartilage tissue within THA-20% dECM group explants (pieces of tissue) had higher glycosaminoglycans (GAG) and collagen content compared with the THA group, which are essential for cartilage elasticity and strength. At the same time point, the expression levels of ACAN, COL2, and SOX9 were higher in the 20% dECM explant hydrogels. THA-dECM explants group showed higher proteoglycan staining intensity compared with the THA groups.

**Discussion & Conclusions:** Adding dECM particles to the hydrogel made it more similar to natural cartilage, which helped chondrocytes maintain their functions better. This is important because chondrocytes need the right environment to stay healthy and produce good-quality cartilage. Culturing the hydrogel within osteochondral explants (bone and cartilage samples) improved its stability and reduced the loss of essential cartilage components like GAG and collagen, making the hydrogel more durable. This approach also positively regulated the chondrocyte characteristics, showing promise for future cartilage repair techniques. By closely mimicking the natural environment of cartilage, this method could lead to better outcomes in cartilage tissue engineering and repair.

Friday, November 8

13:00-14:00

**Session 4    Education and Humanities**

Chairs: Sog Yee Mok / Pädagogische Hochschule Graubünden, Ana Petrus /  
University of Applied Sciences of the Grisons

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-04-education-humanities#resultat>)

## ***Orbita*: a new textbook for teaching Italian in the Canton of Grisons**

Alberto Giudici, Elisa Manetti

University of Teacher Education of Grisons

Italian Grisons – comprising the regions of Moesa, Bernina, and Maloja – is part of the Canton of Grisons, the only officially trilingual canton in Switzerland. The three regions that make up the Italian-speaking part are not contiguous and can be considered a linguistic archipelago (Moretti & Spiess 2002: 261). This territory, with its very complex history, underwent a process of Italianization starting from the mid-sixteenth century (see Bianconi 2013: 37-39). Elementary schooling was a fundamental element for the diffusion of the language thanks to the innovative project of the archbishop Carlo Borromeo. However, after a period of progress, the school system crystallized, leading to the development of an archaic language model (Bianconi 2001: 111-114). In the nineteenth century, linguistic manuals from the eighteenth century were reprinted, which advocated a bookish model of Italian (Lardi 2017).

Given this historical background, the development of contemporary educational tools is essential to address the evolving needs of students in Italian Grisons. This contribution describes the *Orbita* textbook, designed as the Italian L1 teaching tool for compulsory schools in Italian Grisons. The student population in Italian Grisons is approximately 1,200 (Casoni et al. 2021: 201; Todisco et al. 2020: 14-18), and the research by Cangemi & Imhof (2019) highlighted the need for a textbook that aligns with the principles of the Lehrplan 21 (the Swiss Curriculum). The *Orbita* project aims to fulfill this need by providing materials that support the development of all six competency areas indicated by the Curriculum. It promotes mastery of the four language skills (listening, speaking, writing, and reading) and metalinguistic and cultural skills (linguistic awareness and literary awareness).

The *Orbita* teaching tool comprises a textbook and an exercise book for each class. For secondary school classes, there will be two exercise books, divided by levels. Additionally, a digital guide for teachers is planned, providing detailed planning, competencies, objectives, and possibilities for differentiating various activities. The printed manual for language reflection will be available to students starting from the 5th grade and will be based on the valency method. The materials will be structured into 10 units with five thematic categories (language use, books, authors, text types, reflection on language, and multilingualism). Our talk will present some case studies from the manual regarding the difficulties encountered in the realisation of this major project.

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## Border experiences in the microcosm Graubünden

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The presentation offers an interpretation of the text *In quell'albergo sul fiume* by the Italian/Swiss author of Grisons origin, Ketty Fusco. By picturing the events of a destiny profoundly marked by the ideological categorization of the fascist period and its systems of persecution, the text focuses on the multiple aspects of both external and internal boundaries faced by the protagonist and relates them to the construction of individual identity. Significant factors include history and its territorial context, which, by permeating literature, make visible the stratified dynamics of geopolitical border experiences: in an era when the mechanisms of fascist power dominated Italian territory, the Grisons border between Italy and Switzerland represents the division between two existential conditions, between oppression and freedom, and with its crossing becomes a symbol of the transition from persecution to liberation. However, the geopolitical boundary is ambivalent, as it is a relational space between cultures and thus a hybrid space, where different models come into contact with each other, not necessarily a clear cut ideological boundary – as evidenced, for instance, by fascist infiltrations in Switzerland.

The text makes visible both the identity models that populated the Grisons region at the time and those that were reformulated based on the cultural differences coexisting in the area. It highlights the intersection of identity in relation to the linguistic-cultural boundaries dictated by the protagonist's family's bilingualism, with her Grisons mother speaking Swiss German and her father from Naples speaking Italian. The territorial and cultural boundaries also materialize in the landscape through memory: the places where the story unfolds can indeed be defined as 'spaces of memory,' quoting Aleida Assmann, that is, physical and symbolic spaces that have shaped memory and through which memory is now transmitted, and which become constituents of the sense of belonging and thus of the individual identity sphere.

*In quell'albergo sul fiume* is, according to Philippe Lejeune's theories, an autobiographical fiction, that is, an autobiographical retrospection in which there is a non-correspondence between the character's name and the author's name. It is a narrative strategy through which an interchange is created between personal events and elements of fiction that, on one hand, allows the writer to calibrate the expressive force of the events according to her intention, and on the other hand, grants the reader the freedom to find affinities or discrepancies between life and literature, thus interpreting the fictional story and reading it in the register they consider most appropriate. The discourse also extracts itself from historical-individual contingencies and projects into a more general dimension that testifies to historical events and sentiment, and the dimension of memory allows interpreting the events with greater awareness, projecting the past into a renewed construction of identity. Considering this latter aspect and referring to studies on cultural boundaries, the reading allows reflection on the relationship between boundary demarcation processes and identity from a multifaceted and diversified perspective, in which identity can be described as a continuous self-definition process, always provisional, open, and contradictory, shaped through social interactions.

## **Educators, Students, and Industry: A Comprehensive Study of Requirements Engineering in Switzerland**

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University of Applied Sciences of the Grisons, Chur, Switzerland

Requirements Engineering (RE) has emerged as an independent discipline in recent decades and is no longer considered a peripheral topic in software engineering. RE is taught in Switzerland at Universities and Universities of Applied Sciences, including the University of Applied Sciences of the Grisons in Chur. The subject is embedded in various degree programs, including Bachelor's, Master's, and Certificates of Advanced Studies (CAS), focusing solely on RE.

However, teaching this discipline to students poses challenges for educators in higher education, as it requires developing soft skills, decision-making abilities, practical application knowledge, and theoretical content. This Ph.D. project aims to systematically investigate Requirements Engineering in Switzerland from three different perspectives: higher education institutes and educators, students, and the industry.

The first study focuses on the perspective of Switzerland's unique educational landscape, with its research universities and Universities of Applied Sciences (UAS) and their practical orientation. Course descriptions of RE courses will be gathered for quantitative comparison of ECTS, curriculum aspects, embedded degrees, and mentioned prerequisites. Interviews with educators at higher education institutions in Switzerland should get insights into the reasoning behind curricular choices, instructional approaches, and the challenges of teaching RE.

In addition to educators, the students' perspective will be explored through an online questionnaire. How did students experience their RE courses? Did they miss any prerequisites? What instructional methods helped facilitate their understanding of the practical aspects of RE? Did the course encourage them to pursue a career in RE?

The third perspective will be that of future employers in the industry. To gather that perspective, the study will analyze Swiss job advertisements from June 2023 to May 2024 from three job portals (LinkedIn, XING, and jobs.ch). This study seeks to compile a list of top skills and tasks a Requirements Engineer needs to perform. Different industry demands regarding elicitation practices, documentation methods, language qualifications, and certificates like IREB CPRE, HERMES, higher education degrees, or work experience levels will be extracted through content analysis. Regional differences will also be explored.

The results of this half-year review (data collected from XING (N=372) and LinkedIn (N=297) between July 2023 and December 2023) have already revealed some interesting insights into the evolving landscape of Requirements Engineering (RE) within the Swiss job market.

The preliminary analysis of the half-year data revealed a varied landscape of job advertisements in language and structure. Most were in German, with English accounting for 16% of the advertisements (N=92). However, the most intriguing finding was the unexpectedly low numbers of advertisements in French and Italian, with only two in French and one in Italian, all from the same company. These findings are particularly interesting, given the official language status of French and Italian in Switzerland and their respective linguistic regions. Examining certifications commonly requested in RE job advertisements strongly emphasizes industry-specific certificates, particularly those closely linked to Requirements Engineering and Project Management. The prevalence of IREB certificates, alongside other Project Management credentials like HERMES, PMI, and ITIL, suggests a growing recognition of the importance of specialized knowledge and skills in Requirements

Engineering practice. However, the limited mention of Software Engineering-related certifications hints at a divergence from traditional software development pathways, indicating a shift in focus toward interdisciplinary skill sets.

The overall Ph.D. research seeks to understand how RE education in Swiss higher education is aligned with industry needs. The findings will contribute to bridging the gap between academia and industry, enhancing the preparedness of RE students for professional roles, and may improve teaching approaches in REE in Switzerland and beyond.

## **Development of a test instrument for assessing flexible calculation strategies in third grade math**

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### **Theoretical background**

Strong mathematical skills are essential for success in vocational training and university studies. In Switzerland, the “Lehrplan 21” curriculum emphasizes the importance of developing flexible calculation skills in arithmetic in primary school. These skills include the ability to use, explain, compare, and choose appropriate calculation strategies (D-EDK, 2016). Current textbooks such as the “Schweizer Zahlenbuch” (Kocher et al., 2021) contain only few explicit tasks promoting flexible calculation skills. Consequently, many primary school children have insufficient flexible calculation skills and strategies (Csikos, 2016).

Three types of mathematical knowledge are relevant to calculate in a flexible way: Procedural knowledge, conceptual knowledge, and strategy flexibility (Schneider et al., 2011). In equation solving, procedural knowledge means recognizing structures and applying solution steps and strategies, while conceptual knowledge involves understanding mathematical concepts and their relationships (Rüede et al., 2023). Strategy flexibility refers to knowledge of multiple solution strategies and how to compare them with respect to their suitability and efficiency (Verschaffel et al., 2009).

Current primary school didactics show various approaches to promote flexible calculation skills in arithmetic (Arend, 2020). A common approach is comparing multiple strategies showing different solutions per task. This involves simultaneous presentation of strategies for direct comparison of the solution steps which fosters discussions about the similarities, differences, and efficiency of each strategy (Rittle-Johnson et al., 2021; Star & Rittle-Johnson, 2008).

Numerous studies have investigated the development of flexible calculation skills. For example, a study from Arend (2020) with 79 third graders examines whether an explicit or problem-solving approach better promotes flexible and adaptive strategy choice, with tests primarily assessing calculation skills in the German school context. No test instrument currently measures flexible calculation skills in arithmetic for third graders in German-speaking Switzerland. This Master's thesis aims to fill this gap by developing and testing a scientific test instrument for third-grade flexible arithmetic strategies.

### **Research questions**

Which tasks can promote flexible calculation skills for third grade students in German-speaking Switzerland?

### **Methods**

The study used a mixed-methods approach (Roos & Leutwyler, 2022). Theory-guided test items were developed and utilized to construct a performance test instrument, assessing strategy flexibility, procedural knowledge, and conceptual knowledge (Star & Rittle-Johnson, 2008).

Initially, the items were piloted with individual students ( $n = 6$ ) for comprehension and duration (Moosbrugger & Kelava, 2020). Insights from this pilot phase refined the instrument before it was tested with several classes.

### **Sample**

The newly developed test instrument was empirically tested in six third-grade classes ( $n = 90$ ) in St. Gallen and Zurich. Each test session lasted approximately 45 minutes. Personal contacts and snowball sampling was used for the recruitment.

### **Test instrument description**

The developed math test instrument focused on the mathematical operations "addition" and "subtraction". Ensuring scientific rigor, the test adhered to objectivity, utility, and feasibility criteria, with a test manual explaining administration, scoring, and interpretation. Content validity was ensured by expert evaluation of item representativeness (Moosbrugger & Kelava, 2020).

### **Data analysis**

Descriptive item analysis (Moosbrugger & Kelava, 2020) was used to calculate item difficulty, variance, and discrimination, assessing if items differentiated well between students. Results guided the first test adjustments. Furthermore, an exploratory factor analysis (EFA) checked the construct validity, verifying if the items measured the intended constructs and if the theoretical model fit the data (Moosbrugger & Kelava, 2020). Results will be presented at the conference.

**Key words:** test instrument development; mathematic tasks; flexible calculation skills; primary school students; factor analysis

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Friday, November 8

14:10-14:50

**Session 5    Unveiling eosinophilic esophagitis:  
Our journey to understand a rare disease**

Chairs: Sibylle Grad / AO Research Institute Davos, Milena Sokolowska / Swiss  
Institute of Allergy and Asthma Research (SIAF)

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-05-medicine-und-life-sciences#resultat>)

## **Blood speaks: Uncovering biomarkers to decode eosinophilic esophagitis**

Original abstract title: Identifying active vs. inactive eosinophilic esophagitis through blood-based biomarkers

Manal Bel imam<sup>1</sup>, Luc Biedermann<sup>2</sup>, Philipp Schreiner<sup>2</sup>, Andrea Kreienbühl<sup>2</sup>, Anja Heider<sup>1</sup>, Mübeccel Akdis<sup>1</sup>, Alex Straumann<sup>2</sup>, Willem van de Veen<sup>1</sup>

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### **Background**

Eosinophilic esophagitis (EoE) is a chronic, immune-mediated inflammatory condition that has shown increased prevalence in recent decades. The esophagus of affected patients is characterized by rings and furrows and severe cases can result in esophageal narrowing. The esophageal barrier serves as the primary site of inflammation, marked by the recruitment of more than 15 eosinophils per high power field (eos/hpf), in an area physiologically devoid of these cells. Diagnosing and monitoring EoE currently require invasive endoscopies due to the lack of non-invasive biomarkers.

### **Aim**

Our objective is to identify plasma biomarkers capable of distinguishing between active and inactive EoE states to facilitate disease monitoring.

### **Method**

We collected blood samples from 142 EoE patients at the University Hospital Zurich and categorized them into active EoE (>15 eos/hpf) and inactive EoE (<15 eos/hpf). Using the Olink biomarker discovery system, we analysed the expression of 360 proteins in plasma samples from 77 EoE patients and 11 healthy controls.

### **Results**

We identified 56 proteins that were differentially expressed in the groups (active EoE, inactive EoE and healthy controls). Among these, 17 proteins were significantly higher in the active EoE subgroup, including CCL4, TRANCE, and TRAF2. Only 1 protein, ATP6AP2, was higher in the inactive EoE subgroup compared to the active one.

### **Conclusions**

Our analysis identified potential plasma biomarkers in EoE patients. To validate these findings, we will perform a targeted analysis of the proteins in a confirmation cohort. Additionally, we will assess their presence in the esophageal biopsies of the same patients to clarify their origins and better understand the mechanisms underlying the disease. Our research will provide valuable insights into EoE pathophysiology, while improving patients' lives by reducing the number of endoscopies.



## **What is the function of B cells in eosinophilic esophagitis?**

Original abstract title: The role of B cells in the pathogenesis of eosinophilic esophagitis

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Eosinophilic esophagitis (EoE) is a chronic inflammatory disease characterized by esophageal inflammation, resulting in difficulty swallowing and esophageal dysfunction. It affects all age groups and the overall incidence rate has increased during the past decades worldwide, and is currently estimated at 32.2 per 100,000 in Europe. Current available treatments include drugs such as topical corticosteroids, proton pump inhibitors, elimination diets, elemental diet and dilation therapy. Food and aeroallergens are the primary triggers of EoE which stimulate eosinophils, T cells, mast cell, dendritic cells and other inflammatory cells to express type 2-biased mediators and cytokines, impaired esophageal barrier and activated further inflammation. So far, research focused on the role of B cells and antibodies in EoE remains limited. However, it has been demonstrated that food specific antibodies are elevated both in serum and in esophageal biopsies of EoE patients. Indicating that, B cells, IgE and IgG4 may contribute to the pathophysiology of EoE.

This project is focused on the role of B cells in eosinophilic esophagitis, the main purpose and methods of this research can be divided into the following parts: (1) Interrogation of interactions between B cells, T follicular helper cells and eosinophils in EoE in vivo and in vitro. To assess this, purified B cells subsets from PBMCs of healthy donors will be exposed to TSLP and IL-33 in combination with known B cell activation factors such as CD40L, CpG, BCR crosslinkers. We will use bulk RNAseq, flow cytometry, and targeted proteomics approached to assess the response of B cells to these stimuli. We will co-culture epithelial cell organoids with B cells and expose them to supernatants mentioned-above. To determine whether B cells in a type II environment have an effect on the epithelium, we will expose esophageal epithelial cells to supernatants of B cells stimulated with type-2 immune-cytokines.

