

UNI FR UNIVERSITÉ DE FRIBOURG UNIVERSITÄT FREIBURG

Activity Report 2017-18



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Welcome from the President

Anticipating future challenges. The Department of Biology has changed greatly during these last years, notably in the disappearance of the former "units" to form a more flexible and hierarchically uniform structure, the reorganization of the administrative and technical staff, the establishment of platforms in bioinformatics, bioimaging, and proteomics/metabolomics, and the creation of a new master in Bioinformatics in collaboration with the University of Bern. By providing teaching- and research-oriented services, the Botanical Garden is an essential part of the Department. The research conducted under the supervision of its Curator is growing, and the numerous events organized by the Garden place it as a lighthouse for the whole University. In all, our Department is increasing in efficiency and quality. Perhaps the best testimony is the success with external funding, with four Swiss National Science Foundation grants to buy new equipment, with a 100% success rate for the six projects submitted to the SNSF in 2018, and with five prestigious grants for outstanding young researchers (one Eccellenza and two PRIMA Grants from the SNSF, and two ERC Starting Grants from the European Research Council). Our department is now the largest of the Faculty of Science and Medicine, which comes with organizational challenges. However, these challenges are negligible in comparison with those imposed by current global changes. This puts responsibility on institutions of higher-education, and our Department is establishing two new master programs aimed to equip our students with the best knowledge to cope with these challenges. One will be health- and life-science oriented, the other will cover environmental and plant-health domains. All this is only possible with the remarkable involvement of all the members of our Department. May they be warmly thanked.

> President of the Department of Biology Prof. Louis-Félix Bersier

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Research Support

Our research groups benefit from the support of our technical and administrative teams. They ensure the good working of our Department to allow researchers to focus on what they do best.







Tho

Thomas Gruet







Evelyn Boll

Olga Sudan

Alain Werro







Catherine Cuennet Adeline Guélat

Sophie Gross

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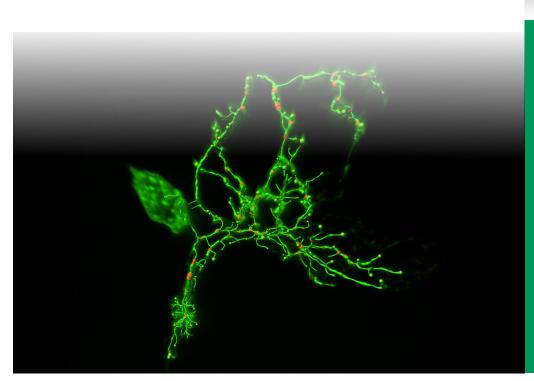
Bioimage

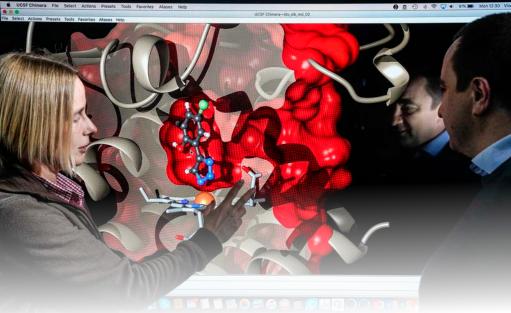
The Bioimage Light Microscopy Facility of the Departments of Biology and Medicine was established in 2013 to accommodate the increasing demand in light microscopy and image processing at the Faculty of Science and Medicine. The facility is managed by Felix Meyenhofer (Bioimage Analyst and Microscopist) and Boris Egger (Facility Coordinator and Microscopist).

Currently, about 100 active researchers from the Departments of Medicine and Biology, the Adolphe Merkle Institute (AMI) and the Swiss Integrative Center for Human Health (SICHH) use the services provided by the facility.

The Bioimage Facility gives training on various high-end microscopes and can be consulted for experimental design, image acquisition and image processing. The facility also organizes master and doctoral courses in light microscopy and image processing for life sciences.

unifr.ch/bioimage





Bugfri

The Bioinformatics Core Facility (established in 2013) is a joint platform between the Department of Biology and the section of Medicine. It is managed by Dr Laurent Falquet. The expertise of the platform is primarily the analysis of Next Generation Sequencing data, with emphasis on genome assembly and comparative genomics, as well as DNA methylation. We also perform other analyses, such as RNAseq, ChIPseq, metagenomics, and any large scale data analysis upon request etc. For more details see page 22.

Please contact us at bugfri@unifr.ch

Metabolomics and Proteomics Platform

The Metabolomics and Proteomics Platform (MAPP) is a service of the Department of Biology of the University of Fribourg. The mission of the platform is to provide expertise, instrumentation, and manpower to enable state-of-the-art implementation of metabolomic and proteomic analyses. To this end, the MAPP offers support in the planning and execution of experiments, including custom-tailored method development, sample preparation, data acquisition and analysis, and researcher training. Since its official start in January 2017, the MAPP has provided its services to many research groups of the Department of Biology as well as to some external customers. Notably, our activities have already contributed to several publications.

Metabolomics and Analytics Unit

The Metabolomics and Analytics Unit provides both analytical services (molecule identification and quantification by the platform staff) and teaching in analytics to researchers that prepare their samples under the supervision of the platform staff. Our mission is to assist the scientific community in implementing currently existing protocols as well as designing specific analytical methods related to their own research. Our unit is currently equipped with two HPLC systems coupled to a diode-array detector, a fluorescence detector and a fraction collector module, and two GC systems coupled to a flame-ionization detector and a single quadruple mass spectrometer. Following the successful R'Equip grant in 2018, we will soon have a novel GC-MS-qTOF that will enlarge our analytical capabilities, in particular for low abundance compounds (March 2019). The Metabolomics and Analytics Unit is currently assisting ongoing research projects developed by nine research groups of the Department of Biology of the University of Fribourg as well as projects currently conducted at the University of Geneva, Bern and Lausanne, at the Leibniz Institute for Zoo and Wildlife research in Berlin, and at a private Swiss company. Research projects notably include the identification and quantification of compounds of interest such as fatty acids, neurotransmitters, bacterial volatiles, hormones or psychotropic alkaloids, from animal samples (mice, Drosophila, bats), plant samples (Arabidopsis, maize, Australian endemic species and legal Cannabis) and from soil samples.

Proteomics Unit

The Proteomics Unit offers mass spectrometric (MS) analyses of protein samples as well as support for the expression and purification of proteins. Due to a successful R'Equip grant application, the Proteomics Unit is since April 2018 in the fortunate situation to have two high-end nanoLC-ESI-MS/MS instruments, the newly purchased Q Exactive HF-X and a Q Exactive Plus (in use since 2016), at their disposition for MS analyses.

In the last two years, twelve of the 27 research groups of the Department, as well as five external research groups, have utilized the services of the Proteomics Unit. For these customers, we have mainly provided the following services: (i) identification of interaction partners in immunoprecipitations either by determining the protein identity within gel bands or by on-bead digestion and label-free semi-quantitative mass spectrometry; (ii) identification of phosphorylation sites after in vitro kinase assays or at a proteome-wide level by deep phosphoproteome analyses; (iii) semi-quantitative (LFQ) or quantitative (SILAC labelling) determination of changes in protein composition within cell or tissue extracts. To overcome limitations of the metabolic SILAC labelling approach, we have established alternative state-of-the-art techniques for quantitative proteomics (i.e., dimethyl and TMT labelling). Besides these MS-analyses, we have also offered our support for the expression and purification of recombinant proteins to several research groups. Moreover, we have provided input for establishing an 'in vivo' kinase assay, relying on the co-expression of the kinase/substrate pair in bacteria.

Selected publications

Fasel N, McMillian K, Jakop U, Mène-Saffrané L, Engel K, Genoud M, Muller K, Christe P. Modification of sperm fatty acid composition during epididymal maturation in bats. Reproduction doi:10.1530/REP-18-0463 (2018)

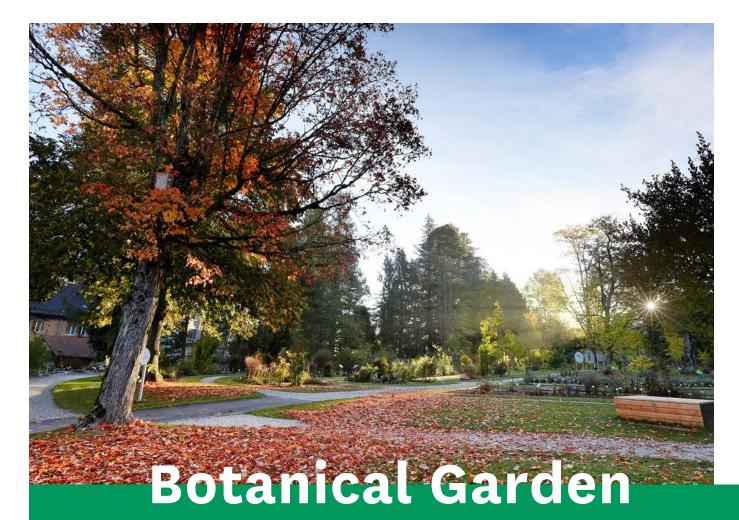
Pellaud S, Bory A, Chabert V, Romanens J, Chaisse-Leal L, Doan AV, Frey L, Gust A, Fromm KM, Mène-Saffrané L. Wrinkled1 and Diacylglycerol Acyltransferase1 regulate tocochromanol metabolism in Arabidopsis. New Phytologist. doi: 10.1111/nph.14856 (2018)

Selected publications

Bise T, de Preux Charles A-S, Jaźwińska A (2019) Ciliary neurotrophic factor stimulates cardioprotection and the proliferative activity in the adult zebrafish heart. NPJ Regenerative Medicine; ePub 24 January 2019

Gerber H, Mosser S, Boury-Jamot B, Stumpe M, Piersigilli A, Goepfert C, Dengjel J, Albrecht U, Magara F, Fraering PC (2019) The APMAP interactome reveals new modulators of APP processing and beta-amyloid production that are altered in Alzheimer's disease. Acta Neuropathologica Communications; in press

Co-workers: Dr Laurent Mène-Saffrané (Head of Metabolomics and Analytics Unit) Dr Dieter Kressler (Head of Proteomics Unit) Dr Michael Stumpe (Platform Manager)



Selected publications

Fragnière Y, Ruch N, Kozlowski E, Kozlowski G (2018) Connaissances botaniques de base en un coup d'œil, 40 familles de plantes d'Europe centrale. Haupt Verlag, Bern. pp. 320.

Fragnière Y, Ruch N, Kozlowski E, Kozlowski G (2018) Botanische Grundkenntnisse auf einen Blick, 40 mitteleuropäische Pflanzenfamilien. Haupt Verlag, Bern. pp. 320.

Co-workers

Curator: Prof. Gregor Kozlowski • Technical Manager: Nicolas Ruch • Communication and events: Annick Monod • Scientific collaborators: Sébastien Bétrisey, Yann Fragnière • Gardeners: Benoît Clément, Marianne Herren, Hélène Huguet-Sahli, Christine Jakob, Manuela Moduli, Josef Schöpfer, Jacques Sciboz, Hans Tschachtli • Trainees: Justine Alvazzi, Mathilde Schouwey

Discovering and learning about the plant world

Knowledge of the diversity of plants and more generally of biodiversity, is essential to protect nature. Among the different missions of the Botanical Garden of the University of Fribourg, vulgarization and teaching of botany are central points. Considerable enhancements have been accomplished during the last two years in order to achieve this mission. Firstly, the "System" has been completely renovated and modernized; this is the area in the Garden where plant species are presented according to their scientific classification. It is now a solid and an up-to-date living tool for presenting the diversity and evolution of plants. Secondly, a new 100% homemade and richly illustrated book published in autumn 2018 will help students and all interested persons to discover botany. This book concentrates on the Central European flora and plant families. It is an essential starting point for beginners, and a precious reference for advanced plant lovers.

To discover other missions of the Botanical Garden and our activities, please visit: www3.unifr.ch/jardin-botanique



The book is available in French and German. It is illustrated with many graphs, diagrams and photographs.

DEPARTEMENT OF BIOLOGY In figures - 2017/2018



167 Collaborators (49% women)

30 Nationalities



138 Researchers

27 Research groups

245 Publications



88 PhD students

78 Master students

291 Bachelor students



3.2 M CHF Internal funding

11.5 M CHF External funding



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Prof. Urs Albrecht

Analysis of circadian clocks and sleep in mammals

Circadian clock and sleep How does lifestyle influence sleep and health?

The earth's rotation around its axis causes periodic exposure of half of its surface to sunlight. This daily recurring event has been internalized in most organisms in the form of cellular circadian clock mechanisms. These cellular clocks are synchronized with each other in various ways to establish circadian networks that build the circadian program in tissues and organs, coordinating physiology and behavior in the entire organism. clocks, as experienced for instance in jet-lag and shift-work conditions, affects normal brain function and can lead to metabolic problems, sleep disturbance, and accelerated neurological decline. We aim to decipher the ways in which the circadian system can coordinate normal brain function and how waste clearance in the brain could be modulated by the circadian clock. Disturbances in these processes will lead to sleep problems and age-related cognitive decline, which are on the rise in modern society.

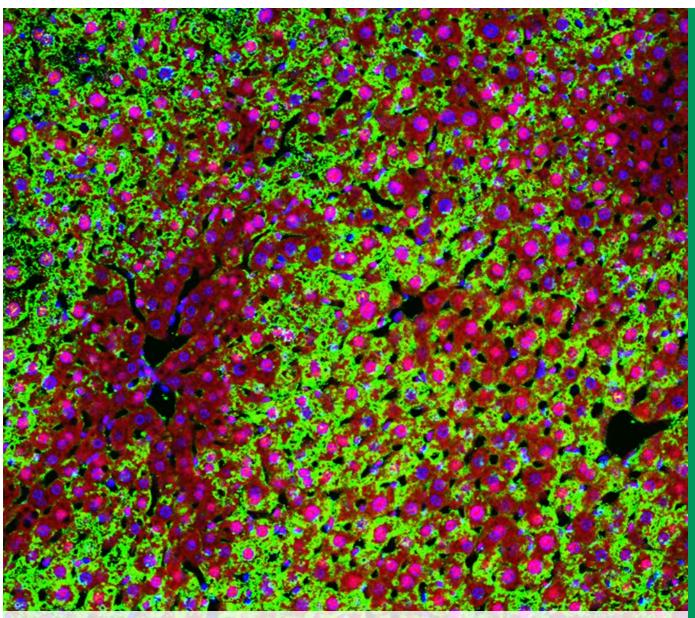
In the mammalian brain, the suprachiasmatic nuclei (SCN) receive light information via the retina and synchronize their own neuronal clocks to the light signal.

" Sleep problems are associated with most chronic and age-related diseases "

We are using normal and genetically modified mice in order to study causal relationships between the circadian clock and these neurological disorders.

Subsequently, the SCN transmits this information to the network of clocks in tissues and organs, thereby synchronizing body physiology and behavior. Disruption of cellular clocks and/or destruction of the synchronization between the A variety of molecular, biochemical, genomic, proteomic and metabolomic methods are applied towards the understanding of clock-sleep-metabolism relationships.





The glucocorticoid receptor (GR) is gated by Rev-erba to the nucleus at a particular time of the day. Murine liver was probed at zeitgeber time (ZT) 20 with antibodies specific for GR (red) and HSP90 (green). Nuclei were visualized using DAPI (blue).