We will analyze the effect on the epithelial barrier by transepithelial resistance (TEER) measurements using a microfluidics-based organ-on-a-chip system. The cellular response will be assessed through bulk RNAseq of esophageal epithelial organoids. (2) Exploring the interaction between T<sub>H</sub>2 and B cells in type II immune responses in EoE. We will assess the capacity of B cells to undergo classic switch recombination (CSR) to IgE and other immunoglobulin isotypes, plasma cell differentiation, and development of different effector B cell types. To achieve this, we will use B cells isolated from healthy donors as well as active and inactive EoE patients, stimulate with CD40L + IL-4 with or without IL-21 and with or without IL-9 and IL-10, Flow cytometry, ELISA RT-qPCR-based quantification will be used to analysis the changes and development of B cells. (3) Elucidate the pathophysiological mechanisms underlying Food-induced Immediate Response of the Esophagus (FIRE) which is a newly identified EoE phenotype.

A pilot project will provide FFPE esophageal biopsies from 53 EoE patients with and without FIRE, we will use more in-depth tissue analysis like visium spatial and Hyperion mass spec imaging to provide a more in-depth characterization of the immune cell composition and their spatial distribution in tissue.

### **Extracellular vesicles for biomarker discovery in EoE patients’ plasma**

Original abstract title: Characterization of extracellular vesicles in the peripheral blood of Eosinophilic Esophagitis patients

Nicolò Marchi<sup>1,2</sup>, Mel Diedro<sup>1,2</sup>, Dagmar Duijzer<sup>3</sup>, Paola Martinez Murillo<sup>1</sup>, Patrick Westermann<sup>3,4</sup>, Christoph Messner<sup>3,4</sup>, Luc Biedermann<sup>5</sup>, Alex Straumann<sup>5</sup>, Pierre-Yves Mantel<sup>1</sup>

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Eosinophilic esophagitis (EoE) is a Th2-mediated chronic inflammatory disorder, whose main hallmark is the recruitment of eosinophils into the esophagus, resulting in chronic inflammation, difficult swallowing, food impaction, and esophageal dysfunction. The prevalence of EoE has increased significantly worldwide, drawing more attention to this disease in the recent years.

Currently, EoE’s diagnosis and disease monitoring are based on histopathologic analyses which require repeated endoscopies and biopsies, representing expensive and invasive approaches for the patients.

Therefore, there is an urgent need for novel technologies based on easily accessible biomarkers, that can be detected in the patients’ blood.

Compelling evidence has demonstrated the central role of epithelial barrier dysfunction in the pathophysiology of EoE, both in skewing the immune system towards allergic inflammation and in enabling the penetration of relevant antigens into the esophageal mucosa, leading to the above-mentioned symptoms. Moreover, numbers of inflammatory cells are increased in the affected epithelial space. Several single-cell RNA-Seq studies have further confirmed that epithelial cells, eosinophils, T lymphocytes (in particular a subtype of Th2 cells), mast cells, B lymphocytes and plasma cells are found in the lesions and might participate to the development of the disease. Interestingly, all these activated cells have the potential to secrete extracellular vesicles (EVs) that might be then found in the blood circulation. EVs are a heterogeneous group of small vesicles involved in a great variety of physiological and pathological functions, which are released in the blood circulation by every cell type in the body and contain many different molecular cargoes derived from their originator cells. For this reason, there is growing attention to use them as biomarkers for difficult-to-diagnose cancers, such as pancreatic, prostate, or glioblastoma.

We are developing and validating a protocol to isolate EVs from plasma based on size exclusion chromatography (SEC). The quality of the isolated-EVs is validated by Transmission Electron Microscopy and Western Blotting to check for the presence of typical EV-markers and plasma protein contaminants. Here, we propose to characterize EVs in EoE patients’ plasma by Mass-spec based proteomics. We will use a cohort of about 100 patients for our discovery cohort. We will compare the EVs from this cohort with healthy controls. With this data, we will build a prediction model based on machine learning to identify a protein signature that identifies the disease. Our predictive model will then be validated by using a validation cohort, made of different patients than the ones included in the discovery cohort.

Friday, November 8

15:45-16:45

**Session 6    Medicine and Life Sciences**

Chairs: Sibylle Grad / AO Research Institute Davos, Willem Van de Veen / Swiss Institute of Allergy and Asthma Research (SIAF)

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-06-medicine-life-sciences#resultat>)

## **A mechanical stimulated 3D in vitro model for treating osteoarthritis**

Original abstract title: Human joint-in-lab: a coculture 3D model to investigate mechanisms and therapeutics of osteoarthritis

Huan Meng<sup>1</sup>, Sophie Verrier<sup>1</sup>, Sonja Häckel<sup>2</sup>, Sibylle Grad<sup>1</sup>, Zhen Li<sup>1</sup>,

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### **Introduction**

Osteoarthritis (OA) is a chronic degenerative joint disease which is currently one of the leading causes of disability in the elderly. Currently there is no effective cue for OA and the investigations for new therapeutics are limited due to the lack of accurate *in vitro* models. Recent studies showed that the pathological vascularisation in subchondral bone, as known as subchondral angiogenesis, plays a vital role in the degradation of cartilage tissue, which is the main pathological change in osteoarthritis. We hereby aim at developing a bilayer 3D OA model, containing a cartilage layer and a subchondral layer, as a platform for better understanding the OA mechanisms and accurately testing new targeted therapeutics.

### **Methods**

For the development of the cartilage layer, chondrons were reproduced by stimulating pericellular matrix production of primary human OA chondrocytes in alginate gel. Then chondrons were harvested by dissolving the alginate gel and were characterised by immunofluorescent staining of collagen VI. The comparison of the isolated chondrocytes and the reproduced chondrons in the catabolic and chondrogenic activity as well as the inflammatory response to IL1 $\beta$  were tested at corresponding gene-expression level by qPCR technique.

For the development of the subchondral layer, primary human umbilical vein endothelial cells (HUVECs) were cultured in fibrin-polyurethane (PU) scaffolds +/- pericytes in Endothelial Growth Media 2 (EGM2). Then the vascularisation was analysed by the quantification of micro-tubular structures in histology images.

Finally, the coculture conditions were tested by combining cartilage layer and subchondral bone layer and cocultured in EGM2 media, chondropermissive (CP) media or 50%/50% EGM2/CP media. Cell morphology and viability were analysed by Calcein AM/ ethidium homodimer (EthD-1) assay.

### **Results**

The reproduction of chondrons were confirmed by over 99% of chondrocytes with positive collagen VI staining. Compared to isolated chondrocytes, the reproduced chondrons in PU scaffolds showed significant elevated COL2 and ACAN expression in the absence of IL1 $\beta$ ; while with IL1 $\beta$  treatment, the reproduced chondrons had upregulated COX2 expression. Compared with HUVECs-scaffolds, the number and area of tubular structures showed a significantly increase in pericyte-HUVEC coculture scaffolds.

The chondrocytes and HUVECs/pericytes in coculture in CP/EGM2 mixed media did not show major viability loss.

### **Conclusion and discussion**

In the cartilage layer, the reproduced chondrons in 3D scaffolds had elevated matrix production and upregulated inflammatory response. In the subchondral layer, coculture of pericytes significantly promoted angiogenesis of HUVECs. Coculture of both layers in mixed media did not show any compromised cell viability.

Therefore, our bilayer cartilage/subchondral coculture model offers a novel "joint-in-lab" platform for the deeper understanding of subchondral bone angiogenesis and cartilage degradation related OA mechanisms and for the development of targeted therapeutics. Future enhancements of our model will involve further optimisation of coculture conditions and the application of mechanical loading mimicking multiaxial joint movements, using our unique cartilage bioreactor.

## High-throughput proteomics in lymphoma - mechanistic insights and clinical applications"

Lopamudra Chatterjee<sup>1,2,3</sup>, Patrick Westermann<sup>1,3</sup>, Christoph Messner<sup>1,2,3</sup>

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Lymphoma is a term for cancers that start in the cells of lymph system. Lymphomas account for 5% of all cancers globally and are a significant concern in the spectrum of hematologic diseases. Non Hodgkin Lymphoma (NHL) makes up the majority of lymphoma cases, accounting for approximately 85-90%, while Hodgkin lymphoma is rarer. Among different NHL types, B-cell NHL are more prevalent than T-cell NHLs. Over the last decade, genome based research have identified multiple types and subtypes of lymphomas. However, there are still several key questions about the onset and progression of the disease that remain unanswered. Lymphoma diagnosis, which relies mostly on immunophenotype and morphology, is challenging even for experts because of the disease's intricate mutational landscape. Another major concern in the field of lymphomas is that a significant number of patients cannot be treated with the current treatment methods that include: chemotherapy, radiotherapy, antibodies, kinase inhibitors and Chimeric Antigen Receptor T-cell (CAR-T cell).

Proteomics plays a crucial role in understanding disease characteristics, as alterations in protein expression, modification, and interaction are fundamental to the development and progression of diseases. However, proteomic analysis of lymphomas has been limited thus far primarily due to the technical challenges associated with it.

At the Precision Proteomics Center Davos, we currently have a very robust and sensitive mass spectrometry based approach that can process thousands of patient samples in a month. Our platform is compatible with different sample types like cells, plasma, serum as well as fresh-frozen and formalin fixed paraffin embedded tissue materials. Additionally, to aid with clinical translation, we are currently developing absolute quantification assays for different disease biomarkers, starting with lymphoma. With our technology, we want to generate the largest known proteomic repository of lymphoid malignancies.

The platform will serve as a proteome database encompassing the broadest possible range of B- and T-cell lymphomas. We expect that the comprehensive proteomic information along with molecularly annotated clinical data, will simplify the diagnosis of various lymphoma types and subtypes. Our current focus is mainly on more common lymphoma types like Chronic Lymphocytic Leukemia (CLL), Follicular Lymphoma (FL), Mantle Cell Lymphoma (MCL) and Diffuse Large B-Cell Lymphoma (DLBCL). In the later stages, we will then move onto diagnostically challenging and rarer lymphomas like T cell-Non Hodgkin Lymphoma (T-NHL) and Marginal Zone Lymphoma (MZL). The large-scale analysis of lymphomas using our robust proteomic platform should also enable the application of the database in clinical settings and potentially for routine diagnostics.

To further support clinical diagnostics, we are also conducting mass-spectrometry based drug perturbation assays. Proteomics can potentially measure the molecularly defined targets that the drugs are dependent upon. In the recent times, mass spectrometry has become the most comprehensive approach for proteome-wide characterization of drugs. It can be used to study both effectiveness of drugs and its underlying mechanism of action. These studies can also reveal biomarkers associated with drug response and resistance.

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We are currently investigating how the proteome changes over time in response to drug treatment. Our aim is to identify early response biomarkers that predict treatment efficacy or resistance by comparing patient proteomic profiles at different time points after treatment.

We believe that using our expertise in high throughput proteomics and bioinformatics we will be able improve the diagnostic landscape of lymphomas, paving the way for personalized medicine and better treatment outcomes.

## Metabolic Regulation of Epithelial RIG-I Signaling in Viral Exacerbations of Asthma

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### Introduction

Rhinovirus (RV) infection of airway epithelial cells from patients with asthma results in an abnormal engagement of retinoic-acid inducible gene I (RIG-I) into RIG-I inflammasome formation, which subsequently delays RIG-I dependent interferon (IFN) type I/III responses and enhances proinflammatory signaling in asthma. The exacerbation-prone asthma has been linked with metabolic dysfunctions, however, the metabolic regulation of antiviral responses during those pathogenic viral infections in asthma is not well understood.

### Methods

Basal and differentiated human bronchial epithelium from patients with asthma and healthy controls upon RV were used to analyze the metabolic regulation of RIG-I-dependent signaling with the use of functional metabolism assessment (Seahorse), untargeted proteomics, and small molecule inhibitors of metabolic pathways followed by ELISA, RT-qPCR, WB, and confocal microscopy. Bronchial brushings from the *in vivo* RV infection model were analyzed gene array and pathway analysis.

### Results

Bronchial epithelium of patients with asthma upon RV infection demonstrated increased glycolytic ATP and decreased mitochondrial ATP production, indicating, in contrast to healthy epithelium, continuous reliance on glycolysis for ATP production in asthma. RV infection of bronchial epithelium upregulated expression of molecules involved in metabolic pathways, such as glycolysis, TCA cycle, and oxidative phosphorylation (OXPHOS). Additionally, we determined that RIG-I expression and RV-induced RIG-I inflammasome activation are tightly regulated by glycolysis and OXPHOS. Glycolysis was an energy source for rhinovirus infection and RIG-I inflammasome activation. On the other hand, OXPHOS fueled IFN production. Importantly, functional inhibition of the OXPHOS pathway led to increased RIG-I inflammasome activation. Those *in vitro* mechanistic data were confirmed *in vivo* in transcriptomics of bronchial brushings of asthma patients and healthy controls experimentally infected with RV. In asthma, upregulated glycolysis-HIF1A pathway corresponded with increased inflammasome signaling and lack of viral clearance, whereas in healthy controls significantly downregulated OXPHOS corresponded with downregulation of type I/III IFNs and efficient viral clearance.

### Conclusions

There is a strong link between aberrant metabolic reprogramming signaling in epithelium with inefficient antiviral response in asthma. It might further influence epithelial response to subsequent infections with other respiratory viruses, such as SARS-CoV-2.

## **Developing a new platform for drug delivery**

Original abstract title: Extracellular vesicles for drug delivery

Hadja Simboro<sup>1,2</sup>, Nicolò Marchi<sup>1</sup>, Klara Eriksson<sup>2</sup>, Bibin Subramanian<sup>2</sup>, Mel Diedro<sup>1</sup>, Paola Martinez Murillo<sup>2</sup>, Pierre-Yves Mantel<sup>1, 2</sup>

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The landscape of drug delivery has evolved significantly with the development of various synthetic nanoparticulate systems aimed at enhancing the properties of therapeutics. While liposomes, polymeric nanoparticles, and dendrimers offer targeted drug release, they come with limitations. Viral vectors, including adeno-associated viruses (AAVs), adenoviruses (Ads), and lentiviruses (LVs), have shown efficiency in gene delivery but face safety concerns and production challenges. Lipid nanoparticles (LNPs), such as liposomes and solid lipid nanoparticles (SLNs), offer advantages like biocompatibility and enhanced drug-carrying capacity but struggle with precise control over release kinetics and limited loading capacity. Extracellular vesicles (EVs) are a heterogeneous group of small vesicles released by almost every cell that can transfer functional cargoes between cells. Comprising exosomes, microvesicles, and apoptotic bodies, EVs circulate in the body and cross different barriers to reach specific cells in tissues. They reach target cells through fusion with the cellular membrane of recipient cells, endocytosis, and also receptor-ligand interaction ways. EVs contain many different molecular cargoes such as proteins and nucleic acids derived from their cells of origin. Therefore, EVs can be seen as a natural drug delivery system. Of particular interest, are EVs released by red blood cells (RBCs). Indeed, RBCs harbor several advantages since they are poorly immunogenic and do not contain DNA.

Here, we propose to develop a drug delivery system based on EVs. We are focusing on the optimization of cargo loading and targeting by using HEK and K562 cells. Ultimately, we want to use EVs secreted by red blood cells derived from induced pluripotent stem cells.

For the stable expression of the exporter, we are generating plasmids that contain the exporter gene and express GFP reporter genes, that will be used for the selection of transfected cells. Then we will use the Cre recombinase as a cargo. HEK293 and K562 cells will be transduced and the cells expressing the transgenes will be sorted by Flow Cytometry. We will also use RNA sequencing to measure the specific enrichment of the RNA cargo in EVs versus the total RNA content of the cells. Then we will generate cell lines expressing the targeting nanobodies: anti-EGFR and anti-Her2 nanobodies. EV binding to cells expressing the EGFR or HER2 will be tested by flow cytometry and microscopy. To test the delivery of Cre-encoding mRNA by the donor cells, we will measure the export of RNA from the donor cells and the transfer to the receiver cells, which will activate GFP expression upon Cre recombination.



Friday, November 8

15:45-17:00

**Session 7    Natural Sciences, Robotics, and Photonics**

Chairs: Hannes Merbold / University of Applied Sciences of the Grisons , Matthias Müller / Pädagogische Hochschule Graubünden

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-07-natural-sciences-technology-robotics-photonics#resultat>)

## **Monocular visual odometry**

Original abstract title: Determining the Position of Moving Vehicles Using 2D Camera Imagery: A Keypoint Tracking Approach for Visual Odometry

Mirco Seeli<sup>1</sup>, Tim Barmettler<sup>1</sup>, Joel Flepp<sup>1</sup>, Micha Gelencsér<sup>1</sup>, Sandro Rey<sup>1</sup>, Philipp Roebrock<sup>1</sup>, Udo Birk<sup>1</sup>

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### **Abstract**

In this paper, we investigate the reliability of methods for determining the position of moving vehicles such as cars or drones relative to their origin using images acquired from a 2D camera attached to the moving object. Our software employs keypoints extracted from these 2D images and tracks these keypoints across subsequent images. For this purpose, we evaluate two methods: (a) determination of the field of expansion by analyzing the vanishing point of lines drawn between matching keypoints in consecutive images, and (b) extraction of the essential matrix to derive the transition matrix for the camera's extrinsic parameters (position and orientation). Additionally, we investigate the robustness of these methods in the absence of ground truth position data, such as GPS information. The shift in the position data as extracted by our method in combination with the image acquisition times provides an estimate of the vehicle velocity, yielding visual odometry. We visualize the results to illustrate the effectiveness of our approach and discuss challenges such as environmental factors and camera calibration inaccuracies.

### **Introduction**

The determination of a moving vehicle's position is a critical task in various applications, including autonomous driving, drone navigation, pedestrian tracking, and odometry. Traditional methods rely on GPS; however, in environments where GPS signals are weak or unavailable, alternative methods become necessary. Recent advancements in computer vision have enabled the use of 2D cameras for this purpose. This paper explores two such methods: the field of expansion and the essential matrix extraction. These methods are particularly relevant for visual odometry, where the objective is to estimate the vehicle's trajectory over time using camera images.

### **Methodology**

We make use of a four steps approach: First, we extract keypoints from each image using a robust feature detector from the opencv library such as ORB or SIFT. Second, we track keypoints across consecutive images using a feature matcher, ensuring high accuracy in the presence of environmental changes. For this, we either use a brute force keypoint matching approach or a methodology termed optical flow, implemented in the opencv image processing library. From the matches of two consecutive images, we then determine either the Field-of-Expansion (FoE), i.e. the position of the perspective vanishing point by drawing lines between matched keypoints in consecutive images and calculate the direction and magnitude of motion from the FoE. Or we directly estimate the essential matrix from matched keypoints using the five-point algorithm. In the latter approach, we derive the transition matrix for the camera's external parameters to determine the vehicle's trajectory.

### **Results**

We validated our method using both simulated and real-world datasets, including sequences captured from moving cars and drones. Our approach demonstrated high accuracy in trajectory estimation, with performance metrics compared against ground truth data obtained e.g. from GPS or from street maps when available.

### **Discussion**

Challenges such as environmental factors and camera calibration inaccuracies were observed. Techniques to mitigate these issues include advanced filtering methods and

adaptive calibration procedures. Future work will explore integrating additional sensor data to enhance robustness.

### **Conclusion**

This paper presents an effective method for determining the 3D position of moving vehicles using 2D camera imagery. Our keypoint tracking approach together with the two methodologies investigated for position extraction, shows promise in scenarios where GPS data is unavailable. This method is particularly suitable for visual odometry applications, offering a reliable alternative for estimating vehicle trajectories. Continued advancements in feature detection and matching algorithms will further improve the reliability and accuracy of this method.

## Davos - Digital analysis of townscapes in GIS

Original abstract title: Digital analysis of townscapes

Oliver Hänni<sup>1</sup>, Stefano Balestra<sup>2</sup>, Sandra Bühler-Krebs<sup>1</sup>, Ralf-Peter Mundani<sup>2</sup>, Mirco Blöchlinger<sup>1</sup>, Marc-Alexander Iten<sup>3</sup>

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Settlements in the alpine region have been experiencing a constant change due to socio-economic and social processes. Urban development and *Baukultur* have been active research areas for many years. The Institute for Construction in Alpine Regions (IBAR) at the University of Applied Sciences of the Grisons has developed a tool (*Baumemorandum*) for architecture offices and municipalities that works as guidelines for assuring quality in design and urban development in critical, historical areas. The *Baumemorandum* consists of three elements: fundamentals, context memorandum, and facade memorandum. These are available in printed form. Since most of the essential information for construction projects are today provided by a geographic information system (GIS), it is therefore beneficial to make this tool digitally available within such systems.

By making this tool accessible directly from GIS, the municipality's decision-making process becomes more transparent, and the planning entity can take neighbouring buildings into account. Viewing the planned project in the context of its neighbourhood, spatial connections, design relationships, and architectural exceptions can be considered. As part of this research project, the representation of spatial relationships and the typical characteristics as architectural principles will be automated.

Discovering patterns and geometrical relationships within image data is a distinct strength of deep learning methods. Knowledge is transferred by domain experts annotating multiple masks on point-cloud data collected specifically for this use case. Therefore, creating a customised dataset on which the deep learning algorithms can learn to find design relationships. The deep learning method will be combined with the analogous tool (*Baumemorandum*) to replace time-consuming drawing work and avoid manual errors. The processed data serves as a basis for validation and interpretation by domain experts. Integrating this process and tool into GIS enables usage in a larger context and opens further research questions.

Combining regulations, specifications, and information important to urban development into a single information channel (GIS) is a desirable goal. In the best case, this streamlines decisions and new development, as well as supports decision makers and architects. The digital *Baumemorandum* creates legal certainty, particularly with regard to the question of appropriate integration into the townscape. As a partner of the Innosuisse project, Davos Monstein will be the first municipality to implement the digital *Baumemorandum*.

There are some limitations to this technology, for example, the detection of structures important for spatial connections and design relationships is highly dependent on the quality of data. Furthermore, is it very difficult to find aesthetically pleasing architectural patterns if they have not been trained before. Therefore, artificial intelligence will never decide on its own what is beautiful. However, artificial intelligence will be able to recognize the extent to which a new building is able to take up the typical characteristics of a specific village or city centre. In the end, decisions will still be made by the building authorities and the population. Currently and in the future, there continuous to be a collective interest in ensuring the quality of local living and working environments and retaining the identification with it. The concept of City Information Modelling (CIM), a combination of building data (BIM) and terrain data

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(GIS) with other information sources, works with digital city models to allow future planning to be simulated using a digital twin on district or city level to help the urban development achieving this.

## **Avalanche Safety for Roads: Probability maps of avalanche run-out distance**

Julia Glaus<sup>1,2,3</sup>, Lukas Stoffel<sup>1</sup>, Pia Ruttner-Jansen<sup>1,2,4</sup>, Johan Gaume<sup>1,2,3</sup>, Yves Bühler<sup>4</sup>

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In the Swiss Alps, roads leading through avalanche hazard zones need to be assessed on a daily basis during winter by local hazard experts to decide whether crossing by car is still safe. Crucial decisions that may cut off a lifeline or have significant economic consequences must be made by experts based on experience, weather station data, and gut feeling. In this time of change, experienced experts are retiring, job changes are more frequent, and transferring knowledge about specific roads is becoming increasingly difficult. To address this challenge, we aim to provide maps that combine weather station data and avalanche simulations to show how far and with what intensity an avalanche might evolve on a specific day. We will focus on the maximum pressure and height of the avalanche. These maps can give practitioners an additional perspective on the daily situation and provide a compact overview of avalanche danger.

In the first step, we need to identify a simulation tool capable of calculating different types of avalanches, such as wet and cold avalanches. The tool must be able to simulate the dense flow of an avalanche and, if present, the powder cloud. Traditionally, avalanche simulation tools are used for hazard mapping to show the maximum spread of an avalanche. In our case, we need a tool sensitive enough to represent the daily conditions, given by input values as the snow distribution in the avalanche track, the erosion potential and temperature distribution in the snow.

Next, we will analyse an avalanche cycle from 2019 at Braemabühl in Dischma valley, located in Davos, Switzerland. Three cold avalanches were artificially released, and the dense part of all avalanches reached the Dischma while the clouds with high pressure went till the counter slope. Using our system, we will simulate these avalanches using only the weather station data and forecasts from the day before and do the prediction. Since we have photogrammetric measurements of these events taken by a drone flight, snow pits close to the release are and pictures of the powder cloud, we can compare our simulations to the measured dimensions of the avalanches. This unique data set allows a robust assessment of our modelling results.

Given the high uncertainty of input parameters such as snow distribution on the slope, temperature, and release zone location, we will improve the simulation by running multiple simulations per avalanche track with varied input parameters. For the location of the release zones, we take the proposed zones from the large scale hazard indication tool developed at SLF. We will then calculate the probability of the avalanche reaching the road from this set of simulations.

As the data availability for such a tool strongly depends on the region and infrastructure, we calculate two different scenarios: one where we calculate the avalanche runout based on the weather forecast from the evening before and another map based on the automatic weather stations nearby the avalanche track.

Currently, we have identified a suitable simulation tool called RAMMS::EXTENDED that meets our expectations. We have successfully predicted the Braemabühl event and created the first probability maps for that day. The next step is to apply the system to other events and automate the pipeline from obtaining weather station data to simulating avalanches and

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post-processing the information to generate daily condition-based probability maps.

## **Avalanche Safety for Roads: Mapping and Monitoring Snow Depth Distribution in an Avalanche Release Area**

Pia Ruttner-Jansen<sup>1,2,3</sup>, Julia Glaus<sup>1,2,4</sup>, Annelies Voordendag<sup>3</sup>, Yves Bühler<sup>1,2</sup>

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Avalanches are a danger to people and infrastructure in mountainous regions. There are different risk mitigation measures, such as avalanche defence structures, artificial avalanche releases, hazard indication maps or the temporary closure of traffic routes. The latter, for example as closure of roads can have a drastic impact on people and economy. The aim is therefore to have the closure as short as possible, but still as long as necessary. The decision on whether to close or open a road is taken by local experts, relying on the weather forecast, the avalanche bulletin, if available, local weather stations and most importantly on their personal experience. One important factor influencing the assessment of the situation is the amount of wind-blown snow in the slopes, which can be derived from the spatial variation of snow depth. However, up to date data with high spatial resolution is rarely available.

In this project we present our newly developed system, that is mapping and monitoring the snow depth distribution in an avalanche release area with high spatial (cm-dm) and temporal (hourly) resolution. The main sensor is a laser scanner, which is permanently mounted on a measurement mast, covering an area of approximately 14'500 m<sup>2</sup>. Additionally, we are using a camera for a visual impression and interpretation of the processes in the monitored area. The measurement mast also contains several meteorological instruments (wind speed and direction, relative humidity and air and snow surface temperature), which are needed for snow depth modelling approaches. The measurement system operates fully autonomously, transferring the data to a local server in (near) real time. As a first test case we installed two measurement masts to monitor the release area of the “Wildi” avalanche, at Brämabüel, the north side of Jakobshorn in Davos in October 2023. The Wildi avalanche can reach the road in the Dischma valley, which had to be closed several times in the past years.

After the first operating season we are able to show snow depth distribution maps with high spatial and temporal resolution. Our analysis shows that we can quantify small temporal changes of average snow depth between measurement epochs for small areas (1m<sup>2</sup>). This includes several avalanche events, where we can estimate the release depth and volume. A comparison with state-of-the-art snow depth distribution mapping, using photogrammetric drones, shows a good agreement on a low cm level.

The newly developed system and continuously build up snow depth database delivers a unique dataset from an avalanche release area. Using the additionally recorded meteorological parameters we are working on modelling approaches to predict the snow depth distribution at arbitrary times and also upscale to other and larger areas. The obtained information from avalanche release areas is crucial for the further development and refinement of avalanche simulation approaches. All information is planned to be available on an information platform to aid the practitioners in their decision on road closures and openings.



## **Solid Geometry Modelling: 3D printing helps to find more than one solution.**

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### **Motivation**

The engagement with a fascinating geometric problem involving the creation of a three-dimensional solid model can be traced back to the 18th century: The goal is to find a solid that has a circular base, looks like a triangle from one side, and like a square from the other. The appeal of the problem has not diminished over the years; Mathematicians and mathematics educators are still engaged with similar or slightly modified versions of it. Peter Friedrich Catel was the first, who described the problem in his book “Mathematisches und physikalisches Kunst-Cabinet” in 1790 [1]. As a precision mechanic and toy manufacturer from Berlin, he crafted a board made of plum wood, which was equipped with three openings and is referred to as “The Mathematical Openings” [5].

### **Historical Background**

Despite the addressed solution to this problem in the aforementioned book the Hungarian mathematician George Pólya revisited the problem 200 years later in his book “How to Solve It” in 1966. In it, the sought-after solid is referred to as a universal plug [2, p. 200]. The problem is formulated in a very similar manner. Therefore, three conditions are given which the sought solid must apply [2, pp. 200]. In our contribution we follow this description of the problem, and we call the sought-after solid “universal plug” such as other authors before [3, 4]. However, as the name might suggest, there is no unique solution. Echoing the mentioned historical instances, the problem hints at a singular solution. In fact, there are infinitely many solids that satisfy the mentioned conditions.

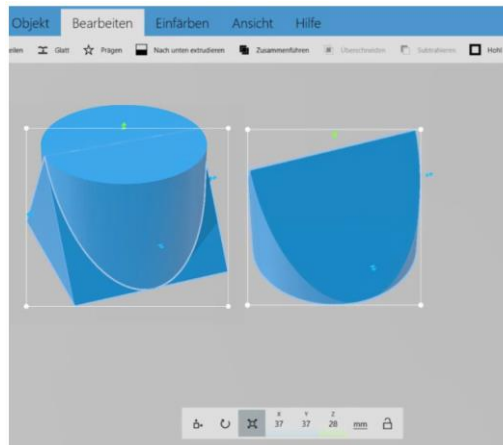
### **Mathematical Background**

In our contribution we investigate the possibility of multiple solids satisfying the geometric problem's specified conditions. We aim to identify and compare the volumes of these qualifying solids. Assuming, that we limit ourselves to convex solids, these can be ordered by their volume. Thus, a solid with the minimal volume and a solid with the maximal volume can be found, which can be considered as the boundaries of a continuum within which all convex solutions can be identified.

### **Comparison of methods (against the background of learning environments)**

The approaches to volume determination of these solids can be illustrated through the creation of models using different methods. As a tactile method to illustrate the infinite number of solutions, shaping the models with modeling clay based on a framework with the three shapes (circle, square, triangle) is suggested. A suitable analog method to create the universal for younger learners is the use of playdough. A framework made of cardboard helps also modelling different versions of the universal plug such as the one of maximal volume. As an analog method creating a universal plug of minimal volume, layering cardboard cuts is recommended. Both methods are suitable for learners of all ages to deal with the given problem.

Of course, 3D printing can be one suitable approach. Especially in computer-based learning environments it might be the best option. One handy software is “3D Builder”, which is easy to use for younger learners. A 3D model of the universal plug of maximum volume could be designed easily in this way (see Fig. 1). A 3D model of the universal plug of minimum volume is much more difficult to design and requires the use of a different program such as “Thinker CAD”. In our contribution we describe all approaches of modelling different solids and compare advantages of the different methods against the background of suitable learning environments for learners of different ages.



**Fig. 1.** Using Microsoft 3D Builder to design a universal plug of maximum volume.

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Saturday, November 9

10:15–11:45

**Session 8    Vielfältige Forschung - Vorträge auf Deutsch**

Chairs: Oscar Eckhardt / Institut für Kulturforschung Graubünden, Peter Bebi /  
WSL Institute for Snow and Avalanche Research SLF

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-08-gemischte-disziplinen-deutsch#resultat>)

## **Semiotics of the Mountain Forest in 20<sup>th</sup> Century Literature from Graubünden**

Deutsch: Bergwälder als Bedeutungsträger in der Bündner Literatur des 20.

Jahrhunderts

Michael D. Schmid<sup>1</sup>

<sup>1</sup> Universität Zürich / Institut für Kulturforschung Graubünden (ikg)

There are different perspectives on the alpine space and landscape of Graubünden in 20<sup>th</sup> century literature. A particularly interesting type of landscape is the mountain forest, as it functions not only as a scenery for diegetic actions, but has specific semiotic connotations of cultural kind. Especially in the romansh literature, trees and forests are important symbols for the cultural identity and resistance. Two examples from engadinian writers may illustrate that. They are both dealing with cultural semiotics and even an anthropomorphisation of the trees.