Co-workers





Antoinette Hayoz



Stéphanie Aebischer



Andrea Brenna



Tomaz Martini

Jürgen Ripperger



Katrin Wendrich

Selected publications

U. Albrecht and J. A. Ripperger. Circadian Clocks and Sleep: Impact of Rhythmic Metabolism and Waste Clearance on the Brain. Trends in Neurosci., 41: 677-688, 2018.

R. Chavan, C.A. Feillet, S. S. Fonseca Costa, J.E. Delorme, T. Okabe, J.A. Ripperger, U. Albrecht. Liver-derived ketone bodies are necessary for food anticipation. Nature Comm., 7: 10580, 2016.

T. Okabe, R. Chavan, S.S. Fonseca Costa, A. Brenna, J. A. Ripperger, U. Albrecht. REV-ERB α influences stability and nuclear localization of the glucocorticoid receptor. J. Cell Sci., 129: 4143-4154, 2016.

G.M. Mang, F. La Spada, Y. Emmenegger, S. Chappuis, J.A. Ripperger, U. Albrecht and P. Franken. Altered sleep homeostasis in Rev-erb α knockout mice. Sleep, 39: 589-601, 2016.



Prof. Sven Bacher Applied Ecology

Ecology in the Anthropocene B³ - Biological invasions, Biodiversity & Biological control

Humans are changing the planet faster than ever before in history. These changes create challenges for science and society, but also opportunities to create better futures. Our research contributes to understanding the mechanisms and consequences of these changes, developing strategies to prevent harmful impacts and to use this knowledge to enhance ecosystem services that we receive from nature. We collaborate with international researchers and organizations such as the International Union for Conservation of Nature (IUCN) and the European Com-

mission (EC).

Which are the worst invasive alien species? The number of alien species is increasing exponentially

worldwide and there are many more species than can be managed. There are more than 14000 alien species in Europe, but not all of them cause problems to the environment or human well-being.

The seemingly simple and straightforward question "which are the worst invaders?" is difficult to answer

because the impacts of alien species can be manifold, and comparisons need to work for species as different as, for example, snails, insects, mammals and plants. We recently developed systems that allow alien species to be classified according to the magnitude of their environmental and socio-economic impacts (S/EICAT), which have been adopted as international standards by the IUCN.

" Alien species are a major threat to biodiversity and human well-being " Can we improve wine quality with biodiversity?

In the European project PromESSinG (www.promessing. eu), we investigate how we can use biodiversity-friendly ag-

ricultural management techniques to improve grape quality.

Improving biological control

In collaboration with the Swiss Federal Research Station Agroscope, we are studying how we can improve biocontrol of important insect pests such as pollen beetles (*Brassicogethes spp.*) and spotted wing fruitfly (*Drosophila suzukii*).

Co-workers







Caroline Curtis

Sonia Eckard









Deborah Kaiser Lara Reinbacher

Silvia Rossinelli



Magdalena Steiner





Andrea Zanetta

Selected publications

Bacher, S et al. (2018) Socio-economic impact classification of alien taxa (SEICAT). Methods in Ecology and Evolution, 9, 159–168.

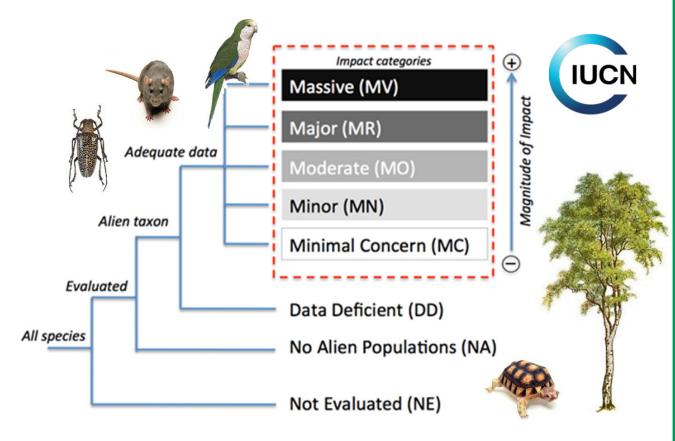
Lara Volery

Pauchard, A et al. (2018) Biodiversity assessments: Origin matters. PLoS Biology, 16, e2006686.

Seebens, H et al. (2017) No saturation in the accumulation of alien species worldwide. Nature Communications, 8, 14435.

Nentwig, W; Bacher, S; Kumschick, S; Pysek, P; Vila, M (2018) More than "100 worst" alien species in Europe. Biological Invasions, 20, 1611-1621.

Seebens, H et al. (2018) Global rise in emerging alien species results from increased accessibility of new source pools. PNAS, 115, E2264-E2273.



The Environmental Impact Classification of Alien Taxa (EICAT) allows to compare impacts of all alien species. It therefore can help answering the question "Who is the worst alien species?". EICAT is adopted by the IUCN as international standard.



Prof. Louis-Félix Bersier

Microbial systems and the structure and organisation of natural communities

Community ecology Community structure and functioning

Natural communities are composed of a myriad of species interacting in many ways among themselves and with their physical environment. Their action is essential as communities deliver "ecosystem services" like food provisioning, carbon sequestration, or nutrient recycling.

Understanding how communities are structured and how they function can be a daunting task given their complexity and variability. However, the microbial systems inhabiting the pitcher-shaped leaves

of Sarracenia purpurea, a carnivorous plant, are perfectly suited to tackle many fundamental questions in community ecology. This system is simple How does global change affect communities? "

From conservation to theoretical questions: in collaboration with Dr Pierre Bize, University of Aberdeen, and Fed-

enough to be captured in mathematical models and to be amenable to replicated experiments, but complex enough to reflect larger-scale systems.

Many natural communities are fragmented, notably because of the increasing impacts of humans on their environment, and form so-called metacommunities (local communities linked by migration of the species). It has been shown theoretically and experimentally that an intermediate rate of migration between the local communities is beneficial for their local diversity. What happens with increased temperature? erico Tettamanti, Game Office of Canton Ticino, we use hunting statistics to study the effect of increased temperatures and of competition with the Red Deer on the distribution and body size of the Chamois. In collaboration with Dr Victor Frossard, Université Savoie Mont Blanc, we explore with models and simulations the effect of potential invaders on lake ecosystems. In collaboration with Prof. Christian Mazza of the Department of Mathematics, we studied a fundamental question related to the so-called stability-complexity debate, a work that was recently published in PloS Computational Biology.

We studied this question with our microbial communities in incu-

We find that temperature does not change the shape of the dis-

persal-diversity relationship, but decreases diversity globally. We

studied two kinds of communities (early and late communities), and the results show that they are very different at the start of the

experiment, but converge to similar structure with time. These results provide important information for our understanding of co-

existence mechanisms in metacommunities.

bators where temperature and migration were manipulated.



How can global change affect the structure and functioning of metacommunities? This is one of the questions that can be answered thanks to our studies on aquatic communities living in the leaves of Sarracenia purpurea.

Co-workers





Samantha Coinus

Sarah Gray

Bachel Korr

Selected publications

Sandau N, Naisbit RE, Fabian Y, Bruggisser OT, Kehrli P, Aebi A, Rohr RP, Bersier L-F (2019). Understanding negative biodiversity-ecosystem functioning relationship in seminatural wildflower strips. Oecologia, 189(1), 185–197.

Parain EC, Rohr RP, Gray SM, Bersier LF (2018). Increased temperature disrupts the biodiversity-ecosystem functioning relationship. The American Naturalist, in press.

Dougoud M, Vinckenbosch L, Rohr RP, Bersier L-F, Mazza C (2018). The feasibility of equilibria in large ecosystems: A primary but neglected concept in the complexity-stability debate. PloS Computational Biology, 14(2), e1005988.



Dr Simon Blanchoud

Whole-body regeneration in Botrylloides leachii

Marine biology and regeneration Bringing the oceans to Fribourg

Oceans represent more than 90% of the Earth's biosphere, around 3 billion years of evolution prior to life on land and an estimated 2.2 million species spanning all phylogenetic kingdoms. Among this immense variety, marine and aquatic invertebrates show the largest biodiversity on Earth. In addition, they illustrate a profusion of exciting stem-cell-based phenomena, including regeneration and immortality. Consequently, research on these

organisms is of significant interest both for fundamental research as well as for human welfare. However, the study of these animals is hina drastically different body plan during their adulthood, tunicates have a tissue complexity related to ours, including a heart and a brain. In addition, we believe that tunicates can provide a more straightforward access to evolutionarily conserved biological processes. In particular, our laboratory is interested in the powerful regenerative capacity of *Botrylloides leachii*. These animals are resilient and invasive colonial tunicates that nowadays have spread

"These invertebrates are our closest relatives with such a powerful regenerative capacity to almost every sea worldwide. Extraordinarily, a colony of Botrylloides leachii can regenerate a fully functional

dered by the distance to their natural habitat. It is thus important to artificially recreate environmental conditions favorable to their development. Our laboratory has taken up this technical challenge by developing the first inland controlled breeding setup for tunicates. We thus host in Fribourg hundreds of wild invertebrates collected in the Venitian lagoon for many months already.

But why are we fascinated by tunicates? Because they are our closest invertebrate relatives! Studying these animals can thus shine new lights into our own origins. Accordingly, and despite

adult from a minute fragment of its vascular system in just 10 days. In this species, one tissue has the stem-like capacity to recreate all other tissues of an animal!

To study this dramatic process, our laboratory is using an interdisciplinary approach combining biology, microscopy and computer science. We are mapping the position, type and lineage of all cells involved in the regenerative process onto a 3D atlas of whole-body regeneration. This unique resource will allow us to characterize with unprecedented resolution the powerful regeneration capacity of Botrylloides leachii.



Two colonies of Botrylloides leachii, which have settled on microscopy glass slides, having a tour of their new environment.

Co-workers



Lluis Matas

Selected publications

Blanchoud, S., Rinkevich, B., & Wilson, M. J. (2018). Wholebody regeneration in the colonial tunicate *Botrylloides leachii*. In Results and Problems in Cell Differentiation (pp. 337–355). Springer International Publishing. https:// doi.org/10.1007/978-3-319-92486-1_16

Blanchoud, S., Rutherford, K., Zondag, L., Gemmell, N. J., & Wilson, M. J. (2018). De novo draft assembly of the Botrylloides leachii genome provides further insight into tunicate evolution. Scientific Reports, 8(1). https://doi. org/10.1038/s41598-018-23749-w

Blanchoud, S., Zondag, L., Lamare, M. D., & Wilson, M. J. (2017). Hematological analysis of the ascidian Botrylloides leachii (Savigny, 1816) during whole-body regeneration. The Biological Bulletin, 232(3), 143–157. https://doi. org/10.1086/692841



Prof. Jörn Dengjel

Regulation of protein homeostasis by autophagy

Cellular recycling How does a cell decide what to degrade when and where?

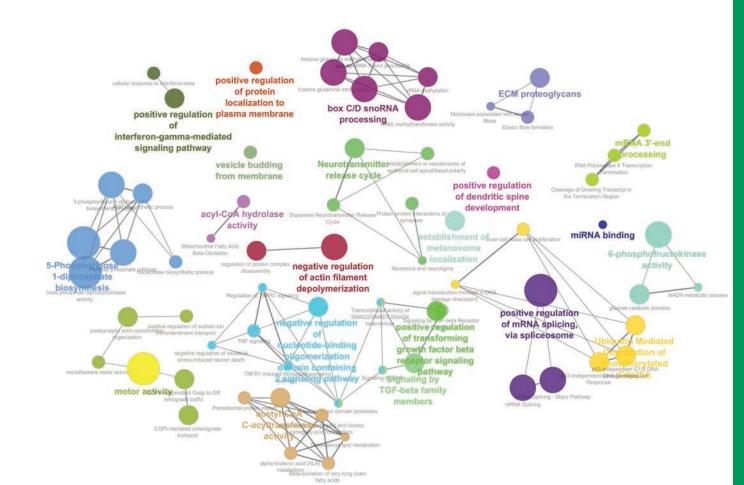
Macroautophagy, hereafter referred to as autophagy, is an evolutionary conserved, cytoprotective cell homeostasis pathway. We study the regulation and function of autophagy by analyzing proteins, which carry out the underlying molecular reactions. As many autophagy processes are characterized as being regulated on a post-translational level, we rely on quantitative mass spectrometry-based proteomics approaches to characterize mechanisms driving autophagy and regulating protein turnover.

Autophagy summarizes specific and non-specific lysosomal degradation pathways. Non-specific autophagy is a constitutive process, whereas specific autophagy leading to the degradation of defined subsets of organelles and/ or proteins is regarded as stress-induced.

Dysregulation of autophagy has been linked to many human diseases, most notably to neurodegeneration and cancer, as well as to ageing. We aim to characterize new proteins that are crucial for functional autophagy, or that are specifically degraded by autophagy, presumably to ensure cell survival under stress conditions. In parallel, we study proteins known to be involved in autophagy regulation, specifically kinases and phosphatases, to better understand their function and to be able to better assess their potential for use in therapeutic approaches targeting human diseases. A special focus is the crosstalk between the cellular microenvironment, i.e. extracellular matrix and soluble proteins, and autophagy regulators.

Keep on recycling ** Here, we use skin as a model system to study the role of auto-phagy in wound healing, employing primary skin fibroblasts and keratinocytes in 3D cell culture systems.

> We combine mass spectrometry method development with mass spectrometry-based screens, biochemical analyses of single proteins, and characterizations of phosphorylation and ubiquitination events to identify new players that are relevant in autophagy function. Our aim is to generate new insights into a fundamental biological process that is crucial for human health.



Characterization of regulated protein networks in autophagy-inducing conditions.

Co-workers





Stéphanie Kaeser-Peb<u>ernard</u>





Zehan Hu





Regine Tölle

Carole Roubaty De

Devanarayanan Siva





Christine Vionnet

Jianwen Zhou

Michal Rackiewicz

Selected publications

Becker, AC, Gannage, M, Giese, S, Hu, Z, Abou-Eid, S, Roubaty, C, Paul, P, Buhler, LK, Gretzmeier, C, Dumit, VI, Kaeser-Pebernard, S, Schwemmle, M, Munz, C, & Dengjel, J (2018). Influenza A virus induces autophagosomal targeting of ribosomal proteins. Mol Cell Proteomics 17:1909-1921.

Thriene, K, Gruning, BA, Bornert, O, Erxleben, A, Leppert, J, Athanasiou, I, Weber, E, Kiritsi, D, Nystrom, A, Reinheckel, T, Backofen, R, Has, C, Bruckner-Tuderman, L, & Dengjel, J (2018). Combinatorial omics analysis reveals perturbed lysosomal homeostasis in collagen VII-deficient keratinocytes. Mol Cell Proteomics 17:565-579.



Prof. Claudio De Virgilio

Nutrient signaling and control of quiescence in yeast.