A great example is the famous poem *Tamangur* (1923), written by Peider Lansel. It describes an old arolla pine forest called “Tamangur” way up in the Val S-charl. The arolla pine often grows in high alpine zones on rocky grounds and has an extraordinary strength against wind and weather. These characteristics make that tree a perfect symbol for the romansh culture, which, according to Lansel’s poem, is also deeply connected with and “rooted” in the high mountain regions, and need to be strong against external influences as well. Wind and weather stand semiotically for the foreign cultural influences that threaten the Romansh. The loneliness of the forest stands for the isolation of the romansh community due to emigration. The age of the wood represents the ancient dignity, that makes it worthy to stand against the threats and defend the local language and culture. Thus, the mountain forest serves as a multi-levelled symbol of the people of romansh Graubünden and their collective cultural identity.

The motif of the mountain forest as a bastion against change has been retaken by many authors from romansh Graubünden. The tale *La jürada* (1967) from Jon Semadeni for instance, shows a complex reflection of the dichotomy of conservative and progressive approaches onto culture. The plot narrates the life of a young forester in a mountain village. As he has learned at university, the forest has to be rejuvenated, to keep him strong. This means, to cut down some older trees and plant younger ones. Obviously, this reflects the idea, that a culture only can be conserved by reforming it and include newer elements – a middle path between the extremes of cutting down all trees (abolish culture and tradition) and leaving the forest untouched, although it grows old and weak (let culture become outdated). The story reflects on the opportunities to handle with tradition and change, and creates by its own poetical aesthetics an innovative artwork between those poles.

Of course, the semiotics of the mountain forest in literature from Graubünden are not fixed and only related on resistance and tradition. Forests appear in stories and poems as

- a space for individual or collective retreat from the every-day’s life
- a magical world of fantasy legends and fairy tales
- a symbol of nature in opposition to civilisation (especially the expansion of tourism and energy infrastructure)
- a religiously connoted space, that symbolises the creation or even the eternal
- an idyllic place for amorous experiences
- a location of traditional economic activities like wood cutting and hunting
- an entity that is protecting, but needs protection as well (cultural and ecological)

This list shows a bright variety of possible cultural meanings, a mountain forest can stand for or being associated with. But all these cultural meanings of forests have something in common: they construct in different and often complex ways the forest as a constant counterpart to the changes of the modern world. The analysis of this literary reflection of the mountain forest can help to understand the complexity of collective and individual cultural identity building.

## **Bark beetle in mountain forests in the canton of Grisons: challenges and opportunities**

Deutsch: Buchdrucker in Gebirgswäldern im Kanton Graubünden: Herausforderungen und Chancen

Theresa Banzer<sup>1,2</sup>, Peter Bebi<sup>1,2</sup>, Simon Blaser<sup>3</sup>, Yves Bühler<sup>1,2</sup>, Marco Conedera<sup>4</sup>, Anna Feller<sup>1,2</sup>, Christian Ginzler<sup>3</sup>, Martin Gossner<sup>3</sup>, Frank Krumm<sup>3</sup>, Concetta Lisella<sup>1,2</sup>, Andrea Minetti<sup>4</sup>, Gianni Boris Pezzatti<sup>4</sup>, Achilleas Psomas<sup>3</sup>, Andreas Stoffel<sup>1,2</sup>, Marco Vanoni<sup>5</sup>, Alessandra Bottero<sup>1,2</sup>

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In the canton of Grisons, approximately 30 % of the total area is forested, providing a wide array of ecosystem functions and services to both the local inhabitants and tourists. However, these mountain forests face growing threats from natural disturbances, notably the European spruce bark beetle (*Ips typographus*). This insect has already caused substantial damage to many spruce forests across Europe. In mountainous regions, rising temperatures accelerate the bark beetle's development, while increased drought frequency reduces tree defences, making mountain spruce forests more susceptible to infestation. Consequently, this poses risks to their protective role against natural hazards, and other ecosystem functions and services.

Given these circumstances, timely planning and effective implementation of control and adaptation measures are therefore crucial tasks for maintaining the protective role and the ecosystem functions and services. To assist various stakeholders in fulfilling their responsibilities, the development of methods for the early detection of both vulnerable and infested trees is essential to limit the extent of bark beetle outbreaks. However, prompt intervention and removal of infested trees are not always feasible. Therefore, at the same time, it is also important to define intervention strategies for the post-disturbance phase to ensure continuity of functions and services.

By focusing on these challenges, we examined six study sites in the canton of Grisons, Switzerland. We are exploring different methods for early detection of bark beetle damage in mountain spruce forests using a combination of multispectral data, field observations, pheromone traps, and real-time data on new infestations. Additionally, we are examining the impact of bark beetle disturbance and subsequent management strategies on the protective effect of these forests against natural hazards like rockfall and avalanches, as well as the occurrence and diversity of tree-related microhabitats as a proxy for biodiversity.

Our results show that different vegetation indices (e.g., NDVI, EVI, VARI) present characteristic patterns for different tree health categories. Most indices show significant differences between healthy trees and trees in a late stage of infestation. In some cases, also the vegetation index values of trees in an early phase of the attack are different from other health categories. The presence of bark beetle-killed trees reduces the protective effect against rockfall by 2 % on average (range 0 - 24 % depending on disturbance severity), mainly due to the lower energy dissipation ability of dead trees. Salvage logging further impairs this protective effect (-12 % on average, range 0 to - 92 %). A similar pattern is observed for the protective effect against avalanches, with salvage logging reducing the protective effect by 8 % (range 0 - 83 %). In terms of potential biodiversity, retaining bark beetle killed trees leads to a greater abundance of tree-related microhabitats. Disturbed areas exhibit on average almost twice as many microhabitats per study site compared to undisturbed sites, with counts of 82 and 42 microhabitats, respectively. Insect galleries, bark losses and bark pockets are mainly observed within areas affected by bark beetle disturbance.

Given the likelihood of increased bark beetle disturbances in mountain forests due to global change, we will face new challenges but also opportunities to maintain the protective function of forests. At the same time, these disturbances will also contribute to increased tree-related microhabitat diversity and abundance, thus enhancing the availability of suitable habitats for forest biodiversity. Our results help to understand the impacts of disturbance in these forests, and support the implementation of proactive measures crucial for sustainable forest management and for preserving their essential ecosystem functions and services.

**Mountain forests in transition: analysing the spatial shift of forest forest regeneration over time**

Deutsch: Bergwald im Wandel: Analyse der räumlichen Verschiebung der Waldverjüngung über die Zeit

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Shorter winters and rising temperatures are altering vegetation conditions in mountain regions, significantly impacting natural forest regeneration. This regeneration is crucial for the adaptability of mountain forests. To better understand these natural processes, further research is essential. Remote sensing, particularly Light Detection and Ranging (LiDAR), has proven to be an efficient and reliable method for forest measurement. HAFL has introduced a LiDAR-based method for detecting forest regeneration, developed and tested in mixed deciduous forests on the Central Plateau.

This paper presents a case study investigating whether climatic changes over the past 20 years have caused a spatial shift in natural forest regeneration. Additionally, it examines the applicability of the HAFL method in quantifying regeneration in mountain forests. Field data from 2003, 2012 and 2022 on regeneration and browsing in the Il Fuorn area of the Swiss National Park (SNP) were analyzed. Topographic factors such as altitude, slope gradient, and exposure were tested as potential drivers of regeneration using Generalized Linear Mixed-Effects Models (GLMM). The study explored interactions between these topographic factors and survey years to determine any spatial shifts over time. The LiDAR-based HAFL method was applied to the study area with various parameterizations, and the results were statistically compared with the field data.

The findings indicate that while the survey year is a significant positive driver for forest regeneration in most models, a spatial shift over time is observed only for mountain pine regeneration, which has moved upslope. The LiDAR method performs well for detecting regeneration between 1.3 and 5 meters but is less accurate for regeneration <1.3 meters. No reliable results were obtained for regeneration <1.3 meters.

The time factor significantly influences the probability of forest regeneration for all tree species except spruce, with an overall increase in sites with existing regeneration over time. Due to the varying spatial distributions of the analyzed tree species, cross-species statements are not feasible. Only pine regeneration has shown a spatial shift, moving upslope. With parameter adjustments to local conditions, the HAFL LiDAR-based method yields good results for regeneration between 1.3 and 5 meters. For detecting regeneration <1.3 meters, it is advisable to supplement LiDAR data with other sources and explore alternative methods.

## **Increased number of Th1 cells and monocytes is associated with infected non-union in patients with long bone fracture**

Deutsch: Bestimmte Immunzellen unterscheiden Patienten mit infizierten Knochenbrüchen von geheilten Kontrollpersonen

Pia Fehrenbach<sup>1,2</sup>, Ferdinand Weisemann<sup>1,3</sup>, Claudia Siverino<sup>1</sup>, Katharina Trenkwalder<sup>4,5</sup>, Laura Bürgli<sup>6</sup>, Simon Hackl<sup>1</sup>, Sebastianus A. J. Zaat<sup>2</sup>, Esther C. de Jong<sup>2</sup>, T. Fintan Moriarty<sup>1</sup>

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Approximately 36 million surgeries for bone fracture repair happen annually. However, up to 10% of fractures suffer from delayed healing or non-union. Bone fracture non-union is classified as a failure of bone healing at least 6 months after fracture fixation. It's a challenging clinical problem, with treatment approaches varying depending on the underlying causes. Treatment of infected non-union demands intra- and postoperative protocols that differ fundamentally from those in case of aseptic non-union. In case of septic non-union caused by biological or mechanical failure, the treatment takes between 3-6 months. However, in case of an infection the treatment takes up to 2 years with quite a burden for the patients. Nevertheless, confirming infection as the underlying cause is challenging, particularly in low grade cases without clear infection signs. Preoperative blood testing would be valuable in diagnosing infectious causes and facilitate early initiation of appropriate treatment. The aim of this study was to characterize blood cells (peripheral blood mononuclear cells (PBMCs)) from patients with septic and aseptic non-union and compare with patients with uneventful healing.

Patients were recruited from eight level-one trauma centres in Germany, after appropriate ethical approval. Blood from healed ( $n=18$ ), septic non-union ( $n=20$ ) and aseptic non-union ( $n=24$ ) patients was taken before surgical revision for routine implant removal or treatment of septic or aseptic non-union respectively. PBMCs were characterized by their expression of specific blood cell surface markers using high-dimensional mass cytometry with a total of 43 markers.

The cell groups investigated originated from both the adaptive and the innate immune system. Innate immune cells were monocytes, granulocytes and NK cells. T and B cells were examined as part of the adaptive immune system. CD4<sup>+</sup> T cells assist in the activation of B cells to secrete antibodies and assist in the activation of CD8<sup>+</sup> T cells to kill infected cells. Among the different cell types analyzed, CD4<sup>+</sup> T cells subgroups showed most of the significant differences between the three groups. T regulatory cells regulating the response of immune cells. These cells were increased in aseptic ( $p=0.0119$ ) non-union patients compared to healed patients. Furthermore, Th1 cells were elevated in septic non-union patients compared to both healed ( $p=0.0004$ ) and aseptic non-union patients ( $p=0.0074$ ). Th1 cells are playing an important role in inflammatory responses and cell-mediated immunity. Activation marker CD38 was decreased in CD4<sup>+</sup> T cells in aseptic non-union patients compared to healed patients ( $p=0.0004$ ). Exhaustion (PD-1, OX-40 and ICOS) and activation markers (HLA-DR and CD69) showed no significant differences in CD4<sup>+</sup> and CD8<sup>+</sup> T cells. Additionally, monocytes were significantly increased in septic non-union patients compared to both healed ( $p=0.0094$ ) and aseptic non-union patients ( $p\leq 0.0001$ ). Monocytes are involved in processes that occur during an immune response, both inflammatory and anti-inflammatory.

In summary, septic non-union patients show an elevated number of monocytes and Th1 cells and reflect a state of infection. In addition, T helper cell subsets seem to play a fundamental role in non-union patients, as they all differ between healed and non-union patients. These



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findings suggest that preoperative blood testing might be used to provide distinct biomarkers to identify non-union patients.

## **Machine learning methods for classifying wild red deer behavior**

Deutsch: Vergleich maschineller Lernalgorithmen zur Verhaltensklassifizierung von Rothirschen mit Beschleunigungsdaten

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To effectively conserve a species, it is necessary to understand its behaviors. However, some species can be difficult to observe in the wild, as they are nocturnal, shy or travel over large distances. One such species is the red deer (*Cervus elaphus*). To overcome these challenges, researchers frequently use GPS collars fitted with accelerometers to better understand the behaviors of wild red deer and other ungulates. While the GPS data provides information regarding spatial behaviors, the accelerometers can be used to infer knowledge regarding the animals' physical activity. Furthermore, combined with classification models, data collected by accelerometers on a collar can be used to determine an animal's actual behaviors, and therefore allow us to “observe” these animals without visually seeing them. This data can be used as a basis for conservation practices or to answer questions such as how climate change or human activity might impact the behavior of these animals.

Previous ungulate classification studies have mostly trained their models using data from GPS-collared captive animals. While this is more efficient and convenient than using data from GPS-collared wild animals, data from captive animals may not be representative of the behaviors displayed by wild individuals. To fill this gap, we decided to train our models with wild red deer. As such, we spent 60 days in the Swiss National Park, observing GPS-collared red deer and recording their behavior. In a second step, we used a supervised learning approach with the data collected from the wild red deer to train the behavioral classification models. While the accelerometer data collected on multiple axes served as an input variable, the simultaneously observed behavior was used as the output variable. Further, we used a variety of machine learning algorithms, as well as combinations and transformations of the accelerometer data to identify those that generated the most accurate classification models. To determine which models performed most accurately, we derived a new metric which considered the imbalance between different behaviors.

We found significant differences in the models' performances depending on which algorithm and combination of input variables was used. In essence, discriminant analysis generated the most accurate classification models when combined with multiple input variables and was able to accurately differentiate between the behaviors lying, feeding, standing, walking, and running. In contrast to using data from captive animals, collecting enough observational data from wild red deer required a significant amount of field work and physical effort. However, our results were comparable to models trained on captive ungulates, with the distinguishing knowledge that our models are well-suited to classify the behaviors of wild red deer living in an Alpine environment. We plan to use these classification models as a basis for future studies to analyze what effects the hunting regime has on the behavior of wild red deer. We also hope that our comparison of the various machine learning algorithms and transformation methods can be used in future behavioral classification projects when deciding which algorithms and methods to use. Finally, we hope that the metric we used to compare the various models may shed some insight on the benefits and limitations of such acceleration-based behavioral classification models.

## **The (r) of the upper Surselva Valley: an unwanted regional and social marker in Swiss German?**

Deutsch: Das (r) der oberen Surselva: ein unliebsamer regionaler und sozialer Marker im Schweizerdeutschen?

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To date, only little is known about the phonetics of the variable (r) in Romansh. (r) is generally said to be produced as alveolar liquid (i.e. [r] or [r̥]) in Romansh (Liver, 2010, S. 132). People however are well aware that uvular variants such as [ʀ] are widespread in the varieties spoken in the upper Surselva Valley. It is thus no surprise that Eckhardt (2021, S. 282–284) has found these variants to be transferred into the L2 Swiss German varieties of Romansh speakers from Trun. Another recent study has looked at the variable from a perspective of perceptual dialectology. Adam-Graf (2020) demonstrates that uvular variants are very salient and even more so function as sociolinguistic stereotype. This means that in the Grison context, people using these variants are quite readily recognised as Romansh speakers and sometimes even stigmatised because of their L2 variety of Swiss German (Büchler, 2023).

The first research question is concerned with what variants of (r) Romansh speakers from the upper Surselva Valley use in Swiss German if they live outside the canton of Grisons, in German-speaking Switzerland. The second research question focuses on variation and asks which linguistic and social constraints determine the use of (r). For this, a sample of 19 speakers was taken from a larger corpus containing spontaneous conversational data in Swiss German by Romansh speakers who have migrated from Grisons to Bern (Büchler, 2023). 13 (6 women and 7 men) grew up in the upper Surselva Valley and six (3 women and 3 men) in other places of the Romansh area thus forming a control group. Variationist sociolinguistic methods were used: The *r*-sounds in the conversational data were coded auditorily and with the aid of the spectrogram (Leemann et al., 2018; Sebregts, 2015). Four variants were differentiated: alveolar (i.e. [r], [r̥]) – uvular voiced (i.e. [ʀ], [ʁ]) – uvular unvoiced (i.e. [χ]) – vocalised/deleted. Different social (e.g. gender or place of residence) and linguistic factors (e.g. phonological environment or stress) were tested statistically for correlations to the use of the four variants.