Nutrients and cell proliferation Rag-time for baker's yeast

All living cells can exit the normal cell cycle and enter into a resting state termed quiescence or GO. Interestingly, most eukaryotic cells, whether they exist as single cells or as part of a multi-cellular organism, spend most of their lifetime in such a quiescent state. The regulatory mechanisms controlling entry into or exit from quiescence, however, are still largely elusive. Because the disruption of these mechanisms is thought to be associated with cellular transformation (in multi-cellular organisms) or dramatically reduced lifespan (in

unicellular organisms), it is likely that research in this area will not only enhance our basic understanding of diseases such as cancer, but also be instrumental

"We cherish an EGOcentric view of growth control "

Notably, amino acids are important and primeval cues that stimulate TORC1 to promote anabolic processes (such as ribosome biogenesis and protein translation initiation) and inhibit catabolic processes (such as macroautophagy) via the conserved Rag guanosine triphosphatases (GTPases).

The latter assemble into heterodimeric complexes consisting of Gtr1 and Gtr2 in yeast, or RagA or RagB and RagC or RagD in mammalian cells. These heterodimers are integral to larger com-

plexes coined EGO (exit from rapamycin-induced growth arrest) complex (EGOC) in yeast or

for the development of diagnostic and therapeutic tools to treat these diseases. To address the basic aspects of quiescence experimentally, we have chosen the unicellular eukaryote baker's yeast as a model system.

Our current data indicate that a conserved protein complex, coined target of rapamycin complex 1 (TORC1), plays a central role in yeast in coordinating both entry into and exit from GO in response to nutrient levels. This fits well with the reported role of TORC1 in coupling nutrient, energy, and hormonal signals with cell growth, division, and metabolism in higher eukaryotic cells.

Rag-Ragulator complex in mammalian cells, which are predominantly tethered to vacuolar or lysosomal membranes, respectively.

In this context, our current research is focused on deciphering the amino acid-sensitive events upstream of the Rag GTPases in yeast, which likely involve both vacuolar and cytoplasmic amino acid sensors. Due to the evolutionary conservation of the EGOC and its regulators, our studies in yeast are expected to contribute to the understanding of the molecular mechanisms leading to diseases that are associated with hyperactive mammalian TORC1, including cancer, type 2 diabetes, and neurodegeneration.



Baker's yeast cells grow and divide by budding in nutrient-rich environments. When starved of nutrients, however, they arrest as unbudded, quiescent single cells.

Co-workers





Ladislav Dokládal

Malika Jaquenoud





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M.-Pierre Péli-Gulli

Serena Raucci

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Selected publications

Péli-Gulli MP, Raucci S, Hu Z, Dengjel J & De Virgilio C (2017). Feedback inhibition of the Rag GTPase GAP complex Lst4-Lst7 safeguards TORC1 from hyperactivation by amino acid signals. Cell Reports 20, 281-288.

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UNI FR

Dr Boris Egger

Neural stem cell states in the brain of Drosophila melanogaster

Neural stem cells and development Building brains in flies

Brain development goes through phases of organ growth, differentiation and cell type specification. Initially, neural stem cells proliferate through symmetric divisions to rapidly expand a stem cell pool. At later developmental stages, neural stem cells switch to more restricted progenitor cell type states to generate neurons and glial cells through differentiative divisions. In disease situations, in which the transition from cell proliferation to differentiation is misregulated, we might observe tumorous overgrowth.

In other cases, premature а cell state transition can lead to small brains. also called microcephaly. investigate We the molecular and cellular mechanisms that regulate the transition of

" To what degree does oxygen availability control the formation and maintenance of neural stem cell states?"

stem cell states in the brain of the fruit fly Drosophila melanogaster. We try to understand how environmental factors interact with cell intrinsic regulators to control neural stem cell states. In collaboration with other research groups we have developed a biosensor to monitor oxygen availability in different neural stem cell compartments.

The biosensor reveals an intriguing correlation between hypoxia and various neural stem or progenitor cell types. An open question is to what degree does oxygen availability control the formation and maintenance of neural stem cell states. We also identified the nuclear hormone transcription factor *Tailless* as a crucial

> cell intrinsic factor during neural development in the fly visual system. Early Tailless gene function is required to prevent cell death and to maintain a pool of undifferentiated neuroepithelial cells. During later stages Tailless is necessary for

the timely generation of more restricted progenitor cells and the correct specification of neurons. We investigate how *Tailless* interacts with other intrinsic and environmental factors to control neural stem cell states.

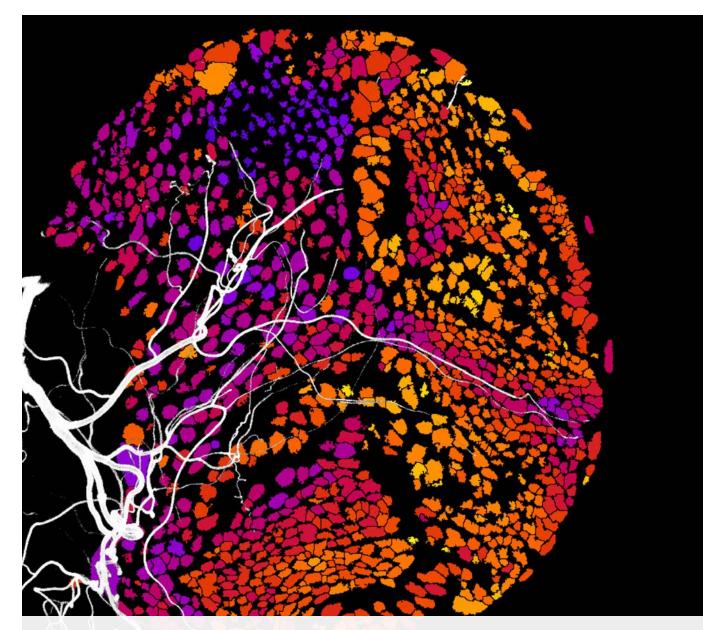


Image by Martin Baccino-Calace shows segmented brain nuclei that have been assigned a color according to the readout of a ratiometric hypoxia biosensor. The brain's air supply system, the tracheal system, is shown in white.



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Co-workers





leleye Oria Ika

Oriane Guillermin

Selected publications

Misra T, Baccino-Calace M, Meyenhofer F, Rodriguez-Crespo D, Akarsu H, Armenta-Calderón R, Gorr TA, Frei C, Cantera R, Egger B & Luschnig S (2017). A genetically encoded biosensor for visualizing hypoxia responses in vivo. Biology Open 6: 296-304

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Dr Laurent Falquet

TASmania: a bacterial toxin-antitoxin systems database

Toxin-antitoxin systems Devils and angels in bacteria controlling antibiotic resistance?

Toxin-Antitoxin Systems (TAS) are involved in several key biological functions in bacteria (e.g., persistence, plasmid maintenance, phage defense). They have been described in nearly all phyla and classified in six different types based on the activity and molecular type (ncRNA or protein) of their components, the Type II being the best studied and characterized. We developed **TASmania**, an *in silico* discovery pipeline min-

ing the >41'000 assemblies of Ensembl Bacteria database for known and uncharacterized protein components of Type I to IV TAS loci.

First, our pipeline annotates

the proteins based on a list of curated HMMs (Hidden Markov Models), which gives >2 million loci candidates, including orphan toxins and antitoxins. Second, it organises the candidates in pseudo-operon structures, in order to identify new Toxin/Antitoxin (TA) candidates based on a guilty-by-association strategy. In addition, we classify the two-component TAS by an unsupervised method on top of the pseudo-operon (pop) gene structures leading to 1'567 "popTA" models that offer a more robust classification of the TAS families. These results give valuable clues in understanding the toxin/antitoxin modular structures and the TAS phylum specificities. For example, only one TAS could be detected in three main phyla simultaneously (Bacteroitedes, Firmicutes, Proteobacteria).

Preliminary laboratory validations confirm putative **TASmania** new hits as promising candidates. Eleven putative toxins discovered by

" Persisters escape the treatment by sleeping "

TASmania in *M*. tuberculosis were tested *in vivo*, out of which six were confirmed to be toxic. In all of them, the simulta-

neous expression of the cognate putative antitoxin was shown to rescue the bacterial growth to normal, confirming the TAS pheno-type of these six pairs of genes.

The **TASmania** database is available on the following server: bugfri.unibe.ch/tasmania



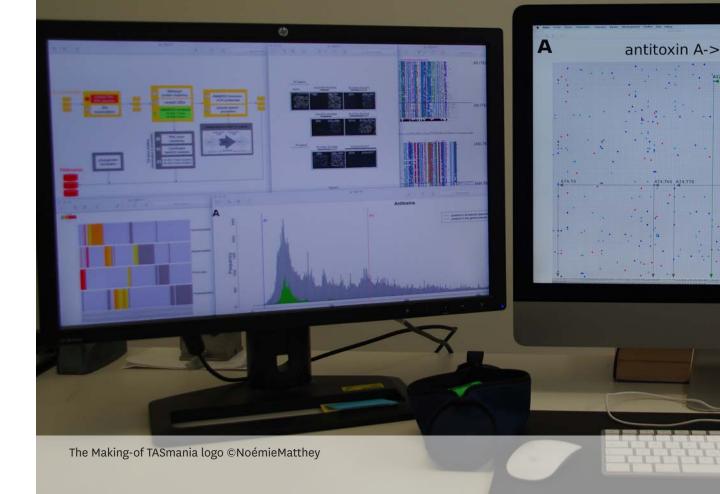






Hatice Akarsu-Egger

José Antonio Agüero



Selected publications

Genetic Separation of Listeria monocytogenes causing central nervous system infections in animals. Aguilar-Bultet L, Nicholson P, Rychener L, Dreyer M, Gözel B, Origgi FC, Oevermann A, Frey J, Falquet L. Front Cell Infect Microbiol. 2018 Feb 5;8:20. doi: 10.3389/fcimb.2018.00020.

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Prof. Thomas Flatt

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The genetics and genomics of adaptation in *Drosophila*

Genomics of adaptation Using fruit flies to find the genes that underlie adaptation

A fundamental aim of evolutionary biology is to understand the genetic basis of how organisms adapt to their environment. Our laboratory seeks to identify the genes and molecular polymorphisms that underpin adaptations by applying genomics and genetics to natural and laboratory populations of the vinegar fly, Drosophila melanogaster, a powerful, experimentally tractable model organism with a very rich history of fundamental discoveries in genetics, evolution and development over the last 100 years.

To do so, we employ populations of flies that differ genetically and phenotypically in fitness-related traits (so-called life history traits), for example in

"Finding the genes that underlie adaptation is a central problem in evolutionary biology"

terms of growth, size, fecundity and lifespan; such traits are the direct targets of natural selection and hence of major importance for our understanding of adaptation.

By investigating the genomes and transcriptomes of such flies with next-generation sequencing and by using population genetics, we can identify candidate genes and alleles that are tributes to adaptive variation in size and stress resistance; and how immunity genes in the Toll signaling pathway underlie the evolution of longevity.

Our current main focus is on understanding the role of chromosomal inversion polymorphisms in adaptation and how such polymorphisms are maintained by balancing selection.

likely shaped by selection. In a next step, we use the versatile genetic tool box available in *Drosophila* (e.g., mutants, transgenes, deletions, balancers, CRISPR/Cas9, recombinant populations) to test how the most promising candidate genes and alleles affect fitness-related traits.

In our recent work we have used this "pipeline" to discover how a large chromosomal inversion (a "supergene") affects multiple fitness traits, including body size, lifespan and stress resistance,

> along environmental gradients; how a central transcription factor of the insulin/insulin-like growth factor signaling (IIS) pathway con-



To examine genetic changes in natural populations we regularly collect fruit flies in the wild, in collaboration with the European Drosophila Population Genomics Consortium (DrosEU).

Co-workers





Marta Bellone

Esra Durmaz





Martin Kapun

Laurent Boualit



Katja Hoedjes

Envel Kerdaffrec







Margot Paris

Marisa Rodrigues

Sara Santi

Selected publications

Kapun, M., and T. Flatt. 2018. The adaptive significance of chromosomal inversion polymorphisms in *Drosophila melanogaster*. Mol Ecol, in press.

Durmaz, E., Benson, C., Kapun, M., Schmidt, P., and T. Flatt. 2018. An inversion supergene in Drosophila underpins latitudinal clines in survival traits. J Evol Biol 31: 1354-1364.

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Dr Markus Geisler

Biochemical analysis of transport complexes in plants

Hormone transport and development **Plant lessons: comparing plant** and mammalian transport systems

My group has a long-lasting interest and expertise in analyzing transmembrane transport processes in plants on a biochemical level. While we have been able over the years to assign transporters of different sub-classes to distinct plant hormones, our focus still lies on the fascinating cell-to-cell movement of the plant signaling compound, auxin. This event, called polar auxin transport, represents a unique, plant-specific mechanism that controls virtually all aspects of plant growth and performance and represents a hotspot in plant biology. "Think twisted!

Another relevant function of TWISTED DWARF1 is connected with its ability to affect cytoskeleton dynamics by regulating the bundling of actin filaments. Currently, we are studying how TWISTED DWARF1 interferes with actin and membrane dynamics by using pollen tubes and tobacco cells as a model system.

Moreover, we are investigating the clinically relevant phenomenon of multidrug resistance by dissecting dual substrate specificity in the ABC transporter, ABCG36/PEN3/PDR8, which is involved

Presently, we are exploring the functional relevance of the interaction between

the auxin exporter, ABCB1, and the FKBP42, TWISTED DWARF1. It appears that TWISTED DWARF1 functions as a co-chaperon for so-called Heat-Shock Proteins (HSPs) that stabilize ABCB-type auxin transporters at the plasma membrane. This complex module of ABC transporter regulation seems to be conserved between plant (green pump in figure) and mammalian ABC transporters (red pump).

expect a deeper understanding of transmembrane transport in general. In the last two years, we have been performing a structure-function analysis of the ABC-ty auxin transporter, ABCB1, in the model plant Arabidopsis. Using a mutational approach, we were able to identify a short motif that is essential for auxin transport and that seems to define Auxin-transporting ABCBs, socalled ATAs.

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in plant devel-

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ease resistance.

these "twisted"

approaches we

all

Employing



Plant transporters (green pump) share many features with mammalian transporters (red pump), but reveal also some unique features that might be useful for an understanding of transporter functionality.

Co-workers





Bibek Aryal

_____Laurence Charrier

Martin Di Donato





lio

Selected publications

Geisler M (2018) Seeing is better than believing: Visualization of membrane transport in plants. Curr. Opin. Plant Biol. 46: 104-112

Zhang Y, Naser V, Pisanty O, Omary M, Wulff N, Di Donato M, Tal I, Hauser F, Hao P, Roth O, Fromm H, Schroeder J, Geisler M, Nour-Eldin H and Shani E (2018) A transportomescale amiRNA-based screen identifies redundant roles of Arabidopsis ABCB6 and ABCB20 in auxin transport. Nat. Comm. 9: 4204

Mao H, Aryal B, Langenecker T, Hagmann J, Geisler M and Grebe M (2017). Arabidopsis BTB/POZ protein-dependent PENETRATION3 trafficking and disease susceptibility. Nature Plants 3: 854-858



Prof. Dominique Glauser

Analysis of nociception and avoidance behaviours in *Caenorhabditis elegans*

Nociception and plasticity A small worm teaching us how to shut off pain signal

Like most animals, we are able to detect damaging or potentially damaging stimuli, through a process called nociception. Nociception underlies important protective behaviours to avoid injuries and favour healing. However, in pathological situations pain may also become persistent with no actual benefit. Chronic pain affects more than a billion people worldwide. Because available drugs are either only moderately effective or have detrimental side effects, there is an essential need for improved pain management solutions. controlling nociception. Using forward and reverse genetic screens, we identify conserved genes required for thermal nociception and avoidance behaviours. For example, we have discovered mutants with impaired sensitivity to noxious heat, as well as mutants unable to habituate to repeated noxious stimuli, or that habituate faster.