As expected, results show that the place of residence is a key social factor: only the speakers from the upper Surselva Valley used the uvular variants, whilst the speakers from the control group used alveolar variants. Somewhat suprisingly, the former group also showed a pronounced tendency to use vocalised/deleted variants. However, the distribution is highly dependent on linguistic factors: vocalisation/deletion is most prominent after a vowel and before a consonant (e.g. [fa:t] for *faart* ‘(he) drives’). Further linguistic and social factors will be presented and discussed with respect to the sociolinguistic context.

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Saturday, November 9

10:15–11:45

**Session 9    Diverse research - Talks in English**

Chairs: Lucas Lombriser / University of Geneva, Helena Jambor / University of Applied Sciences of the Grisons, DAViS

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-09-mixed-disciplines-english#resultat>)

## **Driving forces of land cover change in the Kauner valley and Martell valley since the 1950s**

Mattia Sartori<sup>1</sup>, Katharina Ramskogler<sup>1</sup>, Moritz Altmann<sup>2</sup>, Florian Haas<sup>2</sup>, Tobias Heckmann<sup>2</sup>, Toni Himmelsotß<sup>2</sup>, Florentin Hofmeister<sup>3</sup>, Ben Marzeion<sup>4</sup>, Norbert Pfeifer<sup>5</sup>, Madlene Pfeiffer<sup>6</sup>, Camillo Ressler<sup>5</sup>, Jakob Rom<sup>2</sup>, Michael H. Wimmer<sup>7</sup>, Erich Tasser<sup>1</sup>

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### **Introduction**

The impact of climate change around the world is much more evident in high alpine regions. The European Alpine region is a good example for this phenomenon. In fact, this region is undergoing a rapid transformation in climate dynamics, which are influencing the evolution of land cover types. The glaciers retreat and the forest and tree line, as well as the alpine vegetation types, rise. At the same time, however, agriculture is increasingly retreating from the higher elevations, which is also leading to shifts in vegetation. These processes are initiated and accelerated by a multitude of influencing factors, necessitating an interdisciplinary approach to comprehend their causes and potential future developments. This research is integrated within the broader context of the SEHAG project, an interdisciplinary approach for investigating the sensitivity of Alpine geosystems to climate change since 1850.

### **Aim**

The Martell Valley (South Tyrol, Italy) and Kauner Valley (Tyrol, Austria), emblematic of the fragile alpine regions, have undergone significant transformations over the past seventy years. The aim of our study was to investigate the intricate relationship between land cover changes and various environmental drivers, such as geomorphology, glaciation, hydrology, topography, and land use, particularly under the influence of climate change, since 1952. Thus, we wanted to address the following research questions: (i) What were the specific drivers leading to land cover change and how did they interact with each other? (ii) Were there area-specific drivers that caused certain patterns in one study area or the other?

### **Methods**

To conduct this study, we used aerial images to create high-resolution land cover maps for the two study areas for 1952, 1985, and 2020. We performed yearly automated image segmentation based on spectral differences, followed by manual classification into nineteen predefined land-cover classes. Historical ground-level photographs helped identify ambiguous land surface types. We also collected data on key drivers of climate, geomorphology, land use, glacier condition, and topography. Multivariate analysis and geographically weighted regression accounted for spatial variations in environmental impact and identified correlations between land cover change and drivers.

### **Results and outlook**

Results from the land cover classification show that significant changes have taken place in the last 70 years. We observed that the class “ice/snow” decreased by 46% in the Martell Valley, and by 28% in the Kauner Valley. The total area covered by vegetation increased by 10% in the Kauner Valley and by 4,5% in the Martell Valley since 1950. The land cover class “alpine grassland” showed a particularly strong growth gaining 2.8 km<sup>2</sup> during the investigation period, which is 5% of the total surface. Differences between the two

investigation areas could also be observed. The land cover class “alpine grassland” that showed a gain in coverage of 60% in the Kauner Valley, lost 20% of coverage in the Martell Valley. We identified the Drivers affecting land cover change dynamics to be mostly related to microclimate and topological factors. Furthermore, differences between the two study areas can be led back to differences in the geological composition of the sites.

Overall, this study not only helps us to advance our scientific understanding of the response of high alpine ecosystems to climate change, but also emphasises the importance of interdisciplinary approaches in understanding and subsequently managing environmental problems. It also shows the opportunities for research offered by historical ground level photographs taken. We are therefore currently working on a citizen science initiative in which we offer all the opportunity to re-photograph historical photographs on site via an app. We will then analyse the collected images scientifically.

## **Evaluating the efficacy of pretrained large language models for automated ICD-10 diagnosis coding**

Original abstract title: Benchmarking pretrained large language models for automated ICD-10 coding from clinical text

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The medical coding of patient diagnoses and therapies in hospitals and other institutions plays a crucial role in the Swiss healthcare system. By converting clinical information into standardized codes, they enable more efficient data analyses, resource allocation and evidence-based policymaking. The usual medical coding process in Switzerland involves transforming clinical notes by doctors or other medical personnel, often only available in unstructured free-text format, into structured codes using classification systems like the “International Classification of Diseases – German Modification” (ICD-10-GM) for diagnoses and the “Schweizerische Operationsklassifikation (CHOP)” for treatments. At the national level, coded health data allows for epidemiological studies, monitoring health inequalities and strategic allocation of resources. For individual healthcare providers, like hospitals, these accurate clinical data also offer several optimization possibilities through efficient cost auditing, patient segmentation and patient journey mapping, decision support system development and ensuring appropriate reimbursement for services rendered. Currently many hospitals in Switzerland struggle to find enough personnel for the necessary medical coding work. To further support their work, automated clinical coding systems are being developed to further enhance efficiency and accuracy, addressing challenges such as handling long or incomplete medical records. Due to their performance and potential, Large Language Models (LLM) such as ChatGPT have emerged over the last few years as a disruptive technology across various research fields. Utilizing their architecture on huge amounts of unstructured text data, LLMs can emulate a deep understanding of language semantics. In their functionality, LLMs calculate the conditional probability of word sequences by taking into account the contextual information from foregoing words, so they can predict the probability of subsequent words. With their large context windows for inputs, their utilization requires fewer tedious tasks like chunking in comparison to traditional methods. As well, due to abundantly available extensive high-level libraries for working with LLMs, e.g. the Hugging-Face Transformers library, scripts are more accessible to a non-technical audience and less prone to error in their functionality implying more medical staff can make use of these scripts. The ease of LLM scripts also means they are easier to reproduce, making research more comprehensible and replicable.

In our research we evaluate and benchmark the capabilities of different publicly available Large Language Models for automated ICD-10 coding of diagnoses. Using multilabel sequence classification as a downstream task for matching text sequences to their respective corresponding ICD-10 codes, we used the publicly available MIMIC-IV dataset to fine-tune cross-domain and domain-specialized biomedical LLMs spanning from 1 billion to 7 billion parameters. To optimize and reduce the necessary computing time, we employed multiple parameter-efficient fine-tuning (PEFT) methods to reduce the number of parameters of the LLMs, while maintaining satisfactory performance. One such prominent methods we employed is “Low-Rank Adaptation” (LoRA), which reduces the dimensionality of parameter matrices needed for computation. With another technique called “Quantization” we reduced the necessary GPU-bound memory space and the necessary number of calculations by converting the data representation of the weights and activations within an LLM from high to low-precision, e.g. a 32-bit floating-point number to an 8-bit integer.

For both the fine-tuning and the model evaluation process, the MIMIC-IV dataset provides more than 100'000 clinical notes of individual patients matched together with all corresponding ICD-10 diagnosis codes. Within our results we benchmark multiple LLMs with

different parameters-sizes by comparing their F1-scores and observed necessary compute times for our defined downstream task. Our results show that even small cross-domain models like “Falcon-1B” achieve surprising results in predicting the corresponding ICD-10 codes for previously unknown text sequences.



## What links volcanic and solar eruptions?

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### Introduction

The Earth's climate is ever changing on various time scales. Most recently anthropogenic climate change has become the dominating driver for climate trends. However, natural drivers have modulated Earth's climate in the past and continue to play a role today and into the future. While stable, long-term drivers lastingly alter climate, episodic events can modulate regional and global climate on short time scales of years to decades. Two prominent examples of such events are volcanic and solar eruptions. While there are limited direct observations of such events, due to their sporadic nature, knowledge about their occurrence in the past can be inferred from proxies for various climate variables.

### The project

“Volcanic and solar particle events in the past: Atmospheric Effects and cosmogenic Nuclides in ice cores” (AEON) is a project carried out by the two partnering institutes CEREGE in France and PMOD/WRC in Switzerland. The aim of the AEON project is to reconcile observations and theoretical understanding of the two natural climate forcings: volcanic activity and solar variability. Eruptions of both volcanic and solar nature (also called solar superflares) may - besides the anthropogenic forcing - play an important role in today's climate and strong events can be hazardous for humans and modern technology (e.g. satellites, planes). In the past, these forcings have not been modelled in full complexity, i.e. with all involved Earth system components being interactive in models and have been poorly constrained. For volcanic eruptions, detailed records spanning over the past millennia exist and can be used to force models. A complete record of solar superflares in the same time period, conversely, does not yet exist. In the scope of this project, new, high-precision observational data will be extracted from isotope measurements in ice cores. CEREGE is especially well equipped to measure the new, promising Chlorine-36/Beryllium-10 ratio proxy, which allows the reconstruction of solar superflare energy spectra. All these data will then be used to simulate volcanic and solar eruptions in the state-of-the-art atmosphere-ocean-aerosol-chemistry-climate model SOCOLv4. Both the volcanic and cosmogenic particles enter the atmosphere after being produced, but ultimately leave their fingerprints in various locations on the surface, especially in the remote ice shields. Therefore, the entire physical and chemical evolution of the particles in the atmosphere contributes to the signal found in the records. Thus, to perform useful simulations, we will further develop the model to include relevant chemical reactions and microphysical processes, alongside the already well described detailed atmospheric transport. Notably, cosmogenic nuclides interact with aerosol particles and may be scavenged and deposited. When the atmospheric aerosol is enhanced after a volcanic eruption, interactions between volcanic and cosmogenic particles may leave their own fingerprint in the record. This effect would need to be accounted for in proxy interpretation. Ultimately, this work will allow for a more sophisticated analysis of atmospheric and climate effects of volcanic eruptions and solar variability compared to previous work.

### My role in the project

For my doctoral thesis, I will run SOCOLv4 and analyse the data produced in the various simulations. Mainly I will focus on the volcanic and solar impacts on the atmosphere and climate, and the interactions between volcanic aerosol particles and cosmogenic nuclides. Within the atmosphere, I will give special attention to stratospheric chemistry and circulation, stratosphere/troposphere coupling and tropospheric circulation. While we are obviously interested in the troposphere because we live in it and weather takes place here as well, it is

itself strongly connected to the stratosphere above and reacts to changes therein. Also, the stratosphere contains the ozone layer, which is vital to life on Earth and can react strongly to volcanic eruptions.

### **How common food emulsifiers are breaking down your gut's defense**

Original abstract title: Packaged Food Emulsifiers Trigger Pro-Inflammatory Activation and Disruption of the Gut Epithelial Barrier

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The barrier function of the epithelia is crucial for maintaining homeostasis. Environmental exposures may alter the epithelial barrier integrity and influence the development of diseases. Recent studies have shown that certain surfactants and emulsifiers damage the epithelial barriers. We investigated the effects of three commonly used food emulsifiers, sunflower-derived lecithin (SunLec), soy lecithin (SoyLec) and diacetyl tartaric acid ester of mono- and diglycerides (DATEM) on gut organoids and organs-on-a-chip and adult stem cell derived intestine-on-a-chip. All emulsifiers were examined at consumer-relevant doses using transepithelial-electrical resistance (TEER), RNA-seq, and targeted proteomics. SunLec, SoyLec and DATEM elicited a dose- and time-dependent decrease in epithelial barrier function in TEER measurement. RNA-seq analysis indicated that both lecithins upregulated the pathways of response to lipid and cell death at 6.25 mg/ml. Specifically, wound healing was upregulated with SunLec exposure, while cell migration, oxidative stress and angiogenesis pathways were upregulated with SoyLec. DATEM showed increased cell death, regulation of metabolic processes and response to oxygen-related compounds. An increase in type 2 cytokine levels such as IL-4, IL-13 and IL-33 in response to SunLec, while SoyLec induced the production of proinflammatory cytokines (IL-6, IL-18) as well as alarmins (TSLP, IL-33). DATEM induced the production of not only the alarmin, TSLP, but also proinflammatory and cell death-related proteins such as caspase 8, IL-18, DDX58 and peroxiredoxins. Irregular and heterogeneous confocal microscopy staining of ZO-1 was observed after exposure to all three emulsifiers, additionally demonstrating the disruption of the intestinal epithelial barrier. In conclusion, the present study provides direct evidence on the detrimental effects of food emulsifiers, SunLec, SoyLec and DATEM on intestinal epithelial integrity, due to extensive proinflammatory, oxidative stress, tissue healing, angiogenesis and alarmin release of the epithelial cells, namely causing epithelitis. Studies are going on to examine the epithelial damaging and inflammatory effect of emulsifiers on mice in vivo and to verify the related pathways mechanistically in human intestinal organoids using CRISPR/Cas9.

## **Is your sports routine protecting your health or pushing your immune system to its limit?**

Original abstract title: Immune-inflammatory proteomic fingerprinting of elite athletes, amateur athletes, and non-sportive controls

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Physical exercise is known to impact our immune system in various ways, depending on its intensity, duration and training load. Many factors have been implicated in the ability of exercise to modulate the immune response, such as variations in circulating levels of cytokines and chemotactic factors, changes in adhesion molecules, the generation of reactive oxygen species as well as nutritional status, which is of main interest for immune-metabolic studies. Regular moderate-to-vigorous physical activity is associated with an anti-inflammatory phenotype, enhanced immunosurveillance, and has a protective effect against chronic non-communicable diseases, infections and likely cancer. The reduction in adipose tissue and changes in hormonal, myokine, and cytokine levels that result from regular exercise are thought to be the main contributors to its anti-inflammatory effects. On the other hand, vigorous exercise can potentially lead to an overall pro-inflammatory state and have detrimental effects on immune function. This is especially the case for elite athletes, whose long-term training loads often exceed the recommended upper levels for physical activity and who tend to face further stressors that can impair adequate immune responses, particularly during competitions and heavy training phases. Additionally, endurance sports involve prolonged activities engaging slow-twitch muscle fibers, while anaerobic sports focus on high-intensity efforts using fast-twitch fibers for power and speed. In its 2016 consensus statement, the International Olympic Committee pointed out the importance of further investigation into the relationship between training load and risk of illness to minimize illness-related training absence, decrease in performance, and overtraining syndrome in professional athletes. Studies have shown that illnesses during competitions and tournaments are more frequently observed in winter sports athletes. In this study, we used proximity extension assay (PEA)-based targeted proteomics to investigate the impact of different levels of exercise on organ damage-, immune response-, and inflammation-related proteins in three different cohorts: winter sport athletes, amateur athletes and non-sportive controls. Based on our results, endurance training reduces the levels of IL-6, IL-15, and FGF-21, inversely proportional to the higher exercise intensities. Chronic intense training without recovery could potentially suppress immunity, but regular exercise improves chemotaxis and immune functions. Parvalbumin, crucial for muscle relaxation, is found more in fast-twitch fibers and TNNI3 up-regulation could improve cardiac performance. The PI3K-Akt pathway is able to support cardiac hypertrophy and its changes, together with MAPKs, are activated by IL-18, promoting pro-inflammatory cytokine production, which are important for tissue regeneration. High-intensity physical exercise up-regulates the innate immune response to viral infection, particularly in the acute training phase. This elevated immune activity promotes chemokine up-regulation, leukocyte chemotaxis, T cell activation, adaptive immune responses, angiogenesis, and smooth muscle cell proliferation. IL-8, involved in neutrophil migration and angiogenesis, is produced locally in muscles during exercise with a minimal systemic response observed only after intense exercise. High-exercise loads can also increase circulating anti-inflammatory cytokine IL-10, causing immunosuppression. Ultimately, professional athletes exhibit an overall pro-inflammatory profile, with different endotypes linked to activity type and intensity. The endurance groups, show a more anti-inflammatory immune profile when compared to the others. In conclusion, advances in omics approaches could offer detailed assessments of athlete health and fitness,

enhance our understanding of exercise-immune system interactions, mechanistic processes, functional differences, and pathways associated with various sports. This could also lead to the detection of biomarkers to distinguish between normal recovery and overtraining, ultimately aiming to balance immune health and maximize athletic performance.

## Effects of Exercise-based Cardiac Rehabilitation on Body Composition of Cardiovascular Patients

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### Background

Nutritional status plays an important role in disease management in cardiovascular patients. Improvement of body composition can bring several benefits for blood pressure, cholesterol levels, insulin resistance and glucose control in cardiovascular disease (CVD) patients. Hence, optimization of body composition might reduce the risk for metabolic syndrome. Data in kilograms body weight or the body mass index (body weight/body height<sup>2</sup>), do not distinguish between muscle mass and fat mass, and consequently fail to provide a realistic assessment of persons' actual body composition. Visceral fat or intraabdominal fat defines stored fat in the abdominal cavity. In contrast to subcutaneous fat, visceral fat releases proinflammatory cytokines and negatively influences fat and carbohydrate metabolism. Excessive visceral fat reduction has shown more noticeable effects than subcutaneous fat reduction. Ideally, weight loss should be derived almost exclusively from the fat mass compartment since this is the main driver of metabolic disease. However, several studies have shown that there is an accompanying loss of mass from the fat-free compartment, especially skeletal muscle mass. To induce targeted fat reduction, particular metabolic stimuli are required. Exercise-based cardiac rehabilitation (EBCR) including dietary management and exercise are considered stimuli to trigger targeted fat reduction. Therefore, the aim of our research project is to investigate the effects of EBCR on body composition.

### Methods

Participants will be recruited at the Hochgebirgsklinik Davos to participate in this study. We aim to include 1000 patients to participate after signing a general consent. Body composition analysis, by means of bioimpedance analysis (BIA) will be performed with every patient on admission and discharge of their rehabilitation hospitalization (usually 24±4 days). During their in-patient EBCR, patients will perform EBCR including exercise training, mediterranean diet, risk factor and lifestyle education, smoking cessation if indicated, optimization cardiovascular risk factors. Rehabilitation programs will be performed according to patients' physical condition and based on cardiologists' decision and according to current guidelines. The training sessions include approximately 20 sessions per week, including cycle ergometer training, cardiological gymnastics, walking and resistance training.

### Relevance of the expected results

There is an urgent need to further elicit aspects on the effectiveness of a in-patient EBCR on body composition, particularly fat distribution in the visceral area and muscle mass. BIA is a rapid, safe, valid, and reliable method to assess these parameters. Moderate weight loss can achieve clinically meaningful reductions in markers of cardiometabolic risk and may offer the opportunity for patients to defer or reduce medication. To target fat reduction effectively, and preserve muscle loss in CVD patients, insights into training adaptations are essential. Possible body composition shifts could give valuable insight into physiological mechanisms triggered by EBCR, and the different sub-components including medication. BIA parameters significantly impact treatment outcomes, quality of life, and disease progression. The therapeutical consequence would comprise individually tailored exercise programs and treatment plans for CVD patients, to reduce morbidity and mortality, and enhance quality of life for patients.

Saturday, November 9

14:00-15:30

**Session 10 Vielfältige Forschung - Vorträge auf Deutsch**

Chairs: Barbara Haller Rupf / Academia Raetica, David Niederseer /  
Hochgebirgsklinik Davos

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-10-gemischte-disziplinen-deutsch#resultat>)

**„Unheimliche Eistrümmer“ – Or: How to Read a Historical Description of the Morteratsch Glacier in Times of Climate Heating**

Deutsch: «Unheimliche Eistrümmer» - Oder: Wie liest man eine historische Beschreibung des Morteratschgletschers in Zeiten der Klimaerwärmung?

Jann Duri Bantli<sup>1</sup>

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On 13 September 1850, the topographer and forest engineer Johann Coaz (1822-1918), together with the brothers Jon and Lorenz Ragut Tscharner, made the first ascent of Piz Bernina, the highest mountain in Graubünden. Four years later, Coaz published a description of the first ascent, in which the Morteratsch glacier takes a prominent role. However, from the current perspective of increasing glacier retreat, the text appears in a different light. This raises the fundamental question of how to read a historical description of glacier ice in times of climate heating.

In this context, my paper is interested in the portrayal of the fascinating "Eistrümmer" (fragmented formations of glacier ice; literally translated as 'ice debris') that the pioneers admire and overcome. However, during the descent, which partly takes place at night, these "Eistrümmer" appear to them in a different form: they had taken on "unheimliche, verschwebende Umrisse" (uncanny, floating contours). According to my argument, this reveals a double shift in perception of the glacier: first, the three alpinists are haunted by the idea that they will not make the descent over the crevassed glacier and that they will die. Here, the uncanniness of the "Eistrümmer" functions as the marker of the potential destruction of the human subject. Second, it means a shift in the perception of the contemporary reader itself: against the backdrop of drastic climate change, the reader realizes that the "Eistrümmer" today are not just mutating and taking on different forms due to the lack of daylight, but above all due to rising temperatures. Therefore, from a contemporary point of view, Coaz' description of the "unheimliche Eistrümmer" announces the death of the glacier itself.

I propose to understand the shift in perception of the "Eistrümmer" with Wittgenstein as a "aspect change". This means that, unlike the constant seeing of an aspect, according to Wittgenstein, the image could contain a second aspect that reveals itself through a "lighting up" of an aspect". Through such an aspect change, the "Eistrümmer" appear as "unheimlich" (Freud), premonishing the death of the alpinists anno 1850 resp. the death of the glacier today. Additionally, I rely on Walter Benjamins famous depiction of his 'Angel of History', in which "Trümmer" (debris) play a prominent role. For in contrast to humanity, for whom a historical look back into history merely reveals a chain of events, Benjamins 'Angel of History' perceives history as a single unfolding of catastrophes, accumulating incessantly "Trümmer auf Trümmer", "debris on debris". Therefore, "Trümmer" represents the trail of destruction left behind by Western 'civilization'. Consequently, and with specific reference to Coaz' description of the uncanny "Eistrümmer", I understand those endangered creations of ice in the context of climate heating as "Trümmer von Eistrümmern", "debris of ice debris". My paper analyzes Coaz' description of the first ascent of Piz Bernina in general and the description of the "Eistrümmer" in particular in the context of climate heating. The conceptual framework of the 'aspect change' (Wittgenstein) - in conjunction with Freud's connotation of the uncanny - invites us to reflect on shifts in perception. Using the concrete example of Coaz' "Eistrümmer", and following Benjamins 'Angel of History', an attempt will be made to retrieve these "Eistrümmer" from the hidden, concealed or even repressed (Freud) realm of a historical text and make them visible as what they are: ephemeral "Trümmer von Eistrümmern" whose future is that of cultural artefacts. In this sense, this work aims to raise awareness of the current drastic transformation of the Alpine habitat in general and disappearance of Alpine glacier ice in particular.



## Towards improved understanding of the surface radiation balance in snow covered mountains

Deutsch: Die Strahlungsbilanz über Schnee im Gebirge

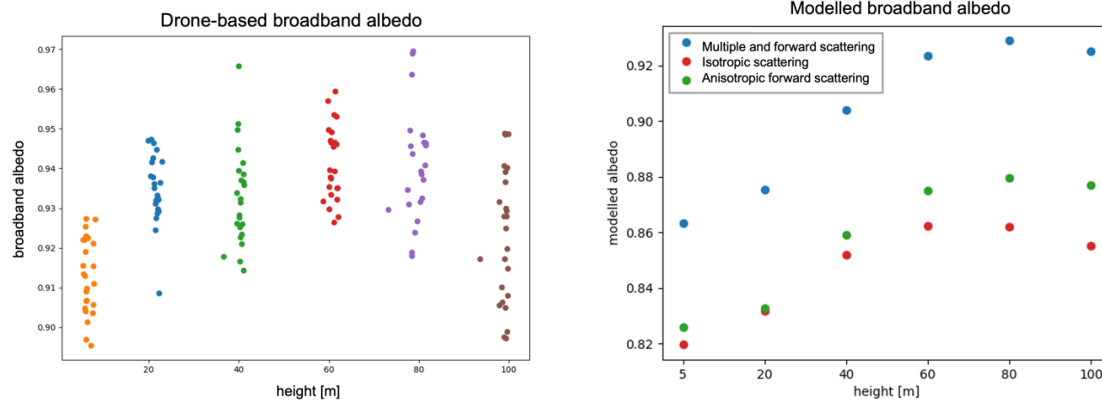
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Knowledge about surface radiation is important for climate change as well as energy harvesting via solar panels, because the surface radiation drives the energy balance on earth. Snow surfaces, scattering large parts of the incoming shortwave radiation back to space, are of special interest. For large scale observations remote sensing is the means of choice, here UAVs bring the advantage to capture also smaller scale heterogeneities. In this context, the radiation received at the sensor largely depends on the observation height above ground and therefore the field of view of the sensor. Especially in complex alpine terrain radiation reflected from the surrounding slopes significantly impacts the radiation balance through effects such as multiple scattering and the forward scattering properties of snow surfaces. We conducted both drone-based measurements and model simulations, with the surface radiation model GROUND EYE, to determine the incoming and reflected radiation at the Totalp site in the Swiss Alps close to Davos. With this we can show that the amount of reflected radiation received at the sensor largely increases with observation height, as more terrain is seen, but levels out where the impact of the slope reflection does not change significantly anymore. The incoming radiation is less impacted by this effect, but slightly decreases with observation height. More precisely, we find that anisotropic forward scattering is most important for higher heights, but in general less important than multiple backscattering effects from the snow covered terrain. This distinct pattern is found both in measurements and modelled results. Further research towards the spectral dependence of the reflected radiation and its influence on the radiation distribution will be done.



## **Snow height sensors reveal phenological advance in alpine grasslands**

Deutsch: Der Klimawandel lässt alpine Wiesen früher spriessen

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Phenology, the science of the timing of annual recurring biological events, is one of the best indicators to demonstrate effects of global warming on organisms. Long term monitoring and experimental studies show that the spring phenology of plants has advanced in the last decades. However, long term phenological data in the alpine region are often limited to few locations and thus, not much is known about climate-change induced phenological shifts above the treeline. In seasonally snow-covered regions, snow melt and spring temperatures are the most important phenological cues that initiate plant growth. Therefore, it is essential to track phenological shifts, snowmelt and near-ground temperatures simultaneously. In this study, we make use of a climate station network in the Swiss Alps to reveal phenological advance and relate them to climatic changes. The climate stations are equipped with a snow height sensor, which measures the height of an underlying object, independently of whether this object is snow or not, allowing study plant growth signal over the vegetation period. To accurately distinguish between a plant- and snow signal we use a machine learning algorithm that classifies the multivariate temporal input signal into snow and plants. We pinned down the timing of snow melt and extracted the start of growth from logistic growth curve that were fitted to the plant growth signal at 40 climate stations between 1500 and 2700m over a time of 25 years (1998 – 2023). We observe a 2.4 days/decade earlier occurrence of green-up coinciding with a shorter time lag between snow melt and the onset of plant growth. Because the timing of snowmelt has not changed significantly, we attribute the observed phenological advance of six days over the study period to the steep increase in spring temperature of 0.75°C/decade. The observed phenological shifts in alpine grasslands are in the same range as the advancing leaf-out timing of forests at lower elevation. Our study provides evidence of the profound impact of climate change on alpine vegetation phenology based on in-situ climatic- and vegetation height data.

## **The influence of foehn winds on cardiovascular parameters**

Deutsch: Der Einfluss von Föhn auf kardiovaskuläre Parameter

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### **Background**

It is well established that weather phenomena, particularly extreme weather conditions, can significantly impact human health, with fatigue, sleep disturbance, headache, and rheumatic pain being the most reported symptoms. Individuals who experience such symptoms due to weather phenomena are therefore termed "weather-sensitive".

Alpine regions are susceptible to foehn winds, which are strong, warm, and dry leeward winds that are known to trigger various symptoms in "weather-sensitive" individuals. Studies have demonstrated a correlation between foehn periods and an increased incidence of headache, pain, fatigue, and even severe traumas. In recent years, wearable devices, which allow continuous tracking of cardiovascular parameters, have revolutionized health monitoring. They therefore provide a novel approach to study physiological impacts of extreme weather events in real-time. Such extreme weather events are increasing due to climate change and therefore, it is important to understand the health effects associated with these conditions. The aim of the present study is to address the current lack of data on the impact of the foehn winds on cardiovascular parameters by using wearable data.

### **Objectives**

The primary objective of this study is to investigate the association between foehn winds and changes in cardiovascular parameters, including respiratory rate (RR), heart rate (HR), heart rate variability (HRV), and wrist skin temperature (WST), recorded by a wearable medical device in a young and healthy population. The secondary objective is to assess whether foehn winds have an impact on cardiovascular parameters (RR, HR, HRV, WST) of those individuals who self-identify as "weather-sensitive".

### **Methods**

A total of 1,163 healthy adults participated in the COVI-GAPP study. In this study, participants wore a CE-certified and FDA-approved sensory bracelet (AVA) that measured seven health parameters during sleep. Initially designed as a fertility tracker, the AVA-bracelet recorded respiratory rate (RR), heart rate (HR), heart rate variability (HRV), wrist skin temperature (WST), and sleep quantity and quality. Data were collected over the course of 11 months. Meteorological data, including the number of foehn days, wind speed, and air pressure, were obtained from nine weather stations across Liechtenstein. These data were used to calculate the foehn index, which is defined as 0 = no foehn, 1 = mixed air (when foehn evolves), and 2 = foehn. These two main data sets will be used for the current study. Initially, descriptive analyses will be conducted to examine the distributions of the variables under consideration and their variances between different population subgroups. To address the research questions, linear mixed effects models will analyse the associations between cardiovascular parameters and foehn, controlling for several demographic covariates. The statistical analyses will be performed using R Studio.

## **Results**

Health data were collected between May 2020 and March 2021, resulting in a total of 1,453,006 recorded hours. Out of the 1,163 recruited participants, 970 wore the AVA bracelet for at least one night. Participant's age ranged from 31 to 51 years with a mean age of 43.28 years (SD = 5.48). Of these participants, 40% (n = 388) were male and 60% (n = 582) were female. Further results will be available in the coming months.

## **Next steps**

Over the next weeks, the data will be preprocessed, after which the statistical tests outlined in the methods section will be conducted over the subsequent two to three months. The results of our study will be discussed and used to draw conclusions that may provide new insights into the physiological impact of foehn winds on cardiovascular parameters in both the general population and people who self-identify as "weather-sensitive".

## **Advancing Precision Dermatology through Tape Strip Proteomics**

Deutsch: Proteomik minimalinvasiver Hautproben - Neue Wege in der personalisierten Dermatologie

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Dermatological disorders are estimated to affect around 1 billion people at any point in time and have a heavy impact on the global population as the 4th leading cause of non-fatal disease burden. This is exacerbated by the lack of personalized and precision medicine available to treat diseases such as atopic dermatitis, psoriasis, and malignant skin carcinoma. Atopic dermatitis especially suffers from a lack of reliable biomarkers to diagnose and characterize the clinical phenotype as well as provide personalized medication and a better understanding of the disease mechanism. Especially pediatric patients are affected by it. This can have further implications not only on their quality of life but even impact their mental health.

Therefore, our objective is to identify these biomarkers and elucidate the underlying disease mechanism through one of the most comprehensive analyses performed so far. For this, we leverage high throughput, bottom-up, proteomics and our newly developed tape strips proteomic workflow to quickly and efficiently sample patients, analyse samples and generate insights. Current methods often rely on biopsies, which can be challenging to obtain, particularly from pediatric patients. Alternatively, when using tape strips, they require the combination of multiple strips, identify fewer proteins, or depend on lengthy gradients during analysis. In contrast, our newly developed tape strip proteomics workflow allows us to non-invasively sample patient cohorts and enables us to also sample pediatric patients.

Our workflow is unbiased and untargeted and combines the Orbitrap Eclipse and EasynLC 1200 as well as DIA-NN. It is capable of identifying between 800-1000 protein per layer of tape in healthy donors and up to 3000 proteins in diseased donors. Additionally, it is unique in its capabilities to analyse a singular layer in a 30-minute gradient. This allows us to prepare up to 400 samples in 2 days, analyse them in a time span of two weeks and identify differences in skin layers. This capability in combination with our collaborations allows us to perform population-wide skin studies which are unique in their reach. For this, we have measured and analyse 70 samples from one cohort, which we have received from our collaborators, in a pilot study. It shows a very low variability in our quality control samples and thus verifies the robustness of our methodology. We identified 300 significantly differentially expressed proteins and measured 3982 unique proteins. We will build upon these preliminary results and conduct a secondary study. It will involve 300 samples from a second cohort and further our knowledge of the disease mechanism of Atopic Dermatitis. We expect to generate valuable new insights into the epithelia barrier and underlying conditions for atopic dermatitis.