These mutants are essential entry points to discover and characterize novel molecular pathways controlling nociception and plas-

Progress in the field is hindered in human and m a m m a l i a n models by ethical concerns, by the size and the complexity

" There is an essential need for improved pain management solutions "

ticity mechanisms in the nociceptive pathway. Furthermore, we use a combination of cutting-edge in

of the nervous system, as well as by the difficulty to bridge the gaps in our understanding at the molecular, neuronal, and physiological/behavioural levels.

To circumvent these limitations, our lab uses the simple model organism Caenorhabditis elegans and has developed a series of fruitful approaches to investigate the mechanisms vivo imaging techniques, proteomic, transcriptomic, optogenetics and computer-assisted analysis of behaviour to better understand the implicated mechanisms at the molecular, cellular and circuit levels. As a whole, our integrative research both provides a fundamental knowledge about the mechanisms underlying pain sensation and aversive behaviours, and brings insight on new potential drug targets for future pain treatment translational development.



Uncovering the functioning logic of the nociceptive circuit in C. elegans. With this optogenetics setup, we can remotely control the activation of different neurons in a population of free-moving animals, while simultaneously recording their behaviour.

Co-workers





Georgina Gomez Domenica Ippolito







Gonçalves Marques

Aurore Jordan

Andrei-Stefan Lia













Gabriella Saro

Lisa Schild







Saurabh Thapliyal

Lola Hostettler

Vanina Lauper

Selected publications

Schild LC and Glauser DA (2015) Dual color neural activation and behavior control with chrimson and CoChR in Caenorhabditis elegans. Genetics Aug 1; 200(4):1029-1034

Glauser DA and Goodman MB (2016) Molecules empowering animals to sense and respond to temperature in changing environments. Curr Opin Neurobiol. Dec;41:92-98.

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Prof. Claire Jacob

Regeneration of the nervous system in rodent models

Chromatin remodeling and regeneration **Reprogram myelinating cells to regenerate the nervous system**

We aim at elucidating basic functions of chromatin-remodeling enzymes in the control of neuroregeneration and testing our findings as exploratory treatments in rodent models for potential cures. We are particularly interested in elucidating mechanisms that can be potentially used to enhance the regeneration of the central nervous system after traumatic lesions such as spinal cord

injuries.

We are also very interested in the study of traumatic lesions of the peripheral nervous system and of degenerative diseases of the peripheral and central nervous systems due to functional "We aim to identify a treatment strategy to cure paraplegia".

repair programs that enables peripheral and central axons to functionally regenerate after lesion.

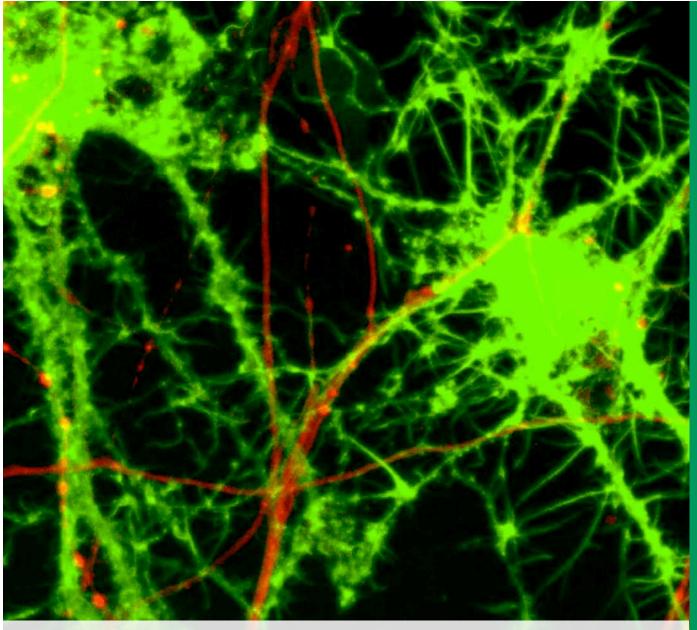
To this aim, we use multiple technical approaches including microscopy, molecular biology, transcriptomics, proteomics, as well as *in vivo* rodent models, in order to fully analyze dynamic

> transcriptome landscape changes controlling neural cell plasticity over time after lesion and the underlying mechanisms, identify key responses of myelinating cells, measure their impact on neuron transcriptional programs after lesion, validate our findings *in*

defects in myelinating cells (Schwann cells in the peripheral nervous system and oligodendrocytes in the central nervous system), such as Charcot-Marie-Tooth disease in the peripheral nervous system and multiple sclerosis in the central nervous system.

Our work is particularly focused on the influence of myelinating cells in the regeneration of neurons and neuronal networks. The main objective of our research is to design a transcriptional blueprint of myelinating cell plasticity and axon vivo and test exploratory pharmacological approaches and gene therapy treatments in mice as proof of concept for potential cures to promote regeneration of the nervous system.

To select the most promising strategies to improve regeneration after lesion, we have recently set up *in vitro* models of peripheral and central nervous system lesion using microfluidics. These models already enabled us to discover a novel plasticity mechanism of the peripheral nervous system that we could induce in the central nervous system model. We will soon test whether this strategy improves regeneration *in vivo*.



Live imaging of F-actin (green) in oligodendrocytes in culture with neurons (red).

Co-workers







Mert Duman

Gianluigi Nocera Antoinette Hayoz





Selected publications

Jacob C (2017). Chromatin-remodeling enzymes in control of Schwann cell development, maintenance and plasticity. Current Opinion in Neurobiology 47: 24-30.

Brügger V, Duman M, Bochud M, Münger E, Heller M, Ruff S & Jacob C (2017). Delaying histone deacetylase early response to injury accelerates conversion into repair Schwann cells and nerve regeneration. Nature Communications 8:14272.

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Dr Gwenaël Jacob Applied population conservation

Evidence-based conservation of populations Tracking the causes of population decline

Many species have declined in the last century, and enormous efforts are currently invested in preventing their extinctions, mostly through management of habitat and reduction of human-induced disturbances. However, the success of conservation measures, including legal protection, is rarely evaluated. Indeed, tracking the response of populations to management actions is complicated by incomplete knowledge of the species biology and methodological challenges. Our group is specialized in the applications of molecular tools to identify individuals from

DNA traces and study population demographic parameters.

" "Tackling methodological challenges in wildlife monitoring"

(forensics) and estimation of abundance from systematic s a m pling. These results

DNA traces

Genetic anal-

yses of non-invasive Eurasian otter (Lutra lutra) samples revealed that the species persisted in France in six different refugia, and allowed to better understand the pattern of rapid spatial expansion observed in France. Evaluation of the Eurasian beaver (Castor fiber) reintroduction in Switzerland confirmed the origin of the stocking populations, and showed low levels of genetic diversity and high levels of inbreeding of the Swiss population. This study was used to inform national management actions for the species and highlighted the role of Switzerland in the restoration of beaver populations at the continental scale. help us better understand the spatial structuring of genetic diversity in the two species, and the role of intrinsic and extrinsic environmental factors driving population susceptibility to habitat fragmentation.

Group activity currently focuses on monitoring programs of two

species listed as endangered in the Canton of Fribourg and in Swit-

zerland, Western capercaillie (Tetrao urogallus) and Hazel grouse

(Tetrastes bonasia). Collaboration and knowledge transfer with

national and international institutions and NGOs allowed us to

implement robust monitoring schemes. Observations and genet-

ic data gave information on the spatial distribution of individuals and highlighted differences in ecological niches between sexes.

Ongoing research is conducted on individual identification from

We combine theoretical work and a wide range of analyses to describe the level of genetic relatedness among males and females within a lek, and understand the factors affecting dispersal in the species. Improving our knowledge of the species ecology is key to designing effective management plans.

Co-workers



Francesco Foletti

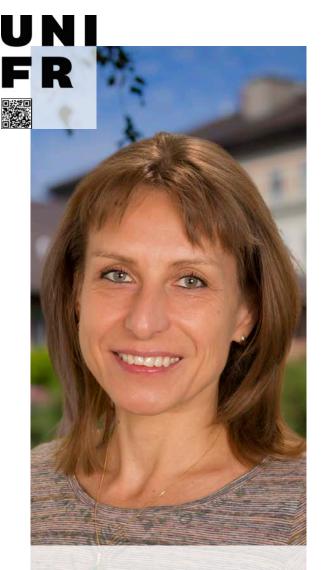
Selected publications

Pigneur L-M, Michaux JR, Jacob G. 2018. Apport de la génétique pour l'étude de la dynamique des populations de Loutre d'Europe Lutra lutra (Linnaeus, 1758) en France. Naturae 2018:63–71.

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Capercaillie (Tetrao urogallus) is a secretive species. Systematic sampling and genetic analyses revealed its ecological peculiarities. These findings pave the way to evidence-based conservation of the species.



Prof. Anna Jazwinska

Exploring heart, fin and retina regeneration in zebrafish

Organ regeneration Zebrafish repair their broken hearts and regrow amputated appendages

Unlike mammals, zebrafish can completely regrow lost structures, such as amputated appendages or injured hearts. This natural restorative ability relies on the plasticity of mature cells in the wounded organs. Activated cells proliferate and reproduce fully functional tissues. We aim to better understand this process.

The zebrafish is a valuable model organism in regenerative biology, thanks to experimental advantages, such as effi-

cient reproduction and a well-annotated genome. For functional studies, we use newly established genetic

" The secrets of regeneration are swimming in aquaria "

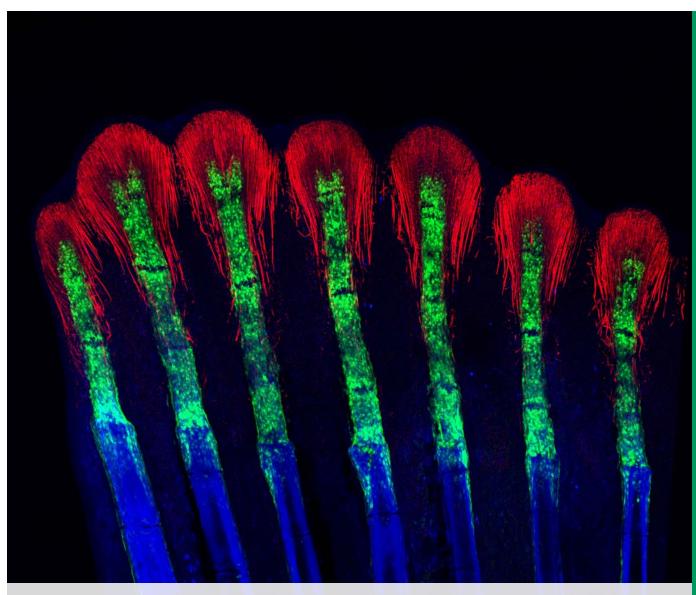
tablished genetic approaches, such as CRISPR/Cas9 mutagenesis, CreERT-loxP cell-lineage tracing, cell ablation, fluorescent gene reporters and inducible gene overexpression.

We describe the biological processes by means of microscopic photography of live animals, histological staining of fixed tissues, multi-color fluorescence imaging and in situ hybridization for visualization of gene transcription. In the last year, we discovered a regulatory element, called careg, which is induced by TGF β /Activin- β signaling in the regenerating hearts and fins after injury.

This allowed new insights into the mechanisms of heart and fin restoration and provided evidence for the existence of common regulatory programs of regeneration that operate in diverse organs. In another study, we focused on regeneration of fin-specific skeletal elements, named actinotrichia, which similarly to our fingers, are positioned at the tip of the appendage. We developed

> sensitive antibodies to monitor morphogenesis of these structures, and showed that the dynamic turnover of actinotrichia is regulated by multiple factors,

including potassium channel (kcnk5b) and FGF signaling. This study revealed the mechanisms regulating actinotrichia formation at the distal position during rapid fin regrowth. In the future, we will investigate cell migration in the regrowing bones, monitor cardiac cell behavior during regeneration and characterize the role of several specific genes during tissue restoration. Knowledge of the mechanisms of organ regeneration in zebrafish could open new directions in medical research.



Skeletal structures of a regenerating fin. Immunofluorescence staining of a zebrafish fin at 5 days post-amputation. Bone matrix of the stump in blue; regenerating bones in green; actinotrichia at the tip of the regenerate in red.

Co-workers







Thomas Bise

Désirée König













Simon Blanchoud

Catherine Pfefferli

Verena Zimmer mann

Selected publications

König D, Page L, Chassot B & Jazwinska A (2018). Dynamics of actinotrichia regeneration in the adult zebrafish fin. Developmental Biology 433: 416-432.

Pfefferli C & Jazwinska A (2017). The careg element reveals a common regulation of regeneration in the zebrafish myocardium and fin. Nature Communications 8: #15151.

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Prof. Gregor Kozlowski

Molecular phylogeny, phylogeography and population genetics of threatened, endemic and relict plants

Conservation biology and biogeography Biological diversity – life insurance for our changing world

During the last centuries, the dimension of anthropogenic alteration of natural habitats and the extinction crisis has attained levels never seen during human history. The destruction of ecosystems can have a very serious effect both on local and global levels.

Our work aims at exploring the evolutionary processes, biogeographical patterns and conservation issues of threatened, endemic and relict species. At the international level, the ma-

group coordinates of the interdisciplinary and international

projects Zelkova and Pterocarya, becoming in the last decade

a leading force in the research and conservation of relict trees.

Our projects address five main objectives: (1) Basic and ap-

plied research; (2) In situ and ex situ conservation activities,

jor focus of our research activities lies on woody species of the Ulmaceae (Zelkova), Juglandaceae (Pterocarya), and Salicaceae (Populus). On a national and local scale, our interest touches members of Sapindaceae (Acer) and Rosaceae (Sorbus). Our

" The extinction crisis has attained levels never seen during human history "

tific drawings, etc.).

The trademark of our group is intensive fieldwork both locally (Switzerland, Alps) and globally (Mediterranean islands,

Transcaucasia, Eastern Asia, North- and Central America).

Our group is associated with the Botanical Garden of the University of Fribourg (G. Kozlowski is a curator of the garden) and is intensively collaborating with the Natural History Museum Fribourg (NHMF), with the Nature and Landscape Office (SNP/ANL) as well as with the Office of Forest, Wildlife and Fisheries (SFF/WaldA) of the State of Fribourg.

action plans and conservation status assessments; (3) Capaci-

ty-building; (4) Public awareness and outreach; and (5) Enrich-

ment of iconographic collections (scientific photography, scien-

The second focal point of our investigations are threatened aquat-

ic macrophytes (e.g., Nuphar pumila) and alpine endemics (e.g., Papaver occidentale). We are applying various modern bio-

geographical, molecular and dendrochronological methods.

More information under zelkova.ch.



Forests of Pterocarya hupehensis (Juglandaceae) in Henan Province, China.