In summary, we aim to conduct population-wide proteomic analysis to elucidate the underlying mechanisms of atopic dermatitis and aim to discover and verify biomarkers which can help to enable precision dermatology. To this length, we have already analysed one cohort and are actively working on processing the second cohort as well as their analysis. In the future we aim to further simplify our processes and increase our throughput as well as the number of detectable proteins.

## **Effects of Mindfulness Exercises on Mental Health, Quality of Life and Risk Factors in Cardiovascular Patients**

Deutsch: Auswirkungen von Achtsamkeitsübungen auf die mentale Gesundheit, Lebensqualität und Risikofaktoren bei kardiovaskulären Patienten

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### **Background**

Cardiovascular Diseases (CVD) are the leading cause for mortality globally and contribute significantly to disability and morbidity. The guidelines on CVD prevention in clinical practice of the European Society of Cardiology (ESC) and the European Association of Preventive Cardiology (EAPC) define blood apolipoprotein-B-containing lipoproteins, elevated blood pressure, smoking, diabetes mellitus and obesity as the main causal and modifiable risk factors in CVD. Stress is reported to highly correlate with behavioral risk factors, such as smoking and poor adherence to a healthy lifestyle. In doing so, it is classified as a potential risk modifier.

Cardiac rehabilitation aims to reduce the risk of further cardiovascular events and cardiovascular mortality. Secondary prevention is one of the main goals of cardiac rehabilitation, part of it being the topic of stress management.

Mindfulness-based stress reduction (MBSR) is a concept originally developed with the purpose of decreasing psychological distress in different somatic diseases. The concept aims to help subjects in discerning primary sensory experiences from emotional or cognitive processes. While there is a body of evidence for the effects of MBSR on chronic pain, symptoms of anxiety and depression, blood pressure and resting heart rate in various patient populations and healthy individuals, available data in cardiovascular patients is scarce. The reduction of resting blood pressure is the only outcome of MBSR-techniques in cardiovascular patients substantiated by statistical significance to date.

Hence, the aim of this research project is to explore the effects of MBSR on mental health, quality of life and risk factors in cardiovascular patients.

### **Methods**

Patients will be recruited at the inpatient cardiac rehabilitation of the Hochgebirgsklinik Davos. The participants will be randomized into an intervention- or a control group, after giving their written consent. The intervention group will visit 2 weekly MBSR sessions, additionally to their usual rehabilitation program for the duration of their stay, while the control group receives written patient education about stress and relaxation techniques on the first week of rehabilitation. Mental health and Quality of Life will be assessed via the Hospital Anxiety and Depression Scale (HADS), the MacNew Heart Questionnaire and the Health- Related Quality of Life questionnaire (HRQoL). Further, the LDL- Cholesterol, smoking history, resting blood pressure, heart rate variability and HbA1c are going to be analyzed. Measurement points are at the clinic entry day and after 24±4 days, at the end of the rehabilitation.

### **Relevance of the expected results for research and clinical practice**

In the face of the challenges that a growing prevalence of CVD and its risk factors poses to the Swiss health care system, the importance of secondary prevention seems crucial. In order to contain increasing health costs, but, more importantly, to empower patients and promote individual responsibility, it is important to explore preventive tools that can be applied simply and without further expense after cardiovascular rehabilitation. The research of the effects of MBSR as one of these tools could contribute to this.

Saturday, November 9

14:00-15:30

**Session 11    Diverse research - Talks in English**

Chairs: Britta Allgöwer / Academia Raetica, David Schmid / CSEM

(Website: <https://gr-forscht.ch/abstracts?kategorie=session-11-mixed-disciplines-english#resultat>)

## Assessing snow water equivalent reconstruction using multi-source high-resolution satellite data and hydrological models in alpine regions

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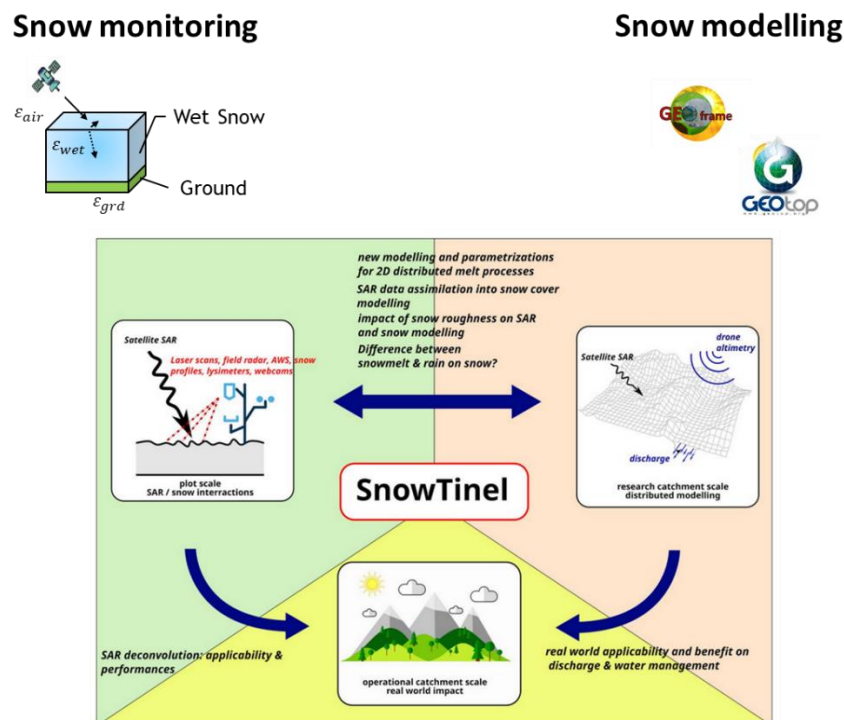
<sup>3</sup> Institute for Earth Observation, Eurac Research, Bolzano, Italy

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Alpine regions are highly sensitive to the impacts of climate change, with snowmelt dynamics playing a crucial role in their hydrological processes. Accurate modeling of snowmelt processes is essential for predicting water availability and hazard assessment in these regions. Recently, the increasing availability of radar remote sensing products has offered great potential for improving our capability to understand and monitor snowmelt processes at high spatial and temporal resolutions.

The “SnowTinel” project aims to better understand the capability of radar remote sensing to detect, monitor, and predict snowmelt processes in mountain regions. This interdisciplinary project involves expertise in snow and hydrological process modeling, in situ snow characterization, and remote sensing monitoring. The project is a collaboration between the WSL Institute for Snow and Avalanche Research SLF (WSL/SLF) in Davos and EURAC Research in Bolzano, supported by the Swiss National Science Foundation and the Province of South Tyrol in Italy.

The project’s primary goal is to improve our understanding of radar interactions with wet snowpack evolution and then evaluate the value of this information to enhance snowmelt modeling at the catchment scale. The melting phase is usually not very accurately simulated in distributed snow models, leading to errors in the exact timing of discharge. Any additional measurement that could help reduce these inaccuracies is welcome.

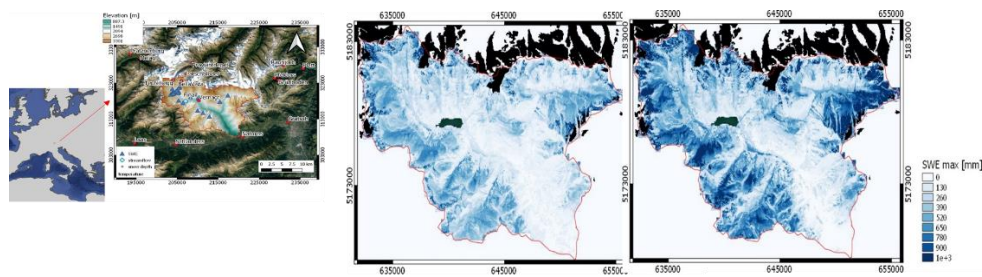


**Figure 1:** Conceptual scheme of the joint Swiss National Science Foundation – South Tyrol “Snowtinel” research project.



In this paper, we focus on the integration of remote sensing into a hydrological modeling framework to improve snowmelt prediction. A representative variable of snowmelt is the snow water equivalent (SWE). However, SWE measurements are rare and limited to point scales, making it difficult to obtain accurate spatialized estimates. Remote sensing products offer a unique opportunity to provide spatialized observations that can be exploited for SWE retrieval. Using optical remote sensing data from MODIS and Sentinel-2, radar SAR data from Sentinel-1, and in situ observations, Premier et al. (2023) developed a multi-source data method to reconstruct daily SWE at high spatial resolution (25 m). More specifically, accurate information about snow persistence, which is linked to the SWE amount, is retrieved from optical satellites, while accurate information about the runoff onset is retrieved from SAR data.

In this work, we investigate the effectiveness of this approach in estimating SWE for the alpine catchments of Dischma, a very well-monitored small catchment located near the city of Davos, Kanton Graubünden, Switzerland (~40 km<sup>2</sup>), and the Venosta catchment, a larger catchment located in the northwestern part of Südtirol, Italy (~1500 km<sup>2</sup>). Accurate snowmelt estimation is needed here as water is intensively used for various purposes, including hydropower and irrigation. We compare the results with those obtained using state-of-the-art hydrological models such as GEOframe (Formetta, 2013) or GEOtop (Rigon et al., 2006) and measurement data.



(a) Hydrological season 2019/20, (b) Hydrological season 2020/21

**Figure 2:** Example of high-resolution SWE estimation for the Senales are in the Venosta catchment in Italy.

Results show that, in terms of total spatial average, hydrological models tend to estimate SWE better than the satellite product of Premier et al. (2023), while the latter has a better capability to estimate spatial patterns at high resolution (~50 m). Moreover, Premier et al. (2023) does not consider glaciers and the presence of reservoirs. In this work, we will evaluate how to combine the Premier et al. (2023) product with GEOframe hydrological model results to substantially improve our ability to estimate snowmelt-related phenomena in alpine regions, especially for poorly monitored catchments.

## **Spatiotemporal variability of turbulent fluxes in snow-covered mountain terrain**

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Turbulent exchange of heat and moisture plays an important role in snow cover dynamics in mountain regions and governs boundary layer dynamics. Having an accurate representation of turbulent fluxes is essential for predicting the snow hydrological cycle, avalanche hazards, and climate in cold regions. Although these processes are subject to great spatial and temporal variability, especially in complex terrain, measurements of heat, moisture, and momentum fluxes are almost exclusively point observations. To quantify the spatial variability, and assess the representativeness of the observations, numerical modeling of the atmosphere and surface is a useful tool. Nevertheless, there is considerable uncertainty regarding the accuracy of surface models in capturing turbulent fluxes, particularly in complex terrain with large spatial variability on small scales. These uncertainties can be attributed in part to (1) the use of parametrization schemes used in such models such as the Monin-Obukhov similarity theory, which has limitations in complex terrain because the assumptions of stationarity and spatial homogeneity are usually not fulfilled and (2) the errors in representing wind speeds and near-surface atmospheric gradients in the model simulations. In this study, we analyze the spatial and temporal variability of the energy exchange over snow during different meteorological events in mountain regions and the sources of errors in representing them. To verify common modelling approaches with observations, we performed model predictions of turbulent fluxes from the novel state-of-the-art model CRYOWRF in the region of Davos, Switzerland. CRYOWRF is developed by the Snow and Avalanche Research Centre SLF and is the atmospheric model WRF coupled to the surface model SNOWPACK. The turbulent fluxes at different model resolutions are compared to turbulent fluxes measured using high frequency measurements of wind, temperature, and moisture by the eddy covariance method and calculated with low frequency measurements using the Monin-Obukhov similarity theory. This model comparison and spatial analysis is carried out for three different meteorological events that are representative of the local climate of Davos, particularly föhn events.

The results from the model indicate that the fluxes vary strongly temporally and spatially. Depending on the weather pattern, elevation plays a large role in the variability of the turbulent fluxes which results in an elevation dependent correlation of turbulent fluxes with wind speed. This shows that locally measured turbulent heat fluxes are not representative of the whole mountain area. This has implications for the calculation of snow melt, sublimation, and accumulation across mountainous terrain and indicates that the spatial variability is important to account for. The resolution within the model also significantly influences the representation of turbulent fluxes, as coarser (1 km) resolutions greatly overestimate wind speeds compared to higher resolutions (200 m). This is due to fewer topography-wind interactions when topography is not accurately represented in the model, leading to an overestimation of turbulent fluxes.

## **Exploring the relationship between mechanical forces and biological outcome in a cartilage model**

Original abstract title: Exploring the relationship between protein activation in a cartilage model and the maximum principal strain calculated through a finite element model

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### **Introduction**

Articular cartilage has a very limited self-healing capacity in case of injury or damage, creating a major clinical challenge. Researchers are focusing on Human Mesenchymal Stem Cells (hMSCs) because they have the potential to form new cartilage tissue, in a process called chondrogenesis. Transforming Growth Factor Beta1 (TGF- $\beta$ 1) is a key protein in chondrogenesis: it is produced by hMSCs in an inactive form and becomes effective when activated (aTGF- $\beta$ 1). There are several mechanisms of activation, among which mechanical force is one. To study this, hMSCs are placed in a structure, named scaffold, and exposed to mechanical forces that mimic daily activities in special machines called bioreactors. The scaffold design and material play a crucial role in activating TGF- $\beta$ 1. A very promising material is Thermoplastic Polyurethane (TPU), which is also 3D-printable. Additionally, finite element (FE) models are effective to predict local distributed forces and relative displacements – known as stresses and strains – in a scaffold under physical forces, helping to improve its design. In this study, as preliminary validation, we aim to correlate the activation of TGF- $\beta$ 1 in a bioreactor loaded scaffold with FE-predicted strain.

### **Methods**

Scaffolds ( $\varnothing$ 8mm, 4 mm height) were obtained from a 3D-printed sheet of TPU (gyroid structure, 83.1% porosity). They were filled with fibrin, a water-based gel that supports cells, covered in media containing 50 ng/mL inactive TGF- $\beta$ 1 and loaded in a mechanical bioreactor [1] for 6h with 10% preload plus 10%, 15% or 20% compression at 1 Hz. The media usually provides nutrients for the cells; however, in these preliminary experiments, cells were not used and therefore TGF- $\beta$ 1 was artificially added to the media. Unloaded controls were prepared the same way. TGF- $\beta$ 1 concentration was quantified in the media and inside the scaffold using ELISA DuoSet TGF-beta1 kit (R&D Systems). Scaffolds were washed with RIPA buffer to recover and quantify TGF- $\beta$ 1. A 3D model of the scaffold was built in Simpleware (v.2017, Synopsys) and imported in Abaqus (v2021, Dassault Systems) to create an FE model of the bioreactor-scaffold system, where pure axial displacements corresponding to the experimental compression levels were simulated. Maximum principal strain [2] was calculated in the FE model within the fibrin region surrounding the 3D printed scaffold and a median value was evaluated at each applied compression step.

### **Results & discussion**

The aTGF- $\beta$ 1 concentration inside the scaffold increased with increasing level of compression, without statistical differences. This trend was not observed in the surrounding media (Fig.1). Preliminary FE results show strain distribution inside the scaffold under different loading protocols, with higher maximum principal strain in the fibrin region due to lower stiffness (Fig.2). The correlation between aTGF- $\beta$ 1 values in the scaffold and FE-predicted median strain resulted in a correlation coefficient of 0.982 (Fig.3). This high value could be due to a low number of replicates, which should be increased in future experiments. Nonetheless, the positive correlation between aTGF- $\beta$ 1 and strain levels is confirmed assuming constant strain and stresses over time. All experiments were conducted in cell-free scaffolds: the action on the protein is fully mechanical and no biological processes are involved, which is captured by the FE model. Further work is ongoing to assess the spatial distribution of aTGF- $\beta$ 1 inside the scaffold and to correlate it with the local strains.

### **Conclusions**

Overall, a methodology to predict scaffold potential for TGF- $\beta$ 1 activation has been developed. This can be potentially applied to other scaffold structures to test them prior laboratory work, speeding up the scaffold optimization process.

[1] Gardner, O.F.W., et al., J Tissue Eng Regen Med, 2017

[2] Zahedmanesh, H., et al., Tissue Eng Part A, 2014

### **Acknowledgments**

Work funded by EU-OSTASKILLS, grant No. 101034412.

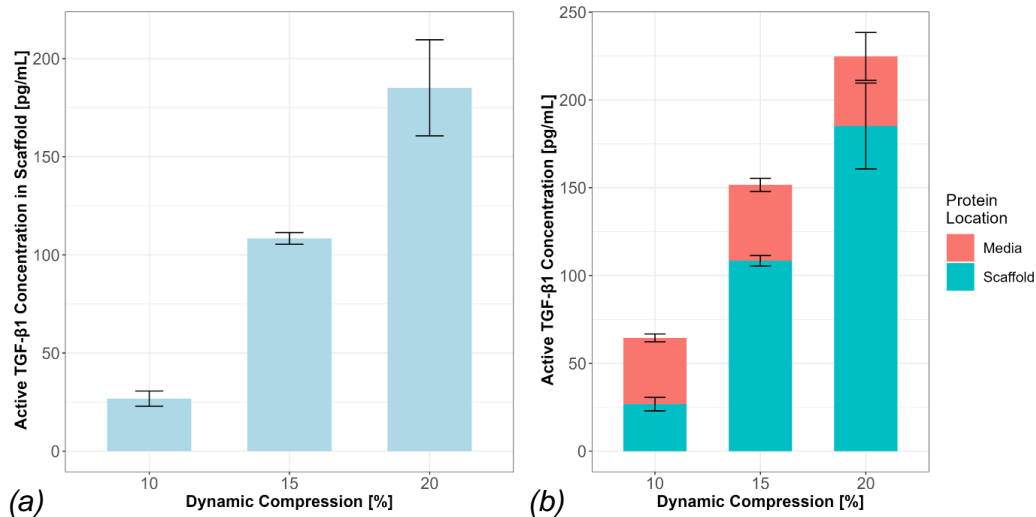


Figure 1: (a) Concentration of active TGF-β1 measured inside the scaffold. (b) Concentration of active protein inside the scaffold and outside in the media. Statistical test: Wilcoxon pairwise test,  $n=3$ ,  $p > 0.05$ .

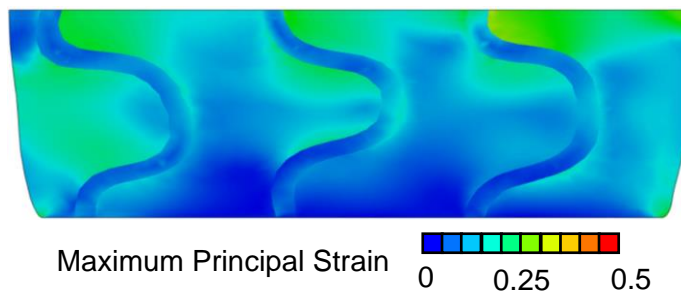


Figure 2: Contour plot of section view of FE model showing maximum principal strain (mm/mm) distribution in a section of the scaffold under the 20% strain loading scenario. Strain is seen to be higher in the fibrin region compared to the stiffer scaffold region.

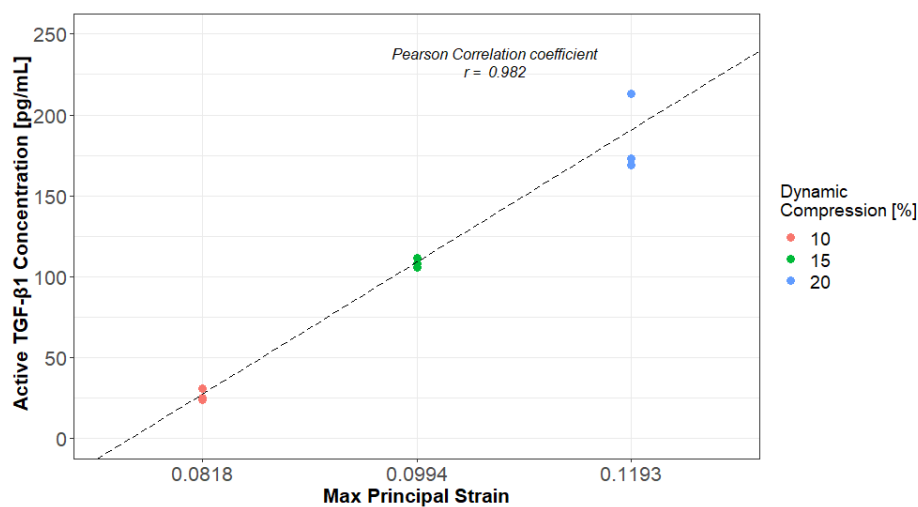


Figure 3: Linear regression analysis between the experimental values of active TGF-β1 and FE-predicted maximum principal strain. Pearson coefficient,  $r=0.982$ .

## **Innovative bone materials promote bone formation and simultaneously reduce the inflammatory response**

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Immunomodulation is becoming more widely recognized as an important element in bone healing, sparking growing interest in osteoimmunology. This new field explores the complex relationship between the immune system and how bones develop and maintain their strength. Key to keeping bones dense, strong, and in good health is the careful balance between the processes that break down bone (bone resorption) and those that build it up (bone formation). Understanding this balance and its modulation by immune processes is crucial for advancing treatments that enhance skeletal health and recovery from bone-related injuries.

This project is focused on developing innovative bone-forming substitutes and using high-throughput techniques to investigate their immunomodulatory effects on immune cells. Peripheral blood mononuclear cells (PBMC) cultures were meticulously optimized using a variety of commercially available compounds, such as beta-tricalcium phosphate, tyramine-modified hyaluronic acid (THA) gel, both filtrated and unfiltered bone particles (in monolayer and transwell cultures), agarose, fibrin sealant (Evicel), and their respective combinations. Phytohemagglutinin and a mixture of anti-CD2, anti-CD3, and anti-CD28 monoclonal antibodies were used as positive controls for stimulation in the assay. The experimental procedures included assessing proliferation through the integration of tritiated thymidine and microscopic observations, evaluating cell viability using propidium iodide in flow cytometry, and conducting targeted proteomics with the Proximity Extension Assay.

The results indicated a modest enhancement in cell proliferation when subjected to specific test materials, including THA gels, filtrated bone particles, and fibrin sealant. Conditions involving agarose resulted in a relatively increased level of proliferation. In the targeted proteomics analysis (OLINK T-92, inflammation and immune response panels), combinations of fibrin sealant and bone particles resulted in the upregulation of proteins linked to bone remodeling and reduced inflammatory response. It is worth noting that conditions involving agarose and bone particles did not produce significant changes in our biomarker panels. Regarding the ultimate results from proteomics analysis, we developed specialized panels (categorized as the bone remodeling and immune response panels) and examined the profiles displayed under various conditions in relation to these markers. We identified pathways related to the matrisome, plasmacytoma, apoptosis, and immune responses for fibrin sealant, both alone and in combination with filtrated bone particles. For optimal bone healing, a balanced dynamic between osteoblastogenesis and osteoclastogenesis is essential. Understanding the molecular basis of bone formation offers insights into the assessment of bone-related diseases and provides potential therapeutic targets for interventions aimed at regulating bone remodeling. In our study, the combination of fibrin sealant with bone particles exhibited beneficial properties in the analysis of both bone remodeling and immune response panels, suggesting its potential to enhance bone

formation and modulate immune activities. In this context, fibrin sealant-related conditions exhibited desired bone remodelling dynamics, regarding CSF-1, IFN-gamma, IL-1 alpha, LAP TGF-beta-1, OPG, TNF, and TRANCE expression. This was also corroborated by downregulation in the NT-3, TSLP, LIF, TGF $\alpha$ , STC1, TNFSF14, UPA, OSM,  $\beta$ -NGF, and FGF21 while upregulation in the TRAIL, CDCP1, MMP1, MMP10, MCP1, VEGFA, FGF19, LIF-R, SCF, CST5, and FGF23 in the fibrin sealant and bone particles combination.

In conclusion, the response of PBMCs to fibrin sealant and its combination with filtered bone particles indicates a decrease in bone resorption and inflammation, suggesting a potentially favorable material for bone formation.

## **Analysis of Eligibility of the S1 Corridor for the Trans-Sacral Screw Placement in Geriatric Patients**

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### **Introduction**

Minimal-invasive placement of a trans-sacral screw represents an increasingly popular method of fixation for Fragility Fractures of the Pelvis (FFP), with variable upper sacral anatomy representing the main challenge. Little is known about the variability of sacral anatomy in the geriatric population and the potential effect of osteoporosis on the upper sacral anatomy and thus S1 corridor morphology. To examine the eligibility (>12 mm) of the S1 corridor for the trans-sacral screw placement in a geriatric population and to analyse what pelvic dysmorphism signs might serve as predictors for an ineligible S1 corridor.

### **Methods**

We analysed S1 corridor in pelvic CT scans of 107 geriatric patients without history of fracture or other pelvic pathology. First, the eligibility for the trans-sacral screw placement was determined by measuring the width and the height of the central portion of the S1 corridor. Then, pelvises were examined for signs of dysmorphism. The correlation of these signs with the ineligible S1 corridor was analysed.

### **Results**

In our geriatric population with average age of  $79,55 \pm 8.79$  years (male:female 0.88) 41% of S1 corridors were not eligible for a trans-sacral screw. In this ineligible group the height was shown to be a more significant limiting dimension (90,9%), compared to the width in 68,2% ( $p < 0.05$ ). Mamillary processes, not recessed sacrum and dysmorphic sacral foramina were present in 38,3%, 34,6%, and 26,2% respectively, with not recessed sacrum demonstrating a significant correlation with a too narrow S1 corridor ( $p < 0.05$ ).

### **Conclusion**

The analysed geriatric population demonstrates a high prevalence of a too narrow S1 corridor, which makes a placement of a trans-sacral screw risky or even impossible. The height of the S1 corridor represents the main limiting factor with a dysmorphism sign of a not recessed sacrum being a significant predictor for the ineligible S1 corridor.



## A CRISPR-based assay for the detection of monoclonal antibodies

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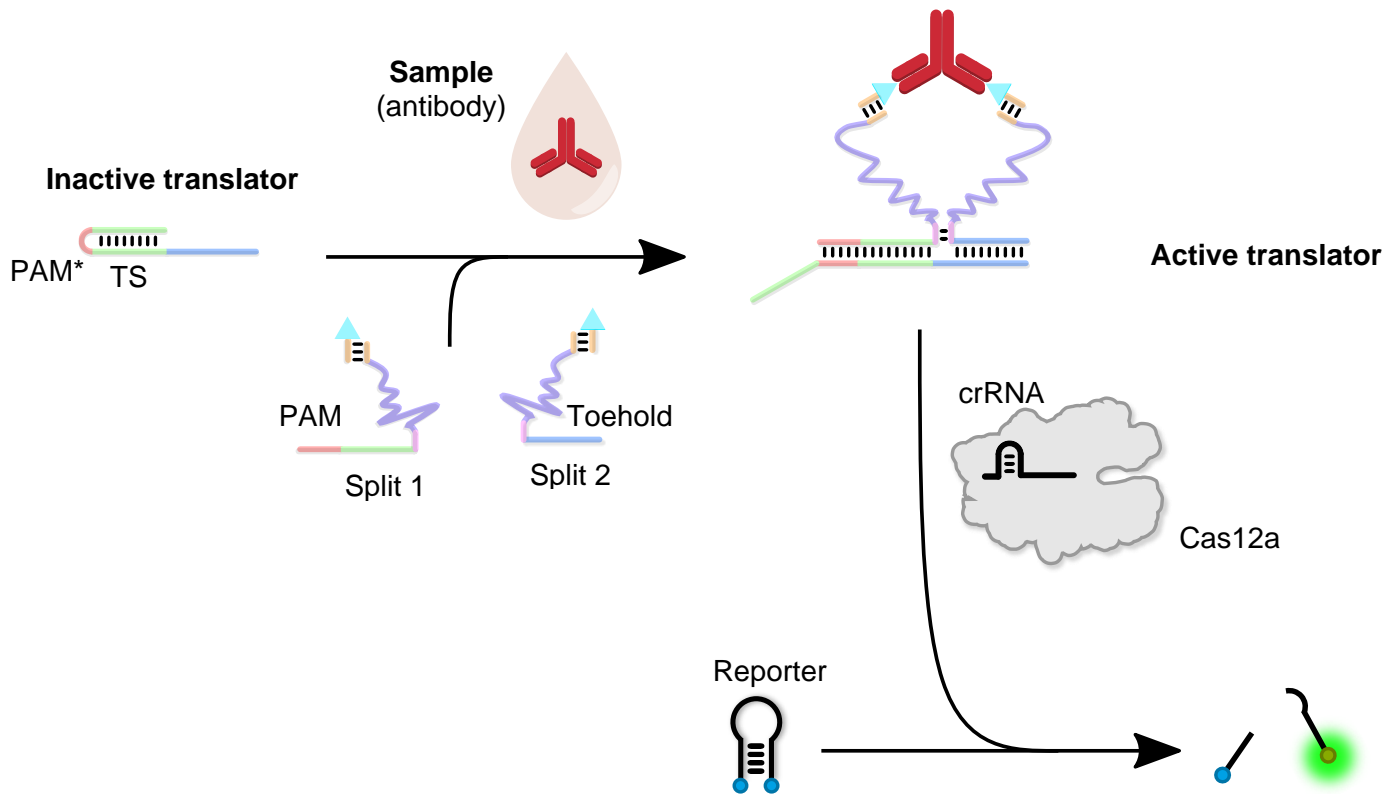
The demand for clinical analyses in hospital is growing, and proteins and nucleic acids (NAs) are the two main biomarker categories that are more relevant for diagnostics. The gold standard techniques for quantitative analysis of the abovementioned biomarkers are the enzyme-linked immunosorbent assay (ELISA) for proteins, the polymerase chain reaction (PCR) for deoxyribonucleic acids (DNA) and reverse transcription PCR (RT-PCR) for ribonucleic acids (RNA). All those techniques require expensive, bulky, and complicated instrumentation to use, making them inaccessible to the average end user at home. The necessity for new point-of-care (POC) devices, over the pregnancy tests, started to become more evident after the COVID pandemic where test kits based on lateral flow enabled to conduct mass testing on the world population: a simple sensing platform provides a positive or negative result without the use of sophisticated instrumentation but just by visual identification. Unfortunately, despite significant effort over the past years, a quantitative POC platform for protein or NAs analysis is still lacking.

In this work, we propose a simple and quantitative protein detection method based on the use of a DNA circuit [1, 2] for the recognition of monoclonal antibodies and the activation of a Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and CRISPR-associated protein (Cas) system (Figure 1). The versatility of CRISPR systems, as well as their lower cost, along with their excellent sensitivity and repeatability, make the developed method suitable for a POC application.

The DNA circuit includes an inactive DNA sequence called translator, which contains the Target Sequences (TS) and the complementary single-stranded Protospacer Adjacent Motif (PAM) in a closed loop conformation to prevent the access to the Cas. In addition to the translator, the reaction solution contains two additional single-stranded DNA (ssDNA) oligos called splits: the split 1 which presents the PAM sequence and the TS's complementary region, and the split 2 which has a toehold region to accelerate the circuit's activation. The antibody sensing element is a Peptide Nucleic Acid (PNA) which contains the epitope of the monoclonal antibody, hybridized to an extremity of each split. After the antibody-antigen peptides binding, the peptide-DNA splits are colocalized and initiate the strand displacement on the translator. This results in the translator activation in which the PAM is now in a double-stranded conformation. The Cas12a and the CRISPR-RNA (crRNA) ribonucleoprotein (RNP) recognizes the PAM and initiate the specific TS cleavage.

We exploit the Cas12a's collateral cleavage (trans-cleavage) activity toward single-stranded DNAs to generate a fluorescent signal from a molecular beacon reporter, which is functionalized with a fluorophore and a quencher in our case. Despite the tremendous potential, the system still needs a prior annealing step at different temperatures to improve the repeatability. Thus, our research focuses on the development of a “one-pot CRISPR-based assay” by maintaining the same performances of a multistep one.

The one-pot CRISPR-based assay has the potential to impact modern diagnostics and revolutionize the clinical market by introducing a new tool for NA and protein diagnostics at the POC. We set a first step in this direction by simplifying the assay procedure for future implementation in a POC device for protein detection.



**Figure 1:** An engineered DNA circuit for the detection of a monoclonal antibody and the activation of the ribonucleoprotein (RNP) made of the Cas12a and the CRISPR-RNA (crRNA) for the recognition of the target sequence (TS). The antibody binding event causes the DNA splits strands-displacement by co-localization. The DNA translator starts to hybridize with the two splits and forms a double-stranded protospacer adjacent motif (PAM), successively the RNP starts the cleavage of the TS. At the same time, other small single-stranded DNA (ssDNA) sequences can diffuse to the accessible active site, and by a collateral cleavage (trans-cleavage) the Cas12a starts to cleave them. We used a molecular beacon ssDNA reporter, fluorophore and quencher terminal labelled, to be able to generate a fluorescence signal after the trans-cleavage.