Co-workers





Benoît Clément



Sébastien Bétrisey

Laurence Fazan







Yann Fragnière

Eveline Kozlowski

Salvatore Pasta



Yi-Gang Song

Selected publications

Kozlowski G, Bétrisey S, Song Y-G. 2018. Wingnuts (Pterocarya) and walnut family. Relict trees: linking the past, present and future. Natural History Museum Fribourg, Switzerland. pp. 128 (book).

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UNIVERSITY OF FRIBOURG - DEPARTMENT OF BIOLOGY



Dr Dieter Kressler

Analysis of eukaryotic ribosome biogenesis in Saccharomyces cerevisiae

Ribosome origami Piecing together the puzzle of life: priming ribosomal proteins for assembly

Ribosomes are the molecular machines that carry out the synthesis of all cellular proteins from mRNA templates. Eukaryotic 80S ribosomes are composed of two unequal subunits, a small 40S and a large 60S subunit, which contain a total of four different mature ribosomal RNAs (rRNAs) and ~80 ribosomal proteins (r-proteins). At first glance, the assembly of these rRNAs with the r-proteins may look like a rather trivial task – however, research carried out over the last 50 years, mainly with the yeast Saccharomyces cerevisiae, revealed that the biogenesis of eukaryotic ribosomes is a tremendously com-

plex process. The act of building a ribosome begins in the nucleolus, where the ribosomal

"The assembly of functional ribosomes is a work of art."

the ribosomal DNA is transcribed into a long precursor rRNA (35S pre-rRNA in yeast), and involves the ordered assembly of the r-proteins with the pre-rRNA, which is concomitantly processed into the mature rRNA species. These assembly and processing events are not only tightly coordinated, but also occur within pre-ribosomal particles that travel, as maturation progresses, from the nucleus to the cytoplasm, where they are ultimately conwill

verted into translation-competent ribosomal subunits.

Given its gargantuan complexity, it is not surprising that this spatially and temporally controlled assembly process strictly depends on a multitude (>300) of mostly essential biogenesis factors. Despite the enormous recent progress, fuelled by ground-breaking advances in cryo-electron microscopy enabling the near-atomic visualization of pre-ribosomal particles, in understanding how this gigantic molecular jigsaw puzzle is pieced together, the precise role of many biogenesis factors and the molecular mechanisms driving ribosome assembly remain in many instances to be determined.

oratory has considerably contributed to the discovery and conceptual appreciation of dedicated chaperones of r-proteins - these selectively protect, in many cases by already capturing their client in a co-translational manner, and promote the assembly of individual r-proteins. To pursue this avenue of research, our ongoing studies are aimed at the identification and functional characteriza-

studies are aimed at the identification and functional characterization of novel dedicated chaperones. We expect that our research will help to better understand the aetiology of ribosomopathies, diseases frequently caused by alterations of r-proteins.

Recent work

from my lab-

Benjamin Pillet

Co-workers

Alfonso

Méndez-Godov

Selected publications

Bioessays 39(1):1-12.

Guillaume Murat

Kressler D, Hurt E, Baßler J (2017) A puzzle of life: crafting ribosomal subunits. Trends Biochem Sci. 42(8):640-654.

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your friends: dedicated chaperones of ribosomal proteins.

Pillet B, García-Gómez JJ, Pausch P, Falquet L, Bange G, de la Cruz J, Kressler D (2015) The dedicated chaperone Acl4 escorts ribosomal protein Rpl4 to its nuclear pre-60S

Kater L, Thoms M, Barrio-Garcia C, Cheng J, Ismail S, Ahmed YL, Bange G, Kressler D, Berninghausen O, Sinning I, Hurt E, Beckmann R (2017) Visualizing the assembly pathway of

Thoms M, Mitterer V, Kater L, Falquet L, Beckmann R,

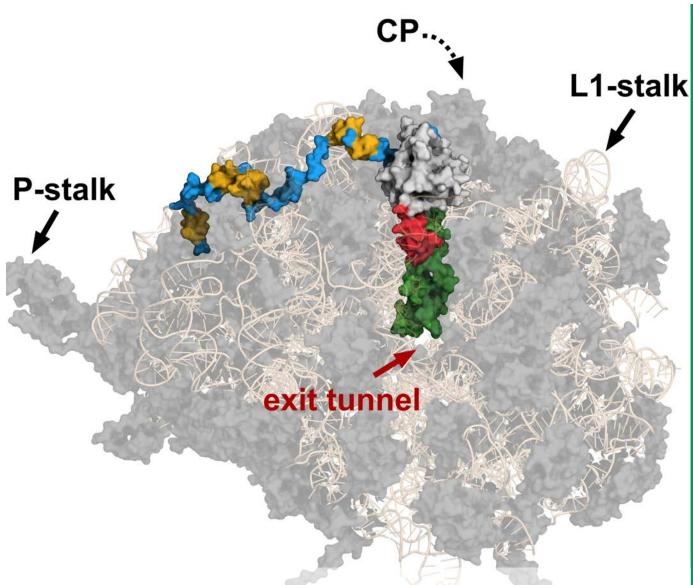
Kressler D, Hurt E (2018) Suppressor mutations in Rpf2-Rrs1

or Rpl5 bypass the Cgr1 function for pre-ribosomal 5S RNP-

nucleolar pre-60S ribosomes. Cell 171(7):1599-1610.

assembly site. PLoS Genet. 11(10):e1005565.

rotation. Nat Commun. 9(1):4094.



Structure of the 60S ribosomal subunit highlighting the position of the r-protein Rpl4, which requires the dedicated chaperone Acl4 for efficient assembly. The different structural features of Rpl4 are coloured as follows: globular domain (grey), long internal loop (green), small internal loop (red), and eukaryote-specific C-terminal extension (blue and yellow). The remaining r-proteins are coloured in dark grey and the rRNA in white. Characteristic features of the 60S subunit are indicated. The image was created with PyMol using the PDB file 4V88 (Ben-Shem et al. 2011 Science 334:1524-1529).





Prof. Félix Mauch

Molecular basis of plant disease resistance and pathogen virulence

Plant immunity Behind enemy lines: How do pathogens sabotage plant immunity?

Research in the Mauch lab focusses on molecular mechanisms of plant immunity and pathogen virulence. The immune system of plants is similar to innate immunity of animals. A number of usually-surface localized immune receptors recognize conserved pathogen-derived molecules and as a result, a multitude of immune reactions are activated, including production of antimicrobial secondary metabolites and proteins, initiation of programmed cell death and local cell wall enforcements at the site of pathogen attack.

The efficacy of the plant immune system has forced pathogens to evolve counter strategies in the form of effector molecules that are delivered as " Virulence of pathogens is defined by their complement of effectors "

such as secretion and cell-to-cell transport and communication via plasmodesmata. These effectors can be used as new molecular tools to better dissect vesicular transport and plasmodesmatal trafficking.

worthwhile to be manipulated for better infection. Interestingly,

we found effectors that interfere with general cellular functions

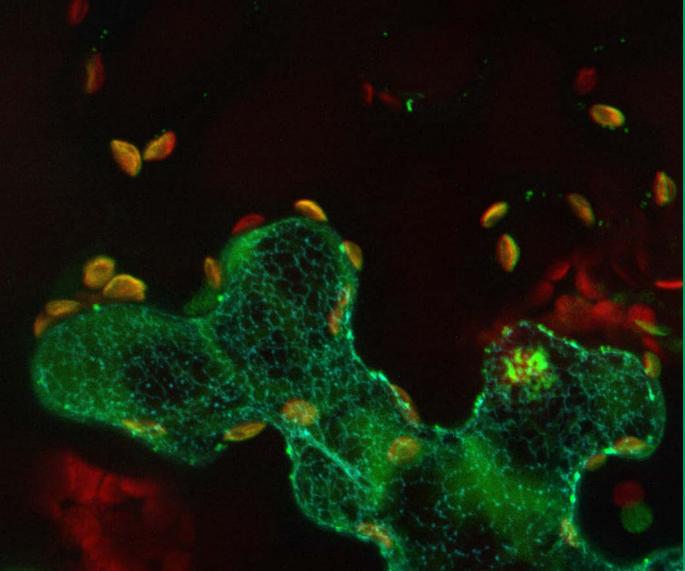
Knowledge about effector targets can contribute to new strategies of plant protection. By changing the sequence of target pro-

> teins or applying a decoy strategy, it may be possible to evade the effect of pathogen effectors and decrease pathogen virulence. A second focus of the Mauch Lab is

virulence factors into potential hosts to suppress plant immunity and create an environment suitable for pathogen invasion.

The main focus of the Mauch lab is to better understand how pathogens manage to undermine plant disease resistance. Our aim is to determine molecular targets of effectors produced by the oomycete pathogen *Phytophthora* in order to learn what the pathogen considers important processes antimicrobial and nematicidal proteins. We wonder, e.g., whether proteins from ink cap fungi, which are known to completely digest their fruiting body during ripening, can be used as tools for plant protection against fungal pathogens.

In a collaboration with ETH Zürich we also have an interest in nematicidal proteins, because nematodes are an underestimated and difficult to control threat to agricultural production.



Subcellular localization of a GFP-tagged effector protein (green) at plasmodesmata, in comparison with ER-CFP (blue) that localizes to the endoplasmatic reticulum. Chloroplasts in red and yellow.

Co-workers



Tu Giang Doan



Brahim Oubaha

Barbara Kalisch









Aboubakr Moradi

Iga Tomczyinska

Katia Zhinder

Selected publications

Tomczynska I., Stumpe M., and Mauch F. (2018) A conserved RxLR effector of the oomycete plant pathogen Phytophthora interacts with host RabA-type GTPases to inhibit vesiclemediated secretion of antimicrobial proteins. Plant Journal 95.187-203.

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Dr Laurent Mène-Saffrané

Plant nutrigenomics bioinformatics & analytics

Plant nutrigenomics The biosynthesis of isoprenoid vitamins

In addition to its hydration and energy functions, the diet must provide thirteen different vitamins that are essential to human growth, health and reproduction. To date, converging epidemiological studies have clearly established that a significant proportion of human populations chronically suffers from mild to severe vitamin deficiencies. In addition to affecting populations of poor countries, these studies have also revealed that vitamin deficiencies frequently occur in human populations of developed countries, notably deficiency in vitamin E.

My research group is currently investigating the molecular mechanisms regulating the biosynthesis and accumulation of isoprenoid vitamins, a group of three lipophilic vitamins encompassing tocopherols (vitamin E), phylloquinones (vitamin K) and carotenoids (pro-vitamin A) that

are notably essential to human health and fertility. By combining high-throughput genetics, whole-genome sequencing and bioinformatics tools, we have recently identified and characterized twelve novel plant genes controlling the quantity and the composition of vitamin E in vegetable oils. The first two mutants that we mapped and characterized are the enhanced vitamin e 1 (eve1) and eve4 mutants that both accumulate twice more vitamin E in seeds. In addition, both eve1 and eve4 mutants overaccumulate other isoprenoid compounds such as chlorophylls and carotenoids (pro-vitamin A) indicating that both mutations favor the accumulation of isoprenoid compounds produced in plastids. The two causative eve1 and eve4 mutations affect genes controlling the accumulation of lipid reserves in seeds. Thus, while the eve1 and eve4 mutants significantly produce more

" Understanding tocopherol biosynthesis to live healtier "

isoprenoid vitamins, they accumulate less lipids in seeds. The analysis of the biosynthetic pathways producing lipids and isoprenoids revealed that they are both produced

in plastids and share the same biosynthetic precursors. This likely indicates the existence of a tradeoff between the lipid and the isoprenoid metabolisms in this organelle. Our findings also suggest that the selection of oilseed crops with higher oil yields might significantly decrease the nutritional quality of these oils by depleting their isoprenoid vitamin contents, a hypothesis that we are currently investigating.

Co-workers





Sébastien Bruisson Laurie Chaisse-Leal

Sébastien Pellaud

Selected publications

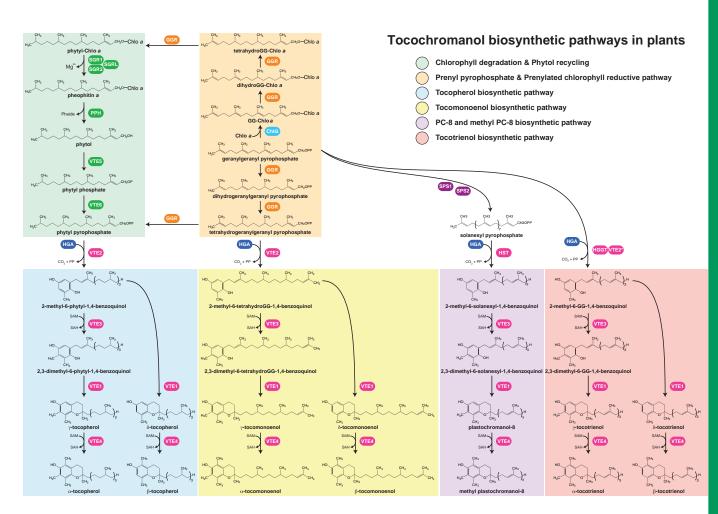
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Mène-Saffrané, L. Vitamin E biosynthesis and its regulation in plants. Antioxidants doi:10.3390/antiox7010002 (2018).

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UNI FR

Prof. Heinz Müller-Schärer

Ecology and evolution of plant-antagonist interactions

Managing plant invasions **Fighting fire with fire**

Biological introductions provide excellent opportunities to study fundamental processes in ecology and evolution, such as adaptive responses to novel local biotic and abiotic conditions. Adaptation can occur rapidly after introductions, likely from selection on the genetic variation available in introduced populations. This holds true also for introductions of potential biological control agents from the area of origin of the plant invader. Because ragweed has severe impacts on human health and is also a crop weed in large parts of Europe, it is one of the economically most important plant invaders in Europe.

In view of improving predictions for future long-term benefits and risks of this potential biological control program, we recently initiated a novel experimental evolutionary approach to assess the

When fighting fire with fire, i.e., using an invasion against an invasion, balancing benefits with risks is key in developing a successful biological control program.

In 2013, we were confronted with the accidental introduction of the North American native ragweed leaf beetle, *Ophraella communa* into Europe, requiring an urgent decision on how to respond to this unforeseen arrival, which is already used in China as a successful biological control agent against common ragweed, *Ambrosia artemisiifolia*.

" Biological weed control could relieve millions of allergy sufferers in Europe "

beetle's potential to select for resistant/ tolerant ragweed populations, as well as the beetle's potential for evolutionary adaptation to novel biotic (host plants) and abiotic (colder tempera-

ture for the yet unsuitable habitats in Central Europe, and considering climate change) conditions, using next generation sequencing and bioassay approaches.

This is the first attempt to rigorously and simultaneously assess the evolvability of a biological control agent and its target weed.



Setting up one of our field experiments at Magnago, MI, Italy, to explore effects of climate warming and biological control on demographic, ecological and evolutionary changes in populations of invasive Ambrosia artemisiifolia.

Co-workers

















Nilgün Sailer





Yongjian Wang

Selected publications

Müller-Schärer H, Sun Y, Chauvel B, Karrer G, Kazinczi G, Kudsk P, Oude Lansink AGJM, Schaffner U, Skjoth CA, Smith M, Vurro M, de Weger LA & Lommen STE. 2018. Crossfertilizing weed science and plant invasion science to improve efficient management: a European challenge. Basic and Applied Ecology, 33, 1-13.

Slodowicz D, Descombes P, Kikodze D, Broennimann O & Müller-Schärer H. (2018). Areas of high conservation value at risk by plant invaders in Georgia under climate change. Ecology and Evolution, 8, 4431-4442.

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Dr Alessandro Puoti

Post-transcriptional regulation of gene expression in Caenorhabditis elegans

RNA biology and development How do germ cells choose their destiny?

Spermatozoans and oocytes are specialized cells that ensure genetic variability through meiosis and fertilization. Usually, sperm and oocytes originate from male and female organisms, respectively. We study one organism that can achieve both: the protandric hermaphroditic nematode *Caenorhabditis elegans* generates spermatids during larval development and oocytes as an adult.

Remarkably, both gametes originate from the same pool of precursors. How is this decision made at the molecular level?

Several lines of evidence indicate that the sperm-oocyte switch is controlled by post-transcriptional mechanisms. Our laboratory focuses on the role of the mog genes, which are needed for the switch from spermato-

" Male or female? It is up to the RNA "

ous mutants, and if needed, the possibility to create mutants by genome editing. *C. elegans* is therefore the ideal model to study fundamental questions in developmental biology, including regulation of gene expression. By comparing the

transcriptomes of mog (loss-offunction) and fem-3(gain-of-

genesis to oogenesis in hermaphrodites. In fact, mog loss-offunction mutants start spermatogenesis but never switch to oogenesis in their otherwise female body.

Because fem-3 gain-of-function mutants show similar defects in gamete production, it is generally believed that mog gene products negatively regulate fem-3. Intriguingly, most mog genes code for proteins involved in pre-mRNA splicing. function) mutants, we have identified several target genes that may bridge the interaction between mog and fem-3.

Central questions in our laboratory include the identification of

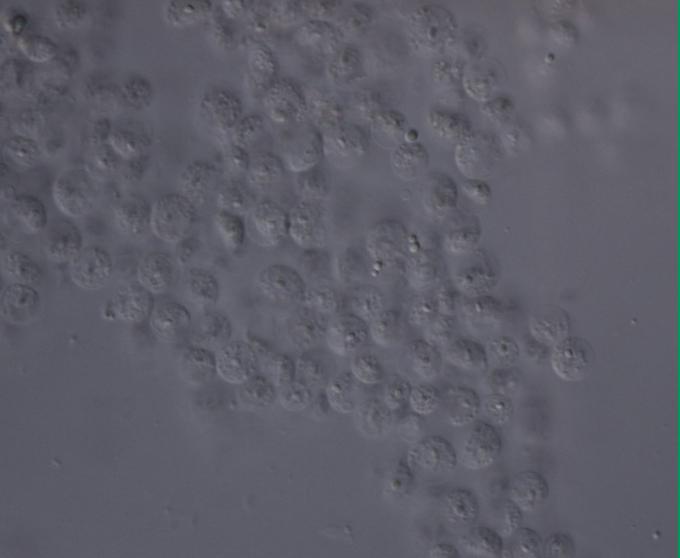
target mRNAs that are up- or down-regulated in mog mutants, and their respective molecular roles. The mechanisms considered

include control of RNA interference, alternative splicing, regula-

C. elegans offers powerful genetic tools, the availability of numer-

tion of mRNA stability and translational control.

In addition because many of the mog target genes identified also occur in higher eukaryotes, *C. elegans* also serves as a paradigm to investigate molecular mechanisms in more complex organisms.



C. elegans spermatids (100X magnification; differential interference contrast). Worm spermatids have no flagellum and feature a highly condensed nucleus.

Co-workers







Kim Charrotton

Christine Déforel

Maria Tarca

Selected publications

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Zanetti S, Grinschgl S, Meola M, Belfiore M, Rey S, Bianchi P & Puoti A (2012). The sperm/oocyte switch in the C. elegans hermaphrodite is controlled through steady-state levels of the fem-3 mRNA. RNA 18:1385-1394.

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Prof. Didier Reinhardt

Regulation of arbuscular mycorrhizal symbiosis in Petunia hybrida

Activation of symbiotic programs How plants engage in symbiosis with beneficial fungi

Most plants live with soil fungi in a symbiotic association, known as *arbuscular mycorrhiza* (AM), that helps them cope with nutrient limitation and environmental stress. AM has been found in the first fossilized land plants, suggesting that plants already relied on the services of AM fungi when they started to colonize the hostile environment that existed before the continents bore life.

How can plants identify AM fungi and distinguish them from ubiquitous fungal pathogens? And how can they accommo-

date AM fungi in their cells? We are using Petunia hybrida to answer these questions by searching genes that are necessary for symbiosis. With this strategy, we have identified a gene that encodes a transcription factor named

REQUIRED FOR ARBUSCULAR MYCORRHIZA1 (RAM1). Mutants in RAM1 are symbiosis-defective. To elucidate the function of RAM1, we determined the genes that depend on RAM1 for transcriptional activation by RNAseq analysis of ram1 mutants.

RAM1 induces several hundred genes, including phosphate transporters that are required for the uptake of phosphate

delivered by the fungal partner. In addition, RAM1 activates a series of genes that are thought to be involved in lipid biosynthesis and modification. These genes are essential for AM, since their mutation results in the abortion of symbiosis. This suggests that AM fungi may receive lipid nutrients in addition to carbohydrates . Indeed, recent evidence from several research groups support this idea. We are currently exploring the function of these genes by genetic and metabolomic analysis. This work will shed light on the mechanisms by which plants can promote and control AM fungal proliferation.

" Most plants are not viable without beneficial microbes "

hypocotyl. This involves high-resolution confocal microscopy and 3D-reconstruction of tissues, and mathematical modeling of cell wall behavior. Finally, we have explored the genetic basis of inflorescence development in *P. hybrida*, in particular the function of a master regulator that is required for the establishment of flower primordia at the shoot tip were leaves and flowers are formed.

on symbiosis, we are exploring growth regulation in Arabidopsis seedlings (SystemsX "Plant MechaniX") with special emphasis on the growth mechanisms in the embryonic stem, the

In addition to the work



Cover illustration to article: M. K. Rich, E. Nouri, P.-E. Courty, and D. Reinhardt (2017b). Diet of arbuscular mycorrhizal fungi - Bread and butter? Trends in Plant Science 22, 652-660. Cover illustration by Bruno Fauser - fauser.ch

Co-workers





Sébastien Bruisson

Nazli Dursun







Mélanie K. Rich

Martine Schorderet

Evert van Schai

Selected publications

M. Rich, P.-E. Courty, C. Roux & D. Reinhardt (2017a). Role of the GRAS transcription factor ATA/RAM1 in the transcriptional reprogramming of arbuscular mycorrhiza in *Petunia hybrida*. BMC Genomics 18, 589.

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S. Robinson, M. Huflejt, P. Barbier de Reuille, S. A. Braybrook, M. Schorderet, D. Reinhardt & C. Kuhlemeier (2017). An automated confocal micro-extensometer enables in vivo quantification of mechanical properties with cellular resolution. Plant Cell 29, 2959-2973.

M. Chen, M. Arato, L. Borghi, E. Nouri & D. Reinhardt (2018). Beneficial services of arbuscular mycorrhiza – From ecology to application. Frontiers in Plant Science 9, 1270.

M. Schorderet, R. R. Duvvuru Muni, A. Fiebig & D. Reinhardt (2018). Deregulation of MADS-box transcription factor genes in a mutant defective in the WUSCHEL-LIKE HOMEOBOX gene EVERGREEN of Petunia hybrida. Plant Signaling & Behavior 13, e1471299.



Dr Rudolf Rohr

Theoretical ecology: coexistence theory, eco-evolutionary dynamics, ecosystem functioning and ecological networks

Biodiversity and ecosystem functioning How biodiversity impacts ecosystem functioning and is impacted by network architecture

The impressive richness of species has long served as a motivation for understanding the key mechanisms allowing their persistence. Moreover, species are not isolated, but interact together and with their environment. We study coexistence theory at the community level and how it relates to the functioning of ecosystems and the architecture of interspecific interaction networks. Our ultimate aim is to develop a coherent and unified theory of coexistence, ecosystem functioning, and interaction network architecture. that the change in species interaction acts as a regulatory control of invasive species in late successional communities, as predicted 50 years ago by E.P. Odum. and R. Margalef.

Observational studied have not been able to conclude whether the persistence of species is positively or negatively linked to the productivity of the ecosystem. We developed a general framework showing that, actually, both outcomes are equally likely, and the direction of the relation depends on the competitive ability of the

We extended the modern coexistence theory, which describes coexistence mechanisms at

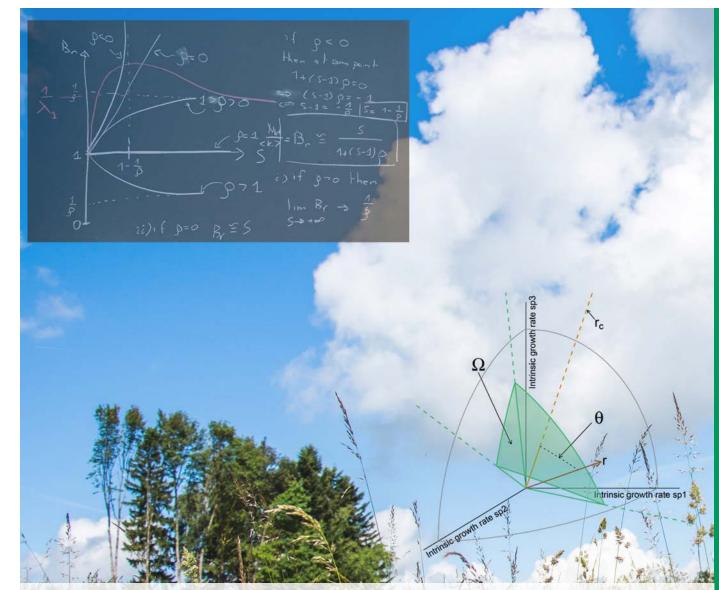
" To unify coexistence and ecosystem-functioning theories "

most abundant species.We developed a mechanistic theory of the biodiversity ecosystem functioning relation-

the level of a pair of competing species, to species-rich communities. Specifically, we introduced a new approach —the structural approach — to study coexistence conditions.

That is, we developed new metrics, the structural niche and fitness difference, to quantify the domain for coexistence. Contrary, to the modern coexistence theory, our structural approach applies to species-rich communities and considers any interaction types (not only competition). In a subsequent work we studied ecological successions and demonstrated ship. Based on community dynamic models, we related the number of coexisting species to their biomass productivity.

We demonstrated that the slope of this relationship is inversely linked to the average level of competition. Then we demonstrated that increasing temperature induces increasing competition, which in turn, decreases the positive effect of biodiversity on productivity. This theory was supported by experiments in collaboration with Prof. Bersier's group.



Left: mathematical models behind the biodiversity ecosystem-functioning relationship (Parin et al. 2018). Right: structural niche and fitness difference in systems of 3 competing species (Saavedra et al. 2017).

Co-workers



Avril Weinbach

Selected publications

Saavedra S, Rohr RP, Bascompte J, Godoy O, Kraft NJB, and Levine JM. 2017. "A Structural Approach for Understanding Multispecies Coexistence." Ecological Monographs 87 (3): 470–86. https://doi.org/10.1002/ecm.1263.

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Prof. Roger Schneiter

Lipid homeostasis, cholesterol, fatty acid transport, immune suppression, pathogen defense

Protect yourself - take a cap What are CAP superfamily proteins doing exactly, apart from binding lipids?

Eukaryotic cells, ranging from fungi to plants and including humans, all synthesize a family of proteins that share a unique three-dimensional architecture, termed the α - β - α sandwich fold. Proteins containing this unique fold form the CAP superfamily, named after its three founding members: the human cysteine-rich secretory proteins (CRISP), the vespid venom antigen 5 (Ag5), and the plant pathogenesis-related protein 1 (PR-1). Their structure is characterized by a central β -sheet flanked by α -helixes above and below the plane of the β -sheet.

In addition, the surface of the CAP domain displays a large cavity that might be important for interaction with other proteins, peptides or glycans (see the Figure). CAP proteins are implicated in many fundamental biological processes, including immune defense in mammals and plants,

sperm maturation and fertilization, prostate and brain cancer, pathogen virulence and venom toxicity. CAP family members are mostly secreted glycoproteins that are very stable in the extracellular fluid. Even though CAP proteins are intensely studied, their mode of action remains elusive. However, the strong structural conservation of the CAP domain suggests a common principle of operation of CAP family members. Using yeast as a model organism, we could recently show that CAP proteins possess two independent lipid binding sites, one for sterols and one for free fatty acids. Through binding to the CAP proteins, sterols and free fatty acids become solubilized and secreted. This lipid export function of CAP proteins is essential under specific growth conditions, for example, in cells that accumulate high intracellular levels of free fatty acids or sterol precursors. In addition, cells lacking these proteins are hypersensitive to small hydrophobic com-

" Survival might depend on a tug-of-war between CAP proteins secreted by the host and the pathogen "

> that CAP proteins may function both intra- and extracellularly to bind and neutralize potential membrane perturbing hydrophobic compounds. Thus, CAP proteins may exert a variety of physiological functions through a common mode of action, the sequestration of small hydrophobic compounds.

pounds, such

as for example

eugenol, an

antimicrobial

agent present

in clove oil. Eu-

genol directly

competes with

cholesterol

for binding to

CAP proteins

in vitro. These

results suggest

Co-workers







Vineet Choudhary

Stéphanie Cottier



 \square





Mykhaylo Debelyy

Ola El Atab

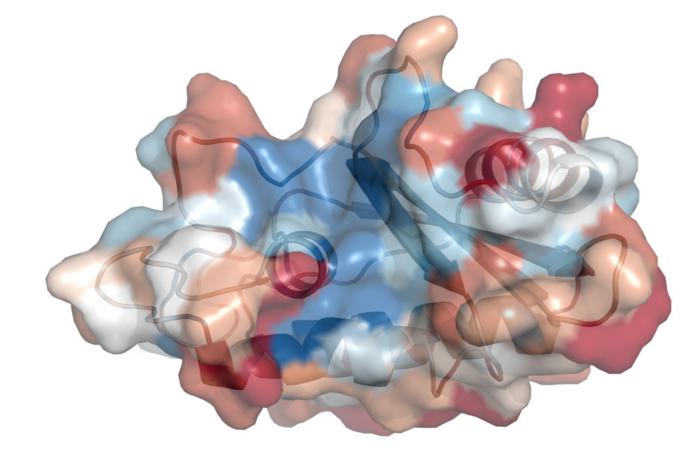
Rasha Khadda



Darwiche, R., El Atab, O., Cottier, S., and Schneiter, R. (2018). The function of yeast CAP family proteins in lipid export, mating and pathogen defense. FEBS Lett. 592, 1304-1311.

Choudhary, V., Golani, G., Joshi, A. J., Cottier, S., Schneiter, R., Prinz, W. A., and Kozlov, M. A., (2018). Architecture of lipid droplets in endoplasmic reticulum is determined by phospholipid intrinsic curvature. Curr. Biol. 28, 915-926e9.

Darwiche, R., El Atab, O., Baroni, R. M., Teixeira, P. J. P. L., Mondego, J. M. C., Pereira, G. A. G., and Schneiter, R. (2017). Plant pathogenesis-related proteins of the cacao fungal pathogen Moniliophthora perniciosa differ in their lipidbinding specificities. J. Biol. Chem. 292, 20588-20569.



Surface view with projection of secondary structure elements of the CAP domain of the yeast Pry3 protein. Strong evolutionary conservation of surface exposed residues is indicated in blue, low conservation is indicated in red. Note the high conservation of an equatorial groove large enough to bind peptides or glycans.



Prof. Simon Sprecher

Cellular, molecular and functional neurogenetics in Drosophila and other invertebrates

Neurogenetics and behaviour How the nervous system encodes the surrounding world and allows memories to be formed and forgotten

How the brain is built and how it actually works remains still poorly understood. Rapid advances in imaging and sequencing techniques as well as the development of versatile genome editing methods open avenues to gain insight into the fundamental question of how the brain does what it does.

We use the powerful genetics of the fruit fly as a model, which

allows us to precisely manipulate or monitor individual cells in the brain in the living animal. Using the fruit fly we address three fundamental questions in neuroscience:

" Looking at small brains allows us to understand how the brain works "

How do is the diversity of neuron types in the nervous system genetically controlled? How do sensory systems encode and decode complex cues from the environment to evoke or adapt behavior? How is the brain able to store and forget this information as memories?

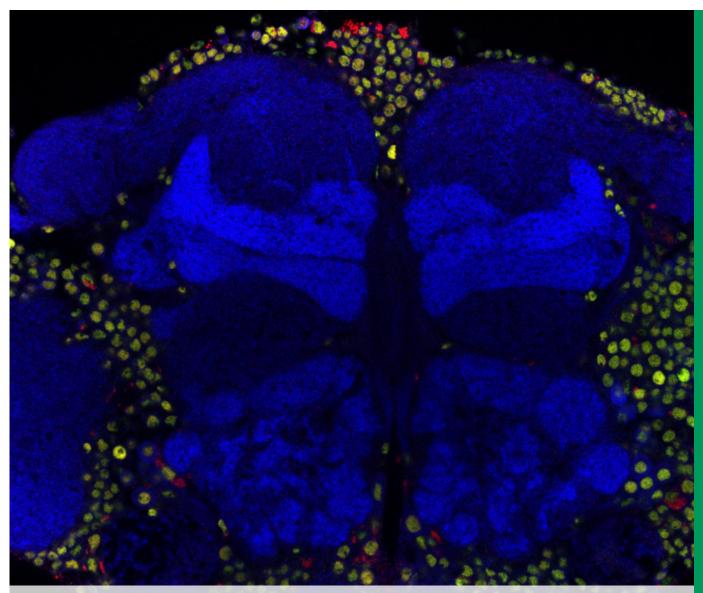
Our research is both fundamental and critical for biomedical

aspects, including studies on Alzheimer and forgetting or neurodegeneration and sleep disorders.

The discovery of underlying molecular mechanisms may be used to design approaches to cure such neurological conditions. However, a critical aspect of biology is not only to cure disease, but rather to understand the fundamental principles of life.

> In order to explore how general these principles are, we explore the earliest animals that evolved nervous systems and brains: cnidarians, the first animals with a nervous system, and

acoel worms, which are the first animals to have a brain. With the advent of CRISPR/Cas9 to edit the genome, we are now in a position to start reconstituting the organization and function of the first nervous system, allowing us to unveil how the brain works from fundamental mechanisms towards the complex actions, such as learning and forgetting.



CRISPR is used to create GFP-tagged proteins that control learning and memory formation.

Co-workers

















Abhishek Mishra

Noemi Sgammeglia

Marta Sprecher



Yves Widmer

Selected publications

Widmer YF, Fritsch C, Jungo MM, Almeida S, Egger B, appetitive long-term memory in the mushroom body circuit. eLife. 2018;7. pii: e39196. doi: 10.7554/eLife.39196.

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RD, Schneider-Mizell CM, Truman JW, Zlatic M, Cardona A, Sprecher SG. Organization of the Drosophila larval visual circuit. eLife. 2017;6:e28387. DOI: 10.7554/eLife.28387.



Prof. Stefano Vanni

Molecular biophysics of cellular membranes

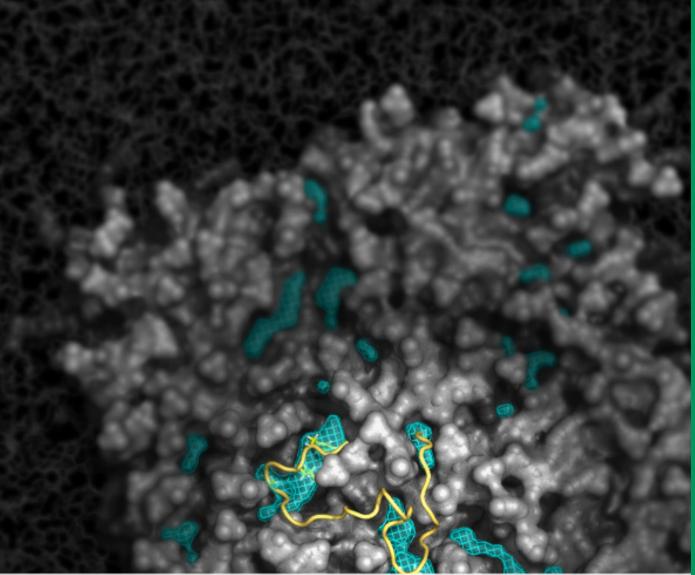
Membrane biophysics What do the walls of cells look like, atom by atom?

In our group, we use computers to understand the inner workings of cells down to molecule-by-molecule and atom-by-atom detail. Traditionally, biologists studied how cells work and behave in living organisms - in vivo – and in their lab tubes - in vitro – but many features are too complex and too small to understand in this way.

To overcome this limitation and understand complex biological problems with atomistic-level resolution, we develop new computational approaches to study biological Currently, the main focus of the lab is to understand how specific lipids and membrane properties influence intracellular trafficking processes and fat storage in eukaryotic cells. In fact, cellular membranes are continually remodelled to achieve communication between intracellular compartments and to selectively exchange materials between them.

[•] We investigate biological systems in silico, to go beyond classical in vivo and in vitro approaches "

systems in silico, and we combine these investigations with biochemical and biophysical approaches. Our main methodology is called molecular dynamics (MD) simulations. Using this approach, we can describe molecular systems in the range of 1-100 nanometers with atom-level accuracy. To use Feynman's words, we investigate living matter by studying the "the jiggling and wiggling of atoms". The energetics of these remodelling processes are governed by the interplay between specialized proteins and membrane properties, but in most cases, we still lack a detailed molecular explanation of how they are controlled. Our goal is to understand these processes, and specifically how lipid sensors, transporters, and lipid remodelling enzymes maintain lipid homeostasis in the cell.



Atomistic representation of a protein peptide binding to a lipid membrane.

Co-workers







Sylvain Adamovicz

Pablo Campomanes

Emanuele Petretto





Valeria Zoni

Selected publications

Interdigitation between triglycerides and lipids modulates surface properties of lipid droplets. A Bacle, R Gautier, CL Jackson, PFJ Fuchs, S Vanni Biophysical Journal 112 (7), 1417-1430.

ER membrane phospholipids and surface tension control cellular lipid droplet formation. KB M'barek, D Ajjaji, A Chorlay, S Vanni, L Forêt, AR Thiam Developmental Cell 41 (6), 591-604.

A sub-nanometre view of how membrane curvature and composition modulate lipid packing and protein recruitment. S Vanni, H Hirose, H Barelli, B Antonny, R Gautier Nature Communications 5, 4916.



Prof. Daniel Wegmann

Bioinformatics and computational biology

Where we come from Computational methods to infer the origin of living things

All living organisms have an evolutionary history. What is ours? Our DNA tells a large part of that story, as it does for any other species. Using modern computational and statistical methods, we seek to extract that information.

The basic idea is simple: genetic data is informative about genealogical relationships. We all have two parents, four grandparents and more than a thousand ancestors 10 generations ago. The more recent ancestors two individuals

share, the more genetically similar they are. Siblings, for instance, share half of their DNA, cousins about one eighth.

Our goal is to link patterns of relationships to evolutionary histories. Two randomly drawn individuals from a

large population, for instance, should not be closely related, but they might easily turn out to be cousins if sampled from a small population (picture the locals of your favorite ski resort). But if used correctly, relationships tell us much more: they are informative about population size changes, migration and mixing of past populations. Using such methods, we could identify newly discovered date palms from remote Oman as the last remnants of the wild date palm, and that modern African cultivars resulted from a mixture of cultivated date palms from the Middle East with now extinct wild date palms of Africa.

Excitingly, we can now extract DNA also from fossils, which gives us an even more detailed glimpse of the past. We pioneer the statistical analysis of such data, and could recently show that hu-

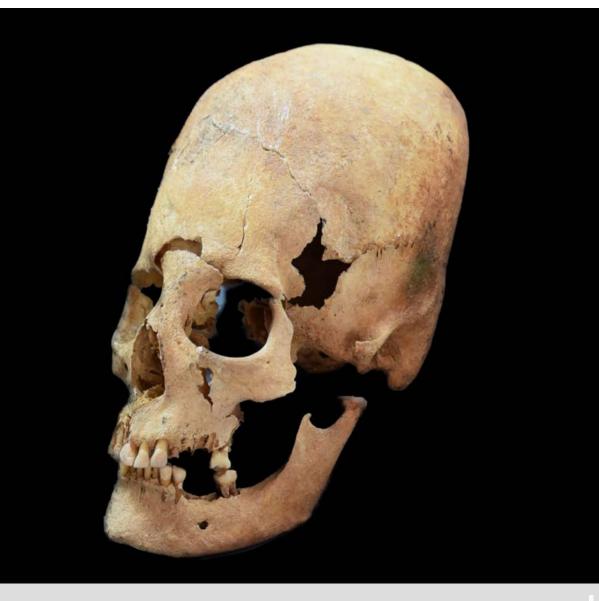
" Ancient DNA is a time-machine to study our past "

mans colonized the Americas using two parallel routes.

We also solved an archaeological mystery: in Bavarian medieval graveyards,

artificially elongated skulls of women were found.

Where did these women come from? Their DNA tells us that they were from south-eastern Europe, from where they migrated more than a thousand kilometers in search of love.



An artificially elongated skull of a woman buried at Altenerding-Klettham, Bavaria, in the fifth century. Genetic analysis indicates that this woman originated from south-eastern Europe and migrated more than a thousand kilometers to Bavaria. Her grave goods suggest that she was fully integrated into the Bavarian society.

Co-workers



Thierry Aebischer





Sadoune Ait-Kaci







Zuzana Hofmanova

Ilektra Schulz

Vivian Link







Selected publications

Scheib C et al. (2018). Ancient human parallel lineages within North America contributed to a coastal expansion. Science 360: 1024-1027.

Veeramah K et al. (2018). Population genomic analysis of elongated skulls reveals extensive female-biased immigration in early medieval Bavaria. PNAS 115(13), 3494-3499.

Gros-Balthazard M et al. (2017). The discovery of wild date palms in Oman reveals a complex domestication history involving centers in the Middle East and Africa. Curr. Biol. 27(14).

Aebischer T et al. (2017). First quantitative survey delineates the distribution of chimpanzees in the Eastern Central African Republic. Biol. Conserv. 213.



Prof. Laure Weisskopf

Deciphering the chemical communication between bacteria, plants and pathogenic fungi

Microbial communication Exploring the smelly world of bacterial volatiles to protect plant health

Like the human skin, plant roots and leaves are densely colonized by diverse communities of bacteria and other microbes. Recent reports indicate that these plant-colonizing bacteria are involved in protecting their host against environmental stress, as well as against diseases caused by phytopathogenic organisms. Our main interest lies in understanding the mechanisms underlying such microbiome-mediated protection against plant pathogens. chemical nature and biological functions of volatile organic compounds emitted by a range of plant-associated bacteria. We mainly work on Pseudomonas, Bacillus and Actinobacteria strains, which have been previously isolated from plants of agronomical relevance such as grapevine or potato. Our work follows basic research lines to understand the modes of action of bacterial volatiles on plant pathogens and to identify the genetic determinants underlying the emission of plant-protecting volatiles by bacteria. In addition, we also pursue more applied projects, in which we investigate the

We focus specifically on the newly discovered ability of plant-associated bacteria to emit volatile organic compounds with a wide range of biological activities on different target organisms. These "bacterial smells" have been

" Plant-associated bacteria are a rich source of biofungicides " potential of microbiome isolates and of their emitted volatiles to protect crops against important diseases like potato late blight or

shown to stimulate plant immunity, to promote root growth, as well as to inhibit the development of various plant pathogens and we therefore consider them as an important source of biofungicides.

Using state-of-the-art methods in analytical chemistry, phytopathology and molecular biology, we aim to decipher the grapevine downy mildew.

We pursue different approaches, such as the application of single or mixtures of bacterial inoculants, or the use of the pure volatiles as plant-protective agents. Our research aims at discovering new strains and active molecules to be used as alternatives to synthetic fungicides, thereby contributing to preserve environmental and human health.



Our lab's motto: happy people and healthy plants.

Co-workers







Abhishek Anand

Floriane L'Haridon





Delphine Chinchilla

Monica Zufferey

Selected publications

De Vrieze M, Germanier F, Vuille N & Weisskopf L (2018). Combining different potato-associated Pseudomonas strains for improved biocontrol of Phytophthora infestans. Frontiers in Microbiology, 9:#2573.

Bailly A & Weisskopf L (2017). Mining the volatilomes of plant-associated microbiota for new biocontrol solutions. Frontiers in Microbiology 8: #1638.

Montes Vidal D, von Rymon-Lipinski AL, Ravella S, Groenhagen U, Herrmann J, Zaburannyi N, Zarbin PHG, Varadarajan AR, Ahrens CH, Weisskopf L, Müller R & Schulz S (2017). Long-chain alkyl cyanides: unprecedented volatile compounds released by Pseudomonas and Micromonospora bacteria. Angewandte Chemie Int Ed 56: 1-6.



Dr Chantal Wicky

Chromatin function in C. elegans development

Chromatin and development Packaging matters

All processes in the nucleus of a cell take place in the context of chromatin, a complex of DNA and proteins. Chromatin is a very dynamic structure that can be altered by specialized enzymatic complexes, which in turn are modulated by gene expression. Several chromatin remodelers function in development and stem cell biology.

Our lab is exploring their functions using a tiny worm, the nematode Caenorhabditis elegans, which presents many

advantages for these studies: chromatin remodelers very similar to humans, well characterized development and many useful molecular tools. Our studies focus on two worm homologs of

" Chromatin is a very dynamic structure "

production.

We are currently studying how these two proteins shape the chromatin of germ cells to allow the production of functional gametes. Packaging

the mammalian Mi2 chromatin remodelers that are required for proper C. elegans development and reproduction. In the freshly hatched worm larvae, LET-418/Mi2 function in a network of chromatin proteins that is required for the initiation of post-embryonic development in response to food. These chromatin proteins regulate the transcription profile of the larvae and repress germline gene expression that would interfere with proper somatic development. of DNA into chromatin matters and our research aims to better understand the molecular mechanisms underlying this process.

To further understand how the genome is regulated at the level of

chromatin, our next challenge will be to identify the binding sites

of this network of proteins onto the genome of the larvae. This will

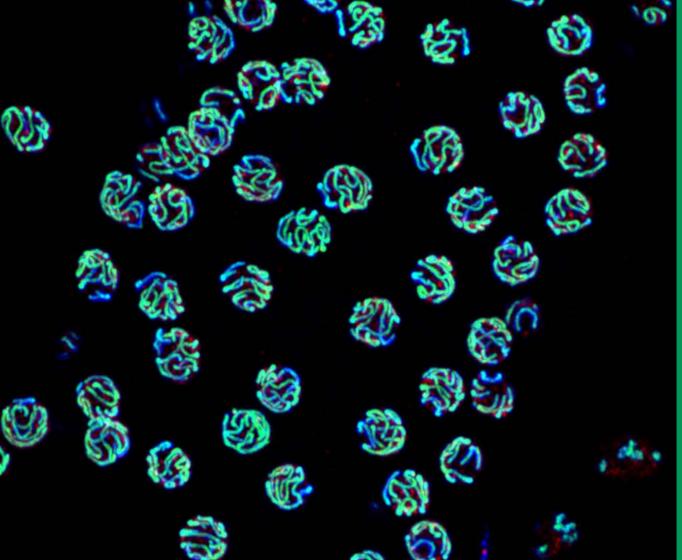
allow us to identify potential genes that are regulated by these

chromatin factors and also to understand how the chromatin is

shaped during this important step in development. In the germ cells, LET-418/Mi2 together with an uncharacterized zinc finger

protein, LSL-1, is required for normal meiosis and successful re-

Our lab also participates in various outreach activities under the name of **Lab2rue** and is part of a nation-wide project to promote sciences at school using the tiny worm *C*. *elegans*.



C. elegans germline nuclei at the pachytene stage of meiosis. Homologous chromosomes are held together by synaptonemal complex proteins (HTP-3 in green). The LSL-1 protein is visualized in red.

Co-workers



David Crespo Rodriguez Shweta Rajopadhye

Selected publications

Käser-Pebernard, S. et al. (2016). Fine-tuning of chromatin composition and Polycomb recruitment by two Mi2 homologues during *C. elegans* early embryonic development. Epigenetics & Chromatin 9, 39.

Erdelyi, P. et al. (2017). A network of chromatin factors is regulating the transition to postembryonic development in Caenorhabditis elegans G3 7, 343.

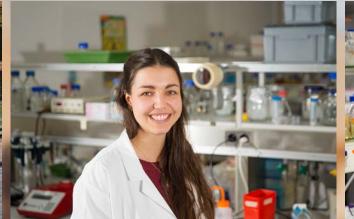
Saudenova, S. and Wicky, C. (2018). The chromatin remodeler LET-418/Mi2 is required cell non-autonomously for the postembryonic development of Caenorhabditis elegans. Journal of Developmental Biology 7,

Personalized teaching and training



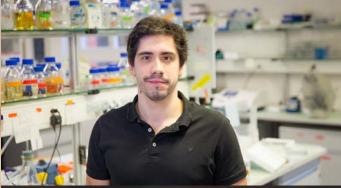
Florian Wagner Bachelor in Biology Germany

Mein Name ist Florian. Ich bin 21 Jahre alt, studiere Biologie und bin Teil des Exekutivkomitees der AGEF als Verantwortlicher der Naturwissenschaftlichen und medizinischen Fakultät. Ich habe noch vor 3 Jahren entschlossen Biologie zu studieren, weil mich die Funktionsweise alles Lebenden schon immer interessiert hat und ich zudem während meiner Maturaarbeit, in Zusammenarbeit mit Laurent Mène-Saffrané, bereits einen kleinen Einblick in die Biologie erhalten habe. Während meines Studiums konnte ich in eine Welt aus komplexen Mechanismen abtauchen, die das Leben zu erklären suchen. Das Studium der Biologie erweitert nicht nur den Horizont und die Denkweise, sondern hilft mir auch in meinem weiteren Leben. In Zukunft möchte ich den akademischen Weg einschlagen und einen Master und später PhD in Biologie erreichen, außerdem möchte ich Teil des universitären Lebens sein und mich weiterhin in verschiedenen Bereichen engagieren.



Réjane Carron Master in Plant & Microbial Sciences Switzerland

I always had interest in sciences and particularly in Biology for its wide panel of different aspects and subjects. I decided to do my Bachelor in Fribourg because of the bilingual curriculum they offer. The Bachelor allowed me to broaden and deepen my knowledge about various fields in Biology and to expand my horizons on many different topics. The Department is on a human scale and teachers are always present and glad to help and discuss with the students. During my Bachelor, I found myself with a strong passion for Plant Biology and decided to stay for my Master and dig deeper into this particular subject. During the Master, we are offered a large choice of different lessons as well as a strong practical work training, allowing us a first step into research work. Within the Department we meet and exchange with PhD students, postdocs as well as professors, who guide and help us through research work and to a future professional path.



Guillermo Miguel Garcia Osuna PhD in Biochemistry Spain

I developed a strong interest in Biochemistry already in High School. I did all my studies up to a Master degree in my home city Granada. Afterwards, I came to Switzerland chasing any opportunity to grow personally and professionally. After working temporarily as a researcher at EPFL and UNIL, I decided it was time to enroll in a PhD program. Something as difficult as doing a PhD is to be able to choose the optimal one for yourself. After months of searching a topic of my own interest and attending several interviews, Prof. Dr De Virgilio gave me the opportunity I was seeking. Within the Department of Biology, the unit of Biochemistry offers the opportunity to learn and master a wide range of techniques related to molecular biology and biochemistry. The challenging environment, autonomy and the research quality give me the option to develop my rational thinking, stress tolerance and communicative skills. About my future, first I need to finish my thesis and then take a break to really know what I want to do next, but no doubt, it will be related to science.



Our study advisor Dr Alessandro Puoti constantly ensures the improvement of our teaching programme.

New Master

In 2018, the Department of Biology paved the way for the establishment of two new Master of Science programs, next to the successful master program in Bioinformatics and Computational Biology, which is organized jointly with the University of Bern.

The classical Master of Science in Biology will be replaced by a Master of Science in Molecular Life and Health Sciences and a Master of Science in Environmental Biology: from Genes to Ecosystems.

With this initiative, the Department aims to strengthen and provide more visibility to its core research areas. Both programs are a continuation of master specializations established in 2017, which were very well received by the students and led to a twofold increase in student numbers in 2018. The two new programs will address current challenges in molecular life and environmental sciences and will teach state-of-the-art approaches. The master program Molecular Life and Health Sciences will focus on basic molecular mechanisms and cell biological processes related to human health. The program Environmental Biology: from Genes to Ecosystems will center on plant health and applied and evolutionary ecology, both aimed at tackling the world's environmental challenges.

Fribourg Graduate School of Life Sciences



The Fribourg Graduate School of Life Sciences - *FGLS* - is an interdisciplinary and international graduate school, which offers a coordinated doctoral programme in life sciences at the University of Fribourg. It addresses doctoral fellows in the fields of biology, biochemistry, molecular medicine, chemistry, physics, bioinformatics and mathematics who have a life science focus. State-of-the-art theoretical and experimental research will lead to a Doctor of Philosophy (PhD) in one of the following areas:

PhD in Biology PhD in Biochemistry PhD in Bioinformatics

Established in autumn 2016, FGLS has supported and coached more than 50 PhD students. Mentoring includes a thesis committee which meets yearly and supports students in their studies. In 2018, a student representatives committee was established. Students organize a yearly retreat and actively participate in the scientific exchange of the department, e.g., via the organization of two department seminars per semester. In 2018, a highlight was the logo commpetition which was won by Thomas Bise, a FGLS student (see new logo above).



FGLS retreat 2018 in Riederalp organized by the student representatives Marisa Almeida, Guillermo Garcia, Rachel Korn & Vivian Link.



Prizes

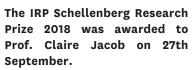


Outreach



Highly cited researchers

The 2017 "Highly Cited Researcher" list of Clarivate Analytics of the most influential researchers in the world contained Prof. S. Bacher and Dr. M. Geisler from the Department of Biology at the University of Fribourg.



The Prize, awarded every two years, rewards a scientist's outstanding work in the field of paraplegia. Priority is given to young but already established and successful scientists working experimentally. The funds awarded, by enabling the recruitment of new co-workers or personnel, and the purchase of equipment or supplies, should help investigate avenues that may, in due course, lead to progress in spinal cord regeneration and functional recovery.



New website

Our new website has been built as part of the University website redesign project. User-friendly and responsive, it integrates the different University data sources.

Goûter scientifique

The Department of Biology and Lab2rue organized a scientific workshop for more than 140 children in November 2018. On a tour in the botanical garden, in white coats or their eyes fixed firmly on a microscope, they observed bacteria, looked out for nematodes from the composter, extracted their own DNA and tracked aliens. A whole programme to get introduced to biology!





Stefano Vanni receives an important ERC grant

By using computer modelling, Professor Stefano Vanni succeeds in studying intracellular communication with an unimaginable precision. His innovative research has won a grant amounting to 1.5 million Euro from the European Research Council.

Research meets public

As an aside to the exhibition "Espèces d'ici et d'ailleurs", the Fribourg Natural History Museum collaborated with Sven Bacher's group in the Department of Biology. They established a small troupe of dressed characters – the Global Trotters – who mingled with the people in Fribourg during the summer. They also prepared two treasure hunts – the Alien Trails - on the subject of exotic species. These activities were made possible thanks to the SNSF as part of the project Agora, which promotes exchange between scientists and the public.

2017

31.01	Automated image analysis, Robert Murphy-Carnegie Mellon University
21.02	Decoding mesodermal cell fates with zebrafish, Christian Mosimann - UZH
11.04	The Hsp90 molecular chaperone machine, Didier Picard-University of Geneva
02.05	Invasiveness in plants, Klass Vrieling - Leiden University
16.05	Atg8-recognition sites mediate Atg4 association, F. Reggiori-University of Groningen
30.05	Proteolytic signaling networks in skin inflammation,Ulrich auf dem Keller-ETHZ
19.09	New insights into the root CLE peptides perception, Ora Hazak-Unil
03.10	Role of antimicrobial peptides in endosymbiosis, Peter Mergaert-CNRS
10.10	Long range gene regulation during evolution, Denis Duboule-University of Geneva
17.10	Regulation of autophagy by the ULK1 complex, Björn Stork-University of Düsseldorf
24.10	Targeting of Perilipins to lipid droplets, Abdou Rahid Thiam-Ecole Normale Paris
31.10	Plant pathogens and disease, Daniel Croll-University of Neuchâtel
07.11	Allelic control mechanism of X-Ch. inactivation, Eric Aebi-Harvard Med School
21.11	Global spread and alien species, Hanno Seebens-Senkenberg University
28.11	Peripheral protein-lipid interactions, Nathalie Reuter-University of Bergen

- 05.12 Nutrient sensing by class III PI3K, Gana Panasyuk-INEM Paris Descartes
- 12.12 Linking development to adult life history, Bas Zwaan-Wageningen University

2018

06.03	Epo in blood development, Hauke Busch-University of Lübeck	06.09
13.03	The roles of pleiotropy and linkage, Catherine Peichel-University of Bern	13-14.09
10.04	Evolutionary agroecology, Jacob Weiner-University of Copenhagen	14.09
24.04	Towards a vaccine against Mycoplasma infections, Joerg Jores-VetSuisse UniBe	21 & 28.11
01.05	Adaptative genetic redundancy in Drosophila, Ch. Schlötterer-Vetmeduni Vienna	22.11
08.05	Scientific computing and cells, Ilpo Vattulainen-University of Helsinki	18.01
22.05	How and why plants degrade chlorophyll, Stefan Hörtensteiner-UZH	26-27.03
29.05	Decoding ligand receptor interactions, Bernd Wollscheid-ETH Zürich	10.04
25.09	Protein structural change, Paola Picotti-ETH Zürich	26-27.04
02.10	Microbial (meta)proteomics-novel insights, Kathrin Riedel-University of Greifswald	15.06
09.10	Woman in academic careers, Susane Gasser-FMI Basel	22.06
23.10	Spread of invasive antsprocesses, Cleo Bertelsmeier-Unil	22-23.06
30.10	Land-use, biodiversity and ecosystems, Martin Gossner-WSL Birmensdorf	
06.11	Microbial range expansions in ecology, David Johnson-Eawag Dübendorf	
13.11	Developmental control of apoptotic cell death, Barbara Conradt-L-M. University	
20.11	Computer science meets ecology, Frank Pennekamp-UZH	
27.11	Consequences of asexual reproduction in animals, Tanja Schanwer-Unil	
04.12	Molecular tumor board, Mélanie Börries-University of Freiburg	
11.12	From immunity to beyond, Cyril Zipfel-UZH	
18.12	Analysis of bacterial persistence, Boris Macek-University of Tübingen	

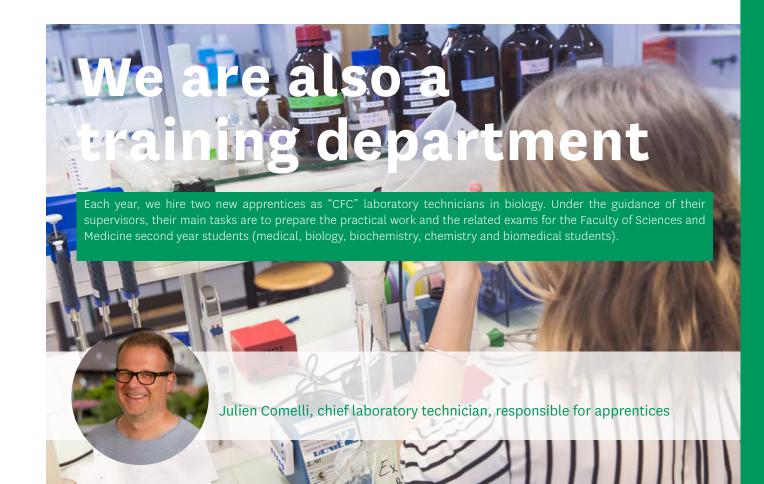
SPECIAL EVENTS

2017

07.09	Chronobiology Meeting
11-12.09	Systems Biology of the Brain Workshop
14-15.09	Biological Invasions Workshop
14.09	Swiss Microscopy Core Facility Day
15.09	Getting Started - Welcome for new students
22 & 29.11	InfoDays
23.11	Bachelor & Master Evening
03.03	BEFRI Research Colloquium
04-05.05	BEFRI Research Retreat

2018

06.09	Chronobiology Meeting
13-14.09	Predicting outcomes of species interactions Workshop
14.09	Getting Started - Welcome for new students
21 & 28.11	InfoDays
22.11	Bachelor & Master Evening
18.01	REPP-SO Winter Meeting
26-27.03	COST BM1408 GENIE Workshop
10.04	BEFRI Research Colloquium
26-27.04	BEFRI Research Retreat
15.06	Swiss Fly Meeting
22.06	BEFRI Genomics Day
22-23.06	FGLS Retreat



Impressum

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